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# Diagnosis, Etiology, and Psychobehavioral Treatment of Premature Ejaculation





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Psychobehavioral Treatment of  
Premature Ejaculation

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# Abstract

Premature ejaculation (PE) is characterized by a pattern of involuntary ejaculation prior to, upon, or shortly after penetration leading to personal or interpersonal distress. Some definitions add a time limit of about 1 minute following penetration. Around 25% of the male population report ejaculating before they wish to do so, while about 4% are estimated to meet current diagnostic criteria. PE has been associated with anxiety, depression, low self-esteem, sexual distress, interpersonal difficulties and a decreased quality of life. Little is known of what causes PE. Many possible etiological factors have been explored, however, none have as of yet been replicated and confirmed in large scale studies. The first-line treatment for PE today is pharmacological, namely using selective serotonin-reuptake inhibitors, sometimes combined with sexological therapy.

**Study I** aimed at clarifying the temporal stability of PE symptoms. Two longitudinal samples were used: a population-based sample followed six years, and a sample of patients previously diagnosed with PE, who were untreated at the time of the study, followed three years. In the population-based sample, less than half of those who reported ejaculation latency times (ELT) of less than 1 minute at the first data collection also reported it six years later. In this sample, 47% reported having experienced a change in ELT between the two measurement points. In the clinical sample, only 5 out of 16 men reported ELTs of less than 1 minute at both time points. In the clinical sample, 63% reported having experienced a change in ELT between the two measurement points.

**Study II** aimed at clarifying the direction of causality between PE symptoms on the one hand, and anxiety, depression, and sexual distress on the other. In a longitudinal, population-based sample followed six years, bivariate analyses revealed that PE and sexual distress were mutually positively correlated across time. Also across time, PE was positively correlated with future anxiety, and depression was positively correlated with future PE. Correlation coefficients were small to moderate. However, when fitting structural equation models to the data, no associations were found across time between PE and the other variables.

**Study III** explored associations between PE and the lifestyle factors alcohol use, physical exercise, and body-mass index. Cross-sectional population-based and clinical samples were used. The most consistent finding was a negative association between PE and physical exercise. While the effect size was small, the negative association was robust, since it was observed when comparing the clinical sample to both the whole population-based sample and to an age-matched subsample, as well as within samples and in multivariate analyses of all study variables.

**Study IV** aimed at developing more effective psychobehavioral treatment protocols for PE. Fifty PE patients were randomized into three groups: 1) a treatment regime consisting of vibrator-assisted start-stop exercises 2) vibrator-assisted start-stop exercises, and additional psychoeducation and exercises aimed to improve the patient's awareness and utilization of physiological cues related to sexual arousal, or 3) waiting-list control group. Both treatment groups improved with large effect sizes after treatment compared to the control group. The treatment groups did not differ on the PE outcome measure at any time. However, the second group also improved on most secondary outcome measures, including anxiety and sexual distress, indicating a favorable outcome for the group receiving additional intervention.

In conclusion, PE symptoms might not be quite as stable over time as previously thought. I suggest that the current cutoff for ELT for PE diagnosis at 1 minute is unnecessarily strict. Increasing the temporal criterion to approximately 2–4 minutes would reduce false negatives, while the criteria for distress and control reduce the risk of false positives. Furthermore, results from the present studies showed no indication that anxiety and depression would be major etiological factors in PE. Hence, these should probably not be targeted in most cases in attempts to improve PE. On the other hand, increased physical exercise may be a promising intervention for PE in some men, and should be further investigated in future studies. Vibrator-assisted start-stop exercises are supported by replicated evidence suggesting that they are viable treatment options for PE.

## Svensk sammanfattning

Omkring en fjärdedel av alla män upplever att de vid samlag får utlösning tidigare än de önskar. Ofrivillig tidig utlösning (prematyr ejakulation, PE) har samband med bl.a. lägre upplevd livskvalitet, ångest och interpersonella problem.

I den första studien följdes för första gången symptomutvecklingen bland obehandlade män. Det fanns betydande variation i symptomnivå över några års tid, och ungefär hälften svarade att de upplevt en förändring i latenstid. Bland en grupp som tidigare hade diagnostiserats med PE var det endast en tredjedel som uppfyllde det mest strika kriteriet för livslång PE vid båda mätningarna.

Lite är känt gällande vad som orsakar PE. I den andra studien analyserades möjliga kausala associationer mellan PE, ångest och depression. Även om förväntade bivariata associationer kunde påvisas över tid var dessa så små att de i strukturekvationsmodeller inte var statistiskt signifikanta över en period på sex år. I den tredje studien analyserades associationer mellan PE och livsstilsfaktorerna fysisk aktivitet, alkoholbruk och kroppsmasseindex. Fysisk aktivitet var associerat med lägre symptomnivå för PE. Effektstorleken var liten, men kvarstod även när övriga faktorer och ålder togs i beaktande.

Syftet i den fjärde studien var att testa och vidareutveckla en psykobehavioral behandlingsmetod för PE. Femtio deltagare randomiserades till tre grupper. En behandlingsgrupp utförde start-stop övningar med en handhållen vibrator, och en annan behandlingsgrupp fick därutöver psykoedukation och utförde övningar för att öka interoceptiv medvetenhet. Kontrollgruppen fick inte någon behandling. Båda behandlingsgrupperna uppvisade förbättringar med stora effektstorlekar efter behandlingen. Den andra behandlingsgruppen uppvisade därtill förbättringar på ett flertal sekundära utfallsmått.

Föreliggande avhandling har visat att det finns betydande variation i symptomnivå över tid, vilket kan innebära att PE ibland inte är fullt så kronsikt som hittills antagits. Detta öppnar dörren för kurativa, snarare än symptomlindrande, behandlingar, av vilka vibratorassisterade start-stop övningar har visats vara ett gångbart alternativ.

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Daniel Ventus

# Abbreviations

BSI	The Brief Symptom Inventory
CAD	Coronary artery disease
CHEES	The Checklist for Early Ejaculation Symptoms
DSM	Diagnostic and Statistical Manual of Mental Disorders
ELT	Ejaculation latency time
IELT	Intravaginal ejaculation latency time
ISSM	The International Society for Sexual Medicine
ITT	Intention-to-treat analysis
MAIA	The Multidimensional Assessment of Interoceptive Awareness
MetS	Metabolic syndrome
PE	Premature ejaculation
PRO	Patient-reported outcomes
PP	Per-protocol analysis
SDS	Sexual distress scale
SSRI	Selective serotonin re-uptake inhibitor
STAI	The State-Trait Anxiety Inventory
VSS	Vibrator-assisted start-stop treatment group
VSS+	Vibrator-assisted start-stop and psychobehavioral intervention group

## List of original publications

- I** Ventus, D., Ristilä, M., Gunst, A., Kärnä, A., Arver, S., Piha, J. & Jern, P. (2017). A longitudinal analysis of premature ejaculation symptoms raises concern regarding the appropriateness of a “lifelong” subtype. *European Urology Focus*, 3, 243-245.
- II** Ventus, D., Gunst, A., Kärnä, A., & Jern, P. (2016). No evidence for long-term causal associations between symptoms of premature ejaculation and symptoms of anxiety, depression, and sexual distress in a large, population-based longitudinal sample. *Journal of Sex Research*, 54, 264-272.
- III** Ventus, D. & Jern, P. (2016). Lifestyle factors and premature ejaculation: Are physical exercise, alcohol consumption, and body mass index associated with premature ejaculation and comorbid erectile problems? *Journal of Sexual Medicine*, 13, 1482-1487.
- IV** Ventus, D., Gunst, A., Arver, S., Dhejne, C., Görts-Öberg, C., Zamore-Söderström, E., Kärnä, A., & Jern, P. (In press). Vibrator-assisted start-stop exercises improve premature ejaculation symptoms: A randomized controlled trial. *Archives of Sexual Behavior*.

The author drafted all manuscripts and performed all statistical analyses; study design and interpretation of results was completed in collaboration with co-authors. The author delivered the interventions and collected all data for Study IV and participated in parts of the data collection for Study II.

# 1. INTRODUCTION

Premature ejaculation (PE) is considered to be one of the most common sexual complaints among men, as approximately 20-30% of all men report that they usually ejaculate before they wish to do so (Althof et al., 2014). However, current diagnostic criteria (e.g., in the DSM-5, American Psychiatric Association, 2013, p.443) do not rely solely on subjective complaints, but also on a time limit of approximately 1 minute. When these criteria are used, prevalence figures have been estimated to around 4% (Althof et al., 2014), as most men who subjectively experience rapid ejaculation engage in intercourse for longer than 1 minute.

Studies have repeatedly shown that PE is associated with a range of negative consequences for the individual, including lower confidence and self-esteem (Rowland, Patrick, Rothman, & Gagnon, 2007; Symonds, Roblin, Hart, & Althof, 2003), personal distress (Giuliano et al., 2008; Patrick et al., 2005; Rowland et al., 2007), anxiety (Dunn, Croft, & Hackett, 1999; Porst et al., 2007; Symonds et al., 2007) and depression (Porst et al., 2007). Individuals suffering from PE report interpersonal difficulties (Giuliano et al., 2008; Patrick et al., 2005; Rowland et al., 2007), including avoiding discussing sexual issues with one's partner (McMahon et al., 2004), and refraining from establishing new relationships (Symonds et al., 2003). For the partner, PE is negatively associated with sexual satisfaction (Riley & Riley, 2005) and orgasmic frequency (Hartmann, Schedlowski, & Krüger, 2005). Taken together, it is clear that PE can lead to a severely decreased quality of life (Rosen & Althof, 2008).

## 1.1 Definitions

### 1.1.1 According to the International Society for Sexual Medicine

The second International Society for Sexual Medicine (ISSM) Ad Hoc Committee for the Definition of Premature Ejaculation (Serefoglu et al., 2014, p. 44) defined PE as follows:

1. Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often to about 3 minutes or less (acquired PE).
2. The inability to delay ejaculation on all or nearly all vaginal penetrations.

3. Negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy.

### 1.1.2 According to the Diagnostic and Statistical Manual of Mental Disorders 5

The 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (American Psychiatric Association, 2013, p. 443) defines PE as follows:

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

According to the manual, PE can be specified as lifelong or acquired (i.e., whether or not the disturbance been present since the individual first became sexually active), generalized or situational (i.e., whether or not it occurs only with certain types of stimulations, situations or partners), and the current severity can be specified as mild, moderate or severe (i.e., intravaginal ejaculation latency times [IELT] of 30-60 seconds, 15-30 seconds, and less than 15 seconds, respectively).

### 1.1.3. According to the International Statistical Classification of Diseases and Related Health Problems - Eleventh Revision (ICD11)

The World Health Organization (2018) defines male early ejaculation (PE) as follows:

*“Male early ejaculation is characterized by ejaculation that occurs prior to or within a very short duration of the initiation of vaginal penetration or other relevant sexual stimulation, with no or little perceived control over ejaculation. The pattern of early ejaculation has occurred episodically or persistently over a period at least several months, and is associated with clinically significant distress.”*

#### 1.1.4 Classification of PE subtypes

In 1943, Shapiro made a distinction between PE of type A and B based on his clinical observations, with one difference between the groups being that group A had gradually developed PE, while group B had experienced PE from the very first act of coitus (Shapiro, 1943). Similarly, Godpodinoff (1989) made a distinction into primary and secondary PE, where patients who reported having had PE their entire lives were classified as having primary PE. This distinction is still reflected in the present diagnostic criteria by the ISSM, in DSM-5, and in the ICD as lifelong and acquired PE. Additionally, the ICD includes an “unspecified” subtype, for patients with PE, which symptoms do not fit into lifelong or acquired PE.

## 1.2 Etiology of PE

The following sections review some of the many genetical, neurobiological, psychological, and lifestyle factors that have been proposed to be part of the etiology of PE. While the mind and the body should not be described as separate entities (Rowland & Motofei, 2007), since there is strong evidence that, for example, cognitive processes have a physiological basis in the brain (Dehaene & Naccache, 2001), the term “psychological etiology” is used here in the sense that psychological problems may contribute to PE.

### 1.2.1 Genetic etiology

Evidence from twin studies indicate a heritable component of around 30% in PE etiology (Jern, Santtila, Johansson, Varjonen, Witting, von der Pahlen, et al., 2009; Jern et al., 2007). This has spawned numerous attempts to identify specific genetic loci, mainly focusing on candidate genes in the serotonergic system, however, no findings have thus far been reliably replicated (Jern &

Ventus, 2017). Regardless, the heritability of PE is lower than complex traits in general (49%; Polderman et al., 2015), and the majority of variance in PE appears to stem from non-shared environmental rather than familial or genetic sources.

### 1.2.2 Neurobiological etiology

The monoamine serotonin is believed to have evolved at least one billion years ago, and is found in fungi, plants, and animals (Azmitia, 2006). Serotonin is involved in a wide number of homeostatically controlled processes, including cell differentiation, temperature, blood clotting, digestion, attention, aggression and mood, with most of the body's serotonin being housed in the gut (Andrews, Thomson, Amstadter, & Neale, 2012). Based primarily on experimental studies on animals, the serotonergic system has been proposed to be involved in the regulation of the ejaculatory reflex. Specifically, hyposensitivity of the 5-HT<sub>2C</sub> and hypersensitivity of the 5-HT<sub>1A</sub> receptors have been hypothesized to be linked to early ejaculation (Waldinger, Berendsen, Blok, Olivier, & Holstege, 1998). It is, however, unclear if these receptors serve the same function in different species. For example, orthologous genes rarely contribute to the same genotype in rats and mice (Vicens-Costa et al., 2013). If mice do not replicate rats on a genetic level, it is questionable whether results from research on mice can be used to derive hypotheses for human contexts. Regardless, selective serotonin reuptake inhibitors tend to delay ejaculation, which implies that men low in 5-HT neurotransmission may have lower ejaculatory thresholds (Althof et al., 2014). Dopamine and oxytocin both appear to stimulate ejaculation in animal studies, but these neurotransmitters are not yet well studied (Clément et al., 2013, 2009). There is some evidence indicating a neural organization in the spinal cord responsible for the ejaculatory reflex in both rats (Staudt et al., 2012) and humans (Chéhensse et al., 2013).

### 1.2.3 Physiological etiology

Experimental studies have found associations between penile sensitivity and ejaculatory latency (Guo et al., 2017; Xin et al., 1996), with higher sensitivity being associated with shorter latency. Results are however not unanimous (Perretti et al., 2003; Salonia, Saccà, et al., 2009). Rowland, Haensel, Blom and Slob (1993) found no significant difference between men with PE ( $n = 9$ ) and

sexually functional controls ( $n = 33$ ), and significantly lower sensitivity in a group of men suffering from both PE and ED ( $n = 8$ ), which taken together speaks against the hypersensitivity hypothesis. Nevertheless, the authors found a strong correlation between sensory threshold and latency within the PE group ( $r = .69, p .039$ ). That penile sensitivity affects ejaculatory function is robustly supported by the evident ejaculation-dealing effect of topical analgesics (Wyllie & Hellstrom, 2011). Note that this does not necessitate an assumption of hypersensitivity among men with PE, since the mechanism is the same regardless of baseline sensitivity. Other proposed physiological etiological components include greater cortical representation of the genital sensory stimuli (Fanciullacci, Colpi, Beretta, & Zanollo, 1988), comorbid erectile difficulties (Jannini, Lombardo, & Lenzi, 2005), prostatitis (Screponi et al., 2001), and pelvic floor dysfunction (Myers & Smith, 2019). Zorba et al. (2012) measured sympathetic activity by means of heart rate variability, and found increased sympathetic activity in patients with PE compared to controls. The authors hypothesize that the increased smooth muscle contractions of the prostate and emission of seminal fluids following sympathetic activation may lead to PE in patients with an overactivation of the sympathetic nervous system.

#### 1.2.4 Psychological etiology

Traditionally, psychological problems have been seen as contributing to PE, especially anxiety (Althof et al., 2014; McMahon et al., 2004). This is still reflected in the DSM-5, as anxiety and depression are considered relevant factors supporting diagnosis (American Psychiatric Association, 2013, p. 444). In a meta-analysis of eight observational studies involving 18,035 participants, Xia et al. (2016) found a statistically significant association between PE and depression (odds ratio = 1.63, 95% CI [1.42–1.87]).

Anxiety and PE in their different operationalizations have been shown to be associated in numerous cross-sectional studies. Examples include associations between self-reported anxiety and subjective PE symptom severity (Porst et al., 2007); associations between generalized anxiety and shorter ejaculation latency time (Corona et al., 2004; Dunn et al., 1999); and increased incidence of PE in patient cohorts diagnosed with social phobia (Corretti, Pierucci, De Scisciolo, & Nisita, 2006). Liu et al. (2019) reported significantly higher levels of anxiety and depression in patients with PE compared to unaffected controls,

and further, negative correlations between stopwatch-measured IELT and anxiety in both patient and control groups, indicating that a shorter IELT is associated with more symptoms of anxiety and depression. In a sample of almost 800 men complaining of PE, Gao et al. (2014) found increased levels of anxiety and depression in men with PE compared to controls, and especially in PE subtypes with more severe symptoms. In addition to the aforementioned studies, where general and trait-like forms of anxiety were measured, PE has also been found to be associated with more transient forms of anxiety, such as performance anxiety (Hartmann et al., 2005; McCabe & Cobain, 1998). In two recent studies utilizing the Spielberg state-trait anxiety scale (Spielberger, Gorsuch, & Lushene, 1970), the researchers found associations between PE and state anxiety, but not trait anxiety (Kempeneers, Andrienne, Cuddy, & Blairy, 2018; Mourikis et al., 2015). While most of these associations have been of a small to moderate effect size, there does seem to be a connection between PE and mood disorders (anxiety and depression), however, the direction of causality between them is unclear (Althof et al., 2014).

Several mechanisms of action between anxiety and premature ejaculation have been proposed. A physiological mechanism could be that anxiety increases sexual arousal. This was demonstrated in rats by Barfield and Sachs (1968) who found that administering electric shocks to male rats led to quicker mounting of receptive female rats. In humans, Barlow, Sakheim and Beck (1983) found that the threat of an electric shock led to increased penile circumference while viewing an erotic film. However, these findings were not replicated in later studies by the same authors (Beck, Barlow, Sakheim, & Abrahamson, 1987), nor by Hale and Strassberg (1990), who found that the threat of an electric shock, as well as (false) feedback that the participant's level of arousal was subnormal, inhibited sexual arousal. In any case, anxiety that results in sympathetic activation will, according to the ejaculation threshold theory, decrease the amount of genital stimulation needed to engage the ejaculation reflex (McMahon, Jannini, Serefoglu, & Hellstrom, 2016; Rowland, 2005).

Another proposed mechanism is that anxiety distracts men from being able to control their ejaculation (Althof, 2006). In line with this, Hartmann et al. (2005) found that PE patients were more preoccupied with thoughts of controlling their orgasm than functional controls. Distraction may also function as a conscious avoidance strategy, or as a way to try to control arousal (Kaplan,

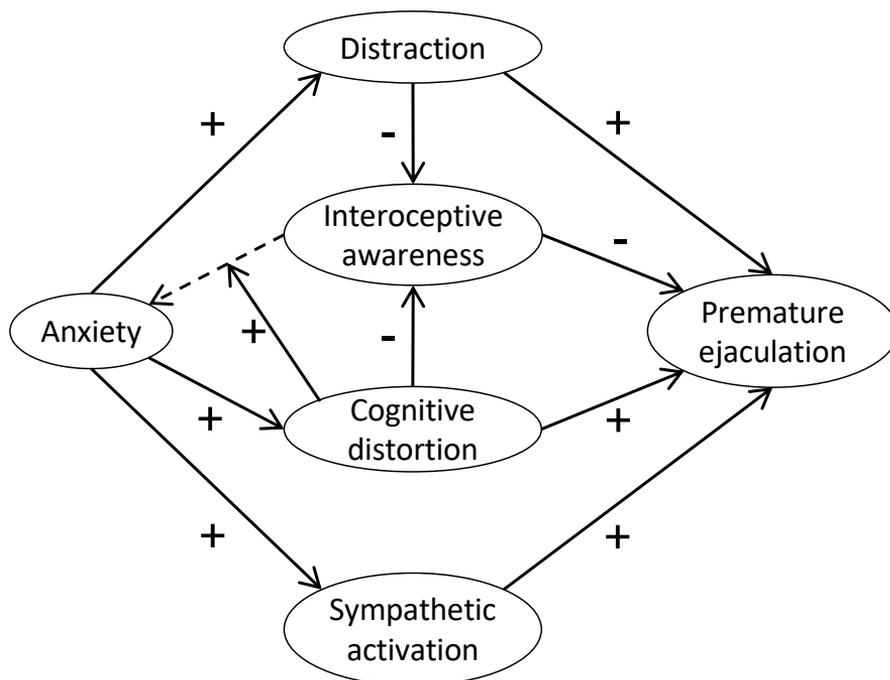
Kohl, Pomeroy, Offit, & Hogan, 1974). The emotional aspect of anxiety may in the same way be distracting, and it has been shown that men with PE fear failure during intercourse (Hartmann et al., 2005) and report emotions of guilt and embarrassment (Rowland, Tai, & Slob, 2003) during sexual stimulation more often than non-affected controls.

From a behavioristic viewpoint, PE is seen as a learned behavior (Althof, 2016), conditioned from early sexual experiences, for example a lack of privacy in the home leading a young person to hasty lovemaking or masturbating in order to not get noticed by his parents (Masters & Johnson, 1970). Performance anxiety has been especially pointed out in men with comorbid erectile dysfunction, who might have learned to ejaculate prematurely in order to evade loss of erection (Zorba et al., 2012).

PE has also been characterized as a lack of awareness of bodily reactions during sex (Kaplan, 1975). In this view, the lack of interoceptive awareness (IA, the sensory awareness that originates from physiological states, processes, actions and functions) deprives men of control over actions that lead up to ejaculation. According to Perelman (2006), men with PE are unable to identify and/or act upon premonitory sensations, such as testicular elevation, increased heart rate, and contraction of muscles, which foretell forthcoming ejaculation. The inability to control the level of arousal through cognitive and behavioral responses to the premonitory signals leads men to cross the ejaculatory threshold unwillingly. For some men, the window of opportunity between emergence of premonitory signals and emission might be small. Kaplan et al. (1974) hypothesized that the inability to control one's level of arousal is due to never having learned the necessary skills, and that the phenomenon is caused or exacerbated by anxiety in the sexual situation. In line with this, Barlow (1986) noted that participants with sexual dysfunctions consistently underestimated their arousal, and were unable to perceive any means by which they might be able to control their sexual arousal, even when they were successfully suppressing their arousal.

From a cognitive perspective, some PE patients have cognitive distortions such as catastrophizing or overgeneralization (Althof, 2016; Kempeneers et al., 2018). As an example of an overgeneralization, a man who thinks "If I had trouble controlling my ejaculation last time, I won't be able to control it now" will probably not even try to do something to improve the situation. In relation

to IA, catastrophizing thoughts may lead to interpretations of bodily signals of rising sexual arousal as a sign of impending failure. Consequently, instead of treating bodily signals as useful information (i.e., because such sensory information can be used to regulate arousal by modifying behavior, e.g., switching position or thrusting more slowly) they are interpreted as threatening, and thus induce anxiety. Alternatively, individuals may actively avoid paying attention to them. In a sample of 49 sexually functional men, Winters, Christoff and Gorzalka (2009) asked participants to consciously down-regulate their sexual arousal while viewing sexual videos. While participants were able to reduce their arousal on average, some men experienced increased physical and cognitive arousal while trying to regulate. The authors suggest that this can be understood through a failure in emotion regulation, where suppression of exciting thoughts in itself may increase excitement in some men (Wegner, Shortt, Blake, & Page, 1990) through increased sympathetic arousal, leading to a cycle where attempted suppression leads to increased emotional response.



**Figure 1.** Theoretical associations between anxiety and premature ejaculation. Arrows depict possible causal associations between variables. Plus signs

indicate a positive association (i.e., an increase in the first variable leads to an increase in the second variable) and minus signs indicate negative associations (i.e., an increase in the first variable leads to a decrease in the second variable.) The dashed arrow between interoceptive awareness and anxiety depicts a conditional relationship, where interoceptive awareness may lead to anxiety, depending on how the physiological signals are cognitively interpreted.

The relationship between anxiety, PE and IA is complex (Figure 1). As noted earlier, higher IA ought to give a better basis for controlling ejaculation, because sensory information can be used to predict when the ejaculatory reflex will be triggered. At the same time, IA is suggested to play an etiological role in anxiety, as anxiety patients report increased somatic sensitivity and hypervigilance (Domschke, Stevens, Pfleiderer, & Gerlach, 2010), and IA and emotional states show similar brain activation in the right anterior insular/opercular cortex (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004). In other words, IA seems putatively to play a double role, both decreasing PE by providing necessary information about current sexual arousal, and increasing PE via increased anxiety if the bodily signals are interpreted as threatening.

### 1.2.5 Lifestyle factors

Lifestyle factors such as alcohol consumption, physical exercise, and being overweight have clear associations with overall health. Lifestyle has also been linked to sexual dysfunctions, primarily erectile dysfunction, but also premature ejaculation.

Alcohol has an acute ejaculation-delaying effect (Malatesta, Pollack, Wilbanks, & Adams, 1979), and surveys suggest that at least some young men may use alcohol with the intention of achieving ejaculatory delay (Santtila, Sandnabba, & Jern, 2009). At the same time, alcohol can also act arousal-inducing (George & Stoner, 2000), which perhaps could counteract some of the ejaculation-delaying effect. The association between alcohol consumption and cardiovascular disease is thought to be U-shaped, with a moderate consumption being protective of disease, while a large consumption is associated with increased risk of cardiovascular disease (Marmot & Brunner, 1991; Ronksley, Brien, Turner, Mukamal, & Ghali, 2011). This may in turn have

a detrimental effect on sexual function, at least erectile function (Kumsar, Kumsar, & Dilbaz, 2016). It is perhaps noteworthy in this context, that erectile dysfunction (ED) displays considerable comorbidity with PE (McCabe et al., 2016). Furthermore, the serotonergic system has been demonstrated to be regulated by alcohol intake, in that the neurotransmitter is itself a likely contributor to the pharmacological effects of alcohol, and different serotonin receptors have been found to play an important role in alcohol use disorders (Agudelo, Yoo, & Nair, 2015). Thus, in combination with the hypothesized role of serotonin in ejaculatory function, alcohol intake is an interesting candidate to study in terms of identifying lifestyle factors that can affect ejaculatory function.

The role of physical exercise has not been extensively studied in the context of PE. Verze et al. (2018) found no statistically significant difference in physical activity between men with and without PE ( $n = 1104$ ). In another study involving men of European and South Asian origin, no association was found between physical inactivity and PE (Malavige, Wijesekara, Ranasinghe, & Levy, 2015). Recently, however, physical exercise was tested as a treatment intervention for PE (Kilinc, Aydogmus, Yildiz, & Doluoglu, 2018). The researchers reported 3.5-fold increases in IELT in a group performing moderate exercise 30 minutes, five times a week during one month. The effect was of the same magnitude as a control group using dapoxetine 30mg on-demand.

Meta-analyses show that physical exercise is associated with decreased depression and anxiety (Rebar et al., 2015), increased global self-esteem (Spence, McGannon, & Poon, 2005), and improved body-image (Campbell & Hausenblas, 2009). A reciprocal relationship between anxiety and PE has been suggested (e.g., Althof et al., 2014; Jern, 2009), where previously experienced perceived failures lead to heightened anxiety, which leads PE, thus sustaining the dysfunction. Improved self-esteem and body-image, along with decreases in depression and anxiety could plausibly break this cycle. According to Biddle and Mutrie (2008), experiences of achievement and progression following physical exercise can lead to enhanced self-efficacy and give patients insights that there is a potential to control one's body, which could be an important insight to some patient suffering from PE.

Another supposed mechanism through which physical exercise could affect ejaculatory function is its effect on the serotonergic transmission. Chaouloff (1997) showed that physical exercise is associated with increased levels of tryptophan as well as increased synthesis of 5-HT. Likewise, Post, Kotin, Goodwin, and Gordon (1973) showed experimentally that physical activity was associated with an increase of 5-HIAA, a metabolite of serotonin, in the cerebrospinal fluid. Given the ejaculation-delaying effect of serotonin, this makes physical exercise an interesting target of study in the context of PE research.

Physical exercise has also been found to be associated with lower stress reactivity. In a meta-analysis of 34 experimental and correlational studies, Crews and Landers (1987) found that fitter individuals displayed lower reactivity to or shorter recovery from brief psychosocial stressors (e.g., change in heart rate in response to cognitive performance demands), with a moderate standardized mean effect size of 0.48 ( $p < .01$ ). Lowered reactivity of the sympathetic nervous system could possibly explain part of the effect physical exercise has on PE, since men with PE have been observed to exhibit a disruption of autonomic processes, with decreased parasympathetic activity and increased sympathetic activity compared to functional controls (Ertekin, Colakoglu, & Altay, 1995; Rowland, 2010).

Given the possible effects of physical activity on PE, it is also interesting to look at connections between physical inactivity and PE. It is well established that lack of exercise is a major contributor to many chronic diseases (Booth, Roberts, & Laye, 2012), and several studies have found associations between chronic diseases and PE. Salama, Eid, Swedan and Hatem (2017) found increased prevalence of PE among patients with metabolic syndrome (MetS; 25.2%) compared to controls (7.6%,  $p < .001$ ). Likewise, Serefoglu et al. (2011) reported that men with PE had significantly more diabetes mellitus, hypertension, cardiovascular disease than men without PE. The same associations were also found in a large Chinese sample (Gao et al., 2013).

Several reports note higher prevalence of chronic diseases in acquired PE compared to other subtypes of PE, as well as compared to nonaffected controls. Jeh et al. (2018) found men with acquired PE having more metabolic syndrome than men without PE. Bolat et al. (2017) compared 100 men diagnosed with acquired PE to 100 control cases, found higher prevalence of metabolic

syndrome in men with PE (51%) than controls (24%,  $p < .001$ ). Further, several components of metabolic syndrome were significantly correlated with shorter IELT and higher scores on the Premature Ejaculation Diagnostic Tool. Compared to other subtypes of PE, men with acquired PE more often suffer from diabetes, hypertension and ED (Gao et al., 2013; Serefoglu et al., 2011; Zhang et al., 2013).

ED has known associations with coronary artery disease (CAD), MetS, obesity and diabetes mellitus (Gorgel, Gorgel, & Sefik, 2014; Han et al., 2011; Salem et al., 2009), and there is evidence that ED symptoms may be an early indicator of underlying heart disease, that sometimes become manifest before direct CAD symptoms can be observed (Inman et al., 2009). Majzoub et al. (2016) showed that PE and ED were more prevalent in patients with diabetes type 2, and that diabetic patients with ED showed higher incidence of PE and shorter ELT. Possible mechanisms, hypothesized by the authors, include that hypoglycemic episodes and diabetic neuropathy may inhibit serotonergic activity and are associated with impaired nitric oxide metabolism, which in turn might increase sympathetic nervous system activity (Francomano, Donini, Lenzi, & Aversa, 2013; Saenz de Tejada & Goldstein, 1988).

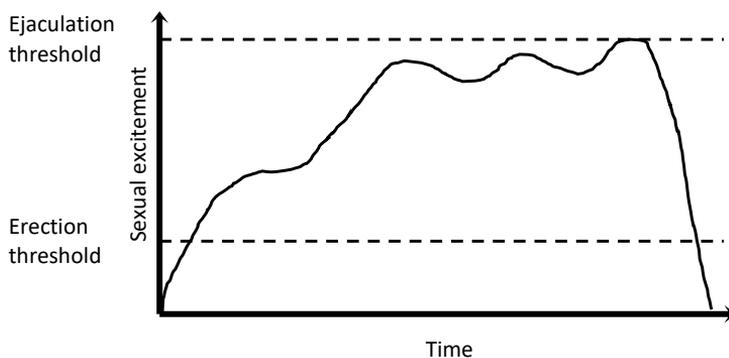
Findings regarding associations between lifestyle factors and PE are not, however, unanimous. Verze et al. (2018) found no statistically significant difference in BMI, alcohol consumption, or physical activity between men with and without PE ( $n = 1104$ ). Likewise, in a study focusing on couples, Rosen et al. (2016) found no association between any sexual problem (including PE) and lifestyle factors such as BMI, alcohol consumption, and frequency of physical exercise. There are possible explanations for why Rosen et al. (2016) found no link between lifestyle factors and sexual problems. For example, their study involved only couples, which may exclude individuals with the most pronounced PE problems, since studies have suggested that some PE sufferers avoid forming new intimate relationships due to their dysfunction (Symonds et al., 2003). Moreover, their median age of their sample was relatively high at 55 years, with most individuals in long-term, stable relations (the average relationship duration for men was 25 years). This could have excluded many individuals with sexual problems, as they are known to be associated with relationship problems.

Lifestyle factors are an important topic of research related to PE, since they could be very attractive targets for therapeutic intervention, not least considering their secondary health benefits.

### 1.2.6 Summary

A plethora of physiological as well as psychological factors in PE etiology have been proposed and explored, but these are yet to be confirmed and replicated in large scale studies (Althof et al., 2014). Cross-sectional studies have found associations between PE and psychological problems, but research on the direction of causality between them is limited (Althof et al., 2014). It is also conceivable that PE and psychological problems reciprocally reinforce each other (Althof et al., 2014; Jern, 2009).

PE is associated with lifestyle factors such as physical exercise through a network of lifestyle-related non-communicable diseases. Possible mechanisms involve dysregulation of the serotonergic neurotransmission, increased sympathetic nervous system activity and erectile dysfunction.



**Figure 2.** An example of a sexual excitement curve during a sexual encounter (inspired by de Carufel & Trudel, 2006).

Figure 2 presents a model of how sexual excitement is related to ejaculation. When a man becomes sexually aroused he first achieves erection, and when the arousal increases sufficiently, he finally crosses the ejaculation threshold. There may be variation between individuals regarding the level of the ejaculation threshold, which might be partly genetically predisposed. Penile

sensitivity could also be understood in light of the model, where the ejaculation threshold would be lower when sensitivity is higher. Interoceptive awareness is associated with men's ability to determine their current level of sexual excitement, which allows them to make necessary adjustment to the sexual activity, since the level of sexual excitement is associated with the activities taking place (e.g., vaginal sex is associated with shorter ELT than other modes of ejaculation; Jern, Santtila, Johansson, Varjonen, Witting, Von Der Pahlen, et al., 2009).

## 1.3 Treatment of PE

Following general trends in psychiatry, there has been a shift from understanding PE as primarily a psychological problem to understanding it mainly as a biological problem (Rowland & Motofei, 2007). According to guidelines by the ISSM, pharmacological agents are currently considered first-line treatment for lifelong PE, and behavioral psychotherapy for acquired PE. A combination of different approaches can sometimes be necessary (Althof et al., 2014).

### 1.3.1 Pharmacological treatment

Serotonin (5-HT) exerts an inhibitory effect on ejaculation (Hull, Muschamp, & Sato, 2004; Waldinger, Berendsen, et al., 1998). Consequently, the currently recommended first-line treatment for PE are selective serotonin reuptake inhibitors (SSRIs; McMahon, 2015). Studies on dapoxetine, the only SSRI specifically approved for treatment of PE, have demonstrated 2.5- to 3.0-fold increases in IELT, increased feelings of control, decreased distress and increased satisfaction (McMahon et al., 2011).

However, 61% of participants reported adverse events, such as nausea, dizziness, headache and diarrhoea following use of dapoxetine 60 mg (Kaufman et al., 2009). Three independent studies on the acceptability of Dapoxetine in naturalistic settings have found discontinuation rates ranging from 70.6% to 89.6% after one year of use, most often because of low efficacy, side effects, financial cost, and loss of interest in sex (Jern, Johansson, Piha, Westberg, & Santtila, 2014; Mondaini et al., 2013; Park et al., 2017). Another SSRI prescribed off-label for treatment of PE, Paroxetine, has been better tolerated, but still associated with considerable discontinuation rates of about

30% (Jern et al., 2014; Salonia, Rocchini, et al., 2009). Regardless of acceptability, a recent review on drug safety concluded that long-term use of SSRIs is to be avoided if alternative treatments are available (Carvalho, Sharma, Brunoni, Vieta, & Fava, 2016). In light of this, further research on treatment options are warranted.

### 1.3.2 Topical anesthetics

Ejaculation consists of coordinated reflexes of emission and expulsion, modulated by the sensory cortex and the lumbosacral spinal cord. The onset of reflexes are facilitated by penile sensory input. A possible means to delay onset of ejaculatory reflexes is thus to reduce neuronal transmission in sensory afferents, which can be achieved using topical anesthetics. Wyllie and Hellstrom (2011) reported that that a mixture of lidocaine and prilocaine applied five minutes before intercourse led to increased feelings of control, sexual satisfaction, and up to six-fold increases in IELT. However, there is a risk of erectile dysfunction due to penile numbness, and further, a risk of diffusion of the topical agent leading to unwanted reductions in sensitivity in the partner (Hatzimouratidis et al., 2010).

### 1.3.3 Psychological treatment

Starting with the “stop-and-start” technique first described by Semans (Semans, 1956), and later altered to the “squeeze” technique of Masters and Johnson (1970), behavioral treatment interventions were long considered first-line treatments for PE (Althof et al., 2014). The techniques consist of manual stimulation of the penis by the man’s partner until the man feels an urge to ejaculate. At this point, the partner either pauses stimulation, or squeezes the penis with the thumb under the frenulum and two fingers wrapped around the penis. When the man loses the urge to ejaculate the partner resumes stimulation. The authors reported somewhat unlikely success rates of 100% (Semans, 1956) and 97.8% (Masters & Johnson, 1970). The purpose is to improve control over ejaculation by de-conditioning of learned behavior, altering the ejaculatory reflex, providing an opportunity to explore new sexual techniques, or desensitizing the patient to anxiety that is assumed to cause PE (Grenier & Byers, 1995).

In recent reviews (Althof, 2016; Melnik et al., 2011) and a meta-analysis (Cooper, Martyn-St James, Kaltenthaler, Dickinson, & Cantrell, 2015) it is noted

that controlled studies of non-pharmacological treatments for PE are scarce and methodologically heterogeneous. However, the existing studies indicate that behavioral treatment alleviate PE, and importantly, that this is achieved without incurring side effects.

Current psychotherapy for PE takes an integrative approach with elements of psychodynamic, systems, behavioral and cognitive influences, with a short-term setup addressing sexual skills/techniques, self-esteem, performance anxiety and interpersonal conflict (Althof, 2016). McCabe (2001) reported 50% remediation of sexual dysfunctions following a 10-week CBT program. Pavone et al. (2017) compared a homogenous group psychotherapy led by an analytically trained psychoterapist to dapoxetine and combination treatment, and found group therapy and combination treatment to be more effective than dapoxetine alone, as measured by IELT and PEDT. Cormio et al. (2015) found a combination of dapoxetine and sexual behavior treatment to be more effective than dapoxetine alone in men with lifelong PE, restoring normal functioning in the majority of them.

Based on behavioral techniques and the penile sensitivity hypothesis, Zamar (2012) developed a treatment where start-stop exercises are performed while stimulating the penis with a handheld vibrator, since prolonged vibratory stimulation is known to lead to feelings of numbness and decreased sensory perception (Herbenick et al., 2009; Malchaire, Rodriguez Diaz, Piette, Gonçalves Amaral, & de Schaetzen, 1998). Zamar noted 11-fold increase of IELT in 61% of the participants (Zamar, 2012). Jern (2014) replicated a somewhat smaller but yet significant treatment effect, but the sample consisted of patients who had responded poorly to pharmacological treatment with SSRIs and thus may have represented a subgroup whose PE symptoms were particularly difficult to treat. In a similar vein, Rodríguez and López (2016) evaluated a device designed for desensitization by adding additional friction and pressure, rather than vibrations, and found that participants reported increased control over ejaculation after completing masturbatory exercises using the device.

In describing a treatment approach combining pharmacological and psychological interventions, Perelman (2006) hypothesizes that the IELT-increasing effect of SSRIs may give the man more opportunities to notice his premonitory sensations. This could in turn enable him to make necessary

behavioral or cognitive adjustments in order to keep his level of arousal below the ejaculatory threshold. If IELT can also be increased by penile desensitization through prolonged vibrational stimulation, this could arguably in the same manner afford the man time and opportunity to notice premonitory sensations and take necessary action to avoid ejaculation. de Carufel and Trudel (2006) showed that a sexological psychoeducational intervention aiming at teaching patients to notice and modulate their level of sexual excitement led to approximately 9-fold increases in IELT.

In order to be able to modulate sexual excitement, however, the patient must first be aware of his level of sexual excitement. Interoceptive awareness has been shown to improve following practices of body scan and breath meditation (Bornemann, Herbert, Mehling, & Singer, 2015). Mindfulness-based interventions (i.e. based on non-judgemental present moment awareness) have been used to improve the ability to register bodily responses to sexual stimuli (Silverstein, Brown, Roth, & Britton, 2011). The methods have also been extensively applied to a range of sexual dysfunctions, including low desire and sexual pain (Brotto & Basson, 2014; Brotto, Basson, & Luria, 2008; Brotto & Goldmeier, 2015; Gunst et al., 2018; Rosenbaum, 2013), however, using samples consisting of women almost exclusively (Goldmeier & Mears, 2010). Improving the ability to register bodily responses may plausibly lead to positive discoveries and experiences of control, simultaneously counteracting resignation and tendencies to catastrophic thinking. Thus, mindfulness-based meditation training could be a novel and useful addition to interventions targeting PE by increasing the patient's awareness of when the ejaculatory reflex will be triggered, which could afford him time to alter his actions accordingly.

Mindfulness-based interventions might also offer patients a form of emotion regulation. Whereas attempts to suppress sexually arousing thoughts and feelings for some leads to the opposite, a reappraisal through emotional distancing may be associated with more successful down-regulation of arousal (Winters et al., 2009). Learning to be non-judgmentally aware of sexual stimuli and one's own reactions, and assume an objective and slightly distanced attitude (as opposed to being enmeshed in or fused with the experience), might provide patients with an opportunity to regulate their arousal appropriately.

#### 1.3.4 Pelvic floor rehabilitation

Pelvic floor rehabilitation has been proposed as a promising treatment option for PE (Myers & Smith, 2019). Using techniques originally designed to rehabilitate urinary and fecal incontinence, la Pera and Nicastrò (1996) applied physiotherapy (i.e., personalized physical exercises to increase awareness and strength of the pelvic floor muscles) and electrostimulation in order to improve contractile strength, as well as biofeedback to learn to recognize and control pelvic muscles. After 20 sessions, 11 out of 18 patients reported better control over ejaculatory reflex, and results were maintained at follow-up (6-14 months). Using similar interventions, Pastore et al. (2012) were able to demonstrate 4-fold increases in IELT after 12 weeks of treatment. In another study by Pastore et al. (2014), 33 of 40 patients gained control of their ejaculatory reflex after treatment, with a mean 3.5-fold increase in IELT.

#### 1.3.5 Surgical interventions

Surgical interventions, including dorsal nerve neurectomy, hyaluronic acid gel glans penis augmentation, and circumcision have also been proposed as treatment options for PE aiming at decreasing sensory input (Moon, 2016). However, due to a dearth of data and conflicting results, in addition to risks of complications following surgery, the ISSM excluded surgical interventions from its recommendations regarding treatment for PE (Anassie, Yafi, & Hellstrom, 2016).

## 2. HYPOTHESES AND RESEARCH QUESTIONS

The general aims of the present dissertation were to: 1) clarify the temporal stability of PE symptoms; 2) clarify the direction of causality between PE symptoms and symptoms of mood disorders (anxiety and depression); 3) explore the associations between PE and lifestyle factors hypothesized to be of relevance for PE; and 4) investigate whether more effective psychobehavioral treatment protocols for PE can be developed by incorporating attempts to improve the patients' ability to identify and monitor physiological signals. The main research questions (Q) are listed below, formulated as directed hypotheses (H) when previous research or existing theory allowed for it:

- H1: PE symptoms are stable over time, both in the general population and in a cohort of patients diagnosed with PE. (Study I)
- Q2: What is the direction of causality in the association between PE and symptoms of mood disorder (anxiety and depression)? (Study II)
- Q3: What are the associations between PE and physical exercise, body-mass index, and alcohol consumption? (Study III)
- H4: Vibrator-assisted start-stop exercises alleviate PE symptoms. (Study IV)
- H5: Additional interoceptive awareness training and psychoeducation further improves the treatment effect of vibrator-assisted start-stop exercises on PE. (Study IV)

### 3. MATERIALS AND METHODS

#### 3.1 Participants

Three independent samples were used in the present studies. A descriptive overview is presented in Table 1.

Table 1

*Description of Samples*

Sample name	Study	Origin	Wave ( <i>n</i> )	
			1	2
Population-based sample	I-III	National population registry	3923	1024
Clinical sample	I, III	Patient databases from two clinics for sexual medicine	175	34
Treatment sample	IV	Participants in treatment study	50	-

*Note.* Wave 1 = data collection in year 2006 for the population-based sample, year 2012 for the clinical sample, and year 2018 for the treatment sample; wave 2 = data collection in year 2012 for the population-based sample and year 2015 for the clinical sample.

##### 3.1.1 Population-based sample (Studies I-III)

A population-based, longitudinal sample was eligible for data analysis in studies I, II and III. This sample (the Genetics of Sexuality and Aggression sample, see Johansson et al., 2013) was collected in 2006, and consists of all Finnish twins aged 18 to 33 who have Finnish as their first language, as well as their biological siblings. As the twins were not selected on any other demographic or geographical grounds, the sample can be regarded as representative of the Finnish population.

Participants were contacted by postal mail and invited to complete an online questionnaire. Addresses were obtained from the Central Population Registry of Finland. An eight-digit code was generated for each participant to be used as logging in to the survey, and to enable anonymous handling of longitudinal

data. Those who did not respond to the initial invitation were sent two reminder letters, one week apart. Participants were informed about all aspects of the study, including that participation was voluntary, in accordance with the Helsinki Declaration of 1975, as revised in 2008. Written informed consent was obtained from all participants and the research plan was approved by the Ethics Committee of the Åbo Akademi University in Turku, Finland.

In the 2006 data collection, 2,559 men responded that they were willing to be contacted again for follow-up studies. These men were contacted again in 2012 and invited to participate in a follow-up survey, yielding a 46% response rate ( $n = 1,173$ ). Of these, 1,024 provided informed consent to participate.

### 3.1.2 Clinical sample (studies I & III)

In 2012 and 2015, we contacted all patients who had been diagnosed with PE by a medical doctor who has worked with male sexual problems for over two decades. No exclusion criteria were applied in the data-collection stage. The patients were not diagnosed in conjunction with participating in the study, but had been diagnosed at an earlier time. While diagnoses in Finland are officially based on ICD-10, which does not include (I)ELT as a diagnostic criterion, the diagnosing specialist holds a fellowship with the European College for Sexual Medicine, and has considered IELT in the diagnoses. Contact information was obtained from the specialist's patient register, and updated postal addresses from the Central Population Registry of Finland.

In 2012, 419 individuals identified in the patient registry as having a diagnosis of PE were invited to take part in the studies. Of these, 175 respondents completed the questionnaire. Seventy of these indicated willingness to participate in follow-up studies, and 34 completed the second survey in 2015.

### 3.1.3 Treatment sample (Study IV)

Study IV was conducted at the Karolinska University Hospital in Stockholm, Sweden. Participants for the study were recruited through advertisement in local newspapers and online using Google AdWords. Prospective participants were screened by telephone. In order to be included participants had to be at least 18 years old, understand spoken and written Swedish, have an ELT under 3 minutes, not experience erectile difficulties that interferes with penetration

or masturbation, not suffer from multiple sclerosis or other chronic illness that may affect ejaculatory function and not use pharmacological agents that may affect IELT, such as SSRIs or opioid analgesics. Additionally, participants had to engage in intercourse during participation in the study in order to be included.

Eighty-six individuals declared interest in participating in the study. Of these, 50 were deemed eligible based on inclusion criteria. At post-treatment, 30 provided data, while 21 and 12 provided data at 3-month and 6-month follow-ups, respectively. Drop-out was handled by utilizing both per-protocol (i.e., including only respondents with complete data sets) and intention-to-treat analysis (i.e., including all participants, with the last observation carried forward for participants with missing data).

### 3.2 Measures

The self-report questionnaire Multiple Indicators of Premature Ejaculation (MIPE; Jern, Santtila, Johansson, Varjonen, Witting, von der Pahlen, et al., 2009; Jern et al., 2007) was used to measure symptoms of premature ejaculation during the last two years. The questionnaire consists of seven items, of which five responded to on a 5-point or and two on a 3-point Likert-type scale, with a range of 7–31. A score of 21 has been proposed as a cut-off, identifying 90% of patients, while keeping false positives at 6 % (Jern, Piha, & Santtila, 2013). In this questionnaire, respondents are asked to report their ejaculatory function during the past two years. Items include questions about ejaculation latency, feelings of control over ejaculation, and number of thrusts before ejaculation. The measure has been validated against both other measures of PE symptoms and stopwatch data, and has been shown to differentiate very well between patients and controls (AUC = .98, see Jern et al., 2013) and confirmatory factor analyses have indicated a good model fit (Jern, Santtila, Johansson, & Sandnabba, 2010). Items were back-translated into Finnish. Reliability coefficients are interpreted as excellent if  $\alpha \geq .9$ , good if  $\alpha = .8-.9$ , acceptable if  $\alpha = .5-.6$ , and questionable if  $\alpha = .6-.7$  (George & Mallery, 2003) In the present studies, internal reliabilities were acceptable ( $\omega_s = .81-.82$  in study II; Cronbach's  $\alpha_s = .75-.76$  in study III).

The CHecklist for Early Ejaculation Symptoms (CHEES; Jern et al., 2013) was also used to measure symptoms of PE. CHEES is an empirically derived composite self-report questionnaire consisting one item from the MIPE

questionnaire, two items from the Premature Ejaculation Profile (PEP; Patrick et al., 2009), and two items from the Premature Ejaculation Diagnostic Tool (PEDT; Symonds et al., 2007). The items cover subjectively estimated ejaculation latency time (ELT), feeling of control, feelings of frustration and relationship difficulties as a consequence of rapid ejaculation, and propensity to ejaculate with very little stimulation. CHEES has been validated against stopwatch-measured ELT and other commonly used self-report questionnaires for measuring PE, in both clinical and population-based samples (Jern et al., 2013). CHEES was shown to differentiate between diagnosed patients and population-based controls very well (AUC = .98, 95% CI [.97, .98]), better than MIPE, PEP, and PEDT. Empirically derived cutoffs for CHEES are as follows: 21-25 is strongly indicative of fulfilling diagnostic criteria for PE (correctly identifies 44% of diagnosed PE patients as PE sufferers and incorrectly identifies 1% of controls as PE sufferers), 17-20 is indicative of PE (correctly identifies 90% of diagnosed patients as PE sufferers and incorrectly identifies 5% of controls as PE sufferers), 5-16 points indicate a low probability of PE. A Swedish (Dhejne, Jern, & Arver, 2017) and a back-translated Finnish version of the scale was used. In study IV, CHEES had a somewhat low internal reliability ( $\alpha = .61$ ), which is likely due to the items covering relevant diagnostic criteria, which do not necessarily correlate highly. CHEES was developed in 2013, and since it outperformed MIPE it was chosen for the subsequent data collections.

Both MIPE and CHEES rely on subjectively estimated ELT. A meta-analysis regarding the relevance of methodological design of studies of PE revealed no significant mean difference between subjectively estimated and stopwatch-measured IELT (Waldinger, Zwinderman, Schweitzer, & Olivier, 2004)

The Sexual Distress Scale (SDS; Jern et al., 2008) was used to measure distress related to sexuality and sexual behavior and performance. The SDS is gender-neutral, and adapted from the Female Sexual Distress Scale (Derogatis, Rosen, Leiblum, Burnett, & Heiman, 2002). Seven questions are answered on a 5-point Likert scale covering topics of distress and embarrassment about sexual problems, and feelings of inadequacy. The SDS items were back-translated into Finnish. Jern et al. reported the items loading on a single factor, with item loadings ranging from .65 to .79, and Cronbach's  $\alpha = .89$ . In the present studies, internal reliabilities were good to excellent (study I  $\alpha = .86$ ; study II  $\omega_s = .89-.91$ ). The SDS was used in Study II to elucidate causal associations between PE and distress, and in Study IV as a secondary outcome measure.

The Brief Symptom Inventory-18 (BSI) was used to measure general psychological distress. The BSI was developed from the Symptoms Checklist (SCL-90; Derogatis & Melisaratos, 1983). The subscales of the SCL-90 have previously been shown to possess good discriminant validity in Finnish (Holi, Sammallahti, & Aalberg, 1998) and Swedish samples (Fridell, Cesarec, Johansson, & Thorsen, 2002). Participants rate how much bother they have experienced during the last week on a 5-point Likert scale. We used two of the subscales measuring anxiety and depression. The anxiety subscale covers symptoms of nervousness, tension, restlessness and panic states, and the depression subscale covers anhedonia, hopelessness and suicidal ideation. In the present studies, internal reliabilities were good to excellent (study II  $\omega_{\text{anxiety}} = .80-.81$ ,  $\omega_{\text{depression}} = .86-.89$ ; study IV  $\alpha_{\text{anxiety}} = .93$ ,  $\alpha_{\text{depression}} = .90$ ). The BSI was used in Study II to elucidate causal associations between PE and symptoms of mood disorders, and in Study IV as a secondary outcome measure.

The State-Trait Anxiety Inventory (STAI; Spielberger et al., 1970) was used in Study IV to measure anxiety as a stable trait and in a specific sexual situation. Unlike the original version, where respondents are asked to rate how anxious they feel in the moment they are filling out the questionnaire, respondents in the present study were asked to rate how anxious they felt during the last few times they had sex with a partner. Each subscale contains 20 questions that are answered on a 4-point Likert scale. In study IV, the reliability was excellent ( $\alpha_{\text{trait}} = .95$ ,  $\alpha_{\text{state}} = .93$ ).

The five-item version of the International Index of Erectile Function (Rosen, Cappelleri, Smith, Lipsky, & Peña, 1999) was used to measure erectile function. Items cover the ability to achieve and maintain an erection sufficient for penetrative sex and satisfaction with intercourse. Items are answered on a five-point Likert scale. In the present studies, internal consistencies were good, ranging from .80 to .89. The index was used to analyze associations between ED and physical exercise in Study III, and was used as a screening instrument in study IV.

The Alcohol Use Disorders Identification Test (Saunders, Aasland, Babor, de la Fuente, & Grant, 1993) was used to measure alcohol consumption in Study III. The ten items relate to frequency and amount of drinking and negative outcomes of drinking, and are answered on a scale from 0 to 4. In study III, the

internal reliability was good in the population-based sample ( $\alpha = .82$ ) and acceptable the clinical sample ( $\alpha = .73$ ).

The Godin Leisure-Time Exercise Questionnaire (Godin, 1997) was used in Study III to measure how much participants engage in physical exercise. The questions ask how many times per week the participant engaged in strenuous (e.g., hockey), moderate (e.g., fast walking), or mild exercise (e.g., golf) for longer than 15 minutes during their free time. The variables are weighted and added into a composite score. In study III, the internal reliability was low both in the population-based sample ( $\alpha = .24$ ) and the clinical sample ( $\alpha = .23$ ). This is due to some respondents reporting engaging in only one or two of the categories, leading to there being many zeros, which drastically reduces internal consistency. In a validation study by Eisenmann et al. (2002), the test-retest reliability over 1 week was  $r = .62$ , and convergent validity was supported by use of an accelerometer.

Body mass index (BMI) was used in Study III to measure respondents' weights in relation to their height. BMI was calculated from self-reported height and weight, according to the standard formula of kilograms per meter squared.

The Multidimensional Assessment of Interoceptive Awareness (MAIA; Mehling et al., 2012) was used in Study IV to measure interoceptive awareness. The measure consists of eight subscales: noticing, not-distracting, not-worrying, attention regulation, emotional awareness, self regulation, body listening, and trusting. Thirty-two items are answered on a six-point Likert scale. Two of the subscales, body listening and noticing, have in women been linked to greater awareness of genital arousal and greater levels of concordance between genital and subjective arousal (Handy & Meston, 2016). No similar studies of concordance have been conducted using MAIA in male samples. In study IV, internal reliabilities for the eight subscales ranged from .59 to .91.

### 3.3 Study designs and statistical analyses

In the following sections I present how each study was designed to answer or test its respective research question or hypothesis, and how results were analyzed.

### 3.3.1 Study I

Study I investigated hypothesis 1 (H1: PE symptoms are stable over time in the general population and in a cohort of patients diagnosed with lifelong PE). We utilized two longitudinal samples measured twice over six years (population-based sample) and three years (clinical sample).

In order to assess the stability of PE symptoms over time, we first looked at how many participants reported an IELT under 1 minute at both, none, or one of the time points. As this time cutoff is considered relevant for diagnosing lifelong PE, it would be expected that participants who reported IELTs under 1 minute at the first measurement would also report IELTs under 1 minute at the second measurement if lifelong PE is, as the name implies, a chronic condition. All respondents in the clinical sample were expected to report IELTs under 1 minute, as they had been diagnosed with PE previously. Secondly, we analyzed how much of the variability in PE symptoms at the later time point could be explained by PE symptoms at the first time point by using linear regression. A high degree of explained variance at the subsequent time point would be expected if PE was a lifelong, stable condition. Thirdly, at the second measurement, participants were asked to provide a self-assessment of any change in PE symptoms since the first measurement three or six years ago, if there was any.

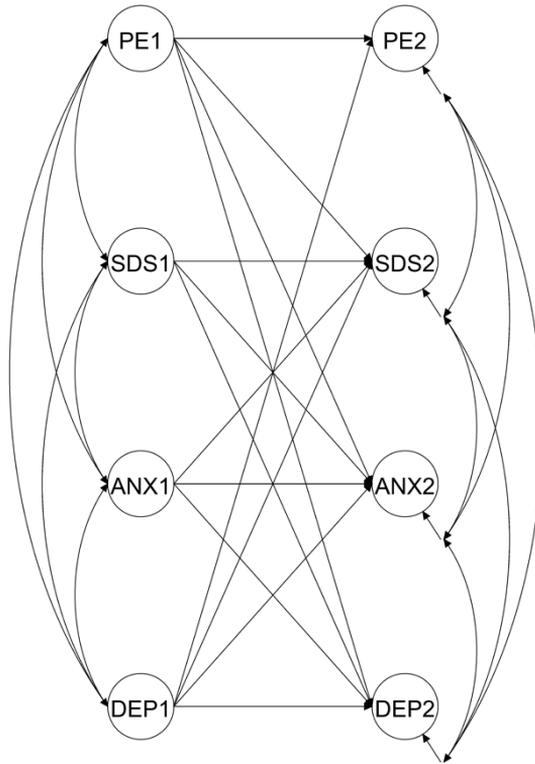
In the population-based sample, 3923 completed the first survey, and 1024 the second. In the clinical sample, 175 participants completed the first data collection and 34 completed the second data collection. After excluding participants who used SSRIs at either time point, and participants who answered less than 40% of PE-related items, the final sample sizes were 843 for the population-based sample and 16 for the clinical sample. Missing data were imputed using the expectation maximization procedure in SPSS 21.0 using intra-scale information. Statistically, analyses were conducted using descriptive statistics and linear regression.

### 3.3.2 Study II

Study II investigated the direction of causality between PE on the one hand, and anxiety and depression on the other (Q2). Using the population-based sample, we tested two competing models regarding the relationships between PE, anxiety, sexual distress and depression. According to the first model, we

expected that anxiety and sexual distress at time 1 would be positively associated with PE at time 2. On the contrary, according to the second model, PE at time 1 was expected to be positively associated with anxiety, sexual distress and depression at time 2. Post-hoc, I ran a model constraining all parameters between PE and the other variables in the structural model to zero (i.e., essentially combining both models), in a more stringent test of there being any longitudinal association between the factors.

Structural equation models were fitted to the data to test the aforementioned models. To test models, relevant structural regression parameters were first omitted (Figure 3). The constrained model was then compared to the saturated model. If the constrained model had a significantly worse fit to data, this was interpreted as indicating that the omitted parameters differed significantly from zero. Because the sample was clustered (twins and siblings in families), maximum likelihood estimation with robust standard errors was used (Muthen & Satorra, 1995). This also allowed handling of missing data.



**Figure 3.** The structural part of first model in study II. Note the omitted parameters between PE2 and SDS1 and ANX1. PE = premature ejaculation, SDS = sexual distress, ANX = anxiety, DEP = depression, 1 = time 1, 2 = time 2. Measurement model not depicted.

### 3.3.3 Study III

Study III investigated associations between PE and physical exercise, BMI, and alcohol consumption (Q3). This was done cross-sectionally and in a case-control manner, using both population-based and clinical samples. For the population-based sample, data were used from the second wave of data collection, and for the clinical sample, data were used from the first wave of data collection, as the relevant variables were gathered only in these waves. Participants were excluded from analysis if they used SSRIs or other medication than may affect PE symptoms, and if they had any missing data. To control for familial dependence (as the population-based sample consisted of genetically related individuals), one person per family was randomly included

in the population-based sample. The total sample sizes were 863 for the population-based and 69 for the clinical sample.

Independent sample *t*-tests were used to compare mean differences between the groups. The clinical sample was compared to the population-based sample, as well as to an age-matched subset of the population-based (as the clinical sample [ $M = 43.8$ ] was significantly older than the population-based sample ( $M = 33.1$ )). Bivariate correlations were used to analyze associations between the variables within the groups. Finally, a multiple linear regression was conducted where PE was the dependent variable and physical exercise, age, erectile function, alcohol consumption, and BMI were entered as independent variables.

### 3.3.4 Study IV

Study IV investigated if vibrator-assisted start-stop exercises alleviate PE symptoms (H4), and whether the treatment effects are further enhanced by additional interoceptive awareness training and psychoeducation (H5). It also provided further data regarding the associations between PE symptom severity, anxiety, depression, sexual distress, and interoceptive awareness.

Participants were randomized into one of two different treatment groups or a waiting list control condition. No statistically significant differences were found between the three groups at the first measurement, with the exception of one MAIA subscale, indicating a successful randomization. Participants in the waiting list control group were randomly allocated to the treatment groups following a 6-week waiting period.

The 6-week intervention involved two visits to the clinic, at the beginning and end of treatment. Participants answered online questionnaires at home before and immediately after treatment, as well as 3 and 6 months after treatment. The waiting list control group additionally completed questionnaires at the beginning of the waiting period (i.e., six weeks before treatment). The study was approved by the Regional Ethical Review Board in Stockholm, Sweden, in accordance with the Declaration of Helsinki. All participants provided written, informed consent.

The first treatment group (VSS; short for Vibrator-assisted Start-Stop) performed vibrator-assisted start-stop exercises three times a week for 6 weeks. Participants were instructed to masturbate while stimulating the underside of glans penis with a handheld vibrator, until ejaculation felt imminent, and then take a break and remove the vibrator. When ejaculation was no longer imminent, participants were to resume masturbation using the device. This was to be repeated three times, and on the third time participants could ejaculate if they so wished, in accordance with the manufacturer's instructions. Participants were not restricted from engaging in any other sexual activities during treatment.

In the second treatment group (VSS+) participants additionally received further psychoeducation and performed interoceptive awareness exercises in the form of 15-minute guided body scan meditations to be completed prior to the vibrator-assisted start-stop exercises. The psychoeducation involved topics such as the connection between interoceptive awareness and PE, and techniques to monitor and control sexual excitement.

Both intention-to-treat (ITT) and per-protocol (PP) analyses were conducted. In ITT analyses, the last observation was carried forward in case of missing data. This can be considered to be a conservative approach in pre-post analyses, as participants who do not provide data are assumed to have had no change. On the other hand, ITT analyses may overestimate long-term effects as any potential treatment effect is assumed to be sustained. Pre-post treatment effects were analyzed using analysis of covariance with post-treatment scores being the dependent variable, treatment group being the between-groups factor (waiting list, VSS, VSS+), and pre-treatment measurement used as a covariate in order to reduce error variance (Dimitrov & Rumrill, 2003). Within-group differences were calculated using dependent sample *t*-tests. Differences between the two treatment groups at follow-up were tested using independent sample *t*-tests.

## 4. RESULTS

### 4.1 Study I

The clinical sample had been diagnosed with PE by a physician specializing in sexual medicine prior to study participation, and the participants were untreated during participation in the study. As such, it would be expected that all participants in the clinical sample met the diagnostic criterion of ELT less than 1 minute. However, only 50% ( $n = 8$ ) reported ELT less than 1 minute in 2012 (Table 2). Of these, five men reported equally short ELT in 2015, while an additional two that did not report ELT less than 1 minute in 2012 did so in 2015. The autoregressive coefficient was high ( $b = 0.83, p < .001$ ). In terms of subjective perception of change, 63% ( $n = 10$ ) reported that their ELT had changed (i.e., that their ELT used to be somewhat shorter/longer; or a lot shorter/longer) between the two measurement points.

In the population-based sample, 16 individuals reported an ELT of less than 1 minute in 2012. Of these, seven reported equally short ELT in 2015, while an additional 13 that did not report ELT less than 1 minute in 2012 did so in 2015. The autoregressive coefficient in this sample was moderate ( $b = 0.58, p < .001$ ), suggesting that ELT was more stable in the clinical sample. In terms of subjective perception of change, 47% ( $n = 397$ ) reported that their ELT had changed (i.e., used to be somewhat or a lot shorter or longer).

Table 2

*Subjectively Estimated Ejaculation Latency Times in the Population-Based and Clinical Samples*

Item response option	Sample			
	Population-based (n)		Clinical (n)	
	Time 1	Time 2	Time 1	Time 2
I usually do not ejaculate	11	6	0	0
More than 10 min	316	282	0	0
Between 5 and 10 min	330	348	1	0
Between 1 and 5 min	170	187	7	9
Less than 1 min	16	20	8	7

*Note.* Time 1 = data collection in year 2006 for the population-based sample, year 2012 for the clinical sample; Time 2 = data collection in year 2012 for the population-based sample and year 2015 for the clinical sample.

## 4.2 Study II

Bivariate correlations between latent factors are presented in Table 3. All variables had statistically significant positive correlations within both time points. PE and sexual distress were mutually positively correlations across time. PE at Time 1 was positively correlated with anxiety at Time 2, while depression at Time 1 was positively correlated with PE at Time 2. These cross-time cross-domain coefficients were small to moderate.

Table 3

*Estimated Correlations between Latent Variables Measuring Premature Ejaculation, Sexual Distress, Anxiety, and Depression*

	PE1	PE2	SDS1	SDS2	ANX1	ANX2	DEP1
PE1	-						
PE2	.659***	-					
SDS1	.563***	.347***	-				
SDS2	.228***	.414***	.467***	-			
ANX1	.121**	.087	.384***	.279***	-		
ANX2	.091*	.209***	.307***	.478***	.544***	-	
DEP1	.156***	.127**	.445***	.349***	.854***	.445***	-
DEP2	.074	.135**	.315***	.533***	.493***	.828***	.529***

Note. PE = premature ejaculation, SDS = sexual distress, ANX = anxiety, DEP = depression, 1 = time 1, 2 = time 2

\*  $p < .05$ , \*\*  $p < .01$ , \*\*\*  $p < .001$

Two models were fitted to the data; the first to test whether anxiety predicted future PE, and the second whether PE predicted future anxiety and depression. Neither of the models had significantly worse fit than the saturated model. A post-hoc model excluding all paths over time between PE and the other variables also did not fit significantly worse than the saturated model ( $\Delta\chi^2(6) = 5.45, p = .49$ ). Thus, no associations across time were found in these models. All models explained approximately the same amount of variance in PE at Time 2 ( $R^2$ s = .431-.440).

### 4.3 Study III

Respondents in the clinical sample were less inclined to engage in physical exercise ( $M = 27.53, SD = 21.01$ ) than the population-based sample ( $M = 34.68, SD = 22.82, t(930) = 2.52, p = .012, d = 0.85$ ). The clinical sample also used less alcohol ( $M = 6.94, SD = 4.46$ ) than the population-based sample ( $M = 8.10, SD = 5.27, t(85.86) = 2.03, p = .045, d = 0.23$ ). No difference in BMI was found between the groups. When comparing the clinical sample to age matched controls, no statistically significant differences between groups remained, although group means were in the same direction as when the full population-based sample was compared to the clinical sample.

Within the population-based sample, PE was weakly negatively correlated with physical exercise ( $r = -.09, p < .05$ ). This correlation was more pronounced in the oldest group, which was age matched to the clinical sample ( $r = -.29, p < .05$ ). PE was not statistically significantly correlated with alcohol consumption or BMI.

In a multiple regression analysis, PE was statistically significantly predicted by physical exercise ( $\beta = -.09, p = .007$ ; Table 4), even while controlling for age, erectile function, alcohol consumption and BMI, suggesting that individuals who exercised less experienced more PE symptoms.

Table 4

*Multiple regression of variables predicting premature ejaculation in the population-based and clinical sample*

	<i>b</i>	<i>SE</i>	$\beta$	<i>t</i>	<i>p</i>
Constant	18.49	1.69		10.92	<.001
Physical exercise	-0.02	0.01	-.09	2.72	.007
Age	0.15	0.02	.21	6.76	<.001
Erectile function	0.31	0.04	.23	7.41	<.001
Alcohol consumption	-0.01	0.03	-.01	0.28	.776
BMI	-0.00	0.04	-.00	0.11	.911

*Note.* BMI = body mass index, SE = Standard error

## 4.4 Study IV

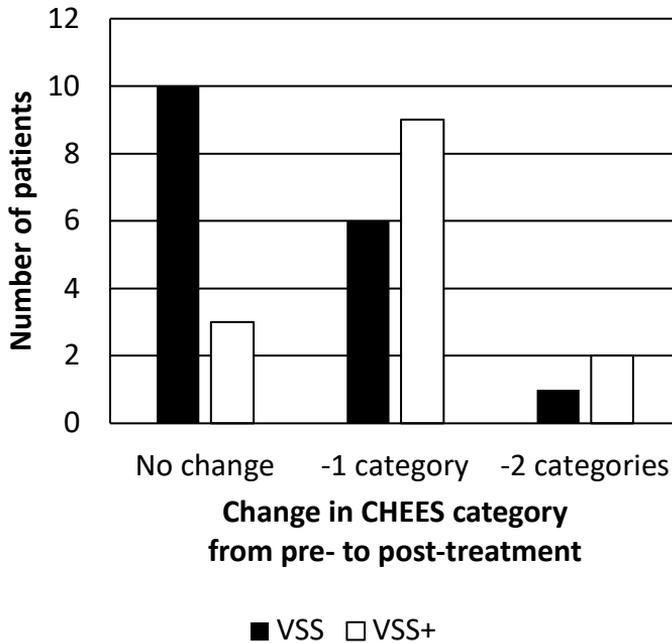
In study IV, there was a statistically significant correlation between PE and sexual distress at the first measurement ( $r = .486, p < .001$ ). PE was not, however, correlated with trait or state anxiety during sex as measured with STAI, nor anxiety or depression as measured with BSI. In addition, PE was not associated with erectile function.

### 4.4.1 Pre-post analyses

The waiting list control group had no statistically significant changes in any variable over the waiting period. The VSS group had a statistically significant improvement of PE symptoms during the treatment period ( $t = 3.22, p = .005$ ), but no statistically significant changes in any other outcome variable. The VSS+ group showed improvements on PE ( $t = 3.78, p = .001$ ) after treatment, and in addition, improvements on the following secondary outcome variables: sexual distress ( $t = 2.48, p = .023$ ), STAI trait anxiety ( $t = 2.77, p = .013$ ), STAI state anxiety during sex ( $t = 2.18, p = .043$ ), and BSI anxiety ( $t = 2.17, p = .044$ ).

An analysis of covariance (ANCOVA) revealed that there were statistically significant differences in PE between the groups at post treatment ( $F = 5.65, p = .006$ , ITT analysis), and the effect size was large (partial  $\eta^2 = .20$ ). Pairwise comparisons showed large treatment effects in both the VSS group ( $d = 1.05$ , 95% CI = [0.27, 1.82]) and the VSS+ group ( $d = 1.07$ , 95% CI = [0.32, 1.82]) compared to the control group. The treatment effect was pronounced when analyzing only items related to dysfunction (ELT, feeling of control, ejaculation

with very little stimulation). The treatment groups did not differ from one another in terms of statistical significance or effect size at post treatment.



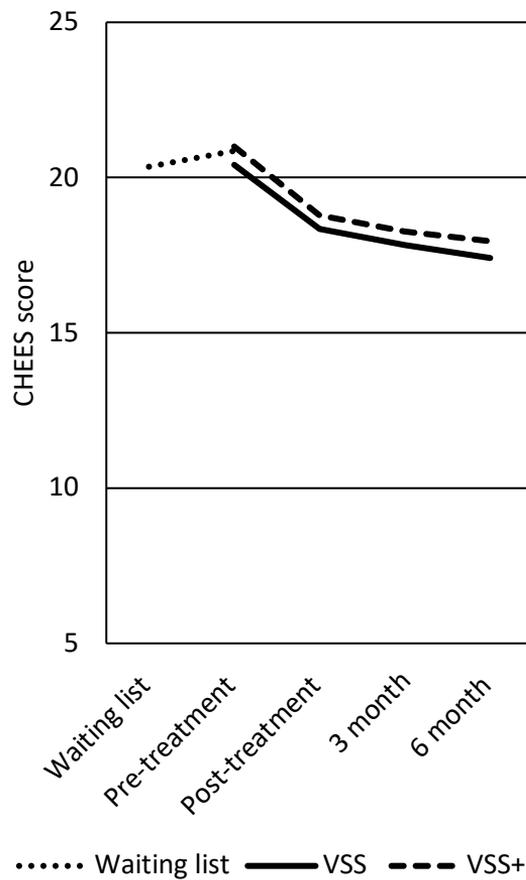
**Figure 4.** Change in CHEES category from pre- to post-treatment. A decrease in category indicates decreased symptoms of PE. The three categories are “strongly indicative of fulfilling diagnostic criteria for PE”, “indicative of PE”, and “low probability of PE” (Jern et al., 2013). No patients had a higher categorization at post-treatment than pre-treatment. VSS = vibrator-assisted start-stop group, VSS+ = vibrator-assisted start-stop and psychobehavioral intervention group.

Comparing the two treatment groups regarding change of categorization on the main outcome measure revealed that more than half of the VSS group had scores within the same category before and after treatment (Figure 4). On the contrary, a majority of the VSS+ had improved one or two categories during treatment. This possibly implies a better treatment effect in the VSS+ group. Prior to treatment, the mean of both treatment groups fall within the category “strongly indicative of fulfilling diagnostic criteria for PE”. In ITT analyses, the means of both groups after treatment are in the lower bound of the “indicative of PE” category in ITT analyses, while the means in PP analyses are in the upper bound of the category “low probability of PE”.

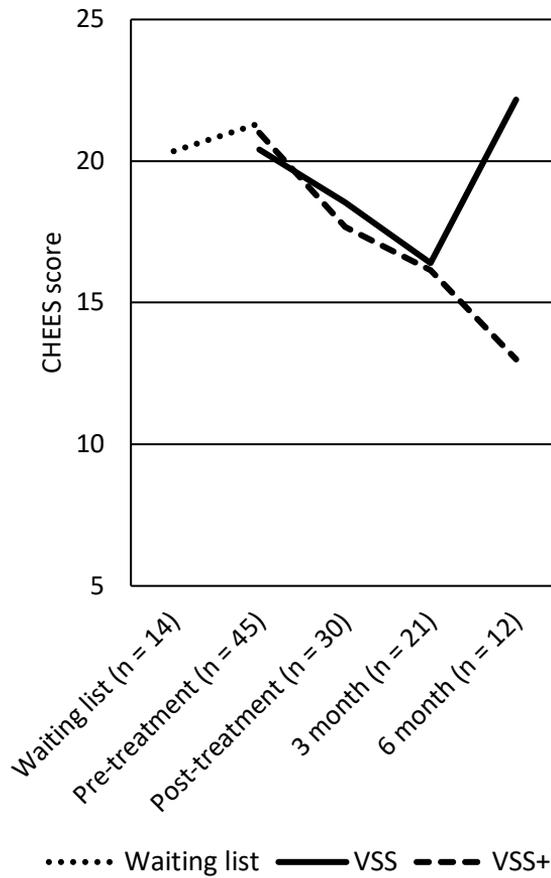
ANCOVA analyses revealed no statistically significant between-group differences on any secondary outcome measure. However, despite not being statistically significant, pairwise comparisons revealed that the VSS+ group displayed larger improvements in sexual distress, and all STAI and BSI measures compared to the VSS group, with medium effect sizes ( $d_s = 0.38-0.66$ ). Surprisingly, interoceptive awareness did not differ significantly between groups, which indicates that the interoceptive awareness exercises performed by the VSS+ did not have had the intended IA-improving effect. All results were similar in ITT and PP analyses.

#### 4.4.2 Follow-up analyses

Participants from the waiting list were included in one of the two treatment groups in the follow-up analyses. No statistically significant differences in PE symptoms were found between the two treatment groups at either follow-up time. ITT analyses revealed that improvements in PE symptoms were sustained after 3 and 6 months in both treatment groups when compared to pre-treatment (Figure 5). However, follow-up analyses were based on a very small number of respondents, and is therefore unreliable. At 6-month follow-up in PP analyses, the mean of the VSS group rises back to baseline (Figure 6). This is however not because of a waning treatment effect, but it can rather be explained by dropout, as the mean of the subgroup of eight participants who provided data at this time point was consistently around 20 at all time points. Consequently, conclusions regarding long-term efficacy should be drawn only with great caution.



**Figure 5.** Premature ejaculation scores from intention-to-treat analyses.  $N_{VSS} = 23$ ,  $N_{VSS+} = 27$ . Range 5–25, higher scores indicate more severe symptoms. Empirically derived cutoff scores: 21–25: strongly indicative of fulfilling diagnostic criteria for PE, 17–20: indicative of PE, 5–16: low probability of PE. VSS = vibrator-assisted start-stop group, VSS+ = vibrator-assisted start-stop and psychobehavioral intervention group.



**Figure 6.** Premature ejaculation scores from per-protocol analyses. Range 5–25, higher scores indicate more severe symptoms. Empirically derived cutoff scores: 21-25: strongly indicative of fulfilling diagnostic criteria for PE, 17-20: indicative of PE, 5-16: low probability of PE. VSS = vibrator-assisted start-stop group, VSS+ = vibrator-assisted start-stop and psychobehavioral intervention group.

## 5. DISCUSSION

The discussion section is structured as follows. In the context of previous relevant research, I first discuss results pertaining to the diagnostic criteria of PE, followed by issues of etiology, and finally treatment of PE. Following this, limitations of the present studies are considered. Finally, some interesting future avenues of research are presented.

### 5.1 Diagnostic considerations

Throughout its history, the definition of PE has been the object of considerable debate (Waldinger & Schweitzer, 2019). With each new edition of the diagnostic manuals presenting somewhat varied definitions, consensus regarding diagnostic criteria has not yet been reached. For example, the latest version of the DSM includes cutoffs for IELT where previous versions did not (American Psychiatric Association, 2013), whereas the new ICD-11 no longer includes any cutoff for IELT while the previous version did (World Health Organization, 2018). The present study adds relevant empirical results for the discussions on IELT cutoff and subtypes of PE.

#### 5.1.1 Ejaculation latency time cutoff

According to the International Society for Sexual Medicine, PE is defined by nearly always having had an IELT of approximately 1 minute (lifelong PE) or a bothersome reduction of IELT to about 3 minutes (acquired PE); inability to delay ejaculation; and negative personal consequences such as distress (Serefoglu et al., 2014, pp. 44). According to this definition, neither a short IELT nor distress about a subjectively experienced short IELT, are in themselves sufficient for diagnosis – a combination of IELT, lack of control, and distress is necessary. These criteria are not always present simultaneously. Rowland et al. (2004) found that some men who ejaculate before they wish do not see it as a problem. Similarly, Patrick et al. (2005) observed that some men with short IELTs were not distressed about their IELTs, while on the contrary, some men with comparably long IELTs were nevertheless distressed. While every patient can express their experienced distress, any objective cutoff for what is to be considered short in terms of IELT is determined by the scientific and professional field. But how is this cutoff-point for IELT determined?

The empirical underpinning for ISSM's definition is partly based on epidemiological stopwatch-measured data. In two studies, unimodal positively skewed distributions of IELT were found with medians of 5.4 minutes in a convenience sample (Waldinger et al., 2005) and 6.0 minutes in a random sample (Waldinger, Mcintosh, & Schweitzer, 2009). This is to say that there is not a clearly distinguishable group with shorter IELTs than the general population, but rather a cutoff point is chosen along the unimodal continuum of the distribution of IELT. The cutoff of approximately 1 minute was chosen based on statistical infrequency (about 2.5% of the population report IELTs less than 1 minute), and on a study which found that 99 of 110 men who sought treatment for lifelong PE reported IELTs  $\leq$  1 minute (Serefoglu et al., 2014; Waldinger, Hengeveld, Zwinderman, & Olivier, 1998).

The reasons for choosing a cutoff of approximately 1 minute has, however, been questioned. Söderfeldt et al. (2017, p. 865) note that "[...] the fact that a phenomenon is statistically rare does not automatically equal pathology as anyone with red hair will confirm". Rowland and Kolba (2015) criticize the validity of relying on stopwatch studies where participants' level of distress was not also assessed, and further, that the self-selected sample of patients used in the study by Waldinger et al. (1998) was not representative of PE patients in general. The authors argue that the 1-minute cutoff excludes many men who otherwise fulfill criteria for PE, and that this creates an artificial dichotomization between men who are in fact very similar. In support of their view, Rowland and Kolba present empirical data by analyzing a total of 1183 men (374 of whom reported ejaculation before they desired). They found very small differences in levels of distress between participants who reported IELTs of  $<$  1 minute compared to 1–2 minutes, while the level of distress was comparably lower in participants reporting IELTs of 2–5 minutes. Furthermore, the authors refer to previous unpublished data comparing distress and bother, demographic variables, general medical history, relationship and sexual parameters (including erectile functioning), and perceived attributions for the problem, and found that men with IELTs  $<$  1 minute were similar to those reporting IELTs of 1–2 minutes. These two groups were more similar to each other than to a comparison group of sexually functional men. Based on these findings, Rowland and Kolba argue that a 2-minute cutoff would reduce false negatives.

The cutoff has been further criticized by Perelman (2017), who reviewed the empirical stopwatch-measured IELT data, and noted that the majority of men (> ~65%) reported an IELT within the range of approximately 4 to 10 minutes. This range, he suggests, could be used as the point of reference, with men who involuntarily ejaculate within 4 minutes, and are distressed by it, could be diagnosed with PE. While suggesting somewhat different cutoffs, perhaps partly due to Rowland and Kolba (2015) using the intervals 0-1, 1-2, and 2-5 for IELT while Perelman (2017) analyzed continuous data, the authors of both reports agree that the current temporal criterion is too strict.

The arguments presented thus far have been based on prevalence and statistics, but what if the issue of a cutoff is not an empirical question? From an evolutionary perspective, Hong (1984) argued that PE could have been selected for, since protohumanoids with shorter IELTs could have had greater opportunity to mate with several partners and were less likely to sustain or afflict physical damage during mating. Further, Hong argues, short IELTs may forestall aggressive competition over chances to mate with a partner, which facilitated group harmony. Taken together, this could mean having a short IELT was associated with increased longevity and chance of passing on genes.

If the distribution of IELT has been shaped by such biological factors, and a short IELT even might have been advantageous at some point, the current experiences of short IELTs being problematic and the need for there to be a diagnosis can only be explained by the meaning that is placed on IELT in today's society. Comparing PE to ED, another common male sexual dysfunction, shows that the dysfunctions are dissimilar on this point. In ED, the penis is not usable for its biological function of penetration, while in PE, the penis arguably performs its biological function with excellence (bar anteportal ejaculation), while not performing according to cultural standards. On an ultimate level of explanation, only anteportal ejaculation can be deemed dysfunctional, since the ultimate function of ejaculation is to fertilize an egg, and there is no evidence to say that the probability of fertilization is higher if intercourse duration is longer. However, on a proximate level of explanation, that is, in the context of sex taking place for recreational purposes, the function can become dysfunctional if it impedes pleasure and causes interpersonal distress (most men probably seek treatment for their PE in order to improve their recreational sex, rather than their fertility.) According to this reasoning, (I)ELT is an inexpedient measure, since the focal point is the subjective experience.

Söderfeldt et al. (2017) argue that PE as a diagnosis reflects strict cultural standards centered around heterosexual coitus, and that the diagnosis itself and the focus on IELT in turn reinforce these narrow male sexual scripts. According to this perspective, the problem emerged when the old biology was situated within a new set of cultural norms. A discrepancy between a man's ejaculatory latency and his conception of how long it should be can lead to suffering. While it is generally not possible for a clinician to alter cultural norms, it is sometimes possible to reduce suffering by altering the man, for example by prolonging the man's ELT. However, with about a third of the male population subjectively experiencing their ELTs being too short (Althof et al., 2014), some form of objective cutoff is useful to guide us in deciding when to accept a man's ELT as too short, and here empirical data are useful.

The present study adds relevant empirical findings to this discussion. Results from Study I indicate that some individuals diagnosed with PE fluctuate in their ELT across both sides of the 1-minute mark. This means that, if a one-minute ELT cutoff were to be abided by, they sometimes fulfilled diagnostic criteria and sometimes did not, even if this does not necessarily reflect their subjective experience. In Study IV, it was interesting to note that a minority (20%) of participants who sought help reported always having had an  $ELT \leq 1$  minute, in contrast to the previously cited study (90%; Waldinger, Hengeveld, et al., 1998). This difference might perhaps be explained by differences in recruitment strategy and wording of recruitment material, cultural differences or decreasing stigma, or that the population of men with PE seeking treatment is indeed more diverse in terms of ELT than what was observed in the study by Waldinger.

In any case, our investigation suggests that that ELT is not always stable over time. Furthermore, not only men reporting  $ELT < 1$  minute seek help for PE. In conjunction with data from a study by Rowland and Kolba (2015), who reported similarities in distress on either side of the 1 minute mark for ELT, I suggest that the current cutoff for ELT for PE diagnosis at 1 minute is unnecessarily strict. Increasing the temporal criterion to approximately 2–4 minutes would reduce false negatives, while the criteria for distress and control reduce the risk of false positives.

### 5.1.2 Subtypes of PE

Results from Study I indicate that a substantial proportion of men had stable symptoms of PE, including individuals with severe symptoms. However, the results of Study I clearly suggest that PE symptoms are less stable over time than previously thought. This is most clearly demonstrated by the fact that around half of the men who reported ELTs less than 1 minute at the first measurement did not do so a few years later. This finding is corroborated by subjectively experienced changes in ELT between the two measurement points in both the clinical sample (63% experienced a change in ELT) and the population-based sample (47% reported change). Furthermore, only a third of the previously diagnosed, but at the time of the study untreated, patients reported ELTs less than 1 minute at both time points. Taken together, hypothesis 1 (i.e., that PE symptoms are stable over time in the general population and in a cohort of patients diagnosed with PE) was not supported.

At present, the chronicity of lifelong PE is accepted as fact, as demonstrated in the ISSM's definition: "Ejaculation that always or nearly always occurs prior to or within about 1 minute of vaginal penetration (lifelong PE)[...]" (Serefoglou et al., 2014, p. 44). The definition is logically sound in itself – if ejaculation always occurs within the same problematic time frame, then it is a chronic condition. However, the evidence presented in the aforementioned article regarding chronicity is based solely on retrospective reports – not longitudinal investigations. Overall, the literature on long-term follow-up of chronicity of PE is nearly nonexistent. Akre, Berchtold, Gmel and Suris (2014) followed the development of PE over 16 months among 3700 Swiss conscripts. Of the 403 respondents who fulfilled the study's criteria for PE at the first time point, a majority (56%) no longer did so at the second timepoint. However, the measure used was not validated and lacked important PE indicators such as ELT, and there were no exclusion criteria, such as receiving treatment for PE or using SSRIs, meaning that no strong conclusions should be drawn from the study. However, the results from Study I corroborate results from Akre et al. (2014), in that both studies suggest considerable variability in PE.

Other purely observational studies of the stability of PE symptoms have only been conducted in the short term (up to 4 weeks), in conjunction with development of patient-reported outcome (PRO) questionnaires (Althof et al., 2006; Patrick et al., 2005; Symonds et al., 2007). Within drug trials, placebo control groups are usually followed a maximum of 12 weeks (Cooper et al.,

2015). There are, however, a few exceptions. Buvat et al. (2009) reported small but not statistically significant mean improvements on IELT and PROs in a placebo group followed 24 weeks. Likewise, no statistically significant group-level changes were found within placebo control groups at 6 month follow-up in two studies by Safarinejad (2007; Safarinejad & Hosseini, 2006). Participants in these control groups may however be affected by the placebo effect, meaning that their experienced level of PE may be affected by their taking part in a drug trial and receiving an intervention. In conclusion, much of the evidence on which current diagnostic subgroups rely can be described as anecdotal or expert opinion, which is the weakest level of evidence according to the Oxford Center for Evidence Based Medicine's Levels of Evidence working group (2009).

Study I presents the best available long-term observational data on PE symptoms. Yet, the data are not optimal for the research question. After making necessary exclusions of participants receiving treatment that could affect PE symptoms, the clinical sample was very small. This reduces the external validity of the findings, as the resulting sample may not be representative of a general population of men with PE. Further, participants were not explicitly asked about chronicity, so the validity of discussing the lifelong subtype based on these data can be questioned. In the study, we analyzed the number of respondents who reported average ELTs of less than 1 minute during the last two years (in the population-based sample) or during the last six months (in the clinical sample). According to the ISSM, acquired PE is characterized by "... [a] reduction in latency time, often to about 3 minutes or less" (Serefoglu et al., 2014, p. 44). Thus, we applied a criterion for ELT that was stricter than what is usually found in patients who suffer from acquired PE. Additionally, the time frame (two years and six months) excludes patients suffering from transient conditions, which Waldinger (2007) would characterize as natural variable PE. While these operationalizations lead to a sample resembling patients suffering from lifelong PE, it is clear that the results from Study I do not disprove the existence of lifelong complaints. Study I does, however, in conjunction with the lack of empirical evidence of stability, raise very important questions regarding the evidence-base that make up the foundation of current diagnoses, the appropriateness of the epithet 'lifelong', and risks of over-diagnosing chronicity.

Researchers' and clinicians' perceptions of a disorder affect how they deal with the problem and the patient. A PE subtype definition including the word "lifelong" may suggest that it is incurable and stable, and that any treatment offered will only be able to temporarily alleviate symptoms (a point of view explicated by, e.g., Waldinger, 2007). Overdiagnosing chronicity reduces hope, and has implications for what treatments are offered by clinicians and accepted by patients: for example, why perform time-consuming exercises, change your lifestyle, or receive somewhat invasive physiotherapeutic interventions if any effects of such endeavors in the end are temporary? All of these interventions, as reviewed in the present thesis, have promising results regarding long-term effects. While pharmacotherapy is helpful and effective for many patients, its status as first-line treatment is partly contingent on the view of PE as being unchangeable, which empirical findings suggest is questionable.

The relevance of diagnostic subtypes themselves are also questionable, at least from a clinical perspective. The second International Society for Sexual Medicine ad hoc committee for the definition of premature ejaculation agreed on a joint definition for lifelong and acquired PE, where the difference being the cutoff for IELT (approximately 1 minute vs. often less than 3 minutes), and whether the complaint had always been present or emerged during the patient's life (Serefoglu et al., 2014). The definition was based on a review of the literature, where the committee found that men with lifelong and acquired PE have similar IELTs, similar experiences of ejaculatory control and similar levels of distress. Regarding treatment, the ISSM has proposed the same treatment (pharmacotherapy and behavioral/psychotherapy) for both lifelong and acquired PE, assuming that the acquired PE is not secondary to some other dysfunction such as ED, which should be treated first (Althof et al., 2014). In light of the similarities in clinical presentation, lack of evidence of different etiologies, and the practically identical treatment recommendations, there is little apparent utility of diagnostic subtypes, at least in clinical settings.

## 5.2 Etiology of premature ejaculation

### 5.2.1 The etiological role of anxiety

In Study II, the direction of causality between symptoms of anxiety and PE was analyzed. While statistically significant bivariate correlations were found across time between variables, both across- and within-time associations between anxiety and PE symptoms were small. In the longitudinal analyses, no

clear-cut causal effects of either anxiety on PE, or PE on anxiety, were detected. At first glance, the results of the present study can be interpreted as suggesting that the role of anxiety as an etiological component of PE is limited. However, lack of support for the role of anxiety is not the same as proof against it, and it should be borne in mind that the present Study II only included measures from two time points several years apart, on which I will elaborate in the following.

Two recent cross-sectional studies found elevated levels of state anxiety, but not trait anxiety, in PE patients as compared to the general population (Kempeneers et al., 2018; Mourikis et al., 2015). The BSI, which was used to measure anxiety in Study II, has been shown to correlate with both Spielberg state anxiety ( $\rho = .69$ , Abu Ruz et al., 2010) and trait anxiety ( $r = .47-.60$ , Lang, Norman, Means-Christensen, & Stein, 2009). While the items of the BSI can be argued to resemble state anxiety (e.g., “Feeling so restless you could not sit still”), the time of reference captures the past seven days rather than a specific moment. Furthermore, the time lag in the present study was six years between measurements, and the autoregressive coefficient for BSI anxiety was high. This would imply that what was measured was quite stable and trait-like, rather than transient states. As such, the present study is in line with Kempeneers et al. (2018) and Mourikis et al. (2015), in that no association was found between PE and trait anxiety. It is quite possible that we were unable to capture a true covariation between anxiety and PE in Study II if the type of anxiety that covaries with PE symptom severity is more state-like.

This was indeed partly corroborated by the findings in Study IV. At baseline, PE was more strongly correlated to STAI state anxiety during sex ( $r = .17$ ) than STAI trait anxiety ( $r = .05$ ) and BSI anxiety ( $r = .06$ ). The effect sizes might be diminished due to restriction of range, since the study design excluded participants without PE and individuals using SSRIs (e.g., to treat some anxiety-related disorder). In summary, our results in combination with other recent investigations concerning the association between anxiety and PE suggest that the possible role of anxiety in PE etiology should be investigated using measures of anxiety in the actual sexual situation (i.e., model state rather than trait anxiety).

In case anxiety was a large etiological factor in PE, it could be expected that improvements in anxiety would be followed by improvements in PE. This was, however, not observed in Study IV. The VSS and VSS+ groups had very similar

mean scores of PE throughout the study. However, the VSS+ group had substantially lower levels of anxiety on all measures than the VSS group following treatment, even if the difference was not statistically significant. The change in anxiety being independent from change in PE speaks against the etiological role of anxiety in PE.

### 5.2.2 The etiological role of depression

In Study II, we found small but statistically significant correlations between depression and PE within both time points ( $r_{T1} = .156$ ;  $r_{T2} = .135$ ). These results are in line with a meta-analysis by Xia et al. (2016), who found a statistically significant association between PE and depression over eight included studies ( $r = .13$ ; the effect size was converted to  $r$  according to Borenstein, Hedges, Higgins, & Rothstein, 2009). While the study selection criteria were not fully transparent in the meta-analysis, and there were also some indications of publication bias, the effect size is of the same magnitude as we found in Study II, providing further evidence that there is link between PE and depression. A plausible explanation for this association is that PE and depression share a common etiological background, with a dysregulation of the serotonergic system, as SSRIs are known to both increase ELT (Buvat et al., 2009; Kaufman et al., 2009; Pryor et al., 2006) and decrease symptoms of depression (Barth et al., 2016). Another reasonable explanation is that PE could lead to lower self-confidence and interpersonal difficulties, including refraining from engaging in new romantic relationship (Symonds et al., 2003), which could lead to loneliness and self-criticism, which are associated with depression (Besser, Flett, & Davis, 2003). A third explanation is that depression is associated with lower self-efficacy (Muris, 2002), which could decrease feelings of control. Depression is also highly associated with anxiety, with a comorbidity of 50% (Hirschfeld, 2001), meaning that that depressive symptoms such as self-criticism may trigger anxiety-related mechanisms of PE. Regardless of possible mechanisms between PE and anxiety, Study II showed that associations were even smaller across a period of six years, and model fitting results indicated that the associations were of little significance. These results suggest that while there may be a small but statistically robust association between depression and PE, depression is probably not a major etiological factor in PE.

### 5.2.3 The etiological role of lifestyle factors

In Study III, no associations were found between PE and the lifestyle factors alcohol consumption and BMI. This is in line with two recent independent

observational studies on a clinical sample of Italian men (Verze et al., 2018) and American men with sexual problems and their partners (Rosen, Heiman, Long, Fisher, & Sand, 2016).

The strongest finding in Study III was a small but statistically significant association suggesting that PE symptoms tended to decrease as physical activity increased ( $r = -.09, p < .01$ ). When comparing the mean level of physical exercise between the clinical and population-based samples, this effect was large ( $t[930] = 2.52, p = .012, d = 0.85$ ). This association maintained statistical significance even controlling for confounding effects of other lifestyle factors and age, albeit with a smaller effect size. Furthermore, the same association was also found within the population-based sample, with a small, but expected, negative correlation between PE symptoms and physical activity.

These results are in line with a recently published observational study by Yildiz, Kilinc, and Doluoglu (2018), who compared men who participated in regular calisthenic and/or fitness exercise programs to men who led a sedentary lifestyle. Men who exercised reported statistically significantly longer IELTs (316 seconds vs. 189 seconds,  $p < .001$ ) and lower scores on the Premature Ejaculation Diagnostic Tool (PEDT; 6.18 vs. 10.02,  $p < .001$ ). According to a validation study of the PEDT (Symonds et al., 2007), the suggested cutoff for having no PE is less than or equal to 8, indicating that men who exercised probably did not have PE, while men who led a sedentary lifestyle were more likely to have PE. There were statistically significant correlations between the measure of physical activity and IELT ( $r = .368, p < .001$ , suggesting longer IELTs as a function of more exercise) and PEDT ( $r = -.383, p < .001$ , suggesting decrements in PE symptoms in individuals who exercised more).

However, in the studies by Rosen et al. (2016) and Verze et al. (2018), no association between PE and exercise was found. Since the publication of these conflicting cross-sectional results, Kilinc, Aydogmus, Yildiz and Doluoglu (2018) conducted a promising intervention study, where they randomized 105 men who met ISSM criteria for lifelong PE into one of three groups: one group using 30 mg dapoxetine on demand; a second group performing moderate exercise for 30 minutes five times a week; and a third group performing minimal physical activity. Results indicated that on-demand use of dapoxetine and moderate physical exercise both resulted in 3.5-fold increases in IELT after

30 days, while no change was observed in the group performing minimal physical exercise. The authors hypothesized that the mechanism of action is through the increased availability of serotonin following physical activity, which has been demonstrated in previous studies (Chaouloff, 1997; Post et al., 1973). This is supported by research demonstrating ejaculation-delaying effects of SSRI medication, which makes physical exercise an interesting target of study in the context of PE research.

This new avenue of research on the relationship between physical exercise and PE still need robust replications and experimental designs to confirm that the direction of causality is such that physical activity alleviates PE symptoms.

It has been suggested that different subtypes of PE could have different etiologies, with lifelong being more strongly influenced by biological factors and acquired having more psychological risk factors, which could indicate different treatment (McMahon et al., 2016; Waldinger, 2007). However, as McMahon et al. (2016) notes, most of these proposed etiologies are speculative at best. In case the proposed mechanism of alteration of serotonergic transmission following physical exercise is correct, interventions aimed at increasing physical activity could be offered to both patient groups, as it has also been reported that dapoxetine is equally effective for lifelong and acquired PE (Porst et al., 2010)

## 5.3 Treatment of premature ejaculation

### 5.3.1 Vibrator-assisted start-stop exercises

In Study IV, we found that six weeks of vibrator-assisted start-stop exercises alleviated PE symptoms at group level, both in terms of ejaculatory function (e.g. ELT, feeling of control) and consequences (e.g. relationship difficulties and distress), thus supporting hypothesis H4. These results are in line with previous studies demonstrating the potential effectiveness of the present intervention. In a pilot study where 11 participants received an intervention equivalent to the VSS group, Jern (2014) found a medium-sized standardized mean difference on CHEES between pre- and post-treatment ( $d = .71$ ), which is comparable to the corresponding within-group effect size for the VSS group in the present study ( $d = 0.54$ ). In the first report on the effect of vibrator-assisted start-stop exercises, Zamar (2012) reported an 11-fold improvement in ELT in 61% of the sample. This effect is larger than what was reported by Jern (2014),

where the outcome was also measured by stopwatch, possibly due to Jern recruiting participants who had previously been unsuccessfully treated with pharmaceuticals (i.e., these individuals could have represented a treatment-resistant subgroup of the PE patient population). Another possible explanation is that Zamar, as the manufacturer of the device used in all three studies, could have arrived at inflated treatment effect sizes, as industry sponsorship and self-evaluation of commercial products generally associated with arriving at slightly larger effect sizes compared to research performed by independent researchers with no conflicts of interest (Lundh, Lexchin, Mintzes, Schroll, & Bero, 2017).

In summary, the concordant results from Study IV, Jern (2014), and Zamar (2012) provide replicated evidence showing that vibrator-assisted start-stop exercises can be used to treat PE.

In the study by Zamar (2012), a larger treatment effect was found for a group performing vibrator-assisted start-stop exercises, as compared to a group performing conventional, vibrator-less start-stop exercises. This indicates that the addition of the vibrating device increases the treatment effect. A possible mechanism of action is reduced penile sensitivity following exposure to vibration, since numbness and decreased sensory perception has been reported following vibrational exposure to genitals (Herbenick et al., 2009) and hands and arms (Malchaire et al., 1998). This suggested mechanism of reduced penile sensitivity is supported by the evident ejaculation-delaying effect of topical analgesics (Wyllie & Hellstrom, 2011).

In case the intervention would lead to a long-term reduction of penile sensitivity, this could perhaps in itself explain the treatment effect. If, on the other hand, a possible reduction of sensitivity was of a more temporary nature, the reduced sensitivity might in some way affect the effectiveness of the start-stop exercises. For example, longer ejaculation latency might contribute to extinction of a conditioned response. Another possible mechanism is that decreased penile sensitivity leads to longer IELT, which Perelman (2006) in turn hypothesized affords the individual time to learn the necessary skills to control ejaculation. However, since penile sensitivity was not measured in Study IV, it was not possible to test this hypothesized mechanism. It would also be interesting to compare the VSS intervention to start-stop exercises while

using a placebo device that does not vibrate, to elucidate whether the vibrations are an essential part of the intervention.

### 5.3.2 Psychoeducation and exercises related to interoceptive awareness

In Study IV, there were no statistically significant differences in outcome measures between treatment groups. This means that, contrary to our hypothesis, there was no additional treatment benefit when receiving psychoeducation and performing exercises meant to improve IA in addition to vibrator-assisted start-stop exercises. There were, however, some indications of larger improvements in the VSS+ than the VSS group. With regard to change in categorization on the primary outcome measure (i.e., strongly indicative of PE, indicative of PE, or low probability of PE) between pre- and post-treatment, 79% of the VSS+ group improved by one or two diagnostic categories (Jern et al., 2013), while the corresponding numbers for the VSS group was 41%. In terms of secondary outcome measures, the VSS+ group showed statistically significant within-group improvements on sexual distress, STAI trait anxiety and state anxiety during sex, as well as BSI anxiety. No statistically significant changes on any secondary outcome was observed in the VSS group. No statistically significant between-group differences were found, probably due to low statistical power, since pairwise comparisons of effect sizes did reveal some differences between the treatment groups (*ds* ranging from 0.38 to 0.66 on secondary outcome measures). Taken together, the added elements of psychoeducation and IA exercises seem to lead to improved outcomes overall. Whether or not to offer any or all of these additional interventions to the patient, considering possible additional benefit in relation to the increased cost in terms of time and effort, must be decided using clinical judgement in collaboration with the patient.

In Study IV, we found no clear indication that IA and PE were related. There was a negative correlation between the total MAIA score at baseline and change in PE from pre- to post-treatment, indicating that higher IA was associated with a larger treatment effect, however, it was not statistically significant ( $r = -.13$ ,  $p = .379$ ,  $n = 50$ ). As a manipulation check of the effect of performing IA exercises, we compared scores on IA scales post treatment. Contrary to our expectation, there were no differences between the treatment groups. Thus, the exercises did not have the intended effect, and we were unable to test whether improved IA would reduce PE symptoms.

A recent laboratory study demonstrated that a higher level of interoceptive awareness was associated with better ability to recognize genital changes following sexual stimuli in a sample consisting of women who experienced difficulties with genital sexual arousal (Handy & Meston, 2018). The researchers went on to recommend that “if a woman reports being unable to detect changes in her genitals during states of sexual arousal, techniques focused on increasing interoception could improve awareness of her genital arousal” (p. 406). In an intervention study, Bornemann, Herbert, Mehling and Singer (2015) had participants attend 13 weekly group sessions and perform daily practices including body scan exercises and breath meditation. Following this, the researchers were able to demonstrate small to moderate improvements on five out of eight subscales of MAIA ( $d$  ranging from 0.2 to 0.7), suggesting that it is possible to improve IA by training.

The hypothesized association between PE and a lack of awareness of bodily reactions during sex (Kaplan, 1975) is theoretically sound, but so far not thoroughly tested. The hypothesis is indirectly supported by the successful physiotherapeutical interventions where participants learn to control their pelvic floor musculature (La Pera & Nicastro, 1996; Pastore et al., 2014, 2012). Since Mehling et al. (2015) found improvements in IA following an intervention more extensive than the one employed in Study IV, where no effects were found, it follows that a more intensive IA training regimen may be necessary in order to elucidate any potential effects of IA training on PE.

### 5.3.3 The role of anxiety in treatment of PE

As anxiety, performance anxiety in particular, has traditionally been seen as an etiological component of PE, some treatment interventions aim at reducing anxiety as a means of reducing PE (Althof, 2016). As observed in Study IV, levels of anxiety and PE changed independently following treatment, since the effect on PE was practically identical in both groups, while the VSS+ group also displayed treatment effects on several measures of anxiety. This speaks against the idea that an improvement in anxiety in general would be followed by an improvement in PE. This is not to say that anxiety should not be a target of intervention in and of itself, however, it is perhaps not the most fruitful way to reduce PE symptoms. Distress directly related to PE could, on the other hand, be an interesting avenue of intervention (e.g., by normalisation of the problem,

improving communication between partners, or a broadening of the sexual script), since a reduction of distress by definition could reduce PE.

#### 5.3.4 Conclusions regarding treatment

An increasing body of evidence suggests that psychological interventions are viable options in the treatment of PE. Study IV shows that behavioral methods can lead to significant decrements in PE symptoms, since a majority of the participants improved in terms of their categorization on a validated scale of PE. In the present study, the treatment incurred no side effects and the available data implied a lasting treatment response. This is the third study to demonstrate the treatment effect, meaning that replicated results show that the vibrator-assisted start-stop technique improves PE symptoms.

Comparing psychological treatment to first-line pharmacological treatment reveals pros and cons with both modes of treatment. Pharmacotherapy of PE is associated with side effects, contributing to making treatment with dapoxetine unacceptable to most patients (Jern et al., 2014; Mondaini et al., 2013; Park et al., 2017). On the contrary, no side effects have been reported for the VSS intervention in the present or previous studies (Jern, 2014; Zamar, 2012). Regarding ease of use, taking a pill is quick and can give results in a few hours, while start-stop exercises require an investment of time and effort, and any payoff is not necessarily immediate. This aspect may however be weighed up if the psychological intervention would lead to long-term effects, whereas pharmacological agents are known to have a time-limited effect. As for convenience, dapoxetine must be taken 1 to 3 hours previous to anticipated intercourse, which hampers spontaneity.

Topical analgesics need also be administrated before intercourse can be initiated, which can be experienced as inconvenient. And while they effectively prolong ELT, optimal dosage might be difficult to attain, with risk of penile hypo-anesthesia, as well as contamination of the partner, with following vaginal or anal numbness (McMahon, 2015). Among other treatment options, pelvic floor rehabilitation has shown promising treatment effects (La Pera & Nicastro, 1996; Pastore et al., 2014, 2012), but is also time consuming, and the procedure can be somewhat invasive if anal electrode probes are used for biofeedback. Physical exercise has recently been tested as an intervention for PE, with results showing similar effectiveness for moderate exercise and

dapoxetine (Kilinc et al., 2018). However, lifestyle changes, such as increasing physical exercise, can be very difficult to attain and sustain, as known from decades of research on treatment of cardiovascular diseases (Teixeira et al., 2015).

Choosing between treatment options depends on how the goal of treatment is formulated. For example, Kilinc et al. (2018, p. 4) state that “The ultimate aim of PE treatment is to increase IELT.” Indeed, prolonging the time of intercourse can be an important goal, giving better opportunities to both everyone involved to enjoy the sexual activity. But it is not in itself necessarily sufficient, as individuals can be distressed regardless of their objectively measured IELT (Patrick et al., 2005). An opposing view was offered by Söderfeldt et al. (2017, p. 866):

*“Doubtlessly, and regardless of their actual IELT, many men experience distress over ejaculatory latency, but methods seeking to prolong the duration of vaginal penetration only confirm the underlying idea that sustained coitus is required in fulfilling (hetero-)sexual interactions. Extension of the sexual repertoire and liberation from the coital imperative have the potential to improve the sexual lives of many more than those who experience relief from SSRI-enhanced IELTs.”*

Broadening of the sexual script is a common theme in sexological therapy. For example, a goal of treatment in de Carufel and Trudels (2006) functional-sexological treatment of PE is to develop an appreciation for visual, emotional, tactile, corporal, verbal, and auditory stimuli, in order to increase enjoyment derived from sex, and decrease reliance on a set pattern or predetermined order of engagement of a sexual encounter.

Choosing the best treatment for PE is not only a question of looking at what treatment shows largest effects. The choice should also be tailored to the specific patient’s wants and needs, and the resources available. For some patients, the best alternative is a quick and convenient pill. For others, an investment of time and effort into learning to control one’s own body is necessary or more suitable. The results from the present study shows that psychological and behavioral interventions can be offered as adequate options for treatment.

## 5.4 Limitations

The prevalence of PE in the general population is estimated to be less than 4% (Althof et al., 2014). Consequently, despite the large size of the population-based sample, the number of men who plausibly could fulfill diagnostic criteria for the most severe subtype of PE is small. This may decrease power to find meaningful associations. However, the sample is still larger than many samples used by other authors in previous studies.

Furthermore, the measures used in the population-based sample does not allow for differentiating between diagnostic subtypes. In Study I, we therefore had to rely on a single diagnostic criterion as a proxy for lifelong PE, albeit the criterion that has often been argued to be the most important PE indicator, namely an ELT of less than 1 minute. It is possible that participants in the population-based sample who reported ELTs of less than 1 minute have experienced a significant reduction in latency time, and thus would fit better in the acquired rather than lifelong subtype. If this was the case, some of the variability could be readily explained by participants acquiring PE. However, the most interesting findings concern the opposite scenario, where participants who previously fulfilled the strictest diagnostic criterion (ELT < 1 minute) cease to do so, despite not receiving treatment. The first data collection was conducted before the current diagnostic criteria were published, and the nosology has varied considerably over time (it could well be argued that the debate regarding how PE should be defined and measured is far from resolved). But while the methods used might not be ideal for resolving the questions about stability over time, and while there were significant dropout which may skew and decrease generalizability of the results, Study I – to my knowledge – still represents the best available published data on the temporal stability of PE, and it points to the need to further examine the definition and diagnostic criteria for PE.

In Study II, the time lag between measurements was six years. If the possible causal associations between anxiety and PE function on a shorter time frame, they would perhaps not be noticed with the current setup. As such, the current null findings should not be interpreted as proof of there being no association over time. Further, with only two measurement points, cross-lagged panel models may not be able to take stable between-person differences into account,

which may bias cross-lagged estimates (Hamaker, Kuiper, & Grasman, 2015). And again, we were not able to differentiate between proposed diagnostic subgroups that may be relevant, since they might have different etiologies (Althof et al., 2014).

In Study III, the number of patients diagnosed with PE was quite small at  $n = 69$ . This was in no small part due to the fact that the majority of the sample was using some kind of pharmacological treatment that affected ejaculatory function, and therefore needed to be excluded from statistical analyses. The sample size is nonetheless sufficient to detect medium effect sizes, which means that the study had enough statistical power to find associations that would be meaningful in terms of etiology. It is, however, possible that there is some systematic difference between participants who do and do not receive treatment, which would reduce generalizability of the results. Regarding measures, the Godin Leisure-Time Exercise Questionnaire explicitly focuses on free time only. Therefore, some individuals who do physically straining work may have come across as leading a sedentary lifestyle in our data when in reality, the opposite was true. BMI is arguably also a flawed measure of physical fitness, since it does not differentiate between different kinds of mass. That is, a fit person who is heavy due to muscle mass may be interpreted as being overweight. These problems increase measurement error, which could possibly diminish observable effect sizes between PE and lifestyle factors.

In Study IV, there was considerable dropout in follow-up measurements, making interpretations of long-term effects difficult. The two treatment groups did not receive an equal amount of attention from the clinician, with the VSS group receiving about 20 minutes and the VSS+ group receiving about 45 minutes during the first meeting. Clinician attention is known to affect treatment response (Freedland, Mohr, Davidson, & Schwartz, 2011), and might thus explain some of the differences between the groups. Moreover, the groups were made more similar to each other than would perhaps have been optimal, as both groups responded to 32 items measuring interoceptive awareness several times. This might in itself mimic the effects of an interoceptive awareness improvement intervention, since all participants would likely know that interoceptive awareness is of interest, in turn decreasing internal validity. Taken together, these aspects of the study design reduce our ability to conclude that observed differences and similarities between groups are due to the intervention they received. Finally, treatment was delivered by the first author

only; having multiple clinicians providing treatment would have reduced the risk of any potential bias (such as the clinician's preconceived hypothesis of which treatment will be more effective) and shown generalizability of treatment effect across clinicians.

## 5.5 Future directions

If the field of sexual medicine, and research focusing on PE in particular, is to continue its move towards evidence-based practice, the most important step would be to collect more data of better quality. Much effort has been directed at ELT cutoffs, and the debate regarding optimal cutoff for diagnosis is ongoing. However, questions concerning the quality of evidence on which diagnostic subdivision have been proposed, and the usefulness of these subtypes, has been overlooked. Diagnostic subdivisions have been proposed based on retrospective self-reports from patients and clinical experience, which is unsatisfactory from an evidence-base point of view. An important first step would be to conduct prospective long-term studies of how PE symptoms vary over time, and also as a function of external factors that could be relevant. For example, how do PE symptoms vary as a function of different partners?

Regarding vibrator-assisted start-stop exercises, it would be interesting to include measures of penile sensitivity. This could test the hypothesized mechanism (i.e., that changes in sensitivity correspond to changes in PE symptoms). To test the effect of the vibrations, the intervention could be tested against an intervention using a placebo device that does vibrate.

In the present study, the exercises intended to produce improvement in IA did not have the expected effect: we assumed that IA would be associated with ejaculatory function, but found no robust evidence to suggest this is actually the case. However, this could be tested, for example, in a laboratory with a case-control design and objective measures of IA (e.g., heartbeat detection tasks). If the hypothesized association was indeed found, future intervention studies could employ a more intensive and comprehensive IA training, in an attempt to accomplish changes in control over ejaculation. It would also be interesting to see if there is any treatment effect of an IA intervention alone, compared to vibrator assisted start-stop exercises.

To further elucidate the hypothesis regarding the etiological role of anxiety in PE, future studies could utilize experimental or more fine-grained temporal observational approaches. Are there any patterns in day-to-day levels of anxiety and severity of PE? How do the physiological, cognitive and emotional aspects of anxiety before and during sex correspond to PE? Ecological momentary assessments as well as experimental methods could provide new insights into the complex phenomenon of PE, such as the possible mediating roles of sympathetic activation, cognitive distortion and interoceptive awareness.

In recent years, the importance of replication in science in general has been highlighted, after reviews suggesting a substantial number of research findings fail to replicate. This has been shown both for behavioral sciences (Gilbert, King, Pettigrew, & Wilson, 2016; Open Science Collaboration, 2015) as well as many areas of biomedical research (Begley & Ioannidis, 2015; Macleod et al., 2014; Prinz, Schlange, & Asadullah, 2011). Regarding the etiology of PE, myriad possible explanations have been proposed and tested, but few have been robustly replicated (Althof et al., 2014). For example, numerous molecular genetic studies aiming to elucidate PE etiology have been published in the past decade, with unconvincing records of replication (e.g., Jern & Ventus, 2017). Other parts of the field of PE research, such as treatment research (especially psychological treatment), is lacking in quantity and comparability of data (Cooper et al., 2015). An important step towards better quality of evidence in the literature concerning PE would be to conduct more replication studies.

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# Diagnosis, Etiology, and Psychobehavioral Treatment of Premature Ejaculation

Premature ejaculation is a common sexual complaint among males, and is often associated with decreased quality of life for the man and his partner.

This dissertation presents new evidence showing that symptoms are sometimes not as stable over time as previously assumed, and implications for diagnosis and treatment are discussed. Associations between anxiety, depression, lifestyle factors, and premature ejaculation are also analyzed. A treatment involving vibrator-assisted start-stop exercises is evaluated.