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1 **Men's beliefs about treatment for erectile dysfunction – What**
2 **influences treatment use? A systematic Review**

3

4 Running title: Systematic review: erectile dysfunction treatment.

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14

15 **1. Abstract**

16 Successful treatment of erectile dysfunction (ED) is associated with improvements in quality of life;
17 however, treatment utilisation is sub-optimal. The aim of this systematic review was to identify the
18 rates of ED treatment utilisation and the barriers and enablers men experience when using
19 treatment.

20 We searched: MEDLINE®, Embase, the Cochrane library; AMED; HMIC; HTA; CINAHL; PsychARTICLES;
21 PsychINFO up to August 2018. Data on rates of treatment utilisation and barriers and enablers of
22 utilisation were extracted and summarised.

23 Fifty studies were included. Discontinuation rates ranged from 4.4-76% for phosphodiesterase type 5
24 inhibitors, 18.6-79.9% for intracavernosal injections, 32-69.2% for urethral suppositories. In relation
25 to those with a penile prosthesis; 30% discontinued having sex due to e.g. device complications, lack
26 of partner or a loss of sexual interest.

27 Most research included in the current review examined barriers to treatment utilisation and
28 therefore focussed on reasons for discontinuing treatment. However, a small number explored
29 factors that men found helpful with regards to treatment utilisation. The most prevalent barriers to
30 utilisation were treatment ineffectiveness, side-effects, the quality of men's intimate relationships
31 and treatment costs. With regards to treatment enablers, the most salient finding was that men who
32 reported side-effects to a health care professionals (HCPs) were significantly less likely to discontinue
33 treatment. There were limitations in methodology in that the studies did not use validated measures
34 of treatment utilisation or barriers and enablers and no study used psychological theory to inform
35 the examination of factors that influenced treatment utilisation.

36 This review identifies a number of influential factors relating to ED treatment utilisation and
37 highlights the importance of men's beliefs with regards to ED and its treatment. Beliefs are
38 potentially modifiable and therefore the findings of this review highlight important considerations
39 for health care professionals with regards to supporting men to make better use of treatment.

40 **2. Introduction**

41 Erectile dysfunction (ED) is defined as the persistent inability to attain and/or maintain a penile
42 erection adequate for sexual performance (1). Prevalence increases with age affecting
43 approximately 1–10% of men up to the age of 40 years, 2-9% of men aged between 40 and 49 years,
44 increasing to 20–40% in those aged 60–69 years and 50-100% in those over 70 (2). ED can have a
45 negative impact on self-confidence, mood and quality of life (3-9). Improvements in psychological
46 status, self-esteem and perceived relationship quality can be achieved by improving sexual function
47 through the use of treatment (10-15).

48 Phosphodiesterase type 5 inhibitors (PDE5Is) are the first line treatment for ED (16). Where PDE5Is
49 are ineffective or contraindicated, alternatives such as intracavernous injections (ICI), urethral
50 suppositories (US), vacuum erection devices (VEDs) and penile prosthesis (PP) remain available (17).

51 PDE5Is are considered safe, effective and tolerable for men with ED (18). Despite this, adherence to
52 PDE5Is has been described as sub-optimal due to factors such as, side-effects, not wanting a sexual
53 schedule dependent on a medication regimen, the delayed response between taking the medication
54 and its effect as well as the financial cost of treatment (19). Psychosocial explanations include
55 performance anxiety, depression, varying arousal patterns and misaligned expectations between a
56 man and his partner (20).

57 To date there has not been a synthesis of research investigating adherence to ED treatment.
58 National guidelines for medication adherence (21) recognise that in order for health care
59 professionals (HCPs) to support patients, a better understanding of factors that influence patients'
60 decisions regarding treatment utilisation is necessary. Therefore, the aim of this systematic review
61 was to identify barriers and enablers to ED treatment utilisation and the extent to which they
62 influence men's decisions to utilise their treatment. The review will serve as a foundation to develop
63 future interventions to facilitate ED treatment utilisation.

64 **3. Material/Subjects and Methods**

65 The protocol was registered on PROSPERO (reference CRD42015023341).

66 **3.1 Search strategy**

67 MEDLINE®, Embase, Cochrane Central Register of Controlled Trials, Health Management
68 Information Consortium (HMIC), Health Technology Assessment, CINAHL plus with full text,
69 PsychARTICLES, PsychINFO and Allied and Complementary Medicine (AMED) were searched from
70 inception to August 2018 . English language key words and MeSH terms for ED, adherence and
71 treatment for ED, were used and combined using Boolean logical operators (see Supplementary
72 Information).

73 **3.2 Inclusion Criteria**

74 Studies had to meet the following criteria:

- 75 • Published in a peer reviewed journal in English
- 76 • Primary research of qualitative, quantitative or mixed methodologies
- 77 • Include an assessment of treatment utilisation
- 78 • Include an assessment of patient barriers and/or enablers to ED treatment utilisation
- 79 • Include participants who were
 - 80 ○ Men aged ≥18 years
 - 81 ○ Diagnosed with ED either using a validated diagnostic tool or by a relevant HCP i.e. a
82 GP or urologist
 - 83 ○ Prescribed PDE5Is, ICI, US, VEDs or PP.

84 **3.3 Exclusion Criteria**

85 Systematic reviews, conference proceedings, commentary articles and letters were excluded.

86 **3.4 Study Selection and Data Extraction**

87 Articles were imported into Thomson Reuters Reference Manager v12.0 and duplicate records
88 removed. Two authors (PW, AA) independently screened titles and abstracts to exclude ineligible

89 studies, followed by full-text screening of the remainder. Any disagreements were discussed with a
90 third author (HM) to reach consensus. Data were extracted using an adapted Cochrane Data
91 Extraction Form (22).

92 **3.5 Quality Assessment**

93 The QualSyst tool was employed to assess study quality due to its ability to cater for both qualitative
94 and quantitative designs (23). Final scores were converted into a percentage where <50% indicates
95 limited quality, 50–70%: adequate; 71–80%: good, and >80%: strong (24). Scoring was carried out by
96 one author (PW) and checked by a second (AA).

97 **3.6 Synthesis**

98 A narrative synthesis, considered the most appropriate method of synthesising qualitative and
99 quantitative evidence (25), was conducted. Barriers and enablers of treatment utilisation were
100 classified into one of six categories:

- 101 ○ Demographic; age, gender, ethnicity, education.
- 102 ○ Clinical; nature of the condition and treatment; including side-effects and medication efficacy.
- 103 ○ Psychological and cognitive: individual-level processes and meanings that influence mental
104 states such as depression, stress and beliefs about ED or its treatment.
- 105 ○ Social: social processes that impinge on the individual, such as relationship quality.
- 106 ○ Behavioural: observable behaviours (as opposed to internal events such as thinking), which
107 can be objectively measured, such as the length of time before seeking help for ED.

108 Depending on the study, the percentage of overall participant's discontinuation, persistence or
109 adherence was reported. Studies indicating the same barriers and enablers to treatment were
110 grouped together and the number/percentage of participants reporting a particular
111 barriers/enablers as being influential were reported (see supplementary material).

112 **3.4 Terminology**

113 The use of the term ‘adherence’ is synonymous with overlapping definitions, such as compliance and
114 persistence. Studies of medication usage lack uniformity in definitions (26), therefore, due to the
115 neutrality of its meaning, the current review will use the term ‘treatment utilisation’ to describe
116 usage patterns.

117 **4. Results**

118 **4.1 Literature search**

119 A total of 3,232 papers were retrieved, 129 underwent full text screening and 50 studies were
120 included (See Figure 1).

121 **4.2 Study Characteristics**

122 All studies used a quantitative study design (Table 1), except one that employed a mixed
123 methodology. The qualitative component of this study was reported as frequency data and was
124 therefore interpreted quantitatively (27). Study designs included retrospective (n=5) and prospective
125 cohort designs (n=29), cross-sectional studies (n=8), randomised trials (n=5), a randomised control
126 trial (n=1), quasi experimental study (n=1) as well as mixed-methodology (n=1). Almost one third of
127 studies were conducted in the USA (n=15). Although all studies examined barriers/enablers to
128 treatment utilisation, this was the primary focus for only 24 studies. Other studies’ primary focus
129 was ED treatment-related factors such as acceptability, safety, efficacy, satisfaction and tolerability
130 (n=25) and one study focussed on help seeking behaviour (n=1).

131 Thirty-three studies (66%) focussed on PDE5I medication, twelve (24%) on ICI therapy, three (6%) on
132 US and two (4%) on multiple treatments, of which one included PP. Studies were conducted
133 between 1991 and 2017.

134 **4.3 Participant characteristics**

135 Data related to 14,371 men. Mean age, reported in 46 studies, ranged from 39.9-69.1 years. Five
136 studies reported ethnicity (28-32), where 67.2-97.8% were classified as white/Caucasian. Seven

137 studies reported on relationship status (27, 29, 33-37), where 61.5–96.0% were described as having
138 a partner (Table 2).

139 **4.4 Clinical characteristics**

140 Twenty-three studies (46.0%) used the International Index of Erectile Dysfunction (IIEF) (38) or the
141 Sexual Health Inventory for Men (SHIM) (39) to assess ED severity, moderate ED was most prevalent
142 (33.3-61.7%). ED duration, reported in 21 studies, ranged from 3-72 months. Twenty studies
143 provided data on ED aetiology, 6.3-86% were classified as having organic ED, 5.0-36.3% psychogenic,
144 and 15-71% as having mixed ED. Twenty studies reported on comorbidities; hypertension (5.0-
145 51.9%) and diabetes (4.4-42.4%) were most commonly reported. Eight studies recruited exclusively
146 men who had undergone a prostatectomy.

147 **4.5 Study quality**

148 Quality scores ranged from 41-100%, 7 (14%) were classified as limited, 22 (44%) as adequate, 4 (8%)
149 as good and 17 (34%) as strong. Lower scores typically related to limited or no provision of
150 definitions of outcome measure/s, neglecting information on power calculations, sample or effect
151 sizes and not controlling for confounding variables.

152 **4.6 Definitions of Treatment Utilisation**

153 There were a variety of different definitions of treatment utilisation and discontinuation (Table 3).

154 Due to the heterogeneity of definitions, synthesis was achieved through a top-down application of
155 the following definitions;

- 156 - Adherence: conforming to recommendations made by the HCP with respect to timing, dosage,
157 and frequency of medication utilisation.
- 158 - Persistence: continuing to take any amount of medication (26).
- 159 - Discontinuation: cessation of treatment.

160 Forty-four studies were classified as measuring discontinuation, three; persistence and three both
161 adherence and persistence.

162 **4.7 Measures of Treatment Utilisation**

163 Thirty-four studies (68%) used self-report measures to investigate treatment utilisation including;
164 questionnaires, patient diaries, consultations and telephone surveys (Table 3). Other methods
165 included for example prescription records (n=2) and twelve studies did not report their method. No
166 validated measures of treatment utilisation were used.

167 **4.8 Rates of Treatment Utilisation**

168 Rates of adherence to PDE5Is ranged from 59.6-70.2%, persistence from 64.9-100% and
169 discontinuation from 4.4-76%. Follow-up periods varied from 3-48 months. ICI discontinuation rates
170 ranged from 18.6-79.9%, in which follow-up ranged from 3-65 months. Discontinuation of US ranged
171 from 32-69.2%, in which follow-up ranged from 9–27 months. The one study that explored PP,
172 followed men over a 65 month period where 30% stopped having sex due to complications with the
173 device itself or due to periphery reasons such as a lacking a partner or a loss of sexual interest (40).

174 It might be expected that longer follow-up periods infer higher rates of discontinuation or poorer
175 adherence; no such pattern emerged. Similarly, there was no pattern of association between rates
176 of treatment utilisation and sample size, study design, or country in which the study took place
177 (Table 3).

178 **4.9 Barriers and enablers of treatment utilisation**

179 Thirty-seven studies (74%) used self-report measures to investigate barriers and enablers to
180 treatment utilisation, mostly self-report questionnaires (Table 3). Other methods included clinical
181 and demographic data (n=2) as well as prescription renewals (n=1). However, ten studies did not
182 clarify their method. Less than half of included studies (n=18) examined whether there was a
183 statistically significant relationship between potential barriers or enablers and treatment utilisation.
184 The remaining 32 studies reported descriptive statistics only. For each barrier or enabler, descriptive
185 data from relevant studies was combined and presented as a total percentage of participants across
186 relevant studies. None of the studies used a validated measure or a theoretical approach to

187 investigate barriers and enablers to treatment utilisation. Based on the studies included, the
188 following sections will consider the most widely reported barriers and enablers to ED treatment
189 utilisation.

190 **4.10 Demographic Factors**

191 Sixteen studies (32%) examined the relationship between demographic factors and use of PDE5Is
192 (n=12) or ICI treatment (n=4) (see Table 4).

193 *Age*

194 Twelve studies examined the relationship between age and PDE5I utilisation (29, 34-37, 41-47). One
195 reported older age as a barrier, however, this was based on descriptive statistics (43). Eleven
196 performed statistical analysis, for which findings were inconsistent. Three studies reported
197 significantly higher rates of discontinuation for men over 60 years (31, 36, 44); however, older men
198 were reported as being significantly more persistent and adherent according to two other studies
199 (35, 42). Six studies reported a non-significant relationship (34, 37, 41, 45-47); as did studies focused
200 on ICI treatment (48-50).

201 *Education*

202 Five studies investigated levels of education and PDE5I utilisation using inferential statistics (34, 37,
203 41-43). Results were conflicting. One study indicated that higher levels of education related to
204 significantly higher rates of utilisation (34). However, after controlling for age, delay in seeking
205 medical help, relationship status and SHIM score; one study reported the relationship to be non-
206 significant (37). A further study reported a higher level of education relating to significantly higher
207 rates of persistence but not adherence (43) and finally, two studies reported a non-significant
208 relationship (41, 42).

209

210

211

212

213 *Employment*

214 Three studies explored the effects of employment on PDE5I utilisation (29, 41, 42). Full-time
215 employment related to significantly higher rates of persistent (42) and adherence (41, 42) compared
216 to being part-time, retired or unemployed. One study, however, reported the relationship to be non-
217 significant (29).

218 *Clinical factors*

219 All fifty studies examined the relationship between one or more clinical factors and treatment
220 utilisation (Table 4).

221 *Treatment Ineffectiveness*

222 Ineffectiveness of PDE5Is was explored by twenty-two studies (27-32, 35, 36, 43, 45, 46, 51-61),
223 eleven on ICI treatment (40, 49, 61-69), four on US (61, 70-72) and one on PP (40).

224 PDE5I ineffectiveness related to hardness and duration of erection. Across all studies 12.1% (range:
225 0.2-60%) of participants reported ineffectiveness as a reason for discontinuation.

226 Ineffectiveness of ICIs related to inadequate erectile response and was explored using descriptive
227 statistics by ten studies, where 15.2% (range: 5–39.3%) discontinued for such reasons. One study
228 used inferential statistics and reported significantly higher rates of discontinuation where treatment
229 was ineffective (49).

230 Ineffectiveness of US was characterised by insufficient erections as well as a lack of a consistent
231 reliable response (70-72); 31.5% (range: 16-50.8%) of participants across studies discontinued for
232 this reason. Finally, 4.7% of participants reported prosthesis malfunction as a reason for
233 discontinuation (40).

234 *Perceived side-effects*

235 The experience of side-effects was reported in twenty-one studies focussed on PDE5Is (27, 29-32,
236 34-36, 45, 46, 51, 52, 54, 55, 59-61, 73-76), twelve on ICI (40, 48, 49, 61, 62, 64-69, 77), three on US
237 (61, 71, 72) and one on PP (40).

238 Across 21 studies, 2.5% (range: 0.9-16%) of men discontinued PDE5Is due to side-effects, which
239 included headaches, rhinitis, Peyronie's disease and chest pain. Three of these studies used
240 statistical analysis, one of which found side-effects to be related to significantly higher rates of
241 persistence (45). Similarly, where men reported side-effects to a HCP they were significantly less
242 likely to discontinue treatment (35). However, one study reported the relationship to be non-
243 significant (31).

244 ICI treatment side-effects included injection pain, priapism, Peyronie's disease and fibrosis of the
245 penile shaft. Across twelve studies, side-effects were reported by 8.1% (range: 0.9-20.9%) of men as
246 the reason for discontinuation. According to one study, side-effects related to significantly higher
247 rates of discontinuation (49), however, a further study found no such relationship (48).

248 Side-effects of US included urethral pain and burning, where 15% (range: 7.4-32%) of men across
249 studies reported side-effects as the reason for discontinuation. Finally, one study reported that
250 infection or erosion was responsible for 9.4% of participants discontinuing PP (40).

251 *Treatment-specific factors: ICI treatment*

252 There were 7.2% (2.0-24%) of men across ten studies (40, 48, 49, 62-65, 68, 69, 77) who reported
253 that they discontinued ICI treatment due to difficulty, inability, being unwilling to self-inject or
254 needle phobia. This was associated with significantly higher rates of discontinuation in one of these
255 studies (48).

256 **4.11 Condition Specific Factors**

257 *ED aetiology*

258 Five studies investigated the relationship between aetiology and PDE5I utilisation (29, 34, 35, 41,
259 43). Men with psychogenic as opposed to organic (34, 43) or venogenic as opposed to arteriogenic,
260 diabetic or iatrogenic ED (35), reported significantly higher rates of persistence. Further studies
261 however, did not replicate these findings (29, 41). In relation to ICI, aetiology that included an
262 organic component was related to significantly higher rates of discontinuation (49).

263 *ED severity*

264 Of eight studies on PDE5Is, five found that less severe ED was associated with significantly higher
265 rates of persistence (36, 37, 42, 43, 47) and adherence (43). However, three studies did not find such
266 a relationship (29, 41, 46).

267 *ED duration*

268 Five studies investigated the relationship between duration of ED symptoms and PDE5I utilisation.
269 Findings were conflicting, shorter duration of ED was reported as being related to significantly higher
270 rates of discontinuation in one study (34), but to significantly higher rates of persistence (43, 45) and
271 adherence (42) in three studies. Finally, one study found the relationship between ED duration and
272 treatment utilisation to be non-significant (41).

273 *Comorbid conditions*

274 The effects of comorbid conditions were explored by eight studies on PDE5Is (29, 34, 36, 41, 42, 46,
275 55, 74) three on ICI treatment (40, 62, 65) and one on PP (40). Across three studies (55, 74, 78) 1.9%
276 (range: 0.8-3.9%) of men discontinued PDE5Is due to comorbid conditions. A higher proportion of
277 men suffering with comorbid hypertension were both more persistent and adherent than those
278 without the condition (42). Similarly, men who had a BMI of ≥ 23 or more indicated significantly
279 higher rates of persistence (34, 36). Conversely, participants with coronary artery disease (41) or
280 who had undergone pelvic surgery (36) were significantly more likely to discontinue PDE5Is. Finally,
281 four studies found no significant relationships (29, 34, 41, 46).

282 Across two studies (40, 65), 4.4% (range: 3.4-5.5%) of men discontinued ICIs due to comorbid
283 conditions. A third study, using inferential statistics, reported the relationship as non-significant (62).

284 **4.12 Psychological and Cognitive Factors**

285 Twelve studies explored one or more psychological or cognitive factors in relation to treatment
286 utilisation, nine on PDE5Is (27, 29, 31, 34-36, 45, 56, 78) and three on ICI (48, 67, 68).

287

288 *Treatment Related Beliefs*

289 In one study PDE5Is were discontinued by 23.4% of men as they caused personal conflict, although
290 the study does not elaborate on its meaning (56). In addition, fear of drug dependency was reported
291 by 3% of men (35) and a lack of confidence in medication by 0.1% (29). However, a lack of
292 confidence in medication was reported as having a non-significant relationship with treatment
293 utilisation according to one study (31). Potential harm to the heart was reported by 6.5% (range: 4-
294 7.6%) of men across two studies (27, 35) and not being willing for one's sex life to depend on
295 medication was reported by 3% (range: 0.4-7.4%) of men across three studies as reasons for
296 discontinuation (29, 34, 78).

297 *Psychosocial well-being*

298 The effects of psychosocial factors were reported by two studies focussed on PDE5Is (27, 36) and
299 one on ICI treatment (48). One study reported that 10.1% of men used PDE5Is only in "special
300 moments" to prolong pleasure or to avoid and/or improve bad performance (27). Similarly, 8.1% of
301 men reported using PDE5Is to improve their psychological and emotional state (27). A lack of self-
302 esteem or self-confidence was given as a reason for PDE5I discontinuation by 0.8 and 11.4% of men
303 (27, 36) and significantly higher rates of persistence to ICI treatment were also associated with
304 higher levels of self-confidence and self-esteem (48).

305 **4.13 Social Factors**

306 Thirty-six studies investigated social factors and their effect on ED treatment utilisation, twenty four
307 on PDE5Is (27-29, 31, 33-37, 41, 43, 45, 46, 51-55, 57, 58, 61, 73, 74, 78), nine on ICI (40, 48, 49, 62,
308 64-66, 69, 77), one on US (72) and PP (40).

309 *Cost of Treatment*

310 Across seventeen studies (27-29, 34-36, 43, 45, 46, 52-55, 61, 73, 74, 78) 6.6% (0.6-47.3%) of men
311 discontinued PDE5Is due to high personal financial cost. Across three studies 4.6% (range: 4.4-5.5%)
312 of men discontinued ICI treatment (40, 62, 65). Finally, 25.4% discontinued US due to cost (70).
313 Studies were from a variety of countries including New Zealand (28), Portugal (27) Korea (34, 78),

314 Taiwan (45) and the USA (46, 52, 53), where some were multi-national (29, 31, 36, 42, 43, 56) (Table
315 1).

316 *Related to Partner and Intimate relationship*

317 Twenty-two studies focussed on PDE5Is (27-29, 31, 33-37, 40, 41, 45, 51-53, 55-58, 73, 74, 78) nine
318 on ICI (40, 48, 49, 62, 64-66, 69, 77), one on US (72) and PP (40) explored couples' sexual relationship
319 and treatment utilisation.

320 The most commonly reported factors were loss of libido or interest in the sexual relationship;
321 reported by 6.6% (range: 0.6-17.3%) of men across nine studies focussed on PDE5Is (34, 35, 45, 52,
322 55, 58, 73, 74, 78), 8.8% (range: 6.9–30%) across four studies focussed on ICIs (40, 62, 65, 77) and
323 8.9% and 6.9% of men using US and PP, respectively (40, 72).

324 A partner's lack of interest in the sexual relationship was given as a reason for PDE5I discontinuation
325 by 5.5% (1.2-9.8%) of men across five studies (27, 34, 45, 58, 74). A lack of emotional readiness for
326 restoration of sexual activity was a reason for discontinuing PDE5Is for 5.5% (13.1-22.7%) of men in
327 two studies (34, 78) and conflict within one's relationship by 4.1% (2.4-5.8%) of men in three studies
328 (27, 28, 51). Conflict within one's relationship was also a reason for 1% discontinuing ICI (62). Low
329 levels of satisfaction with one's sexual relationship, was associated with significantly higher rates of
330 ICI discontinuation (49). Conversely, a better quality sexual relationship was associated with
331 significantly higher rates of ICI persistence (48).

332 **4.14 Behavioural Factors**

333 Seven studies examined the effect of behavioural factors on treatment utilisation; six on PDE5Is (27,
334 33-37) and one on ICI treatment (49). Most commonly a lack of opportunity to engage in sexual
335 intercourse was a reason for 0.9% (2-7.3%) of men to discontinue PDE5Is, across three studies (27,
336 35, 61). A greater number of sexual attempts in the first month of treatment and a higher rate of
337 pre-treatment sexual activity were both associated with significantly higher rates of PDE5I

338 persistence (33, 36). Finally, less frequent masturbation was related to significantly higher levels of
339 ICI treatment discontinuation (49).

340 **5. Discussion**

341 Rates of treatment discontinuation varied considerably across studies, from 4.4-76.0% for PDE5Is,
342 18.6-79.9% for ICI, 32.0-69.23% for US and 30% for PP. This may relate in part to limitations in
343 operational definitions where less than a quarter of studies gave explicit definitions of treatment
344 utilisation. Where provided, however, variation existed. These findings support a previous call for
345 standardisation of adherence definitions to enable more accurate comparisons between studies
346 (26). Other potential reasons for variation in utilisation rates identified by previous research include;
347 differences in methodologies, adherence measures, treatment regimens, and patient characteristics
348 (79).

349 In relation to barriers and enablers of treatment utilisation, no consistent findings were evident for
350 demographic factors. However, clinical factors, examined by all studies included in this review,
351 indicate treatment ineffectiveness and side-effects as the most prevalent reasons given for
352 discontinuation.

353 Only twelve studies examined psychological or cognitive factors, which is surprising considering that
354 psychogenic factors are the cause to some degree of nearly all cases of ED (80). In addition, there is a
355 large body of research which highlights the importance of patient beliefs in relation to a range of
356 acute and chronic conditions and their respective treatments (81-83). Such beliefs have been found
357 to predict adherence in a variety of chronic conditions (84) and are amenable to change which can
358 improve adherence (85). None of the studies included in this review utilised psychological theory to
359 guide their investigations, therefore, future research would benefit from employing psychological
360 theory to advance our understanding of barriers and enablers to ED treatment utilisation.

361 A widely reported social factor was treatment cost (n=21), however, it was not explored by any of
362 the studies using inferential statistics. Therefore, it is difficult to ascertain the extent to which other
363 factors, such as employment status, play a role. Additionally, studies originated from a variety of
364 countries involving a variety of health care systems. In the UK, for example, guidance provided by
365 the Department of Health restricts prescription of ED treatments to those patients who meet
366 specific criteria, meaning that, for example, those men with ED who additionally suffer with
367 diabetes, multiple sclerosis or Parkinson's disease can receive treatment on the NHS for ED (86).
368 Previously, if a patient did not meet such criteria, then the patient incurred a personal cost for
369 treatment. However, with the advent of cheaper medicines becoming available (87), in 2014,
370 legislation was introduced removing the restrictions on NHS prescribing of generic sildenafil. This
371 enabled HCP's the ability to prescribe generic sildenafil for all men with ED on NHS prescription (88).
372 Finally, more recently, Sildenafil has been made available in UK pharmacies for men who wish to
373 purchase the treatment over-the counter (89). It is beyond the scope of this review to consider the
374 impact of varying procurement methods on ED treatment utilisation, however, this remains an
375 important consideration for future research.

376 Loss of libido in men and their partners and its relationship with ED treatment discontinuation was
377 also a widely reported social factor. It is possible that loss of libido was underreported as other
378 factors potentially overlap, such as a lack of emotional readiness for restoration of sexual activity
379 and conflict within one's relationship. Furthermore, loss of libido and ED are both symptoms of
380 testosterone deficiency (90), but studies did not report potential causes of low libido in their
381 participants. The causes of low or a lack of libido are important considerations for HCP's to consider
382 when providing treatment for ED as successful treatment of other conditions such as testosterone
383 deficiency may influence successful treatment with regards to ED. Although treatment
384 ineffectiveness was the most frequently reported barrier to utilisation, operational definitions were
385 absent. Therefore it is possible that a treatment could potentially be described as 'ineffective' due to
386 other factors such as loss of libido or conflict within one's relationship. Underlying factors such as

387 these may have been overlooked and therefore, future research would benefit from investigating
388 individual perceptions of ineffectiveness which, in turn, could enable HCPs to provide appropriate
389 support, potentially reducing discontinuation.

390 It is important to note that results of the current review indicate that men who reported side-effects
391 to a HCP were significantly less likely to discontinue treatment. This suggests that there is potential
392 for HCP's to influence utilisation rates. As discussed, perceived ineffectiveness of treatment has a
393 subjective element and therefore requires exploration with a given patient. We would
394 recommended that if men report that their treatment is ineffective, prescribers seek to identify and
395 clarify any misconceptions patients may have in relation to their treatment. This would enable the
396 possibility of exploring beliefs about medication with patients where changing treatments or altering
397 doses in line with any insights that arise could potentially increase ED treatment utilisation.
398 Additionally, exploring the quality of patients' intimate relationships may indicate the necessity for
399 additional treatments, for example psychosexual counselling, which could potentially work in
400 conjunction with medication/devices and increase treatment utilisation.

401 There were methodological limitations with respect to the studies included. Descriptive statistics
402 were used by 32 studies and only 8 used multivariate statistics to analyse data. Therefore, a
403 substantial amount of frequency data was included, which can indicate the prevalence of a barrier or
404 enabler, but not their unique impact on utilisation when others are taken into account.

405 There was an absence of reliable and validated measures with respect to rates of treatment
406 utilisation, as well as barriers and enablers to utilisation. Although there is no 'gold standard' to
407 measuring treatment adherence (91), there are a variety of validated treatment adherence
408 measures (92). However, existing measures of treatment adherence are potentially unsuitable for
409 assessing ED treatments; taken predominantly on demand. Therefore, this review highlights the
410 need for a validated measure of ED treatment utilisation and echoes the call for simple, valid and

411 reliable methods for detecting the prevalence and types of non-adherence to enable the possibility
412 of building effective and targeted adherence interventions (85) .

413 The methods used to ask men about barriers and enablers to treatment utilisation varied
414 considerably. Use of open-ended questions may result in some barriers or enablers being under-
415 reported if they are not asked about specifically. In order to understand barriers and enablers to ED
416 treatment utilisation, future studies would benefit from using a design that are prospective in nature
417 coupled with the use of validated measures. In addition, analysis of results using multivariate
418 statistics would enable causes to be established rather than associations.

419 This review has several limitations. The inclusion of only published manuscripts introduces the
420 possibility of publication bias and resources dictated that articles were published in English. Due to
421 the nature of some of the barriers and enablers, allocation to one of the overarching themes was not
422 always straight forward. For example, loss of libido was classified as a social factor; however, this is
423 likely to have psychological and/or physiological components. The quality of findings of any
424 systematic review relies in part on the quality of the studies included and although study quality
425 varied, 58% were classified as either 'limited' or 'adequate'. In general, there was an under-reporting
426 of important participant data such as ED duration, ED severity, relationship status, levels of
427 employment and levels of education.

428 In conclusion, treatment ineffectiveness, side-effects, the quality of one's intimate relationship as
429 well as the cost of treatment emerged as important barriers to treatment utilisation. There is a need
430 for study designs to be more rigorous as well as a greater focus on the impact of psychosocial
431 factors. Beliefs about ED and its treatment are potentially modifiable, offering an opportunity to
432 improve treatment utilisation and the quality of life of both men and their partners. Therefore,
433 based on the results of this review, future research would benefit from identifying modifiable factors
434 e.g. beliefs about medication, which could be targeted by interventions to help improve utilisation
435 through the use of a more theoretically informed, evidence-based approach.

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444 **9. References**

445

- 446 1. Nehra A, Jackson G, Miner M, Billups KL, Burnett AL, Buvat J, et al., editors. The Princeton III
447 Consensus recommendations for the management of erectile dysfunction and cardiovascular
448 disease. *Mayo Clinic Proceedings*; 2012: Elsevier.
- 449 2. Lewis RW, Fugl-Meyer KS, Corona G, Hayes RD, Laumann EO, Moreira Jr ED, et al.
450 Definitions/epidemiology/risk factors for sexual dysfunction. *The journal of sexual medicine*.
451 2010;7(4pt2):1598-607.
- 452 3. Fugl-Meyer A, Lodnert G, Bränholm I, Fugl-Meyer K. On life satisfaction in male erectile
453 dysfunction. *International Journal of Impotence Research*. 1997;9(3):141.
- 454 4. Jonler M, Moon T, Brannan W, Stone NN, Heisey D, Bruskewitz RC. The effect of age,
455 ethnicity and geographical location on impotence and quality of life. *British journal of urology*.
456 1995;75(5):651-5.
- 457 5. Guest JF, Gupta RD. Health-related quality of life in a UK-based population of men with
458 erectile dysfunction. *Pharmacoeconomics*. 2002;20(2):109-17.
- 459 6. Feldman HA, Goldstein I, Hatzichristou DG, Krane RJ, McKinlay JB. Impotence and its medical
460 and psychosocial correlates: results of the Massachusetts Male Aging Study. *The Journal of urology*.
461 1994;151(1):54-61.
- 462 7. Shabsigh R, Klein LT, Seidman S, Kaplan SA, Lehrhoff BJ, Ritter JS. Increased incidence of
463 depressive symptoms in men with erectile dysfunction. *Urology*. 1998;52(5):848-52.
- 464 8. Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and
465 predictors. *Jama*. 1999;281(6):537-44.
- 466 9. Moreira Jr ED, Abdo CHN, Torres EB, Lôbo CFL, Fittipaldi JAS. Prevalence and correlates of
467 erectile dysfunction: results of the Brazilian study of sexual behavior. *Urology*. 2001;58(4):583-8.
- 468 10. Turner LA, Althof SE, Levine SB, Bodner DR, Kursh ED, Resnick MI. Twelve-month comparison
469 of two treatments for erectile dysfunction: self-injection versus external vacuum devices. *Urology*.
470 1992;39(2):139-44.
- 471 11. Costa P, Grandmottet G, Mai HD, Droupy S. Impact of a first treatment with
472 phosphodiesterase inhibitors on men and partners' quality of sexual life: results of a prospective
473 study in primary care. *The journal of sexual medicine*. 2013;10(7):1850-60.
- 474 12. McCabe MP, O'Connor EJ, Conaglen JV, Conaglen HM. The impact of oral ED medication on
475 female partners' relationship satisfaction. *The journal of sexual medicine*. 2011;8(2):479-83.

- 476 13. Rosen RC, Fisher WA, Eardley I, Niederberger C, Nadel A, Sand M. The multinational Men's
477 Attitudes to Life Events and Sexuality (MALES) study: I. Prevalence of erectile dysfunction and
478 related health concerns in the general population. *Current medical research and opinion*.
479 2004;20(5):607-17.
- 480 14. Shabsigh R, Zakaria L, Anastasiadis AG, Seidman SN. Sexual dysfunction and depression:
481 etiology, prevalence, and treatment. *Current urology reports*. 2001;2(6):463-7.
- 482 15. Williams G, Abbou C, Amar E, Desvaux P, Flam T, Lynch S, et al. The effect of transurethral
483 alprostadil on the quality of life of men with erectile dysfunction, and their partners. *MUSE Study*
484 *Group. British journal of urology*. 1998;82(6):847-54.
- 485 16. McKernan S. *Erectile Dysfunction Guidance 2015* [Available from:
486 [http://www.lancsmmg.nhs.uk/wp-content/uploads/sites/3/2013/04/Erectile-Dysfunction-Guideline-](http://www.lancsmmg.nhs.uk/wp-content/uploads/sites/3/2013/04/Erectile-Dysfunction-Guideline-Version-1.0.pdf)
487 [Version-1.0.pdf](http://www.lancsmmg.nhs.uk/wp-content/uploads/sites/3/2013/04/Erectile-Dysfunction-Guideline-Version-1.0.pdf).
- 488 17. Hatzimouratidis K, Giuliano F, Moncada I, Muneer A, Salonia A, Verze P. EAU guidelines on
489 erectile dysfunction, premature ejaculation, penile curvature and priapism. *European Association of*
490 *Urology*. 2016;46.
- 491 18. Morales AM, Casillas M, Turbi C. Patients' preference in the treatment of erectile
492 dysfunction: a critical review of the literature. *International journal of impotence research*.
493 2011;23(1):1.
- 494 19. Hackett GI. Patient preferences in treatment of erectile dysfunction: the continuing
495 importance of patient education. *Clinical cornerstone*. 2005;7(1):57-64.
- 496 20. Althof S. When an erection alone is not enough: biopsychosocial obstacles to lovemaking.
497 *International Journal of Impotence Research*. 2002;14(S1):S99.
- 498 21. Nunes V, Neilson J, O'flynn N, Calvert N, Kuntze S, Smithson H, et al. Medicines adherence:
499 Involving patients in decisions about prescribed medicines and supporting adherence. 2009.
- 500 22. Collaboration TC. *Effective Practice and Organisation of Care (EPOC)*. Data collection form.
501 EPOC Resources for review authors. . Oslo: Norwegian Knowledge Centre for the Health Services.
502 2013;7-3-2014.
- 503 23. Kmet LM, Cook LS, Lee RC. Standard quality assessment criteria for evaluating primary
504 research papers from a variety of fields. 2004.
- 505 24. Johnson S, Butow P, Kerridge I, Tattersall M. Advance care planning for cancer patients: a
506 systematic review of perceptions and experiences of patients, families, and healthcare providers.
507 *Psycho-Oncology*. 2016;25(4):362-86.
- 508 25. Mays N, Pope C, Popay J. Systematically reviewing qualitative and quantitative evidence to
509 inform management and policy-making in the health field. *Journal of health services research &*
510 *policy*. 2005;10(1_suppl):6-20.
- 511 26. Cramer JA, Roy A, Burrell A, Fairchild CJ, Fuldeore MJ, Ollendorf DA, et al. Medication
512 compliance and persistence: terminology and definitions. *Value in health*. 2008;11(1):44-7.
- 513 27. Carneiro A, Forjaz V, Pereira NM. Adherence to phosphodiesterase type 5 inhibitors in the
514 treatment of erectile dysfunction in long-term users: how do men use the inhibitors? *Sexual*
515 *medicine*. 2014;2(2):96-102.
- 516 28. Conaglen HM, Conaglen JV. Couples' reasons for adherence to, or discontinuation of, PDE
517 type 5 inhibitors for men with erectile dysfunction at 12 to 24-month follow-up after a 6-month free
518 trial. *The journal of sexual medicine*. 2012;9(3):857-65.
- 519 29. Buvat J, Hatzichristou D, Boess F, Büttner H, Gehchan N, Hennes C, et al. Continuation and
520 effectiveness of tadalafil once daily during a 6-month observational study in erectile dysfunction: the
521 EDATE study. *International journal of clinical practice*. 2014;68(9):1087-99.
- 522 30. McMurray JG, Feldman RA, Auerbach SM, DeRiesthal H, Wilson N, Group MS. Long-term
523 safety and effectiveness of sildenafil citrate in men with erectile dysfunction. *Therapeutics and*
524 *clinical risk management*. 2007;3(6):975.
- 525 31. Buvat J, Büttner H, Hatzimouratidis K, Vendeira PA, Moncada I, Boehmer M, et al. Adherence
526 to Initial PDE5 Inhibitor Treatment: Randomized OpenLabel Study Comparing Tadalafil Once a Day,

527 Tadalafil on Demand, and Sildenafil on Demand in Patients with Erectile Dysfunction. *The journal of*
528 *sexual medicine*. 2013;10(6):1592-602.

529 32. Kim E, Seftel A, Goldfischer E, Baygani S, Burns P. Comparative efficacy of tadalafil once daily
530 in men with erectile dysfunction who demonstrated previous partial responses to as-needed
531 sildenafil, tadalafil, or vardenafil. *Current medical research and opinion*. 2015;31(2):379-89.

532 33. Mazzola CR, Devenci S, Teloken P, Mulhall JP. Exploring the association between erectile
533 rigidity and treatment adherence with sildenafil. *The journal of sexual medicine*. 2013;10(7):1861-6.

534 34. Kim S, Lee Y, Seo K, Jung G, Kim T. Reasons and predictive factors for discontinuation of PDE-
535 5 inhibitors despite successful intercourse in erectile dysfunction patients. *International journal of*
536 *impotence research*. 2014;26(3):87.

537 35. Carvalheira AA, Pereira NM, Maroco J, Forjaz V. Dropout in the treatment of erectile
538 dysfunction with PDE5: a study on predictors and a qualitative analysis of reasons for
539 discontinuation. *The journal of sexual medicine*. 2012;9(9):2361-9.

540 36. Roumeguère T, Verheyden B, Arver S, Bitton A, Belger M, Schmitt H, et al. Therapeutic
541 response after first month of tadalafil treatment predicts 12 months treatment continuation in
542 patients with erectile dysfunction: results from the DETECT study. *The journal of sexual medicine*.
543 2008;5(7):1708-19.

544 37. Salonia A, Abdollah F, Gallina A, Pellucchi F, Molina RAC, Maccagnano C, et al. Does
545 educational status affect a patient's behavior toward erectile dysfunction? *The journal of sexual*
546 *medicine*. 2008;5(8):1941-8.

547 38. Rosen RC, Riley A, Wagner G, Osterloh IH, Kirkpatrick J, Mishra A. The international index of
548 erectile function (IIEF): a multidimensional scale for assessment of erectile dysfunction. *Urology*.
549 1997;49(6):822-30.

550 39. Rosen RC, Cappelleri J, Smith M, Lipsky J, Pena B. Development and evaluation of an
551 abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool
552 for erectile dysfunction. *International journal of impotence research*. 1999;11(6):319.

553 40. Sexton WJ, Benedict JF, Jarow JP. Comparison of long-term outcomes of penile prostheses
554 and intracavernosal injection therapy. *The Journal of urology*. 1998;159(3):811-5.

555 41. Cairoli C, Reyes LA, Hennes C, Sorsaburu S. PDE5 inhibitor treatment persistence and
556 adherence in Brazilian men: post-hoc analyses from a 6-month, prospective, observational study.
557 *International braz j urol*. 2014;40(3):390-9.

558 42. El-Meliegy A, Rabah D, Al-Mitwalli K, Mostafa T, Hussein T, Istarabadi M, et al. A 6-month,
559 prospective, observational study of PDE5 inhibitor treatment persistence and adherence in Middle
560 Eastern and North African men with erectile dysfunction. *Current medical research and opinion*.
561 2013;29(6):707-17.

562 43. Rubio-Aurioles E, Reyes LA, Borregales L, Cairoli C, Sorsaburu S. A 6 month, prospective,
563 observational study of PDE5 inhibitor treatment persistence and adherence in Latin American men
564 with erectile dysfunction. *Current medical research and opinion*. 2013;29(6):695-706.

565 44. Souverein P, Egberts A, Meuleman E, Urquhart J, Leufkens H. Incidence and determinants of
566 sildenafil (dis) continuation: the Dutch cohort of sildenafil users. *International journal of impotence*
567 *research*. 2002;14(4):259.

568 45. Jiann B, Yu C, Su C, Tsai J. Compliance of sildenafil treatment for erectile dysfunction and
569 factors affecting it. *International journal of impotence research*. 2006;18(2):146.

570 46. Lee DJ, Cheetham P, Badani KK. Penile rehabilitation protocol after robot-assisted radical
571 prostatectomy: Assessment of compliance with phosphodiesterase type 5 inhibitor therapy and
572 effect on early potency. *BJU international*. 2010;105(3):382-8.

573 47. Sato Y, Tanda H, Kato S, Onishi S, Nitta T, Koroku M. How long do patients with erectile
574 dysfunction continue to use sildenafil citrate? Dropout rate from treatment course as outcome in
575 real life. *International journal of urology*. 2007;14(4):339-42.

576 48. Lehmann K, Casella R, Blöchlinger A, Gasser T. Reasons for discontinuing intracavernous
577 injection therapy with prostaglandin E1 (alprostadil). *Urology*. 1999;53(2):397-400.

- 578 49. Rowland D, Boedhoe H, Dohle G, Slob A. Intracavernosal self-injection therapy in men with
579 erectile dysfunction: satisfaction and attrition in 119 patients. *International journal of impotence*
580 *research*. 1999;11(3):145.
- 581 50. Purvis K, Egdetveit I, Christiansen E. Intracavernosal therapy for erectile failure—impact of
582 treatment and reasons for drop-out and dissatisfaction. *International journal of impotence research*.
583 1999;11(5):287.
- 584 51. EL-GALLEY R, RUTLAND H, TALIC R, KEANE T, CLARK H. Long-term efficacy of sildenafil and
585 tachyphylaxis effect. *The Journal of urology*. 2001;166(3):927-31.
- 586 52. Fagelman E, Fagelman A, Shabsigh R. Efficacy, safety, and use of sildenafil in urologic
587 practice. *Urology*. 2001;57(6):1141-4.
- 588 53. Green BG, Martin S. Clinical assessment of sildenafil in the treatment of neurogenic male
589 sexual dysfunction: After the hype. *NeuroRehabilitation*. 2000;15(2):101-5.
- 590 54. Incrocci L, Hop WC, Slob AK. Efficacy of sildenafil in an open-label study as a continuation of
591 a double-blind study in the treatment of erectile dysfunction after radiotherapy for prostate cancer.
592 *Urology*. 2003;62(1):116-20.
- 593 55. Ljunggren C, Hedelin H, Salomonsson K, Stroberg P. Giving patients with erectile dysfunction
594 the opportunity to try all three available phosphodiesterase type 5 inhibitors. *J Sex Med*.
595 2008;5:469-75.
- 596 56. Montorsi F, Verheyden B, Meuleman E, Jünemann K-P, Moncada I, Valiquette L, et al. Long-
597 term safety and tolerability of tadalafil in the treatment of erectile dysfunction. *European urology*.
598 2004;45(3):339-45.
- 599 57. Raina R, Lakin MM, Agarwal A, Sharma R, Goyal KK, Montague DK, et al. Long-term effect of
600 sildenafil citrate on erectile dysfunction after radical prostatectomy: 3-year follow-up. *Urology*.
601 2003;62(1):110-5.
- 602 58. Salonia A, Gallina A, Zanni G, Briganti A, Deho F, Sacca A, et al. Acceptance of and
603 discontinuation rate from erectile dysfunction oral treatment in patients following bilateral nerve-
604 sparing radical prostatectomy. *European urology*. 2008;53(3):564-70.
- 605 59. Bai W-J, Li H-J, Dai Y-T, He X-Y, Huang Y-R, Liu J-H, et al. An open-label, multicenter,
606 randomized, crossover study comparing sildenafil citrate and tadalafil for treating erectile
607 dysfunction in Chinese men naïve to phosphodiesterase 5 inhibitor therapy. *Asian journal of*
608 *andrology*. 2015;17(1):61.
- 609 60. Choi H, Kim J, Shim J, Park JY, Kang SH, Moon DG, et al. Comparison of the efficacy and
610 safety of 5-mg once-daily versus 5-mg alternate-day tadalafil in men with erectile dysfunction and
611 lower urinary tract symptoms. *International journal of impotence research*. 2015;27(1):33.
- 612 61. Panach-Navarrete J, Morales-Giraldo A, Ferrandis-Cortés C, García-Morata F, Pastor-Lence J,
613 Martínez-Jabaloyas J. Satisfaction and treatment adherence in erectile dysfunction in the medium
614 and long term. *Actas Urológicas Españolas (English Edition)*. 2017;41(4):258-66.
- 615 62. Sung H, Ahn J, Kim J-J, Choo S, Han D, Lee S. The role of intracavernosal injection therapy and
616 the reasons of withdrawal from therapy in patients with erectile dysfunction in the era of PDE 5
617 inhibitors. *Andrology*. 2014;2(1):45-50.
- 618 63. GROUP EAS. The long-term safety of alprostadil (prostaglandin-E1) in patients with erectile
619 dysfunction. *British Journal of Urology*. 1998;82(4):538-43.
- 620 64. Armstrong D, Convery A, Dinsmore W. Reasons for patient drop-out from an intracavernous
621 autoinjection programme for erectile dysfunction. *British journal of urology*. 1994;74(1):99-101.
- 622 65. Gerber GS, Levine LA. Pharmacological erection program using prostaglandin E1. *The Journal*
623 *of urology*. 1991;146(3):786-9.
- 624 66. Kunelius P, Lukkarinen O. Intracavernous self-injection of prostaglandin E1 in the treatment
625 of erectile dysfunction. *International journal of impotence research*. 1999;11(1):21.
- 626 67. Perimenis P, Gyftopoulos K, Athanasopoulos A, Barbaliás G. Diabetic Impotence Treated by
627 Intracavernosal Injections: High Treatment Compliance and Increasing Dosage of Vaso-Active Drugs.
628 *European urology*. 2001;40(4):398-403.

629 68. Polito M, d'Anzeo G, Conti A, Muzzonigro G. Erectile rehabilitation with intracavernous
630 alprostadil after radical prostatectomy: refusal and dropout rates. *BJU international*.
631 2012;110(11c):E954-E7.

632 69. Raina R, Lakin M, Thukral M, Agarwal A, Ausmundson S, Montague D, et al. Long-term
633 efficacy and compliance of intracorporeal (IC) injection for erectile dysfunction following radical
634 prostatectomy: SHIM (IIEF-5) analysis. *International journal of impotence research*. 2003;15(5):318.

635 70. Mulhall JP, Jahoda AE, Ahmed A, Parker M. Analysis of the consistency of intraurethral
636 prostaglandin E1 (MUSE) during at-home use. *Urology*. 2001;58(2):262-6.

637 71. Raina R, Agarwal A, Ausmundson S, Mansour D, Zippe C. Long-term efficacy and compliance
638 of MUSE for erectile dysfunction following radical prostatectomy: SHIM (IIEF-5) analysis.
639 *International journal of impotence research*. 2005;17(1):86.

640 72. Raina R, Pahlajani G, Agarwal A, Zippe CD. The early use of transurethral alprostadil after
641 radical prostatectomy potentially facilitates an earlier return of erectile function and successful
642 sexual activity. *BJU international*. 2007;100(6):1317-21.

643 73. Cimen S, Demir O, Aslan G, Esen AA. Factors associated with phosphodiesterase type 5
644 inhibitor treatment satisfactions: results of patient interrogation. *The Aging Male*. 2009;12(2-3):58-
645 61.

646 74. Klotz T, Mathers M, Klotz R, Sommer F. Why do patients with erectile dysfunction abandon
647 effective therapy with sildenafil (Viagra®)? *International Journal of Impotence Research*.
648 2005;17(1):2.

649 75. Ricardi U, Gontero P, Ciammella P, Badellino S, Valentino F, Munoz F, et al. Efficacy and
650 safety of tadalafil 20 mg on demand vs. tadalafil 5 mg once-a-day in the treatment of post-
651 radiotherapy erectile dysfunction in prostate cancer men: A randomized phase II trial. *The journal of*
652 *sexual medicine*. 2010;7(8):2851-9.

653 76. Li G, Lan H, Liang J, Zhang C, Huang C. Efficacy of tadalafil de-escalation in the treatment of
654 psychogenic erectile dysfunction. *Urologia internationalis*. 2017;98(2):205-9.

655 77. Irwin MB, Kata EJ. High attrition rate with intracavernous injection of prostaglandin E1 for
656 impotency. *Urology*. 1994;43(1):84-7.

657 78. Son H, Park K, Kim S-W, Paick J-S. Reasons for discontinuation of sildenafil citrate after
658 successful restoration of erectile function. *Diabetes*. 2004;23(9):16.70.

659 79. DiMatteo MR. Variations in patients' adherence to medical recommendations: a quantitative
660 review of 50 years of research. *Medical care*. 2004:200-9.

661 80. Ian Peate O. *Men's health: the practice nurse's handbook*: John Wiley & Sons; 2007.

662 81. Horne R, Clatworthy J, Polmear A, Weinman J. Do hypertensive patients' beliefs about their
663 illness and treatment influence medication adherence and quality of life? *Journal of Human*
664 *Hypertension*. 2001;15(S1):S65.

665 82. Horne R, Clatworthy J, Hankins M, Investigators A. High adherence and concordance within a
666 clinical trial of antihypertensives. *Chronic Illness*. 2010;6(4):243-51.

667 83. Horne R, Chapman SC, Parham R, Freemantle N, Forbes A, Cooper V. Understanding
668 patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-
669 analytic review of the Necessity-Concerns Framework. *PloS one*. 2013;8(12):e80633.

670 84. Petrie KJ, Weinman J. *Perceptions of health and illness: Current research and applications*:
671 Taylor & Francis; 1997.

672 85. Horne R, Weinman J, Barber N. *Concordance, adherence and compliance in medicine taking:*
673 *a conceptual map and research priorities*. London: National Coordinating Centre for NHS Service
674 Delivery and Organisation (NCCSDO). 2006.

675 86. Department of Health. *NHS Executive Health Service Circular 1999*.

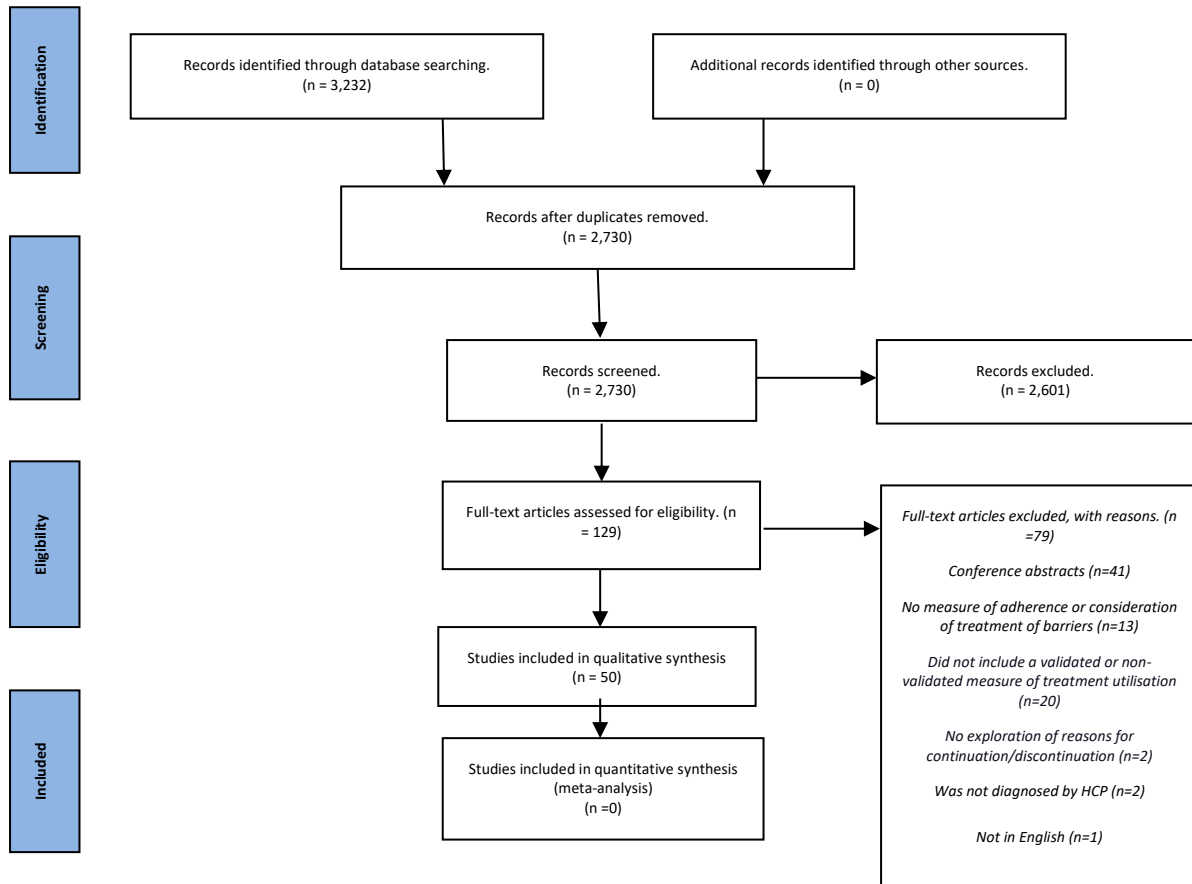
676 87. Partnership M. *Can I get medication for erectile dysfunction (ED) on the NHS? 2019*
677 [Available from: [https://modalitypartnership.nhs.uk/self-help/chq/articles/882-can-i-get-](https://modalitypartnership.nhs.uk/self-help/chq/articles/882-can-i-get-medication-for-erectile-dysfunction-(ed)-on-the-nhs)
678 [medication-for-erectile-dysfunction-\(ed\)-on-the-nhs](https://modalitypartnership.nhs.uk/self-help/chq/articles/882-can-i-get-medication-for-erectile-dysfunction-(ed)-on-the-nhs).

- 679 88. Group CPJP. PRESCRIBING POLICY: DRUGS AND DEVICES USED IN THE TREATMENT OF
680 ERECTILE DYSFUNCTION 2018 [Available from:
681 [https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=157](https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=15703&type=0&servicetype=1)
682 [03&type=0&servicetype=1](https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=15703&type=0&servicetype=1).
683 89. COMMITTE PMAP. PHOSPHODIESTERASE TYPE-5 INHIBITORS for the treatment of erectile
684 dysfunction. 2018 [Available from:
685 https://www.panmerseyapc.nhs.uk/media/2039/phosphodiesterase5inhibitors_201807_v0601.pdf.
686 90. Wu FC, Tajar A, Beynon JM, Pye SR, Silman AJ, Finn JD, et al. Identification of late-onset
687 hypogonadism in middle-aged and elderly men. *New England Journal of Medicine*. 2010;363(2):123-
688 35.
689 91. Garfield S, Clifford S, Eliasson L, Barber N, Willson A. Suitability of measures of self-reported
690 medication adherence for routine clinical use: a systematic review. *BMC medical research*
691 *methodology*. 2011;11(1):149.
692 92. Wagner J, Justice A, Chesney M, Sinclair G, Weissman S, Rodriguez-Barradas M. Patient-and
693 provider-reported adherence: toward a clinically useful approach to measuring antiretroviral
694 adherence. *Journal of clinical epidemiology*. 2001;54(12):S91-S8.

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697 Figure 1: PRISMA flowchart



698

699 Table 1: Study characteristics

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
ICI treatment							
Alvarez et al. (1998)(63)	Europe, South Africa	Evaluate the long-term safety and efficacy.	Prospective cohort study	Aprostadil 20 mg/mL	6 months	848	70%
Armstrong et al (1994)(64)	N. Ireland	To identify factors contributing to patient drop-out from an ICI programme.	Cross-sectional study	NR	n/a	30	45%
Gerber and Levine (1991)(65)	USA	To investigate erectile response, pain after injection and frequency of use.	Prospective cohort study	Aprostadil: 5, 10 or 20 mcg's	M=7 months (2-28 months)	72	41%
Irwin & Kata (1994)(77)	USA	To determine acceptance and durability of treatment.	Prospective cohort study	Aprostadil (mean dosage) = 23 ug (range 5-30 ug).	6 months	60	45%
Kunelius et al (1999)(66)	Finland	To assess the long-term outcome of treatment and overall patient satisfaction with their sexual life.	Retrospective cohort study	NR	36 months	69	54%
Lehmann et al (1999)(48)	Switzerland	To clarify the reasons why experience with self-injection therapy for ED shows high dropout rates.	Retrospective cohort study	Alprostadil 2-mL	M=16 (3-64 months)	86	59%
Perimenis et al (2001)(67)	Greece	Compare patient compliance with treatment and the dosages used for the management of impotence.	Prospective cohort study	Aprostadil initially 5 – 10 ug	84 months	40	64%
Polito et al (2012)(68)	Italy	To assess the rate of compliance in the first 6 months of a rehabilitation protocol for patients undergoing RRPP.	Prospective cohort study	Alprostadil initially 2 – 3 mcg	6 months	273	68%
Purvis et al (1999)(50)	Norway	To examine the impact of treatment on libido, ejaculatory control, quality of life and treatment dependency in men with erectile failure. Furthermore to assess the drop-out rate and reasons for dissatisfaction with the technique.	Cross-sectional study	Aprostadil (10 ± 20mg), papaverine-phentolamine (15 mg; 0.5 mg) and Trimix (10 mg Aprostadil; 15mg papaverine; 0.5 mg phentolamine).	n/a	766	64%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Raina et al (2003a)(57)	USA	Investigate drug efficacy in patients following RP.	Retrospective cohort study	Aprostadil alone (10 or 20 mg/ml in normal saline), high-dose triple therapy (20 mg/ml Aprostadil +1 mg/ml phentolamine +30 mg/ml papaverine), or low-dose triple therapy (5.88 mg/ml Aprostadil +0.59 mg/ml phentolamine+ 17.65 mg/ml papaverine).	M=14.5 months	102	73%
Rowland et al (1999)(49)	USA	Explore satisfaction with and dropout from ICI use.	Prospective cohort study	NR	M=9 months	119	73%
Sung et al (2014)(62)	Korea	To investigate the rate of withdrawal and its associated reasons.	Cross-sectional	Trimix (a mixture of prostaglandin E1 18 ug, papaverine 48 mg and phentolamine 2 mg in 2 mL of distilled water).	18 +/- 23.9	294	82%
PDE5I medication							
Bai et al (2015)(59)	China	To compare treatment preference, efficacy, and tolerability of sildenafil and tadalafil for treating erectile dysfunction (ED)	Randomised Trial	(1) 20-mg tadalafil and then 100-mg sildenafil (2) 100-mg sildenafil and then 20-mg tadalafil	7 Months	383	91%
Buvat et al (2013)(31)	France, Greece, Portugal, Germany, UK	To evaluate the effects of initiating treatment with Tadalafil OaD, Tadalafil PRN, or sildenafil PRN on treatment utilisation.	Randomised Trial	(1) Tadalafil OaD, 5 mg OaD (2) Tadalafil PRN, 10 mg PRN (3) Sildenafil PRN, 50 mg PRN	median = 4.3 months median = 5.5 months median = 2.2 months	770	82%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Buvat et al (2014)(29)	Germany, France, Italy, Greece	To evaluate treatment continuation, effectiveness and tolerability of Tadalafil OaD.	Prospective cohort study	Tadalafil OaD 5-mg	6 months	778	100%
Cairolı et al (2014)(41)	Brazil	To characterize persistence and adherence to PDE5I on-demand therapy over 6 months	Prospective cohort study	NR	6 months	104	81%
Carvalho et al (2012)(35)	Portugal	(i) to analyse discontinuation rates of PDE5Is; (ii) to identify predictors of discontinuation; and (iii) to study the reasons for discontinuation using a qualitative methodology	Mixed methodology	NR	36 months	327	68%
Carvalho et al (2014)(27)	Portugal	(i) To characterize the way men use PDE5I and (ii) analyse treatment utilisation, identifying the factors that influence PDE5I use.	Cross-sectional Study	NR	n/a	148	65%
Choi et al (2014)(60)	China	To investigate the sustainable effect of 5-mg alternate-day tadalafil versus 5-mg once-daily tadalafil	Randomised Trial	(1) Tadalafil) 5-mg once-daily (2) Tadalafil) (5-mg alternate-day	3 months	180	61%
Cimen et al (2009)(73)	Turkey	Retrospective evaluation of ED patients who were recommended a PDE5I treatment in terms of patient satisfaction.	Cross-sectional Study	NR	n/a	345	55%
Conaglen & Conaglen (2012)(28)	New Zealand	To evaluate factors influencing adherence to, or discontinuation of, oral ED medications.	Retrospective cohort study	NR	12 months	155	64%
El-Galley et al (2001)(51)	USA, Saudi Arabia	Evaluation of the long-term efficacy of Sildenafil	Prospective cohort study	NR	24 months	200	54%
El-Meliegy et al (2013)(42)	Saudi Arabia Egypt, United Arab Emirates, USA	To assess on-demand PDE5I treatment persistence and adherence over 6 months in men with ED.	Prospective cohort study	NR	6 months	493	95%
Fagelman et al (2001)(52)	USA	To evaluate the efficacy, side-effects, renewal patterns and other relevant practice issues related to the use of sildenafil.	Prospective cohort study	Sildenafil 50 mg, increasing to 100 mg if necessary.	6 – 12 months	164	54%
Green and Martin (2000)(53)	USA	To evaluate the efficacy and safety of sildenafil in patients with ED caused by spinal cord injury and multiple sclerosis.	Prospective Cohort Study	NR	M=21 months	40	45%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Incrocci et al (2003)(54)	Netherlands	To determine the efficacy of Sildenafil citrate in patients with ED after three-dimensional conformal external beam radiotherapy.	Quasi experimental	50 mg for 2 weeks increasing to 100 mg if necessary.	24 months	50	64%
Jiann et al (2006)(45)	Taiwan	To assess treatment compliance and reasons for dropout.	Cross-sectional Study	NR	M=36 months	434	64%
Kim et al (2014)(34)	Korea	To identify characteristics of ED patients who discontinued PDE5I medication.	Cross-sectional Study	NR	n/a	485	91%
Kim et al (2015)(32)	USA	To evaluate whether TAD-OaD provides similar efficacy in men with ED who had previously demonstrated a partial response to PRN PDE5I therapy.	RCT	(1) Placebo, (2) Tadalafil 2.5 mg (uptitrated to tadalafil 5mg after 4 weeks) (3) Tadalafil 5mg OaD	3 months	623	93%
Klotz et al (2005)(74)	Germany	To determine the rate of abandonment of sildenafil therapy and assess the reasons for abandonment.	Prospective cohort study	Sildenafil 50 or 100 mg	6 months	234	41%
Lee et al (2010)(46)	USA	To evaluate factors that affect discontinuation in men after nerve sparing RAP.	Prospective cohort study	Sildenafil citrate (100 mg) three times a week or Tadalafil (20 mg) three times a week.	6 months)	53	61%
Li et al (2016)(76)	China	To assess the efficacy of tadalafil de-escalation in the therapeutic effects of psychogenic ED	Randomised Trial	(1) 5 mg of tadalafil per day; Group 2: 20 mg tadalafil per day (for 1 month) followed by 10 mg per day (for the 2nd month) and 5 mg for the third month.	3 months	86	61%
Ljunggren et al (2008)(55)	Sweden	To study long-term compliance among patients who were treated according to a "three-drug regime" i.e. able to try all 3 PDE5I medications.	Prospective cohort study	NR	M=27 months	138	45%
Mazzola et al (2013)(33)	USA	To explore the link between erection hardness and treatment adherence.	Prospective cohort study	Sildenafil, 100 mg	17 +/- 4 months	186	82%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
McMurray (2007)(30)	USA	To assess the safety and effectiveness of flexible doses of Sildenafil	Prospective cohort study	Flexible-doses (25, 50, and 100 mg) of Sildenafil.	48 months	979	54%
Montorsi et al (2004)(56)	Italy/Belgium/Netherlands /Germany/Spain/Canada/ Argentina/Mexico/USA	To assess the long-term safety and tolerability of tadalafil for patients with ED.	Prospective cohort study	Initial dose was 10 mg (Tadalafil) taken as needed	18-24 months	493	68%
Raina et al (2003b)(57)	USA	To evaluate the long-term effect and safety of sildenafil citrate for the treatment of ED.	Prospective cohort study	Starting dose was 50 mg, which was titrated to 100 mg if necessary.	36 months	48	73%
Ricardi et al (2010)(75)	Italy	To compare the efficacy and safety of Tadalafil PRN 20-mg (arm A) with Tadalafil 5-mg OaD (arm B) in patients with ED following radiotherapy for prostate cancer.	Randomised Trial	Tadalafil 20 mg PRN (arm A) or Tadalafil 5 mg OaD (arm B)	3 months	52	93%
Roumeguere et al (2008)(36)	Austria/Belgium/Denmark /Greece/Iceland/Netherlands/Norway/Sweden	To determine the effectiveness of Tadalafil and the factors associated with the continuation of treatment for ED.	Prospective cohort study	Tadalafil 10 or 20 mg	12 months	1567	100%
Rubio-Aurioles et al (2013)(43)	Brazil, Mexico, Venezuela	Investigate the factors that may be predictive for PDE5I persistence and adherence.	Prospective cohort study	NR	6 months 6 months	511	100%
Salonia et al (2008a)(58)	Italy	Assess acceptance of and discontinuation rate from ED treatment in patients after bilateral nerve-sparing radical retro-pubic prostatectomy.	Prospective cohort study	NR	18 months	51	82%
Salonia et al (2008b)(37)	Italy	To explore whether the educational status may have a significant impact on the delay before seeking first medical help and compliance with a suggested PDE5I.	Prospective cohort study	Sildenafil 50 mg, Vardenafil 10 mg or Tadalafil OaD 10 mg.	=/< 24 months)	231	91%
Sato et al (2007)(47)	Japan	To study the dropout rate for use of sildenafil after initial prescription and during successful treatment to clarify their risk factors.	Prospective cohort study	NR	36 months	322	68%

Author, year	Country	Study Aim	Design	Dose	Follow Up (months)	n	Quality score (0-100%)
Son et al (2004)(78)	Korea	To investigate the reasons for discontinuations of Sildenafil after the successful restoration of erectile function.	Prospective cohort study	Flexible Sildenafil doses; 25-100 mg according to patients need and side-effects	6 months	156	41%
Souverein et al (2002)(44)	Netherlands	Sildenafil utilization was evaluated in men with ED. Further, some determinants of Sildenafil discontinuation were identified.	Prospective cohort study	NR	M=18 months	317	86%
Urethral Suppository							
Mulhall et al (2001)(70)	USA	To determine the consistency of a successful response to a urethral suppository (Aprostadil)	Prospective cohort study	Aprostadil 1000 mg	M=9 months	68	73%
Raina et al (2007)(72)	USA	To obtain baseline and follow-up data of 54 patients who used medicated urethral system for erection for ED associated with RP.	Prospective cohort study	Aprostadil 125 ug or 250 ug of urethral suppository.	M=9 months	56	61%
Raina et al (2005)(71)	USA	To assess whether early introduction of Aprostadil after RP results in a shorter recovery time for the return to functional erections and successful sexual activity.	Retrospective cohort study	Aprostadil 250 mg flexible to 500 or 1000 mg dose of urethral suppository, if needed	M=27 +/- 14 months	54	82%
Multiple Treatments							
Panach-Navarrete et al (2017)(61)	Spain	To describe the medium and long-term satisfaction and adherence of pharmacological treatments in ED	Cross-sectional	NR	NA	250	85%
Sexton et al (1998)(40)	USA	To compare the long-term outcomes of both penile prostheses and ICI therapy and determine the reasons for discontinuation.	Prospective cohort study	NR	M=37 months (PP) M=63 months (ICI)	130	54%

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701 ICI: Intracavernous injection therapy; M: mean; OaD: once a day; PP: penile prosthesis; PRN: on demand; RAP: robotic assisted prostatectomy; RCT: randomised control trial; US: Urethral suppository

702 Table 2: Participant Characteristics

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n,%	ED Duration, months (sd)	ED severity – IIEF n(%)
ICI treatment							
Alvarez et al. (1998)(63)	52	NR	NR	NR	Neurogenic: 118 (14) Vasculogenic: 215 (25) Psychogenic: 268 (32) Diabetes: 94 (11) Other: 30 (3.5) Mixed causes: 123 (15)	54	NR
Armstrong et al (1994)(64)	50.5	NR	NR	NR	NR	NR	NR
Gerber and Levine (1991)(65)	NR	NR	NR	NR	NR	NR	NR
Irwin & Kata (1994)(77)	64	NR	NR	NR	NR	NR	NR
Kunelius et al (1999)(66)	60.5	NR	NR	NR	Vasculogenic: 30 (28) Psychogenic: 31 (29) Neurologic: 8 (7)	NR	NR
Lehmann et al (1999)(48)	58 (10)	NR	NR	NR	Organic: 52 (60) Mixed: 23 (27) Psychogenic: 11 (13)	NR	NR
Perimenis et al (2001)(67)	54.85	NR	NR	NR	NR	28	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Polito et al (2012)(68)	64.6 (6.5)	NR	NR	NR	NR	NR	M=No ED (= /> 20): 212 (77.6%)
Purvis et al (1999)(50)	57	NR	NR	NR	Vascular: 33% Idiopathic: 31% Psychogenic: 26% Neurologic: 7% Endocrine: 3%	NR	NR
Raina et al (2003a)(57)	60.4 (6.3)	NR	NR	NR	NR	NR	Sev: 68%
Rowland et al (1999)(49)	58	NR	NR	NR	NR	41	NR
Sung et al (2014)(62)	61.8 (7.9)	NR	NR	Diab: 82 (27.9), Hyp: 118 (40.1), CVD: 37 (12.6), CVA: 11 (3.7), Previous RP: 198 (67.3), NSRP: 72 (36.4), Previous pelvic RT: 31 (10.5)	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
PDE5I medication							
Bai et al (2015)(59)	39.94 (11.00)	NR	NR	Diab: 17 (4.4), Hyp 19 (5.0)	Organic: 24 (6.3), Mixed: 272 (71.0)	≥3 to <12 164 (42.8), ≥12 219 (57.2)	Mi 131 (34.2), Mod 133 (34.7), Sev 119 (31.1)
Buvat et al (2013)(31)	53.03 (11.66)	White 753 (97.8), Black/African American 10 (1.3), Multiple 1 (0.1)	NR	Hyp: 266 (34.5), Hyperl: 137 (17.8), Diab: 142 (18.8), BPH: 68 (8.8), Dys: 42 (5.4), Osteo: 36 (4.7), Dep: 36 (4.7), Anx: 30 (3.9)	Tadalafil OaD Psychogenic: 54 (21.0) Organic: 56 (21.8) Mixed: 125 (48.6) Unknown: 22 (8.6) Tadalafil PRN Psychogenic: 59 (23.4) Organic: 65 (25.8) Mixed: 106 (42.1) Unknown: 22 (8.7) Sildenafil PRN Psychogenic: 62 (23.8) Organic: 66 (25.3) Mixed: 111 (42.5) Unknown: 22(8.4)	23.3	Mi 300 (38.9), Mod 261 (33.9), Sev 204 (26.5)
Buvat et al (2014)(29)	57	Caucasian 523(67.2), Other 4(0.5)	Married 639(65.9), Partnered/living together 120(12.4)	CVD: 268 (34.5), Hyp: 260 (33.4), Dysl: 144 (18.5), Diab: 124 (15.9) PS: 89 (11.4), BPH: 49 (6.3), Hypog:12 (1.5)	Mixed: 443 (45.7) Organic: 286 (29.5) Psychogenic: 172 (17.8) Unknown: 68 (7.0)	<3 n=55 (7.1%) 3-12 n=231(29.7%) ≥12 n=490(63.1%)	Mi 160 (20.6), Mod 411 (53.0), Sev 204 (26.3)

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Cairoli et al (2014)(41)	57.8 (10.9)	NR	NR	Hyp: 54 (51.9), Diab: 25 (24.0), Ob: 10 (9.6), CAD: 4 (3.8), BPH: 7 (6.7), LUTS: 5 (4.8), Hyperl: 13 (12.6)	Mixed: 48 (47.1) Organic: 37 (36.3) Psychogenic: 16 (15.7)	24	Mi 13 (13.8), Mod 58 (61.7), Sev 23 (24.5)
Carvalho et al (2012)(35)	56.30 (11.44)	NR	Married: 65.4% Divorced/separated: 18.3% Single: 10.4% Common law: 3.1% Widowed: 2.8%	NR	Venogenic :79 (24.2) Arteriogenic: 75 (22.9) Iatrogenic: 62 (19.0) Psychogenic: 50 (15.3) Diabetic: 40 (12.2) Neurogenic: 21 (6.4)	NR	NR
Carvalho et al (2014)(27)	55.8 (11.11)	NR	Married: 61.5% Divorced/separated: 20.3% Single: 12.2% Common law: 4.1% Widowed: 2.0%	NR	Venogenic:31% Arteriogenic: 23% Psychogenic: 18% Iatrogenic: 13% Neurogenic: 8% Diabetic: 7%	NR	NR
Choi et al (2014)(60)	56.8	NR	NR	Underlying disease 42 (29.1)	NR	NR	Mod – Sev 180 (100)
Cimen et al (2009)(73)	56 (11.2)	NR	NR	Diab: 21.7%, Hyper: 16.1%, CVD: 4.7%	NR	27.7	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Conaglen & Conaglen (2012)(28)	55.85 (8.59)	Maori or Pacific Islander 8 (5.1) Caucasian/European 128 (82.6) Mixed Ethnicity 11 (7) Other 8 (5.1)	NR	NR	NR	NR	NR
El-Galley et al (2001)(51)	58 (10)	NR	NR	NR	Radical prostatectomy: 25 Neurogenic impotence: 12 Arterial insufficiency: 26 Diabetes mellitus: 19 Diagnosed venous leak: 7 Clinical venous leak: 9 Peyronie's disease: 6 Other: 47	NR	NR
El-Meliegy et al (2013)(42)	49.6 (12.03)	NR	NR	Hyp: 222 (45), Diab: 209 (42.4), Ob: 104 142 (28.8), BPH: 105 (21.3) LUTS: 110 (22.3), Hyperl: 169 (34.3)	Tadalafil Psychogenic: 66 (19.3) Organic: 133 (38.9) Mixed: 125 (36.5) Unknown: 18 (5.3) Sildenafil Psychogenic: 14 (18.4) Organic: 32 (42.1) Mixed: 18 (23.7) Unknown: 12 (15.8) Vardenafil Psychogenic: 9 (12.2) Organic: 30 (40.5) Mixed: 28 (37.8) Unknown: 7 (9.5)	18	Mi 78 (15.8), Mod 259 (52.5), Sev 155 (31.5)

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Fagelman et al (2001)(52)	54.1	NR	NR	NR	NR	44	NR
Green and Martin (2000)(53)	40.4	NR	NR	NR	Multiple sclerosis: 7 Spinal cord injury: 33 Quadriplegics: 13 Paraplegics: 20 Complete injuries: 14 Incomplete injuries: 19	NR	NR
Incrocci et al (2003)(54)	68	NR	NR	Diab and/or Hyp 13%	NR	NR	NR
Jiann et al (2006)(45)	66.8 (9.8)	NR	NR	NR	NR	NR	NR
Kim et al (2014)(34)	53.6 (11.8)	NR	Marriage/Co-habit: 416 (85.8) Bereavement: 11 (2.3), Divorce: 14 (2.9) Separation: 13 (2.7), Bachelor: 25 (5.2), Others: 6 (1.2)	Diab: 58 (12.0), Hyp: 102 (21.0), Dys: 39 (8.0), Ob: 46 (9.5), CAD: 14 (2.9), BPH: 119 (24.5), Arthritis: 13 (2.7), Herniated nucleus pulposus: 17 (3.5), Digestive disorder: 25 (5.2)	Psychogenic: 176 (36.3) Organic: 309 (63.7)	<5 years: 276 (56.9) 5–9 years: 125 (25.8) 10–14 years: 48 (9.9) =>15 years: 12 (2.5) Don't know/No answer: 24 (4.9)	Mi: 228 (47.0), Mod: 224 (46.2) Sev: 33 (6.8)
Kim et al (2015)(32)	57.6 (10.4)	Caucasian: 517 (83.0), Black/African American: 88 (14.1), Asian: 8 (1.3), Other: 9 (1.4)	NR	NR	Psychogenic: 31 (5.0) Organic 297 (47.7) Mixed 217 (34.8) Unknown 78 (12.5)	<1 year 39 (6.3) ≥ 1 year 584 (93.7)	Mi/Mod: 123 (19.7) Mod: 472 (75.8), Sev: 28 (4.5)

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IEEF n(%)
Klotz et al (2005)(74)	60.5	NR	NR	Hyp: 40%, Diab: 16%	Organic: 202 (86)	NR	M=Mi-Mod 17
Lee et al (2010)(46)	57.8 (7.0)	NR	NR	NR	NR	NR	Mi 22
Li et al (2016)(76)	24.55 (3.8)				Psychogenic: 86 (100)		Mi 15 (16.6) Mod 30 (33.3) Sev 45 (50)
Ljunggren et al (2008)(55)	60 (7)	NR	NR	NR	Organic: 40 (32%) Psychogenic: 23 (18%) Mixed: 64 (50%)	60	NR
Mazzola et al (2013)(33)	61 (22)	NR	Partnered: 63%	Hyper: 36%, Dys: 38%, CAD: 16%, Diab: 15%	NR	26	Mi 25%, Mod 45%, Sev 30%,
McMurray (2007)(30)	58.2	White: 873 (89.2), Black: 68 (6.9), Asian: 8 (0.8), Other: 30 (3.1)	NR	Hyp: 272 (27.8), Diab: 213 (21.8), Hyperl: 139 (14.2), IHD: 83 (8.5)	Organic: 72 Mixed: 17 Psychogenic: 11	54	NR
Montorsi et al (2004)(56)	NR	NR	NR	NR	NR	NR	NR
Raina et al (2003b)(57)	NR	NR	NR	NR	NR	NR	Sev: 68%
Ricardi et al (2010)(75)	69.1	NR	NR	NR	NR	12	Sev: 88.9%

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Roumeguere et al (2008)(36)	56.5 (11.1)	NR	Currently has a partner 1504 (96)	CHD: 157 (10), Hyp: 674 (43), Diab: 360 (23), Anx/Dep: 219 (14), LUTS: 266 (17), Pros: 78 (5), Ob: 376 (24), PS: 47 (3)	Organic :28% Mixed: 51% Psychogenic: 21%	>12	N: 78 (5), Mi: 517 (33), Mod: 392 (25) Sev: 580 (37)
Rubio-Aurioles et al (2013)(43)	53.2 (12.4)	NR	NR	Hyp: 157 (30.7), Diab: 106 (20.7), Ob: 95 (18.6), BPH: 81 (15.9), LUTS: 75 (14.7), Hyperl: 62 (12.2)	Mixed: 232 (45.6) Organic:168 (33.0) Psychogenic: 94 (18.5)	20	Mi: 114 (22.8), Mod: 272 (54.3) Sev: 115 (23.0)
Salonia et al (2008a)(58)	51.8 (12.7)	NR	No stable sexual relationship: 38 (16.45) Stable sexual relationship >12 months: 193 (83.5)	NR	NR	NR	M=Mi-Mod: 13.75
Salonia et al (2008b)(37)	53; 10.3 51.4; 13.5	NR	NR	NR	NR	NR	NR

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Sato et al (2007)(47)	NR	NR	NR	Diab: 55 (5.3), Hyp: 102 (9.4), CVD: 13 (1.3), IHD: 2 (0.2), AS: 6 (0.6), CBD: 20 (1.9), Dep: 19 (1.8), SCI: 12 (1.2), PC: 19 (1.8), IO: 17 (1.6)	NR	NR	Mi: 291 (28.1), Mod: 352 (34.0), Sev: 393 (37.9)
Son et al (2004)(78)	54.6	NR	NR	BPH: 33 (21), Diab: 26 (17), Hyp: 17 (11) CVA: 4 (3), Others: 4 (3)	NR	28.8	M-Mod: 16.23 (mean)
Souverein et al (2002)(44)	57.2 (10.74)	NR	NR	NR	NR	NR	NR
Urethral Suppository							
Mulhall et al (2001)(70)	46.5 (14.6)	NR	NR	Diab: 11% , Hyp: 29%, Hyperch: 21%, A History of cigarette smoking: 31%	NR	NR	NR
Raina et al (2007)(72)	55.6 (3.78)	NR	NR	NR	NR	NR	Sev: 19.65 (mean)
Raina et al (2005)(71)	63.7 (5.6)	NR	NR	NR	NR	NR	Sev: 68%
Multiple Treatments							

Author, year	Age (yrs), Mean(SD)	Ethnicity, n(%)	Relationship status, n(%)	Co-morbidities, n(%)	ED Aetiology n, %	ED Duration, months (sd)	ED severity – IIEF n(%)
Panach-Navarrete et al (2017)(61)	57.09 (10.63)	NR	NR	Hyp: 115 (46), Diab: 70 (28), Dys: 92 (36.8) Smkr; Yes 79 (31.6)/No 71 (28.4)/Former smkr 97 (38.8), CHD: 27 (10.8), Ldis: 24 (9.6), VasD: 14 (5.6), DigD: 19 (7.6), Endo: 27 (10.8), Neuro: 22 (8.8); OncH: 27 (10.8), PS: 16 (6.4)	NR	NR	NR
Sexton et al (1998)(40)	58.5	NR	NR	NR	NR	NR	NR

703 *Anx: anxiety; AS: Arterial sclerosis; BPH: Benign prostatic hyperplasia; CAD: Coronary artery disease; CBD: Cerebrovascular disease; CHD: Coronary heart disease; CVA: Cardiovascular accident; CVD: cardiovascular*
704 *disease; Dep: depression; Diab: diabetes; DigD: Digestive disease; Dys: Dyslipidaemia; Endo: Endocrinopathy; Hyperch: Hypercholesterolemia; Hyp: hypertension; Hyperl: hyperlipidaemia; Hypog: Hypogonadism; IHD;*
705 *Ischemic heart disease; IO: Intrapelvic operation; LUTS: Lower Urinary Tract Symptoms; Ldis: Lung disease; M: mean; Mi: mild; Mod: moderate; Neuro: Neuropathy; N: normal; NR: Not recorded; NR; Ob: obesity;*
706 *Onco: Oncologic History; Osteo: Osteoarthritis; PC: Prostate cancer; PS: Pelvic surgery; RP: radical prostatectomy; RPS: radical pelvic surgery; RT: radiotherapy; Sev: severe; SHIM: Sexual health inventory for men;*
707 *NSRP: Nerve sparing radical prostatectomy; Pros: Prostatectomy; SCl: Spinal cord injury; Sev: Severe; Smkr: Smoker; VasD: Vascular disease*

708 Table 3: Measures of Utilisation and Treatment Barriers and enablers

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
ICI treatment						
Alvarez et al. (1998)(63)	PD	Reasons for discontinuation were collected monthly.	NR	PD	After each injection: date, time, volume of injection and dose were recorded by the patient.	34% (D)
Armstrong et al (1994)(64)	SRQ	Qs: Reasons for withdrawal from treatment were collected via predefined questions.	NR	SRQ	Qs: covering home injection use including period of time.	64% (D)
Gerber and Levine (1991)(65)	Cons	Patients returned every 3 months and were questioned regarding erectile response, pain after injection and frequency of use.	NR	Cons	Qs: covering frequency of prostaglandin E1 use.	72% (D)
Irwin & Kata (1994)(77)	Cons	Patients were given monthly follow-up visits scheduled to evaluate the patients' acceptance and usage patterns	NR	NR	Monthly follow-up visits to evaluate patients' acceptance and usage pattern.	60% (D)
Kunelius et al (1999)(66)	SRQ	Qs: Patients were invited to a check-up after three years after they had been started on ICI treatment and were sent a questionnaire prior to the appointment.	NR	SRQ	Qs: aspects of sexual function and possible problems with Aprostadil self-injection.	46%.4 (D)
Lehmann et al (1999)(48)	Int & Cons	Included objective and subjective variables which included barriers to treatment use.	NR	Int & Cons	Qs: covering the number of injections used.	20% (D)
Perimenis et al (2001)(67)	NR	NR	NR	NR	NR	42.5% (D)
Polito et al (2012)(68)	SRQ	Qs: multiple choice questions including: lack of, disappointment with the effects, Injection pain/problems with the injection (difficulty/fear), Cost of the drug.	NR	NR	NR	18.6% (D)
Purvis et al (1999)(50)	SRQ	Qs: Twenty eight questions were asked which were multiple choice in the majority of cases.	NR	SRQ	NR	38.6% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Raina et al (2003a)(57)	NR	NR	NR	SRQ, CR	Data collected: treatment effect, frequency of use, duration of erection following penile injections and side-effects.	52% (D)
Rowland et al (1999)(49)	SRQ	Qs: including as section for participants who had discontinued ICI treatment.	NR	SRQ	Qs: items pertained to how ICI was used, its effectiveness, and the patient's general satisfaction.	40% (D)
Sung et al (2014)(62)	TS	Participants were asked about reasons for discontinuation.	NR	TS	Qs: multiple responses.	79.9% (D)
PDE5I medication						
Bai et al (2015)(59)	NR	NR	NR	NR	NR	tadalafil 20mg: 13.7% (D) Sildenafil 100-mg: 10.3% (D)
Buvat et al (2013)(31)	Cons	Time to discontinuation was measured by the number of days from randomization up to discontinuation of treatment. Secondary outcomes included patients who switched and discontinued treatment and were asked about reasons for switches and discontinuations.	NR	Cons	NR	Tadalafil OaD:52% (D) Tadalafil PRN:42% (D) Sildenafil PRN:67% (D)
Buvat et al (2014)(29)	TS	Patients who had no visit within 4–6 months after baseline were followed up with a telephone follow-up call.	D = days to switch or discontinuation.	Cons	A telephone follow-up call was performed if a patient had no visit within 4–6 months after baseline.	13.8% (D)
Cairolì et al (2014)(41)	SRQ	A questionnaire administered at 1, 3, and 6 months post baseline.	P ≥ 1 dose in last 4 weeks A = most recent dose in accordance with prescription	PAQ	Qs: drug administration, dosing compliance, erectile function, sexual performance/satisfaction, relationship status.	70.2% (A) 69.2% (P)
Carvalho et al (2012)(35)	TS	A telephone interview involving a comprehensive, detailed questionnaire which included two open ended questions: (i) How did you take the inhibitor?; and (ii) What reasons led you to stop medication?	NR	SRQ	Qs: quantitative and qualitative variables and including frequency and duration of PDE5 use.	48.9% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Carvalho et al (2014)(27)	SRQ	Qs: 29-item questionnaire including open ended questions with regards to utilisation of PDE5Is.	P=Continued use	SRQ	Qs: demographics, type of PDE5i and frequency of use, other previous treatments, side-effects, expectations regarding the treatment, and partner involvement	100% (P)
Choi et al (2014)(60)	NR	NR	NR	NR	NR	Tadalafil OaD: 18.9% (D) Tadalafil alternate-day: 21.1% (D)
Cimen et al (2009)(73)	TS	Patients were called by phone and asked to answer questions on the phone including questions regarding reasons for discontinuation.	NR	Int	Qs: PDE5 inhibitor usage status (current using/stopped using), patient satisfaction, reasons of treatment interruption (inadequate efficacy, treatment expenses, adverse effects, etc.), drug shift (interchange between different PDE5 inhibitors) and satisfaction with the new drug were interrogated.	32.8% (D)
Conaglen & Conaglen (2012)(28)	Int	The interviewer followed a question schedule that sought details of frequency of usage and preference for the drugs available to participants. Reasons for that choice, or for discontinuation of use, were also sought.	D=stopping medication taking	Int	Qs: details of frequency of usage and reasons for discontinuation of use.	33% (D)
El-Galley et al (2001)(51)	TS	Participants were contacted by telephone. Patients who ended treatment were asked about the main reason for discontinuation.	P=Continued use	TS	NR	48% (D)
El-Meliegy et al (2013)(42)	SRQ	Outcomes were assessed at baseline and at 1, 3, and 6 months after treatment initiation.	P≥ 1 dose in last 4 weeks A= most recent dose in accordance with prescription	PAQ	NR	59.6% (A) 64.9 (P)
Fagelman et al (2001)(52)	SRQ	Qs: At follow-up visits, the patients were given a questionnaire and then interviewed	D=Prescription renewal	SRQ, Int	Qs: demographics, comorbid conditions, duration of ED, length of time taking sildenafil, number of tablets taken, maximum dose, efficacy, safety, satisfaction, and others.	38% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Green and Martin (2000)(53)	SRQ/ TS	The initial forty patients were followed for a two-year interval either by follow-up clinic visits or telephone interviews.	NR	SRQ/ TS	At follow-up clinic visits or telephone interviews.	32.5% (D)
Incrocci et al (2003)(54)	SRQ	Qs: evaluate their current sexual functioning and to ask about sildenafil use.	NR	SRQ	Qs: current sexual functioning and use of sildenafil.	76% (D)
Jiann et al (2006)(45)	SRQ	Qs: multiple choice questions in regard to reasons for discontinuation.	NR	SRQ	Qs: marital status, ED duration, frequency of sexual intercourse, history and current status of usage.	57% (D)
Kim et al (2014)(34)	SRQ	Qs: questionnaire had multiple choice questions regarding discontinuation.	D=not taken PDE5i in the past 1 year	SRQ	Qs: characteristics and treatment of ED.	23.9% (D)
Kim et al (2015)(32)	NR	NR	NR	NR	NR	Placebo: 9.1% (D) Tadalafil 2.5 mg (prrated): 10.1% (D) tadalafil 5mg OaD: 8.7% (D)
Klotz et al (2005)(74)	TS	The reasons for abandonment were determined by a telephone survey.	D=no 2 nd prescription within 6 months	PR	NR	31% (D)
Lee et al (2010)(46)	TS	Reasons for discontinuing PDE5I therapy were recorded by asking each patient..	D=treatment cessation at 2/6 months	NR	Compliance measured at two different time points: at 2 months and again at the 6 month follow-up after.	72% (D)
Li et al (2016)(76)	NR	NR	NR	NR	NR	Tadalafil 5 mg: 4.4% (D) Tadalafil de-escalation: 4.4% (D)
Ljunggren et al (2008)(55)	TS	Participants were contacted by telephone and asked questions regarding reasons for discontinuation.	NR	Int	Qs: current treatment, frequency of use, change of treatment, reason for change, and reason for discontinuation.	14.2% (D)
Mazzola et al (2013)(33)	Cons	On follow-up, patients were questioned regarding continued use of PDE5.	D=stopping medication taking	NR	Qs: regarding continued use of PDE5Is.	67% (P)
McMurray (2007)(30)	NR	At yearly intervals changes in dosing or temporary or permanent discontinuation were recorded.	NR	PD	Compliance was assessed by medication diaries and by continued study participation.	40% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Montorsi et al (2004)(56)	Cons	At patient visits, blood pressure and pulse, adverse events, concomitant medications and the reason for dose modification were recorded.	NR	Cons	NR	21% (D)
Raina et al (2003b)(57)	SRQ	Qs: focussed on sexual satisfaction of the patients' spouses/partners 3 years after the first survey to assess long-term efficacy and compliance.	NR	CR	Data collected: drug efficacy, dose, frequency, compliance, return of erections, new side-effects.	27% (D)
Ricardi et al (2010)(75)	NR	NR	P=taking at least 70% of doses	NR	NR	Arm A (20-mg tadalafil PRN): 86% (P) Arm B: (tadalafil 5-mg OaD): 100% (P)
Roumeguere et al (2008)(36)	SRQ	Qs: At 1, 6, and 12 months, patients completed the IIEF-EF domain questionnaire, EDITS and the relationship questionnaire, and indicated whether tadalafil was used in the previous 4 weeks.	D=not using treatment in past 4 weeks.	Quest	Qs: Tadalafil utilisation in the past 4 weeks: the number of tablets, dosage, and tolerance were recorded.	16% (D)
Rubio-Aurioles et al (2013)(43)	SRQ	Qs: Patients provided assessments of drug administration and dosing compliance, erectile function, sexual performance and satisfaction, and relationship status at 1, 3, and 6 months following the initiation of treatment.	P≥ 1 dose taken within the last 4 weeks A= most recent dose taken according to original instructions	PAQ	PAQ administered to patients at 1, 3, and 6 months after treatment initiation.	67.5% (A) 66.5% (P)
Salonia et al (2008a)(58)	SRQ	Qs: At the 18-mo follow-up, patients were asked to complete a multiple-choice global assessment questionnaire (GAQ) regarding specific reasons for eventual therapy discontinuation.	NR	SRQ	Patients were asked to complete a multiple-choice GAQ	72.6% (D)
Salonia et al (2008b)(37)	Clin, demog data	Patients were subdivided into two groups according to their compliance.	NR	Cons	Data gathered included patient compliance with the suggested PDE5.	42% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Sato et al (2007)(47)	Clin, demog data	Reasons for discontinuation were not asked about due to privacy concerns of the authors, however, significant risk factors for the dropout during successful treatment were analysed.	NR	SRQ, Int, Cons	NR	48% (D)
Son et al (2004)(78)	TS, CR	Six months after the first sildenafil prescription, compliance to medication and the reasons for discontinuation were reviewed by chart or surveyed by telephone.	NR	TS, CR	Compliance to medication and the reason for discontinuity were reviewed by chart or surveyed by telephone.	34.6% (D)
Souverein et al (2002)(44)	PR	The date of sildenafil discontinuation was defined as the last sildenafil prescription date plus the number of tablets dispensed.	D = (1) no refills in 12 months; (2) switched treatment or (3) 6 months between the last refill and the end of follow-up.	PR	Sildenafil use during follow-up was assessed using information on the number of Sildenafil refills during follow-up	45% (D)
Urethral Suppository						
Mulhall et al (2001)(70)	SRQ	Qs: to determine whether they were continuing to use MUSE as a treatment. Those who had discontinued therapy were asked to complete a questionnaire regarding the reasons for stopping.	NR	SRQ	Qs: to determine whether they were continuing to use MUSE as a treatment.	69.2% (D)
Raina et al (2007)(72)	NR	NR	NR	NR	NR	32 (D)
Raina et al (2005)(71)	NR	NR	NR	CR	Data gathered: treatment effect, frequency of use, duration of erection following treatment and side-effects.	52 (D)
Multiple Treatment						
Panach-Navarrete et al (2017)(61)	TS	To collect information about the use (including time of use) and dropout (including reason) of the prescribed treatment.	NR	TS	To collect information about the use (including time of use) and dropout (including reason) of the prescribed treatment.	1 st PDE5I: 62.07% (D) Other PDE5I: 41.94% (D) US: 69.23% (D) ICI: 65.11% (D)

Author, year	Measure of Treatment Barriers/Enablers	Description of Barriers/Enablers Measure	Definition (A,P,D)	Measure of Treatment Utilisation	Description of Utilisation Measure	% Adherent (A), persistent (P) discontinued (D)
Sexton et al (1998)(40)	TS	Telephone interviews were conducted with all patients to determine levels and frequency of sexual activity, current form of therapy and reasons for discontinuing therapy, side-effects and overall satisfaction.	NR	NR	NR	ICI:59%(D) PP:30%(D)

709 CR: chart review; Cons: consultation; Int: interview; NR: not reported; PAQ: persistence adherence questionnaire; PD: patient diaries; PR: prescription records; Qs: questions; Quest: questionnaire; SRQ: self-report
710 questionnaire; TS: telephone survey; Y: year

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714 Table 4: Treatment barriers and enablers

	Factor	TT	Descriptive results	Inferential results
Demographic	Age			
	Being of older age	PDE5I	(-): 43	(0): 34,37,41,45,46,47 (-): 29,36,44 (+): 35,42
		ICI		(0): 48,49,50
	Education			
	Higher level of education	PDE5I		(0): 41,42 (+): 34,37,43(P, not A),
Employment				
Being in FT employment	PDE5I		(0): 29 (+): 41 (A, not P),42(A/P),	
Clinical	Related to Treatment			
	Medication Ineffective	PDE5I	(-): 27,28,29,30,31,32,35,36,43,45,46,51,52,53,54,55,56,57,58,59,60,61	31; - Hardness of erection (0): Tad OaD Vs Sild PRN Vs Tad PRN - Duration of erection: (0): Tad OaD vs. Tad PRN (+): Tad OaD sig increased P compared to Sild PRN (+): Tad PRN sig increased P compared to Sidl PRN
		ICI	(-): 40,61,62,63,64,65,66,67,68,69,	(-): 49
		US	(-): 61,70,71,72	
		PP	(-): 40	
	Side-effects/Fear of side-effects	PDE5I	(-); 27,29,30,32,34,36,46,51,52,54,55,59,60,61,73,74,75,76	(0): 31 (between PDE5Is) (+): 35; (Men who reported side-effects were less likely to discontinue treatment) (-): 45
		ICI	(-): 40,61,62,64,65,66,67,68,69,77	(0): 48 (-): 49
		US	(-): 61,71,72	
		PP	(-): 40	
	Medication lacks spontaneity	PDE5I	(-): 34,35,78	
		ICI	(-): 40, 62	
		US	(-): 70	
	Specific to PDE5I Treatment			
	Initial treatment	PDE5I		(0): 41
	Having a history of ED treatment utilization	PDE5I		(0): 62 (+): 44

Factor	TT	Descriptive results	Inferential results
Using; Tadalafil/Sildenafil or Vardenafil	PDE5I		42; (0): Tad Vs Sild (0): Tad Vs Sild (+): Using Sild at initial prescription rather than Vard 43; (0): Sild Vs Vard (0): Sild Vs Vard (0); (+): Tad sig increased utilisation compared to Sild (P/A)
Able to tolerate treatment at 1 month	PDE5I		(+): 36; Having good toleration for treatment after 1 month was associated with sig continued utilisation.
Higher incidence of trying dose titration	PDE5I		(+): 45
Having a dose greater than 50mg	PDE5I		(+): 45
Short window of time in which the drug is effective	PDE5I		31; (0): Tad OaD Vs Tad PRN (+): Tad OaD sig increased utilisation compared to Sild PRN (P) (+): Tad PRN sig increased utilisation compared to Sild PRN
Slow onset of action	PDE5I		(0): 31 (Tad OaD Vs Sild PRN Vs Tad PRN)
Specific to ICI Treatment			
Administration	ICI	(-): 40,49,62,63,64,65,68,69,77	(-): 48
Type of vasoactive substance	ICI		(-): 49
Disposable 1ml syringe	ICI	(0): 50	
Fully automatic RFSU pistol	ICI	(0): 50	
Manual Injection (d-penn) as opposed to semi-automatic BD pistol	ICI	(0): 50	
Using papaverine-phenolamine (15 mg; 0.5 mg)	ICI	(0): 50	
Using; Low dose Aprostadiil (0 ± 10 mg)/High dose Aprostadiil (0 ± 20 mg)/TRIMIX/D-penn Aprostadiil	ICI	(0): 50	
Condition Specific Factors			
Aetiology	PDE5I	(+): 43 (psychogenic associated with continuation)	(0): 29,41 (-): 34 (psychogenic associated with discontinuation) (+): 35 (venogenic associated with continuation compared to arteriogenic /diabetes/iatrogenic)
	ICI		(-): 49 (ED including an organic component)
Having more severe levels of ED	PDE5I		(0): 29,41,46 (-): 36,37,42,43,47
A shift of => 2 or a score of 4 on the erection hardness score (EHS)	PDE5I		(+): 33
Shorter Duration of ED symptoms	PDE5I		(-): 34 (+): 43 (≥ 4 years versus <1 year; P=+, A=0),42 (<1 year P=0, A=+), 45 (0): 41 (P=0, A=0)
Comorbidities			
Due to the effects of co-morbidities	PDE5I	(+): 42 (Hypertension) (-): 55,74 (tumor/hip prosthesis),78	(0): 29,46 (BMI score/Charlson Comorbidity Index score). 34;

	Factor	TT	Descriptive results	Inferential results
				(0): Number of comorbidities/Stress/Smoking/alcohol (+): Sig increase in utilisation by those of higher weight and those with a BMI of ≥ 23 41; (0): Diabetes Mellitus/Dyslipidemi/Hypertension/Depression (+): Those with Coronary artery disease had sig higher rates of utilisation. (+): 36 (Sig increase in utilisation by those with pelvic surgery)
		ICI	(-): 40,65	(0): 62 (diabetes mellitus/hypertension/cardiovascular disease/cerebrovascular attack/previous radical pelvic surgery including prostatectomy and cystectomy/unilateral or bilateral nerve sparing prostatectomy/previous pelvic radiotherapy)
		PP	(-): 40	
	Illness (ongoing health issues, deteriorating health or recent injuries or operations)	PDE5I	(-): 28,36	
		ICI	(-): 63,64	
	Other medications and treatments			
	Due to other Medications and Treatments	PDE5I	(-): 34	44; (-): incontinence materials/antidepressants/nitrate therapy/Insulin (0): antihypertensive agents/oral anticoagulants/low dose acetylsalicylic acid/benign prostatic hyperplasia products (+): Lipid-lowering drugs
	Other clinical factors			
	Type of physician	PDE5I		31; (0): Endocrinologist/diabetologist/urologist/Other (+): diagnosed by a GP rather than a urologist sig higher utilisation.
	-Presence of erections prior to treatment -Low response during psychophysiological screening (investigation of pharmacological effects on sexual response). -Lack of spontaneous erections	ICI		(-): 49
	Penile rigidity adequate for sexual intercourse	ICI		(+): 62
	Premature ejaculation	ICI		(-): 49
Psychological and	Treatment Related Beliefs			
	Lack of confidence in medication	PDE5I	(-): 29	(0): 31 (Tad OaD/Tad PRN/Sild PRN)
	Fear of drug dependency	PDE5I	(-): 35	
	Fear that medication is harmful for the heart	PDE5I	(-): 27,35	
	Averse to taking medication	PDE5I	(-): 27	
	Medication caused personal conflict	PDE5I	(-): 56	
	Don't want to take a pill everyday	PDE5I	(-): 29	31; (0): Tad PRN vs Sild PRN (-): Tad OaD sig increased discontinuation compared to Tad PRN/Sild PRN

	Factor	TT	Descriptive results	Inferential results
	Prefer a pill every day, not on demand	PDE5I		31; (0): Tad PRN vs Sil PRN (+): Tad OaD sig increased utilisation compared to Sild PRN/Tad PRN
	Not willing for sex life to depend on medication/medication controls sex life	PDE5I	(-): 29,34,78	31; (0): Tad PRN vs Sild PRN (0): Tad OaD vs. Tad PRN (-): Sild PRN sig increased discontinuation compared to Tad OaD
	Inconvenience/embarrassment in obtaining medication	PDE5I	(-): 27,45	
	Forgetting to buy or to get medical prescription	PDE5I	(-): 27	
	Satisfaction with treatment	ICI		(+): 48
	Disappointed with treatment	ICI	(-): 67,68	
	Would recommend treatment to a friend	ICI		(+): 48
	Psychosocial Well-being			
	Lack of self-confidence/self-esteem	PDE5I	(-): 27,36	
		ICI		(-): 48
	Improve Sexual performance	PDE5I		(+): 27
	To improve psychological and emotional state	PDE5I	(+): 27	
Social	Cost of Treatment			
	Cost	PDE5I	(-): 28,27,29,34,35,36,43,45,46,52,53,54,55,61,73,74,78	
		ICI	(-): 40,62,65,	
		US	(-): 70	
	Related to Partner and Intimate relationship			
	Loss of libido/interest in sex	PDE5I	(-): 34,35,45,52,55,58,73,74,78	
		ICI	(-): 40,62,65,77	
		US	(-): 72	
		PP	(-): 40	
	Partner lack of interest in sexual relationship	PDE5I	(-): 34,45,58,74 (+): 27	
	Lack of emotional readiness for restoration of sexual activity	PDE5I	(-): 34,78	
	Higher level of Partners sexual activity	PDE5I		(0): 27
	Conflicts within one's relationship	PDE5I	(-): 27,28,51	
		ICI	(-): 62	
	Low satisfaction with sex life	ICI		(-): 49
Better quality of sexual relationship	ICI		(+): 48	
Person within the dyad who most often initiated sexual activity	ICI		(0): 49	
Partner Related				
Partner's difficulty in accepting treatment	PDE5I	(-): 27,29,36	(0): 31	
	ICI	(-): 66		
Partner satisfaction with treatment (reported by patient)	ICI		(+): 48	
Partner aware of and involved in the use of treatment	PDE5I		(+): 27	

	Factor	TT	Descriptive results	Inferential results
	Having no partner	PDE5I	(-): 28,36,53,57	(+): 33 (having a partner)
		ICI	(-): 40,64,69,77	
		PP	(-): 40	
	Marital Status/Relationship Status	PDE5I		(0): 34,37,41
		ICI		(0): 49
	Living with partner	PDE5I		(0): 34
	Longer duration of living arrangement	PDE5I		(-): 31
	Length of marriage/relationship	PDE5I		(0): 34,37
		ICI		(0): 49
	Geographical distance from partner	PDE5I	(-): 27	
Partner being of younger age (=>10 years younger)	PDE5I		(0): 34 (+): 33	
Partners illness	ICI	(-): 66		
Behavioral	Help seeking			
	Length of time before seeking help for ED	PDE5I		(0): 37
	Personal behavior			
	Lower frequency of masturbation	ICI		(-): 49
	Related to sexual relationship			
	Lack of opportunity for sexual intercourse	PDE5I	(-): 27,35,61	
		ICI	(-): 61	
		US	(-): 61	
	Pre-treatment sexual activity (=>4 times per month)	PDE5I		(+): 33
	Greater No of sexual attempts in the first month of treatment	PDE5I		(+): 36
Life style				
Level of exercise	PDE5I		(0): 34	

715 Key: A=adherence; OaD=Once a day; P=persistence; PRN=On demand; Sild=Sildenafil; Tad=Tadalafil; Vard=Vardenafil; (-) = Barrier to treatment utilisation; (+) = Enabler of treatment utilisation; (0) = Not
716 significant

1.1 Supplementary Material

Prisma Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3-4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supp. Material p 4-7
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5

Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	N/A
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I ²) for each meta-analysis.	5 Supp. Material p 8-47

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Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6 Figure 1 - PRISMA flowchart
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6 Table 1 – Study Characteristics
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	N/A
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9 Table 4 – Treatment barriers and enablers
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A

DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15-18
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	18
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	18

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

1.1.1 Systematic Review Search Terms

General Terms		
Erectile Dysfunction	Adherence	Treatment for ED
Erectile Dysfunction*	Medication AND (adher* OR -use OR taking)	PDE5 Inhibitor*
Impoten*	(complan* OR non-complan*)	Phosphodiesterase type 5 inhibitor*
penis erection*	(adhere* OR non-adhere*)	Sildenafil Citrate (Viagra)
male erectile disorder*	(persistence OR non-persistence)	Tadalafil (Cialis)
Sexual dysfunction*	Patient complian*	Vardenafil (Levitra)
Male reproductive disorder*	Non-fulfilment	PDE5I
Sex disorder*	Drug-use	Uprima
Penile Erection*	Mean possession ratio	Intracavernosal injection*
Erection*	Medication possession ratio	Alprostadil pellet
	Treatment refusal	Vacuum device
	Uptake	Viagra
	adheren*	Cialis
	non?adheren*	Levitra
	persist* or non?persist*	penile prosthesis
	compla*	Psychosexual counselling
	non?complan*	Apomorphine hydrochloride
	Drug utilization	Medicated urethral system for erections (MUSE)
	Health rationing	Viridal duo
		Caverject
		Caverject dual chamber
		urethral suppositories

MeSH Terms		
Embase 1974 to 2015 July		
Erectile Dysfunction	Adherence	Treatment for ED
Erectile dysfunction	Medication compliance	Phosphodiesterase V inhibitor
Impotence	Patient compliance	Sildenafil
Penis erection	Compliance	Vardenafil
Sexual dysfunction	Drug utilization	Apomorphine
	Drug use	intracavernous drug administration
	Treatment refusal	prostaglandin E1
		Tadalafil
		penis prosthesis
		prostaglandin E1
Ovid MEDLINE(R) 1946 to 2015 July		
Sexual dysfunction, Physiological	Medication Adherence	Alprostadil
Sexual dysfunction, Psychological	Patient Compliance	penile prosthesis
Sexual dysfunctions, Psychological	Compliance	Apomorphine
Penis	Treatment Refusal	
Penile Erection	Drug Utilisation	
AMED (Allied and Complementary Medicine) 1985 to July 2015		
Sex disorders male	Patient compliance	Enzyme inhibitors
Impotence	Treatment refusal	Sex Counselling
Sexual dysfunctions	Patient acceptance of health care	Phosphodiesterase 5 Inhibitors
Penis		Penile prosthesis
Genital diseases, male		Apomorphine

		Alprostadil
HMIC Health Management Information Consortium 1979 to July 2015		
Male reproductive disorders	Drug compliance	
Impotence	Patient compliance	
Penis	Drug Consumption	
Sex disorders	Drug administration	
	Patient non-compliance	
	Patient participation	
	Patient response to treatment	
	Decision making	
	Health rationing	
	Patient consent to treatment	
Cochrane Central Register of Controlled Trials		
Erectile dysfunction	Medication adherence	Phosphodiesterase 5 Inhibitors
Sexual dysfunction, Psychological	Compliance	Penile prosthesis
Sexual dysfunction, Physiological	Patient compliance	Apomorphine
Penis	Treatment refusal	Alprostadil
Health Technology Assessment 2 nd Quarter 2015		
Impotence	Patient compliance	Phosphodiesterase Inhibitors
Sexual dysfunction, physiological	Treatment Outcome	Penile prosthesis
Penile Erection	Drug utilization	Alprostadil
	Decision making	
	Health care rationing	
CINAHL plus with full text®		
Impotence	Medication compliance	Phosphodiesterase Inhibitors

Sexual dysfunction, Male	Patient compliance	Sildenafil
Penile erection	Treatment refusal	Tadalafil
Penile prosthesis	Drug utilization	Vardenafil Hydrochloride
	Decision making, patient	penile prosthesis
		Couple counselling
		Sexual counselling
PsychARTICLES®		
Erectile Dysfunction	Treatment compliance	Phosphodiesterase
Erection (penis)	Treatment refusal	Sildenafil
Male genital disorders	Decision making	Apomorphine
PsychINFO®		
Erectile dysfunction	Treatment compliance	Phosphodiesterase
Erection (penis)	Treatment refusal	Apomorphine
Male genital disorder	Decision making	Sildenafil

1 1.1.2 Barriers and Enablers to Treatment Utilisation

	Factor	Treatment type	Barrier to treatment utilization <i>Descriptive results</i> (n (%) reporting reason for discontinuation unless otherwise stated)	Barrier to treatment utilization <i>Inferential results</i>	Enabler of treatment utilization <i>Inferential results</i>	Non-significant <i>Inferential results</i>
Demographic	Age					
	Being of older age	PDE5I	<p>Rubio-Aurioles (2013)#</p> <p>(P) Higher rates of persistence in younger men (mean age of 52.3 years versus 54.9 years for non-persistent patients).</p> <p>(A) Higher rates of adherence in younger men (mean age of 52.1 years versus 55.5 years for non-adherent patients).</p>	<p>Buvat (2014):</p> <p>>65 y significantly higher rates of discontinuation than those ≤65 y (p=0.038).</p> <p>Roumeguere (2008):</p> <p>>60 y significantly higher rates of discontinuation than those 51-60 y (OR = 1.88; 95% CI: 1.18–2.99; P = 0.008)</p> <p>Souverein (2002):</p> <p>=/>60 y significantly higher rates of discontinuation than <60 y (RR 1.71 (95% CI: 1.20 – 2.44).</p>	<p>Carvalho (2012)</p> <p>Older men less likely to discontinue (OR = 0.956, p =0.005).</p> <p>EI-Meliegy (2013)# Older men were likely to be both more persistent (P) (OR =1.03, p=0.002) and adherent (A) (OR =1.02, 0.034)</p>	<p>Cairoli (2014) (P) (A)</p> <p>Jiann (2006)</p> <p>Kim et al (2014)</p> <p>Lee et al (2010)</p> <p>Salonia (2008b)</p> <p>Sato et al (2007)</p>

	ICI					Purvis (1999) Lehmann (1999) Rowland (1999)
Education						
Higher level of education	PDE5I			Kim et al (2014) Significantly greater discontinuation for middle school graduate or below compared to high school graduate or above p=0.049. OR: 0.48, p= 0.05 Rubio-Aurioles (2013) (P) Significant higher rates of persistence for primary, secondary or tertiary education in comparison with no education) p=0.047	Cairolì (2014) (P)(A) Rubio-Aurioles (2013) (A) Postgraduate Vs no formal education (P)(A) Primary education Vs formal education (P)(A) Secondary education Vs formal education (P)(A) Tertiary education Vs formal education (P)(A)	

					<p>Salonia (2008b)</p> <p>high education group indicated significantly higher rates of persistence compared to patients in the low education group UVA: OR = 2.46, p=0.005</p>	<p>University education Vs formal education (P)(A)</p> <p>Salonia (2008b)</p> <p>higher level of education not significant using MVA</p>
Employment						
Being in FT employment	PDESI		Overall work status		<p>El-Meliegy (2013)</p> <p>(P): FT employment was related to a significantly higher rates of persistence p= 0.010</p> <p>(P): being employed FT opposed to being unemployed was associated with significantly higher rates of persistence OR: 0.28, p=0.024</p> <p>(P): being employed FT as opposed to retired was associated with significantly higher rates of persistence OR: 0.411, p=0.009</p> <p>(A): FT employment was related to a significantly higher rates of adherence p= 0.006</p>	<p>Buvat (2014)</p> <p>Pensioner/retired vs. employed/student</p> <p>Unable to work vs. employed/student</p> <p>Unemployed/other vs. employed/student</p> <p>Cairolì (2014) (P)</p> <p>FT/PT/retired/unemployed</p> <p>El-Meliegy (2013)</p> <p>(P) FT as opposed to PT</p> <p>(A) FT as opposed to Unemployed</p>

					<p>(A): being employed FT opposed to PT was associated with significantly higher rates of adherence OR: 0.59 p=0.007</p> <p>(A): being employed FT as opposed to retired was associated with significantly higher rates of adherence OR: 0.411, p=0.010</p> <p>Cairolì (2014)</p> <p>(A) Being employed FT compared to part time, retired, unemployed significantly increased adherence p=0.022</p>	
Other						
Height / Residential area / Occupation / Number of children	PDE5I					Kim (2014)
Being of Catholic religion	PDE5I		Kim (2014) Continuers 24 (20.7), discontinuers 36 (9.8), p=0.015 OR: 2.31, p=0.01			Kim (2014) Protestant Buddhist

						Other
	Ethnic background	PDESI		<p>Buvat (2014)</p> <p>France vs. Germany 0.045 HR 1.62 (1.01, 2.59)</p> <p>Italy vs. Germany 0.022 HR 0.41 (0.19, 0.87)</p> <p>Greece vs. Germany 0.010 HR 0.32 (0.13, 0.75)</p>		<p>Cairolì (2014)</p> <p><i>Black</i></p> <p><i>African American</i></p> <p><i>White</i></p>
Clinical	Related to Treatment					
	Medication Ineffective	PDESI	<p>Bai (2015)#</p> <p><i>Ineffective:</i></p> <p>Tad 1 (3.8)</p> <p>Buvat (2013)#</p> <p><i>Hardness of erection:</i></p> <p>Tad OaD: 55 (21.4)</p>	<p>Buvat (2013)</p> <p><i>Duration of erection</i></p> <p>Tad OaD was related to significantly increased persistence compared Sild PRN: p=0.035</p> <p>Tad PRN was related to significantly increased persistence compared Sil PRN: p=0.003</p>		<p>Buvat (2013)</p> <p><i>Hardness of erection</i></p> <p>Tad OaD vs. Sild PRN</p> <p>Tad PRN vs Sil PRN</p> <p>Tad OaD vs. Tad PRN</p> <p><i>Duration of erection</i></p>

		<p>Tad PRN: 46 (18.3)</p> <p>Sild PRN: 55 (21.1)</p> <p><i>Duration of erection</i></p> <p>Tad OaD: 11 (4.3)</p> <p>Tad PRN: 7 (12.8)</p> <p>Sild PRN: 24 (9.2)</p> <p>Buvat (2014)# Total: 35 (4.4)</p> <p><i>Hardness of erection: 33 (4.2)</i></p> <p><i>Duration of erection: 2 (0.2)</i></p> <p>Carvalho (2012)# 61 (38.1)</p> <p>Carvalho (2014)#: 23 (15.5)</p> <p>Choi (2014)# Total: 14 (15.5)</p> <p>Insufficient response:</p> <p>Tad OaD: 5 (5.5)</p> <p>Tad alternative days: 9 (10)</p> <p>Conaglen (2012)# 1 (0.6)</p>			OaD vs. Tad PRN
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		<p>El-Galley (2001)# 14 (7)</p> <p>Fagelman (2001)# 64 (39)</p> <p>Green (1999)#</p> <p><i>Minimal response:</i> 6 (15)</p> <p>Incrocci (2003)#: 30 (60)</p> <p>Jiann (2006)# 104 (23.9)</p> <p>Kim (2015)# Tad 2.5mg; 2 (0.9)</p> <p>Lee (2010)# 8 (15)</p> <p>Ljunggren (2008)# 3 (2.3)</p> <p>McMurray (2007)# Total 52 (7.5)</p> <p><i>Year 1:</i> 22 (2.2)</p> <p><i>Year 2:</i> 19 (2.3)</p> <p><i>Year 3:</i> 14 (1.9)</p> <p><i>Year 4:</i> 7 (1.1)</p> <p>Montorsi (2004)# 173 (23.8)</p> <p>Panache Navarrete (2017)# 90 (38.8)</p>			
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		<p>Raina (2003b)# 5 (10.4)</p> <p>Roumeguere (2008)#: 38 (2.4)</p> <p>Rubio-Aurioles (2013)#</p> <p><i>Tad:</i>60 (19.0)</p> <p><i>Sild:</i> 17 (15.0)</p> <p><i>Vard:</i>13 (17.0)</p> <p>Salonia (2008a)# 28 (54.9)</p>			
	ICI	<p>Alvarez (1998)# 69 (8.0)</p> <p>Armstrong (1994)# 3 (10.0)</p> <p>Gerber (1991)#</p> <p><i>Inadequate erectile response</i> 9 (12.5)</p> <p>Kunelius (1999)# 9 (13.0)</p> <p>Panache Navarrete (2017)# 11 (39.3)</p> <p>Perimenis (2001)#3 (7.5)</p> <p>Polito (2012)# 33 (12)</p> <p>Raina (2003a)# 18 (17.6)</p>	<p>Rowland (1999)</p> <p>Those that reported a lack of efficacy were more likely to discontinue $p=0.009$.</p>		

		<p>Sung (2014)# 111 (37)</p> <p>Sexton (1998)#: 16 (18.3)</p>			
	US	<p>Mulhall (2001)# 30 (50.8)</p> <p>Panache Navarrete (2017)# 14 (28)</p> <p>Raina (2005)# 16 (29.6)</p> <p>Raina (2007)#: 9 (16.0)</p>			
	PP	<p>Sexton (1998)#</p> <p><i>Malfunction:</i> 2 (4.7)</p>			
Side-effects/Fear of side-effects	PDE5I	<p>Bai (2015)#</p> <p><i>Adverse event</i></p> <p>Tad 20mg: 3 (0.9)</p> <p>Buvat (2014) # Total: 23 (2.9)</p> <p><i>Adverse event;</i> 22 (2.8)</p> <p><i>Un-wanted spontaneous erections</i> 1 (0.1)</p> <p>Carvalho (2014)#:</p> <p>Fear of/side effects 15 (10.1)</p>	<p>Jiann (2006)</p> <p>A higher incidence of adverse events in continuers than discontinuers 63% and 47% respectively, p=0.01</p>	<p>Carvalho (2012):</p> <p>Men who reported side-effects were less likely to discontinue treatment OR: 0.396, p=0.002.</p>	<p>Buvat (2013)</p> <p><i>Un-wanted spontaneous erections / Adverse event</i></p> <p>Tad OaD</p> <p>Tad PRN</p> <p>Sild PRN</p>

		<p>Choi (2014)# Total: 5 (4.5)</p> <p><i>Side effects;</i></p> <p>Tad OaD: 3 (2.7)</p> <p>Tad alternate days: 2 (1.8)</p> <p>Cimen (2009)# 4 (1.3)</p> <p>El-Galley (2001)# Total: 10 (8)</p> <p><i>Side-effects:</i> 2 (1.6)</p> <p><i>Worsened Peyronie's disease:</i> 2 (1.6)</p> <p><i>Un-wanted spontaneous erections</i></p> <p>6 (4.8)</p> <p>Fagelman (2001)# Total: 13 (6.9)</p> <p><i>Side-effects:</i> 7 (3.1)</p> <p><i>Peyronie's disease:</i> 3 (1.9)</p> <p><i>Chest pain:</i> 3 (1.9)</p> <p>Incrocci (2003)#: 8 (16)</p> <p>Kim (2014)# 19 (3.9)</p>			
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		<p>Kim (2015)# Total: 6 (2.8)</p> <p>Tad 2.5mg: 3 (1.4)</p> <p>Tad 5mg: 3 (1.4)</p> <p>Klotz (2005)#</p> <p><i>Adverse (headache and rhinitis) 4 (1.7)</i></p> <p>Lee (2010)# 4 (7.5)</p> <p>Li (2016)# Total: 4 (4.6)</p> <p>Tad 5mg :</p> <p>headache and dyspepsia: 1 (1.15)</p> <p>Myalgia: 1 (1.15)</p> <p>Tad 20mg:</p> <p>Headache/back pain: 1 (1.15)</p> <p>Flushing and headache: 1 (1.15)</p> <p>Ljunggren (2008)# 3 (2.4)</p> <p>McMurray (2007)# Total: 11 (1.3)</p> <p>Year 1: 5 (0.5)</p>			
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		<p>Year 2: 2 (0.2)</p> <p>Year 3: 1 (0.1)</p> <p>Year 4: 3 (0.5)</p> <p>Panache Navarrete (2017)#</p> <p>Fear of/ADR:13 (6.4)</p> <p>Ricardi (2010)#</p> <p><i>Intolerable adverse events:</i> 3 (5.78)</p> <p><i>Headache:</i> 1 (1.9)</p> <p><i>Anaphylactic reaction:</i> 1 (1.9)</p> <p>Roumeguere (2008)#: 23 (1.4)</p>			
	ICI	<p>Armstrong (1994)# 1 (3.0)</p> <p>Gerber (1991)#:</p> <p><i>pain due to injection:</i> 12 (16.6)</p> <p>Irwin (1994)#</p> <p><i>pain:</i> 2 (3.3)</p> <p>Kunelius (1999)#: Total: 7 (10.1)</p>	<p>Rowland (1999)</p> <p>Those that discontinued were more likely to report side-effects p=0.038</p>		<p>Lehmann (1999)</p> <p><i>Pain from injection</i></p> <p><i>Aching pain in corpus cavernosum</i></p> <p><i>New scar tissue</i></p> <p><i>Bleeding from injection site</i></p> <p><i>Secondary penile deviation</i></p>

		<p><i>Fibrosis in the penile shaft</i> 3 (4.3%)</p> <p><i>Pain after injection</i> 4 (5.8%)</p> <p>Panache Navarrete (2017)#</p> <p><i>Fear of/ADR</i> 9 (20.9)</p> <p>Perimenis (2001)#</p> <p><i>Peyronie's disease:</i>1 (2.5)</p> <p>Polito (2012)#</p> <p><i>Injection pain:</i> 23 (8.4)</p> <p>Raina (2003a)#</p> <p><i>Priapism:</i> 1 (0.9)</p> <p>Sexton (1998)#</p> <p><i>Side-effects:</i> 12 (23)</p> <p>Sung (2014)#</p> <p><i>Adverse side-effects:</i> 16 (4.4)</p>			<p><i>Erection lasting longer than desired</i></p> <p><i>Priapism</i></p>
	US	Panache Navarrete (2017)#			

		<p>Fear of/ADR 16 (32)</p> <p>Raina (2007)#</p> <p><i>urethral pain and/or burning: 4 (7.4)</i></p> <p>Raina (2005)#</p> <p><i>urethral pain and/or burning: 4 (7.4)</i></p>			
	PP	<p>Sexton (1998)#:</p> <p><i>Infection or erosion: 4 (9.4)</i></p>			
Medication lacks spontaneity	PDE5I	<p>Carvalho (2012)# 14 (2.6)</p> <p>Kim (2014)# 11 (2.2)</p> <p>Son (2004)# 2 (1.2)</p>			
	ICI	<p>Sexton (1998)# 14 (16.1)</p> <p>Sung (2014)# 43 (14.6)</p>			
	US	Mulhall (2001)# 20 (34.0)			
Specific to ICI Treatment					
Administration	ICI	<p>Alvarez (1998) #</p> <p>Inability/unwilling to self-inject: 18 (2.0)</p>	Lehmann et al (1999)		

		<p>Armstrong (1994)#</p> <p><i>reluctance to use injections/difficulty with technique/method regarded as unacceptable: 7 (24.0)</i></p> <p>Gerber (1991)#</p> <p><i>did not like injections: 7 (9.7)</i></p> <p>Irwin (1994)# Total: 4 (6.65)</p> <p><i>physical limitations: 3 (5)</i></p> <p><i>needle phobia: 1 (1.65)</i></p> <p>Polito (2012) #</p> <p><i>difficulty, fear, pain when using injections: 18 (15)</i></p> <p>Raina (2003a)# Total: 12 (11.8)</p> <p><i>fear of injections: 6 (5.9)</i></p> <p><i>troublesome procedure: 6 (5.9)</i></p> <p>Rowland (1999)#</p> <p><i>procedural aspects surrounding the injection: 10 (8.4)</i></p>	<p>The effort to prepare and inject was substantial for those who discontinued, $p=0.001$.</p>		
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		<p>Sexton (1998)# Total: 9 (10.3)</p> <p><i>Fear of needles or injection procedure: 5 (5.7)</i></p> <p><i>manual dexterity: 4 (4.6)</i></p> <p>Sung (2014)#</p> <p><i>inconvenience of use 43 (14.6)</i></p>			
Type of vasoactive substance	ICI				<p>Rowland (1999)</p> <p><i>No difference across vasoactive treatments.</i></p>
Disposable 1ml syringe	ICI	<p>Purvis (1999)#</p> <p><i>Did not influence the decision to use the treatment.</i></p>			
Fully automatic RFSU pistol	ICI	<p>Purvis (1999)#</p> <p><i>Did not influence the decision to use the treatment.</i></p>			
Manual Injection (d-penn) as opposed to semi-automatic BD pistol	ICI	<p>Purvis (1999)#</p> <p><i>Discontinuers: 35.3%, compared to 27.7% continuing</i></p>			

		<i>semi-automatic BD pistol (13.1% compared to 23.7% continuing)</i>			
Using papaverine-phentolamine (15 mg; 0.5 mg)	ICI	Purvis (1999)# <i>Continuers 24.3%, discontinuers 14.6% (n=766)</i>			
Using; - Low dose Aprostadiil (0 ± 10 mg) - High dose Aprostadiil (0 ± 20 mg) -TRIMIX - D-penn Aprostadiil	ICI	Purvis (1999)# <i>Did not influence the decision to use the treatment.</i>			
Specific to PDE5I medication					
Initial treatment	PDE5I				Cairolì (2014) (P) (A) <i>Tad/Sild/Vard</i>

	Having a history of ED treatment utilization	PDE5I			<p>Souverein (2002)</p> <p>Discontinuation was less frequent among patients with a history of ED treatment use compared with those with no prior history: 28.6% and 43.9% respectively. Adjusted RR 0.48 (95% CI: 0.31 – 0.76).</p>	<p>Sung (2014)</p>
	Using Tadalafil, Sildenafil or Vardenafil	PDE5I			<p>El-Meliegy (2013)</p> <p>(P) using Sild at initial prescription rather than Vard was associated with increased persistence OR: 0.450, p=0.023</p> <p>(A) using Sild at initial prescription rather than Vard was associated with increased adherence OR: 0.42, p= 0.015</p> <p>Rubio-Aurioles (2013)</p> <p>(P) Tad was associated with increased persistence when compared to Sild OR: 1.6 p=0.006.</p> <p>(A) Tad was associated with increased adherence when compared to Sild OR: 1.3, p=0.021.</p>	<p>El-Meliegy (2013)</p> <p>(P) Using Tad as opposed to Sild</p> <p>(A) Using Tad as opposed to Sild</p> <p>Rubio-Aurioles (2013)</p> <p>(P) Using Sild as opposed to Vard</p> <p>(A) Using Sild as opposed to Vard</p>

Able to tolerate treatment at 1 month	PDE5I			<p>Roumeguer (2008)</p> <p>Toleration of treatment after 1 month (N = 1,350; 98% of total) was associated with continued use compared to patients who did not well tolerated at 1 month (N = 31; 2% of total): adjusted OR = 9.47; 95% CI: 4.04–22.18; P < 0.0001).</p>	
Higher incidence of trying dose titration	PDE5I			<p>Jiann (2006)</p> <p>Dose titration was associated with significantly higher rates of continuation p=<0.01</p>	
Having a dose greater than 50mg	PDE5I			<p>Jiann (2006)</p> <p>Having doses greater than 50mg was associated with significantly higher rates of continuation p=<0.01</p>	<p>Jiann (2006)</p> <p><i>Having a responding dose greater than 50mg</i></p>
Short window of time in which the drug is effective	PDE5I	<p>Buvat (2013)#</p> <p>Tad OaD: 0 (0.0)</p> <p>Tad PRN: 1 (0.4)</p> <p>Sild PRN: 11 (4.2)</p>	<p>Buvat (2013)</p> <p>Significantly higher rates of continuation for those using;</p> <p>-Tad OaD compared to those using Sild PRN p=<0.001</p>		<p>Buvat (2013)</p> <p>Tad OaD compared to Tad PRN</p>

			- Tad PRN compared to those using Sil PRN: p=0.006		
Slow onset of action	PDE5I	Buvat (2013)# Tad OaD: 9 (3.5) Tad PRN: 5 (2.0) Sild PRN: 10 (3.8) Buvat (2014)# 3 (0.4)			Buvat (2013) Tad OaD vs. Sild PRN Tad PRN vs Sil PRN Tad OaD vs. Tad PRN
Condition Specific Factors					
Aetiology	PDE5I	<u>Psychogenic ED as opposed to organic:</u> Rubio-Aurioles (2013)# (P) Higher rates of persistence for men with ED of psychogenic aetiology (79 persistent patients [23.2%] versus 15 non-persistent patients [8.9%]). (A) Higher rates of adherence for men with ED of psychogenic aetiology (78, [22.6%] of adherent patients versus 16 [9.8%] of patients who were non-adherent).	<u>Psychogenic ED as opposed to organic:</u> Kim (2014) <i>Psychogenic ED:</i> The proportion of the patients with psychogenic ED in the discontinuation group (47.4%) was significantly greater than in the continuation group (32.8%) (P%0.004). <u>Venogenic ED opposed to Arteriogenic, Diabetic and Iatrogenic etiologies:</u>		Buvat (2014) Cairolì (2014) (P) (A)

			<p>Carvalho (2012):</p> <p>Compared to venogenic aetiology participants with the following aetiologies indicated significantly higher rates of discontinuation;</p> <p>arteriogenic OR = 3.4, P = 0.01</p> <p>diabetes OR = 6.9, P = 0.001</p> <p>iatrogenic OR = 7.5, P < 0.001.</p>		
	ICI				<p>Rowland (1999)</p> <p><i>ED including an organic component</i></p>
	Having more severe levels of ED	PDE5I		<p>El-Meliagy (2013)</p> <p>(P) Having moderate as opposed to severe was associated with increased persistence 0.017.</p> <p>Roumeguer (2008)</p> <p>Patients with lower ED severity were more likely to continue compared to severe ED:</p> <p>- normal ED (adjusted OR = 6.88; 95% CI: 3.68–12.86; P < 0.0001);</p>	

			<p>- mild ED (adjusted OR = 7.83; 95% CI: 4.25–14.44; $P < 0.0001$);</p> <p>- moderate ED (adjusted OR = 2.06; 95% CI: 1.01–4.19; $P = 0.05$).</p> <p>Rubio-Aurioles (2013)</p> <p>(P) Moderate as opposed to severe ED was associated with higher rates of persistence OR: 0.6, $p=0.029$</p> <p>(A) Mild and Moderate as opposed to severe ED was associated with higher rates of adherence OR: 0.5, $p=0.037$ and OR: 0.5, $p=0.016$ respectively.</p> <p>Salonia (2008b)</p> <p>Compliant patients indicated a significantly greater SHIM score i.e. had less severe ED: UVA: $p=0.01$ / MVA: $p=0.01$.</p> <p>Sato (2007)</p> <p>Patients with lower ED severity were more likely to continue compared to severe ED HR: 0.960 CI: 0.931–0.990, $p=0.025$</p>		<p>El-Meliegy (2013)</p> <p>(P) having mild as opposed to severe ED</p> <p>(A) having mild OR moderate as opposed to severe ED</p> <p>Rubio-Aurioles (2013)</p> <p>(P) having mild as opposed to severe ED</p> <p>Lee (2010)</p> <p>SHIM score</p>
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A shift of \geq 2 or a score of 4 on the erection hardness score (EHS)	PDE5I			<p>Mazzola (2013)</p> <p>Significantly higher rates of continuation were reported for those with such a score on the EHS, $p < 0.001$</p>	
Shorter duration of ED symptoms	PDE5I		<p>Jiann (2006):</p> <p>Those that continued had a shorter duration of ED (49.6 ± 77.5 months) opposed to those that discontinued (52.5 ± 50.0), $p < 0.05$</p> <p>Rubio-Aurioles (2013)</p> <p>(A) Those that were adherent had a shorter duration of ED symptoms (those that had ED symptomology for ≥ 4 years compared to those that had ED symptomology for < 1 year) OR: 0.4 $p = 0.004$</p>	<p>El-Meliegy (2013):</p> <p>(A) Those who were adherent had a longer duration of ED (31.0 versus 24.0 years) OR: 1.008</p> <p>Kim (2014)</p> <p>Those that persisted had a longer duration of ED ($m = 5.13 \pm 3.87$ years, sd) compared to those with a shorter duration ($m = 4.22 \pm 3.33$ years, sd) $p = 0.026$. OR: 0.93, $p = 0.03$</p>	<p>Cairoli (2014) (P) (A)</p> <p>El-Meliegy (2013) P</p> <p>Rubio-Aurioles (2013)</p> <p>(P) (A) 1–2 years versus < 1 year</p> <p>(P) (A) 2–4 years versus < 1 year</p> <p>(P) ≥ 4 years versus < 1 year</p>
Comorbidities					
Due to the effects of co-morbidities	PDE5I	<p>El-Meliegy (2013)#</p> <p><i>Hypertension</i></p>	<p>Cairoli (2014)</p> <p><i>Coronary artery disease</i></p>	<p>Roumeguer (2008)</p> <p><i>Pelvic surgery</i></p> <p>Treatment was continued by 71% of the patients with a history of pelvic surgery</p>	<p>Buvat (2014)</p> <p><i>Co-morbid conditions</i></p> <p>Cairoli (2014) (P) (A)</p>

		<p>(P) Higher proportion of persistent patients had hypertension (154 [48.1%] versus 68 [39.3%])</p> <p>(A) A higher proportion of adherent patients had hypertension (146 [49.7%] versus 76 [38.2%])</p> <p>Klotz (2005)#</p> <p><i>tumour/hip prosthesis: 3 (1.3)</i></p> <p>Ljunggren (2008)#</p> <p><i>co-morbid conditions: 1 (0.8)</i></p> <p>Son (2004)#</p> <p><i>co-morbid conditions: 6 (3.9)</i></p>	<p>those with the condition had higher rates of discontinuation p=0.002</p>	<p>(N = 48) vs. 88% of those with no history (adjusted OR = 0.40; 95% CI: 0.18–0.93; P = 0.03).</p> <p>Kim (2014)</p> <p><i>BMI</i></p> <p>Those with a BMI of ≥ 23 were more likely to continue (273, 85.3%) compared to those that discontinued (75, 72.1), p=0.002</p> <p>Overall participants who had a higher BMI (kg/m²; m=24.60 \pm 2.38, sd) were more likely to continue compared to those that discontinued (m=23.99 \pm 2.60, sd) p=0.019. OR: 0.92, p=0.09</p> <p><i>Weight (kg)</i></p> <p>Those who continued had a higher weight (m=71.93 \pm 8.55, sd) compared to those that discontinued (m=69.37\pm8.95, sd) p=0.006</p>	<p><i>Diabetes Mellitus</i></p> <p><i>Dyslipidemia</i></p> <p><i>Hypertension</i></p> <p><i>Depression</i></p> <p>Kim (2014)</p> <p><i>Number of comorbidities</i></p> <p><i>Stress</i></p> <p><i>Smoking</i></p> <p><i>alcohol.</i></p> <p>Lee (2010)</p> <p><i>BMI score</i></p> <p><i>CACI (Charlson Comorbidity Index) score</i></p>
	ICI	<p>Gerber (1991)#</p> <p><i>Developed a significant inter-current illness: 4 (5.5)</i></p>			<p>Sung (2014)</p> <p>DM</p> <p>Hypertension</p>

		Sexton (1998)# <i>co-morbid conditions: 3 (3.4)</i>			Cardiovascular disease Cerebrovascular attack Previous radical pelvic surgery including prostatectomy and cystectomy unilateral or bilateral nerve sparing prostatectomy Previous pelvic radiotherapy
	PP	Sexton (1998)# <i>co-morbid conditions: 1 (2.3)</i>			
Illness (ongoing health issues, deteriorating health or recent injuries or operations)	PDE5I	Conaglen (2012)# 13 (8.4) Roumeguere (2008)# 14 (1.1)			
	ICI	Alvarez (1998)# 36 (4.0) Armstrong (1994)# 4 (13.0)			
Other medications and treatments					
Due to other Medications and Treatments	PDE5I	Kim (2014)# More important to treat other conditions: 7 (1.4)	Souverein (2002) Discontinuing was highest among patients using:	Souverein (2002) <i>Lipid-lowering drugs</i>	Souverein (2002) antihypertensive agents oral anticoagulants

			<p><i>incontinence materials</i>: 85.7%; adjusted RR 2.61, 95% CI: 1.41 – 4.83</p> <p><i>antidepressants</i>: 80.0%; adjusted RR 3.41, 95% CI: 1.19 – 9.77)</p> <p><i>nitrate therapy</i></p> <p>73.9%, adjusted RR 2.23, 95% CI: 1.30 – 3.82.</p> <p><i>Insulin</i></p> <p>adjusted RR 1.71, 95%CI: 1.06 – 2.93.</p>	Were associated with increased continuation; adjusted RR 0.59, 95% CI: 0.36 – 0.97.	low dose acetylsalicylic acid benign prostatic hyperplasia products
Other clinical factors					
Type of physician	PDESI		<p>Buvat (2014)</p> <p>Those diagnosed by a GP rather than a urologist showed significantly higher levels of continuation OR: 0.27 (0.12, 0.56) p= <0.001</p>		<p>Buvat (2014)</p> <p>Endocrinologist</p> <p>diabetologist</p> <p>urologist</p> <p>Other</p>

	<p>-Presence of erections prior to treatment</p> <p>-Low response during psychophysiological screening (investigation of pharmacological effects on sexual response).</p> <p>-Lack of spontaneous erections</p>	ICI				Rowland (1999)
	<p>Penile rigidity adequate for sexual intercourse</p>	ICI			<p>Sung (2014)</p> <p>More patients were able to achieve penile rigidity adequate for sexual intercourse in the continuing group than in the withdrawal group: 94.9% vs. 51.5%, respectively, p< 0.001.</p>	

Psychological and Cognitive	Premature ejaculation	ICI		Rowland (1999): Higher rates of drop out in those with co-existent premature ejaculation: OR: 2.29, p=0.026		
	Treatment Related Beliefs					
	Lack of confidence in medication	PDE5I	Buvat (2014)# 1 (0.1)			Buvat (2013) Tad OaD Tad PRN Sild PRN
	Fear of drug dependency	PDE5I	Carvalho (2012)# 10 (3.0)			
Fear that medication is harmful for the heart	PDE5I	Carvalho (2012)# 25 (7.6) Carvalho (2014)#: 6 (4.0)				

Averse to taking medication	PDE5I	Carvalheira (2014)#: 7 (4.7)			
Medication caused personal conflict	PDE5I	Montorsi (2004)# 94 (12.9)			
Don't want to take a pill everyday	PDE5I	Buvat (2014)# 12 (1.5)	<p>Buvat (2013)</p> <p>-Higher rates of discontinuation for those taking Tad OaD compared with Sild PRN: $p < 0.001$</p> <p>-Higher rates of discontinuation for those taking Tad OaD compared with Tad PRN: $p < 0.001$</p>		Buvat (2013) Tad PRN vs Sild PRN
Prefer a pill every day, not on demand	PDE5I		<p>Buvat (2013)</p> <p>-Higher rates of discontinuation for those taking Sild PRN compared to Tad OaD, $p < 0.001$</p> <p>- Higher rates of discontinuation for those taking Tad PRN compared to Tad OaD, $p < 0.001$</p>		Buvat (2013) Tad PRN vs Sil PRN

Not willing for sex life to depend on medication/medication controls sex life	PDESI	<p>Buvat (2014)# 3 (0.4)</p> <p>Kim et al (2014)# 36 (7.4)</p> <p>Son et al (2004)# 4 (2.5)</p>	<p>Buvat (2013)</p> <p>Higher rates of discontinuation for those taking Sild PRN compared to those taking Tad OaD, p= 0.015</p>		<p>Buvat (2013)</p> <p>Tad PRN vs Sil PRN</p> <p>Tad OaD vs. Tad PRN</p>
Inconvenience/embarrassment in obtaining medication	PDESI	<p>Carvalho (2012)# 4 (1.2)</p> <p>Jiann (2006)# 71 (16.3)</p>			
Forgetting to buy or to get medical prescription	PDESI	<p>Carvalho (2014)#: 3 (2.0)</p>			
Satisfaction with treatment	ICI			<p>Lehmann (1999):</p> <p>Continuers were more satisfied with treatment than those who discontinued, p=0.02</p>	
Disappointed with treatment	ICI	<p>Perimenis (2001)# 7 (17.5)</p> <p>Polito (2012)# 33 (12)</p>			
Would recommend treatment to a friend	ICI			<p>Lehmann (1999):</p> <p>A higher proportion of those who continued would recommend the</p>	

Social					treatment to a friend (continuers 65, 94.0%), discontinuers 7, 41.0%), p=0.01		
	Psychosocial Well-being						
	Lack of self-confidence/self-esteem	PDESI	Carvalho (2014)#: 17 (11.4) Roumequere (2008)#: 12 (0.8)				
		ICI				Lehmann (1999) Continuers showed increased levels of self-esteem p=0.012	
	Improve Sexual performance	PDESI	Carvalho (2014)# Total: 25 (16.8) <i>To avoid bad performance</i> 15 (10.1) <i>To improve performance</i> 10 (6.7)				
	To improve psychological and emotional state	PDESI	Carvalho (2014)# 12 (8.1)				
Partner related							
Having a partner	PDESI				Mazzola (2013)		

					Having a partner was reported as significantly Increasing persistence: $p < 0.01$	
Having no partner	PDESI	Conaglen (2012)# 4 (2.6) Green (1999)#: 5 (12.5) Raina (2003b)# 1 (2.0) Roumeguere (2008)#: 27 (1.7)				
	ICI	Armstrong (1994)# 4 (13.0) Irwin (1994)#: 9 (15) Raina (2003a)# 4 (3.9) Sexton (1998)#: 10 (11.5)				
	PP	Sexton (1998)#: 3 (6.97)				
Marital Status/Relationship Status	PDESI					Cairolì (2014) (P)(A) Kim et al (2014) Salonia (2008b)
	ICI					Rowland (1999)
Living with partner	PDESI					Kim (2014)

Longer duration of living arrangement	PDESI		Buvat (2014) associated with an increased risk of treatment discontinuation, p=0.019		
Length of marriage/relationship	PDESI				Kim (2014) Salonia (2008b)
	ICI				Rowland (1999)
Geographical distance from partner	PDESI	Carvalho (2014)#: 13 (8.7)			
Partner being of younger age (=>10 years younger)	PDESI			Mazzola (2013) Having a partner =>10 years younger increased persistence significantly, p=<0.01	Kim et al (2014)
Partners illness	ICI	Kunelius (1999)#: 2 (2.9)			
Personal					
For extra marital relations	PDESI			Carvalho (2014): 8.1%	
Work commitments	ICI	Armstrong (1994)# 1 (3.3)			

Cost of Treatment					
Cost	PDE5I	Buvat (2014)# 16 (2.0)			
		Carvalho (2012)# 22 (6.7)			
		Carvalho (2014)#: 8 (5.4)			
		Cimen (2009)# 51 (16.5)			
		Conaglen (2012)# 18 (11.6)			
		Fagelman (2001)# 5 (0.6)			
		Green (1999)#: 2 (5)			
		Incrocci (2003)#: 12 (24)			
		Jiann (2006)# 93 (21.4)			
		Kim (2014)# 31 (6.4)			
		Klotz (2005)# 9 (3.8)			
		Lee (2010)# 24 (45.3)			
		Ljunggren (2008)# 1 (0.8)			
		Panache Naverette (2017)# 20 (8.62)			
		Roumequere (2008)# 34 (2.2)			

		Rubio-Aurioles (2013)# Total: 161 (31.5) <i>Tad:117 (37.0)</i> <i>Sild:26 (23.0)</i> <i>Vard:18 (25.0)</i> Son (2004)# 2 (1.2)			
	ICI	Sung (2014)# 13 (4.4) Gerber (1991)#: 4 (5.5) Sexton (1998)#: 4 (4.6)			
	US	Mulhall (2001)# 14 (25.4)			
	Related to sexual relationship				
Loss of libido/interest in sex	PDE5I	Carvalho (2012)# 8 (2.4) Cimen (2009)# 18 (5.8) Fagelman (2001)# 1 (0.6) Jiann (2006)# 75 (17.3) Klotz et al (2005)# <i>Lack of opportunity or desire 33 (14.1)</i>			

		<p>Kim (2014)# 9 (1.8)</p> <p>Ljunggren (2008)# 1 (0.8)</p> <p>Salonia (2008a)# 1 (1.9)</p> <p>Son et al (2004)# 2 (1.2)</p>			
	ICI	<p>Irwin (1994)# 18 (30)</p> <p>Sung (2014)# 16 (5.4)</p> <p>Gerber (1991)# 5 (6.9)</p> <p>Sexton (1998)# 6 (6.9)</p>			
	US	<p>Raina (2007)#:5 (8.9)</p>			
	PP	<p>Sexton (1998)# 3 (6.9)</p>			
	Partner lack of interest in sexual relationship	<p>PDESI</p> <p>Carvalheira (2014)#: 9 (6.0) *Lack of emotional and physical stimulus by the partner increased utilisation of treatment.</p> <p>Jiann (2006)# 36 (8.2)</p> <p>Kim (2014)# 6 (1.2)</p> <p>Klotz (2005)# 19 (8.1)</p> <p>Salonia (2008a)# 5 (9.8)</p>			

	Lack of emotional readiness for restoration of sexual activity	PDE5I	<p>Kim (2014)# 15 (13.1)</p> <p>Son (2004)# Total: 20 (12.8)</p> <p><i>Of partner:</i> 12 (7.7)</p> <p><i>Of patient:</i> 8 (5.1)</p>			
	Partners level of sexual activity	PDE5I				Carvalho (2012)
	Conflicts within one's relationship	PDE5I	<p>Carvalho (2014)#: 5 (3.3)</p> <p>Conaglen (2012)# 9 (5.8)</p> <p>El-Galley (2001)# 2 (2.4)</p>			
		ICI	Sung (2014)# 3 (1.0)			
	Low satisfaction with sex life	ICI		<p>Rowland (1999):</p> <p>Higher rates of drop out associated with a lower level of satisfaction with one's current sexual life OR: 1.24, p= 0.054</p>		
	Better quality of sexual relationship	ICI			<p>Lehmann (1999):</p> <p>Continuers 63 (91.0) reported better quality of sexual relationship than discontinuers 5 (30.0) p=0.001</p>	

	Person within the dyad who most often initiated sexual activity	ICI				Rowland (1999)
	Partner's difficulty in accepting treatment	PDE5I	Buvat (2014)# 5 (0.6) Carvalho (2014)#: 5 (3.3) Roumequere (2008)#: 12 (0.8)			Buvat (2013) Tad OaD Sild PRN Tad PRN
		ICI	Kunelius (1999)#: 2 (2.9)			
	Partner satisfaction with treatment (reported by patient)	ICI			Lehmann (1999): Those that persisted were more significantly more satisfied with treatment p=0.02	
	Partner aware of and involved in the use of treatment	PDE5I			Carvalho (2012): Continuers were less likely to discontinue compared with men whose partner was not involved in the treatment OR: 0.345, p= 0.01	

Behavioral	Help seeking					
	Length of time before seeking help for ED	PDE5I			Salonia (2008b)	
	Personal behavior					
	Lower frequency of masturbation	ICI		Rowland (1999): Higher rates of drop out indicated for those with a lower frequency. OR: 1.35, p=0.027		
	Related to sexual relationship					
	Lack of opportunity for sexual intercourse	PDE5I	Carvalho (2012)# 18 (5.5) Carvalho (2014)#: 3 (2.0) Panache Naverette (2017)# 17 (7.3)			
		ICI	Panache Naverette (2017)# 3 (6.9%)			
		US	Panache Naverette (2017)# 2 (4%)			
Pre-treatment sexual activity (PDE5I			Mazzola (2013)		

	=/>4 times per month)				Pretreatment sexual activity increased persistence significantly, p= <0.001	
	Greater No of sexual attempts in the first month of treatment	PDE5I			Roumeguere (2008): Patients with a greater number of sexual attempts in the first month were significantly more likely to continue the treatment at 12 months (adjusted OR = 1.09; 95% CI: 1.03–1.16; P = 0.003).	
	Life style					
	Level of exercise	PDE5I				Kim (2014)

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