# PREMATURE EJACULATION AMONG MEN ATTENDING OUTPATIENT CLINIC IN UNIVERSITI SAINS MALAYSIA HOSPITAL AND IT'S ASSOCIATED FACTORS

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# Table of contents

# LIST OF TABLES

# LIST OF FIGURES

# ABBREVIATIONS

| | |
|---|---|
| 5-HT-1A | 5-hydroxytryptamine (serotonin) receptor 1A |
| AIPE | Arabic index of premature ejaculation (AIPE) questionnaires |
| APE | Acquired Premature Ejaculation |
| BMI | Body Mass Index |
| DASS | Depression, Anxiety, Stress Scale |
| DSM | Diagnostic Statistic Manual |
| ED | Erectile Dysfunction |
| GSSAB | Global Study of Sexual Attitudes and Behaviours |
| HUSM | Hospital Universiti Sains Malaysia |
| ICD-10 | International Classification of Diseases, Tenth Revision |
| IELT | Intravaginal Ejaculatory Latency Time |
| IIEF-5 | 5-item International Index of Erectile Function |
| ISSM | International Society for Sexual Medicine |
| KRK | Klinik Rawatan Keluarga |
| LPE | Lifelong Premature Ejaculation |
| MHQ | Middlesex Hospital Questionnaire (MHQ) |
| NHSLS | National Health and Social Life Survey |
| NVPE | Natural Variable Premature Ejaculation |
| PE | Premature Ejaculation |
| PEDT | Premature Ejaculation Diagnostic Tool |
| PEP | Premature Ejaculation Profile |
| PEPA | Premature Ejaculation Prevalence and Attitudes (PEPA) Survey |
| PLED | Premature-Like Ejaculatory Disorder |
| PRO | Patient Report Outcome |
| ROC | Receiver Operating Characteristics |
| SAS, DAS | Self-Rating Anxiety and Depression Scale |
| SD | Standard Deviation |
| SHIM | Sexual Health Inventory for Men |
| SPSS | Statistical Package for the Social Sciences |
| TSH | Thyroid Stimulating Hormone |
| UK | United Kingdom |
| UMMC | Univesiti Malaya Medical Centre |
| USA | United States of America |
| WHO | World Health Organization |

# ABSTRACTS

English version

## PREMATURE EJACULATION AMONG MEN ATTENDING OUTPATIENT CLINIC IN USM HOSPITAL AND ITS ASSOCIATED FACTORS

**BACKGROUND**: Premature ejaculation (PE) is a common male sexual disorder. Several factors have been proven to be associated with PE namely erectile dysfunction, general medical condition and psychological illness. However, there is little data on prevalence of premature ejaculation according to its four subtypes; lifelong PE, acquired PE, natural variable PE and premature-like ejaculatory dysfunction.

**OBJECTIVES:** To determine the prevalence of premature ejaculation and its associated factors among men attending outpatient clinic in USM hospital.

**METHOD:** A cross sectional study among men aged 18 to 60 years old was conducted from January 2014 to January 2015. Premature Ejaculation Diagnostic Tool (PEDT) and 5-item International Index of Erectile Function (IIEF-5) questionnaire were distributed. Participants who were identified as having premature ejaculation were further assessed with 21-item Depression, Anxiety and Stress Scale. Premature ejaculation was defined as PEDT score of 9 and above.

**RESULTS:** A total of 294 men recruited in this study with the mean (SD) age of 46.3 (10.1) years. The prevalence of PE was 21.4% (n=63). Among those with PE, 7.9% (n=5), 15.9% (n=10), 58.7% (n=37), 17.5% (n=11) were identified as lifelong PE, acquired PE, natural variable premature ejaculation and premature-

like ejaculatory dysfunction respectively. Multiple logistic regression showed that only mild erectile dysfunction (ED) [*adj. OR (95% CI):* 5.65 (1.89, 16.91)], p=0.002) mild-moderate ED [*adj. OR (95% CI):* 8.2 (2.72, 24.46), p: <0.001] and moderate-severe ED [*adj. OR (95% CI):* 6.0 (1.15, 31.23), p=0.03] were significantly associated with premature ejaculation. The proportion of depression, anxiety and stress among men with PE in this study were 20.6%, 33.3% and 14.3% respectively. More than two third of them discussed their ejaculatory problem with others.

**CONCLUSION:** The prevalence of premature ejaculation in this study was comparable with other regions. Erectile dysfunction was the only factor that significantly associated with PE but no association were seen between age, ethnicity, educational and occupational status, frequency of sexual intercourse, smoking status or underlying comorbidities. Men who were detected as having PE in this study also reported certain degree of anxiety, depression and stress.

**KEYWORDS:** premature ejaculation, erectile dysfunction, Premature Ejaculation Diagnostic Tool.

Versi Melayu

## EJAKULASI PRAMATANG DI KALANGAN LELAKI YANG HADIR DI KLINIK PESAKIT LUAR HOSPITAL USM DAN FAKTOR-FAKTOR BERKAITANNYA

**LATAR BELAKANG**: Ejakulasi pramatang (PE) adalah masalah seksual lelaki yang biasa. Beberapa faktor telah dibuktikan berkaitan dengan PE seperti erektil disfungsi (ED), masalah kesihatan umum dan penyakit psikologi. Walaubagaimanapun, hanya sedikit sahaja data mengenai prevalen PE berdasarkan empat sub kumpulan iaitu 'lifelong PE', 'acquired PE', 'natural variable PE' dan 'premature-like ejaculatory dysfunction'.

**OBJEKTIF:** Menentukan prevalen ejakulasi pramatang di kalangan lelaki yang hadir di klinik pesakit luar Hospital USM dan farktor-faktor yang berkaitan dengan nya.

**METODOLOGI:** Kajian hirisan lintang melibatkan 294 lelaki berumur 18 hingga 60 tahun yang hadir ke klinik pesakit luar. Peserta di rekrut semenjak Januari 2014 sehingga Januari 2015. Setiap peserta melengkapkan soalan yang diisi sendir mengandungi maklumat sosiodemografik, latarbelakang penyakit, soalan "Premature Ejaculation Diagnostic Tool" (PEDT), dan soalan 5 item "International Index of Erectile Function" (IIEF-5). Peserta yang dikesan menghadapi PE akan di teruskan dengan set soalan yang kedua mengandungi soalan-soalan berunsurkan sejarah sexual dan 21-item "Depression, Anxiety and Stress Scale" (DASS21)..

**KEPUTUSAN:** Sejumlah 294 lelaki yang menyertai kajian ini, dan purata umur adalah 46.3 (±10.1) tahun. Pecahan PE adalah 21.4% (n: 63), Dikalangan lelaki PE, pecahan empat jenis PE adalah seperti berikut 7.9% (n=5), 15.9% (n=10), 58.7% (n=37), 17.5% (n=11) untuk “lifelong PE”, “acquired PE”, “natural variable PE” dan “premature-like ejaculatory dysfunction”. Analisa multivariate menunjukkan hanya masalah erektil disfungsi (ED) ringan [*adj. OR (95% CI):* 5.65 (1.89, 16.91)], p=0.002) ED ringan-sederhana [*adj. OR (95% CI):* 8.2 (2.72, 24.46), p: <0.001] dan ED sederhana-teruk [*adj. OR (95% CI):* 6.0 (1.15, 31.23), p=0.03] yang berhubungkait dengan PE. Kekerapan masalah depresi, anxiety dan stress dikalangan lelaki PE adalah 20.6%, 33.3% dan 14.3%. Lebih dari dua per tiga dari mereka membincang masalah ejakulasi mereka bersama orang lain.

**KESIMPULAN:** Ejakulasi pramatang adalah masalah kesihatan seksual lelaki yang biasa dan prevalen nya adalah setara dengan kajian prevalen di tempat lain. Hanya masalah erektil disfungsi (ED) didapati berhubung kait dengan ejakulasi pramatang (PE), tetapi bukan faktor umur, bangsa, status pelajaran dan pekerjaan, frekuensi hubunagn kelamin, status merokok dan latar belakang penyakit. Lelaki yang dikesan mengidapi PE juga melaporkan masalah anxieti, kemurungan dan stres.

# CHAPTER 1: INTRODUCTION

Premature ejaculation (PE) has been hailed as the most common sexual disorder among men by most of studies (1-3). Unfortunately, the figure of the prevalence is highly variable depend on the location and operational definition of PE itself. Relatively ‘new’ among practitioner, mainly due to its uncertainty in arriving the diagnosis especially prior in the 80’s, PE is always underdiagnosed and under treated due to various barriers that exist in both patient and health practitioner (4, 5). Having said that, PE has been proven causing certain degree of negative impact to the men himself and subsequently to his spouse. The clinical attitude and understandings of PE have interestingly evolved over the years along with emerging of new data.

As the understanding of PE evolved over the years, recent evidence has discover another two PE variant in addition to two traditional PE subtypes (lifelong PE and acquired PE). The discoveries of Natural variable PE (NVPE) and premature-like ejaculatory disorder (PLED) are results from several large stopwatch epidemiological studies measuring ejaculatory latency time (term as IELT) where it revealed wide discrepancy with men’s own perception as having PE (6). The emerging of this data has suggested that the two new subtypes might suggest that the men in this subgroup (NVPE and PLED) do not ‘truly’ suffer from unintended early ejaculation, but rather as normal variation in men’s ejaculatory profile. Consequence of this, debate has started to raise whether the prevalence of true pathological PE is really that high among our population.

A renown sexologist, Waldinger emphasized that there was a misconception theory in most literature review in regards of PE, where PE were always thought to represent as male sexual disorder in general, rather than acknowledging the importance of the distinction between the syndrome [Lifelong PE (LPE) and acquired PE (APE)] and complaints [natural variable PE (NVPE) and premature-like ejaculatory disorder (PLED)]. Although PE is often reported as the most common male sexual disorder, these report were based on patient self-diagnosis and most likely reflect the community of NVPE and PLED rather than the actual syndromes of LPE and APE (which actually represent much lower prevalence) (7).

To date, the pathophysiology and pathogenesis of PE are still not well understood. Traditionally, PE is consider as a disorder as a consequence of psychopathology namely sexual performance anxiety and relationship performance distress (5). However, new emerging data has suggested that there are possibilities that neurobiological and genetic variation might contribute in lifelong PE (8). On the other hand, several recent epidemiological studies have significantly correlate certain chronic medical condition (e.g. diabetes, hypertension and obesity) and cardiovascular risk factors with PE (9, 10).

PE has been strongly associated with negative psychological impact. It is postulated that psychological factors (namely anxiety, depression and distress) may play a contributing role to PE and subsequently causing significant similar negative psychological impact to men with PE as well as to his spouse (11). Having said that, not much research are in cohorts as there in cross sectional in regards to this area hence only suggesting strong association, rather than labelled as contributing factors (12).

## 1.1 Justification of study

Much effort and focus has been allocated by the governing body in research of premature ejaculation. Prevalence and epidemiological study as well as clinical trial in premature ejaculation had therefore gained momentum for the past decades in searching new evidence for better understanding of PE. Having said that, lack of standardized operational definition have resulted in disparity among the outcomes (13). On the other hand, the emerging recent data that suggest hefty and significant discrepancy between the incidence of self-perception PE and community based stop watch prevalent studies, where this highlight current polarization of opinion as what defines PE into several subtypes for this moment (6).

Until this study was conducted, there were still little data regarding the prevalence of the four subtypes of PE except for Serefoglu et al. as well as Zhang and Gao et al. The determination of the prevalence of 'true' PE (lifelong and acquired PE) will illustrate the true figures for PE patient who are really indicated for pharmacological treatment and further specialized management.

On the other hand, although men's sexual health and issues are currently in increasing trend and interest among the investigators, data regarding the epidemiology and associated factor pertaining to PE are still scarce in our local context (14). Therefore, analyses regarding associated factor among the PE patient will later add to our understanding regarding the nature of this sexual problem particularly among east coast community in Malaysia.

# CHAPTER 2: LITERATURE REVIEW

## 2.1 Definition of premature ejaculation

First reported as rapid ejaculation in 1887, over the years, PE has been widely debated and studied in term of its operational definition. Past decades had seen generally 4 defining period in term of PE definition's evolution. The evolution of understanding regarding the disease from regarded as a psychosomatic disturbance and overanxious behaviour toward the latest understanding that involved neurobiological disturbance involving serotonin metabolism and genetic predisposing factors (15). First official definition was introduced by American Psychiatric Association in 1980, since then, debates ongoing among psychologist and sexologist to improve it definition and scope of treatment hence catalysing further epidemiology research and clinical trials pertaining to PE.

Further study searching and creating evidence based data mainly focused on standard operation in diagnosing PE had taken places overwhelmingly across the continent, mainly to redefine the construct in arriving at the diagnosis of PE.

### 2.1.1 Definition of premature ejaculation by ISSM (International Society for Sexual Medicine)

In 2007, International Society for Sexual Medicine has convened a meeting in Amsterdam, appointed a committee consisted of 21 international expert in premature ejaculation worldwide, to develop a consensus in reaching a diagnosing premature ejaculation. The aim was to create a first contemporary evidence based definition of PE with focused on lifelong PE. In previous years, PE which was defined by various leading organization namely American Psychiatric Association (DSM) and ICD (WHO)

which differ substantially among them, were considered all based from expert experience and authority nature instead of evidence based (15, 16). With the scarcity of literature review regarding PE, the earlier definitions were initially developed based on expert opinion with no definitive critical appraisal, without support from standardized clinical and epidemiological data. Therefore, after critical evaluation of published data, the 2007's committee unanimously agreed that the constructs that were necessary to define lifelong PE are time from penetration to ejaculation, inability to delay ejaculation, and negative personal consequence from PE (16). The meeting also highlighted a preliminary baseline data from a landmark Phase 3 dapoxetine trials that the two different classification of PE (lifelong and acquired) shared similar ejaculatory latency characteristic as well as negative personal impact to the men himself (17).

Second meeting took place in April 2013 in Bangalore, India where this time the new appointed committee comprise of 19 experts in PE and honorary ISSM member from underlying various medical specialty. Resonance from the first meeting in 2007 that there was insufficient published data, the latest meeting was mainly focused in proposing an evidence-based definition of acquired PE. Results from second ad hoc meeting, the committee unanimously agreed that lifelong and acquired PE are two distinct entity with diverse in etiology (18). However they agreed that lifelong and acquired PE in parts of their definition, shared a single unifying definition which are the constructs of time of penetration to ejaculation, inability to delay ejaculation and negative personal consequence from PE, where these can be mutually joint define both of these two subtypes (18).

Despite this, lifelong PE and acquired PE are still two different entities in context of demographically and etiologically where the presenting patient characteristics and/ or symptoms reported by these two subtypes differed from each other. The later ad hoc meeting also highlighted an additional key defining dimension of acquired PE in term of latency time of about 3 minutes or less will present a clinically significant and bothersome in men with this subtype as compare to lifelong PE which was set for less than 1 minute.

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

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

The Committee agreed that published objective evidence on PE is limited to studies of men with PE engaging in vaginal intercourse. There is insufficient information to objectively define problematic early ejaculation in the context of oral sex, anal sex, and same-gender sexual activity (18).

### 2.1.2 Definition of Premature Ejaculation by APA (American Psychiatric Association)

American Psychiatric Associations established the first definition of PE in their DSM-III in 1980. The definition stated that someone is consider as PE when ejaculation that occurs before the individual wishes it, because of recurrent and persistent absence of reasonable voluntary control of ejaculation and orgasm during sexual activity. Toward the evolution and emergence of new evidence, the definition

has evolved in each DSM edition where it saw the shifted of from using the criterion of control but not that of time, towards the definition that embraced the criterion of time not that of control. This evolution were partly parallel toward the favour definition by objective criteria (including ejaculation latency time and the number of penile thrusts) rather than subjective criteria (including diminished feelings of control and ejaculation at moment without wishing it) prior this, where may as well provide a clearer baseline definition to facilitate the emergence of new research and trials.

The recently published DSM-5 in 2013 defined PE includes an objective ejaculatory latency criterion and yielded based upon the same data that supported the ISSM definition of lifelong PE. The latest definition by APA also requires clinician to specify whether PE is lifelong or acquired and whether it is generalized or situational. The DSM-5 defines PE by four major criteria (19):

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

In addition, the DSM-5 define PE into the classification of mild PE, moderate PE and severe PE via the cut off time limit of intravaginal ejaculatory latency time (IELT) which is 30 seconds to 1 minute, 15–30 seconds and ejaculation occurring prior, at the start or 15 seconds into sexual activity respectively (19).

### 2.1.3 Definition of PE by ICD-10 (International Classification of Disease)

ICD10 by the World Health Organization published in 1992 defines PE as:

1. Inability to control ejaculation sufficiently for both partners to enjoy sexual interaction
2. An inability to delay ejaculation sufficiently to enjoy lovemaking, and manifest as either of the following:
    a. occurrence of ejaculation before or very soon after the beginning of intercourse (if a time limit is required: before or within 15 seconds of the beginning of intercourse)
    b. ejaculation occurs in the absence of sufficient erection to make intercourse possible

The ICD-10 uses both the criterion of “control” and that of a “very short” ejaculation time, defining the latter as a maximum of 15 seconds after penetration (20).

## 2.2 Classification of premature ejaculation

In earlier years, majority of specialist agreed that there were at least 2 distinguish type of premature ejaculation (PE). Proposal had been made as early as 1943 regarding the classification of PE. Schapiro et al came with the idea of PE consist of type A (the sexual hypotonic type) and type B (the hypertonic or hypererotic type). It was until 1989 that Godpodinoff et al reclassified this as lifelong (primary) and acquired (secondary) PE. The debates regarding classification continuous over the years as attempts had been made to classify PE into several subtypes (e.g. global vs. situational PE). In basic principal, clinician had agreed that to sub classify PE may involves several parameters among others were the time of onset; meaning lifelong PE might started this problem since his first ever sexual encounter) whereas acquired PE develop this problem later in life after a period of normal ejaculatory control. Some isolated expert has classified as ‘unintended’ ejaculation before penetration (ante

portas) or suddenly during coitus (intra moenia). Finally, it can also be labelled as in the presence (complicated) or absence (simple) of other sexual disorder that can be cause or caused of/by PE (1).

Subsequently, world of men's sexual health witnessed another ground breaking discoveries where in addition to lifelong and acquired PE, Waldinger and Schweitzer proposed another 2 new subtypes which are Natural Variable Premature Ejaculation (NVPE) and Premature-like Ejaculatory dysfunction (PLED). This discoveries were the results of several landmark observational studies of men with PE since 2005 added with community-based ejaculatory latency time (IELT) research (13, 21). These total 4 subtypes vary according to the duration of IELT, the course of the IELT duration throughout life, the frequency of occurrence of short IELTs and the cognitive and subjective experience of the IELT (7). Waldinger et.al explained that men with NVPE is not regarded as a disorder where they occasionally experience an early ejaculation and this is considered as a natural variation of the ejaculation time in men. On the other hand, men with PLED complain of PE while actually they are having a normal or even extended ejaculation time (8). All these subtypes of PE except for lifelong PE is probably related to psychological and/or cultural factors and/or interpersonal causes. In contrast, the consistent early ejaculation of lifelong PE is postulated caused by an underlying neurobiological functional disturbance.

This new classification and continuous research into the diverse phenomenology, aetiology, and pathogenesis of PE is expected to provide a better understanding of the four PE subtypes. Recently, using a similar methodology, Serefoglu et al and Zhang et al confirmed the existence of these four PE subtypes in a cohort of men in Turkey and China respectively (9, 10). Although the aetiologies and characteristic of PE subtype differ from each other, the new emerging data still suggest

that lifelong and acquired PE shared similar elements such as a lack of ejaculatory control and the presence of negative personal consequences suggest a potential for a single unifying definition; apart from another two new subtypes which are NVPE and PLED.

In concordance with this, doubt have been raised in past years whether PE prevalence rate is true in 20-30% worldwide. Lack of standardization in definition, especially most of prevalence study utilised the DSM-IV-TR definition which used vague terminology that is not well defined such as “complaints” or “marked distress” and there are ongoing debate as to whether or not this true rate of PE in general population. Based on consistent several epidemiological stopwatch studies, Waldinger and Schweitzer whom proposed to classify PE according to “syndrome” approach which consisted of LPE, APE, NVPE and PLED; suggest that the latter two subtypes (NVPE and PLED) were the reason for the high prevalence rate of PE previously reported in general population surveys (13). This statement that later evidence by several more specific epidemiological studies estimates the prevalence of lifelong and acquired PE to be around 2-5%.

Table 1: Summary of the symptoms of four premature ejaculation subtypes used in the classification of males with complaints of ejaculation prematurely (adapted by Waldinger et al. (6)

| Lifelong PE | Acquired PE | Natural variable PE | Premature-like ejaculatory dysfunction |
|---|---|---|---|
| Ejaculation occurs too early nearly in each intercourse | Early ejaculation occurs at some point in a man's life | Early ejaculation are inconsistent and occur irregularly | Subjective perception of consistent or inconsistent rapid ejaculation |
| With nearly every woman | The man had normal ejaculation experiences before | The ability to delay ejaculation may be diminished or lacking | Imagined early ejaculation or lack of control of ejaculation |
| From about the first sexual encounter | The onset is either sudden or gradual | The impression of diminished control of ejaculation | IELT is in the normal range or may be of longer duration |
| The majority of cases (80%) within 30-60 seconds or between 1 and 2 minutes (20%) | The dysfunction may be a result of urological or thyroid dysfunction | Ejaculation time maybe short or normal | Availability to delay ejaculation may be diminished or lacking |
| Remains rapid throughout the lifetime of the subject | The dysfunction maybe because of psychological or relational problems. | Psychotherapy should be considered as first-line treatment | The preoccupation is not better accounted for by another mental disorder |
| PE= premature ejaculation, IELT= intravaginal ejaculation latency time | | | |

In treatment aspect, NVPE and PLED were not a symptom or manifestation of real biological pathology, but rather a normal variation on sexual performance (13) hence the distinction between these four syndromes illustrates that prescribed medication only indicated as treatment for men with lifelong PE and in certain case of acquired PE. Obviously, one may combine medication with counselling or psychotherapy, but current consensus agreed that NVPE and PLED indicated only for counselling or psycho-education (7, 22). In addition, although these subtypes should be considered provisional, this may help healthcare professional addressing the concerns of men who do not qualify for the diagnosis of PE but seeking consultation help.

## 2.3 Prevalence of premature ejaculation

Review on the literature pertaining to premature ejaculation showed marked variability in prevalence rate among the population and mostly this is because they were lack of standardization and difficulty in defining what constitutes clinically relevant PE (22). Dubious definition without specific operational criteria, variation in modes of sampling and non-standardized data acquiring have led to tremendous variability in approximated prevalence. Among the causal factor of this variability that can be elicited were the difference when the operational definition used in each study (DSM-IV-TR vs. self-reported PE vs. IELT), different methodology (face to face interview vs. online/ mail self-assessment questionnaire) and venue of the study (random sampling among community vs. appointment clinic patient). Environment and local social culture had also believed to be contributing this variability of prevalence rate among different population.

The Global Study of Sexual Attitudes and Behaviours (GSSAB) was an international survey of various aspects of sex and relationships among adults aged 40–80 years old has interviewed 11205 men from 29 countries. Using a self-administered questionnaire the participants were assessed about their possible raised sexual issues for the past 12 month where the problem lasted for at least 2 month. Premature ejaculation was screened using the question “reached climax (experienced orgasm) too quickly?” and further relative severity were assessed by participants to classify among “occasionally, sometimes, or frequently” (1).

The surveys showed that East Asia and Southeast Asia reported the highest prevalence of sexual disorder compare to other regions of the world. In detail, 30.5 % (27.0, 34.1) of men in South East Asia complaint early ejaculation whereas, erectile

difficulties among men was also relatively common and showed identical prevalence across most regions (23). As a matter of fact, most remarkable finding was that the prevalence of both sexual disorder (PE and ED) from the aforementioned continent has reported approximately double as compared that reported in other regions (1).

In another comprehensive study showed a variety of prevalence rate among Asia-Pacific country. Using a PEDT questionnaire among the 4997 men had shown that the prevalence were ranging from 3% in Indonesia and 33% in South Korea with overall the prevalence in this continental was 31% (2). Malaysia in this study revealed the prevalence of 29% (19% probable PE and 10% PE). Interestingly, this study has highlighted the disparity of prevalence based on different diagnostic method where apart from the total prevalence of 31% diagnosed from PEDT, only 13% of the participant perceived themselves as PE (using of self-reported PE questionnaire). Similar unparalleled results was seen on the IELT demographic among the participant. Using the cutting points of IELT less than 1 minutes (22), the PEDT-diagnosed patient has shown only 18% of them of having IELT less than 1 minutes.

In explaining the wide discrepancy in the percentages of men who self-reported and those who were diagnosed with this condition using the PEDT, the author postulates that this may because the respondents might not fully understand regarding PE to essentially self-diagnose the condition and there might be possibilities of misunderstanding with other sexual dysfunctions namely ED (2). On the other hand, another revealing data was that majority of respondents who were classified as PE and probable PE based on PEDT questionnaire surprisingly recorded IELT values of greater than 2 minutes (74% and 85%, respectively), despite these men clearly have symptoms or complaints of PE and may be experiencing negative personal consequences related to these symptoms. Regarding this, the author explained that

there is possibility that these group of men fall under the categories of natural variable PE (NVPE) and premature like ejaculation disorder (PLED) (2). In addition, one hypothesis is that these differences may be also related due to the differences in cultural or religious backgrounds among the country in Asia-Pacific region.

A prevalence study of sexual problem done among urban population in Malaysia involve 430 men. Self-administered questionnaire were distributed among them and PE was defined as patient's estimation of IELT ≤ 2minutes. The study revealed that the prevalence of PE was 22.3% where the highest rate was seen among age group less than 39 years old (24).

On the other hand, a cross sectional study done by Tang et al which took place in a primary care clinic a teaching university hospital in Kuala Lumpur involved a bi-language version of PEDT questionnaires (original English version and translated Malay version) among 222 men. Using the PEDT questionnaire, this number was summed up by probable PE (N: 42, 20.3%) and confirmed PE (N: 42, 20.3%) hence producing a prevalence number of 40.6% (25).

An online or in person questionnaire study which utilised PEDT questionnaire as well as self-assessment of PE status was done in Singapore. The study involved 243 men aging from 14-55 years of age who were or had been active in heterosexual relationship for the past 2 years. The results based from PEDT questionnaire has showed that 34% of the respondent is having PE (20% confirm, 14% probable) while surprisingly another sets of questionnaire assessed on similar group of men (self-assessment of PE) results showed only 16% of the respondents felt that they had PE (26).

Serefoglu et al was believed to be the first who study regarding the prevalence of four PE subtypes. Took place in 2009, the study involved 2593 heterosexual couple across the urban and rural era in Turkey, whom had active sexual relationship 6 month prior this study. All participants were interviewed by a trained interviewer where they were screened with Turkish version Premature Ejaculation Diagnostic Tool (PEDT), Premature Ejaculation Profile (PEP) and Arabic Index of Premature Ejaculation (AIPE). Those who were identified as men with ejaculated prematurely (basically a group of men who not satisfied with their estimated ejaculation latency time) where then evaluated their medical and sexual history regarding their according to the description describe by Waldinger et al.(6) to be further classified into LPE, APE, NVPE and PLED.

The study has found that the prevalence of PE among their participant was 20.0% (n=512 men). Furthermore, among the entire study population, they founded that the prevalence for each subtypes of PE were as follow; lifelong PE 2.3% (n=58), acquired PE 3.9% (n=100), natural variable PE 8.5% (n=213), and premature-like ejaculatory disorder 5.1% (n=131). The author concluded that the prevalence of four subtypes PE yielded in this study was correspond with the presumption by Waldinger et. al. (6) that the large number of men with PE were in fact contributed by natural variable PE (NVPE) and premature-like ejaculatory dysfunction (PLED), whereas the actual prevalence of lifelong and acquired PE is much smaller between 2 and 5%.

Table 2: Summary of the prevalence rate of premature ejaculation.

| Year | Author | Origin | Operational criteria for PE | Number of sample | Prevalence rate |
|---|---|---|---|---|---|
| 2007 | H.Porst et al. (27) | USA, Germany, Italy | Distress and control over ejaculation | 12133 | USA:24% Germ:20.3% Italy: 20.0% |
| 2008 | Giuliano et al. (28) | France, Germany, UK, Poland, Italy | Premature Ejaculation Profile (PEP), IELT | 1115 | 18.0% |
| 2008 | KF Quek et al. (24) | Malaysia | Self-reported PE and IELT | 430 | 22.3% |
| 2010 | HJ Park et al. (29) | Korea | Suffering from PE (local questionnaire by PE study group) | 2037 | 27.5 |
| 2010 | H Son et al. (30) | Korea | Suffer from PE (DSM-IV-TR) | 600 | 18.3% |
| 2011 | PG Andaikan et al. (26) | Singapore | PEDT | 243 | 20.0% |
| 2011 | WS Tang et al. (25) | Malaysia | PEDT | 207 | 40.6% |
| 2012 | Mialon et al. (31) | Switzerland | Distress and control over ejaculation | 2507 | 11.4% |
| 2012 | O Shaeer et al. (32) | Middle east | Ejaculate before the person wishes to ejaculate at least sometimes, IELT | 804 | 83.7% |
| 2012 | McMahon et al. (2) | Asia Pacific | PEDT questionnaires | 4997 | 31.6% |
| 2013 | Zhang et al. (33) | Hong Kong | Self-reported Premature ejaculation | 728 | 4.7% |
| 2014 | Gao et al. (34) | China | Self-reported PE | 3016 | 25.8% |
| 2014 | Silangcruz et al. (35) | Philippines | PEDT questionnaire | 101 | 27 |
| 2014 | Lee JH (36) | Korea | PEDT questionnaire | 2591 | 25.5% |

Further analysis in this study also revealed that comorbidities were more prevalent among men with PE complaints especially with the subject with acquired PE. The author presumed that this group of subtype whom in view they had normal ejaculation experience before the onset of either psychological or biologic problem, they report comorbidities more than patients with other symptoms or subtypes of PE.

Among comorbidities that significantly (P value of <0.001) related to acquired PE was hypertension (50.2%), sexual desire disorder / dysfunction (44.3%), diabetes mellitus (35.7%), and prostate enlargement (26.5%). In addition, the component of health seeking behaviour of the study has revealed that significant proportion of men who were classified as lifelong PE and acquired PE were the group who seek treatment via consulting a physician regarding their problem.

Gao et al also conducted almost a similar study in 2011 (37). The aim was to determine the prevalence of these four subtype of PE as well as the impact of IELT and erectile dysfunction on depression and anxiety among patients with PE. This cross sectional study was done among 3016 sexual active men in Anhui province, China. Face to face interview was conducted regarding their satisfactory of timing of ejaculation, as well as estimated IELT and further detail of PE such as duration and experience. In addition, they also utilised the International Index of Erectile Function – 5 (IIEF-5) and Zung Self-Rating Anxiety and Depression scale (SAS/SDS).

This study has found that among 3016 men interviewed, 778 men (25.8%) complained of PE. The distribution of the four types of PE was as follows; LPE 12.34% (n=96), APE 18.77% (n=146), NVPE 44.09% (n=343) and PLED 24.81% (n= 193). They summarized that men whom they identified as PE presented significantly shorter IELT and higher rates of ED, anxiety and depression as compared to men without PE. Further analysis has shown that among the four subtypes of PE, APE reported higher rates of ED (38.36%), anxiety (35.62%) and depression (13.01%). In regards the self-estimated IELT, men with PLED estimated the highest mean IELT 3.36 ± 1.18 minutes whereas men with LPE reported the lowest IELT with 1.33 ± 0.74 minutes. Overall, all men in four subtypes of PE showed negative relationships between IELT/IIEF-5 score

and SAS/SDS score with after an adjusted r values, these negative relationship were strongest in PLED patients than in men with other subtypes of PE (37).

2.4 Intravaginal Ejaculatory Latency Time (IELT)

Intravaginal Ejaculatory Latency Time (IELT) has been established as one of the important quantitative parameter in assessing one's ejaculatory status; apart from subjective patient-reported outcome (PRO), number of thrust and PEDT score. In modern era, IELT had been the favourite dimension or criteria as operational definition of PE among PE related studies and clinical trials. Introduced in 1994, Waldinger has introduced a straightforward and measurable method to describe PE where it's define as the time from the start of vaginal intromission to the start of intravaginal ejaculation (38). IELT can be obtain by two ways; which is by stopwatch or via estimation from the man himself. Several authors have proven that patient self-estimation of IELT correlates reasonably well with correspond stopwatch IELT (39). Patient self-estimation IELT may be useful as a compliment to arrive in diagnosing PE where usually can be adequately achieved via patient's sexual history and perceive control of ejaculation.

In a large observational epidemiologic study to quantify IELT consisted of 1587 men documented that men without PE had recorded mean IELT of 9 minutes (range of 7–13 minutes) as compared 3 minutes for men with PE (n=207). Despite the difference, the study emphasized on the finding that suggest considerable overlap between the two groups (39). In addition, men with PE in this study has also perceived themselves as having poor ejaculatory control, dissatisfaction with sexual intercourse, interpersonal difficulty with their partner as well as higher ratings for personal distress if compare with men without PE. This has lead the establishment by the researcher to consider the importance of subjective factors (patient-reported outcomes) including of

control, distress, and satisfaction when diagnosing and treating PE. The researchers emphasized that PE is actually not a ‘uni-dimensional disorder of time’ but rather a multidimensional dysfunction that encompasses both objective (time duration) and subjective parameters (39).

Waldiner et al. also famously introduced the ‘ejaculation distribution theory’ in which they postulated that PE is part of a normal biological variation of the ejaculatory latency time among men rather than merely a psychological disorder. In description, any random group of men can be part of a small subgroup of men with early ejaculation, another subgroup with delayed or even absence of ejaculation alongside the majority of men who have a ‘‘normal’’ or ‘‘average’’ ejaculation time. In addition, they also in principle believed that possible genetic and neurobiological contributed in determining in the duration of the IELT (8).

Consistent with this notion, Waldinger et al. proved his theories with several studies including a statistic in five nation stopwatch study where he concluded that IELT values lower than 0.5 and 2.5 percentile should be used as cut-off points for abnormality (where in this study yielded duration of less than 1-1.5 minutes) (7). Subsequently, in a clinical cohort study among men with lifelong PE, majority ejaculated less than 1 minutes, whereas 10% remaining within 1-2 minutes. In addition, the author also came with the idea of lifelong PE is a probably manifestation of a neurobiological phenomenon. It is also should be noted that the prevalence of about 2% of men having IELT values of 1-1.5 minutes (which were labelled as possible lifelong PE) does not resemble to the high prevalence of 20-30% of PE seen in most of epidemiology study of PE (7).

In conjunction with this, ISSM in its second committee meeting had unanimously agreed that a self-estimated or stopwatch IELT of 3 minutes was identified as a valid IELT cut-off for diagnosing acquired PE, on top of less than 1 minutes for diagnosing lifelong PE (22). The admission of dimension of IELT cut-off point was also followed by APA in their new edition of DMS-V where cut-off point of less than 1 minutes is required in arriving of PE diagnosis (19).

Having said that, stopwatch measures of IELT during intercourse have the potential disadvantage of being intrusive and potentially disruptive of sexual pleasure or spontaneity (22). Furthermore, IELT may not adequately categorised patients as 'pathological premature ejaculation' because some patient with brief IELT report little or no bother and are therefore asymptomatic and not 'suffering' from PE. Alternatively, other subjective measures including Premature Ejaculation Diagnostic Tool (PEDT), Patient Reported Outcome (PRO) or even self-perception regarding poor ejaculatory control, may and should be consider the best measure in detecting PE.

## 2.5 Aetiology of premature ejaculation

Although premature ejaculation has been reported as early as in 1800s, the exact pathogenesis is yet to be well understood. Early PE investigations and researches did not often differentiate between the types of PE, but majority of aetiological study involve lifelong PE (8). Lifelong PE has been described as the most severe form of PE where men that suffer from this ejaculates too early nearly in each intercourse and believed to be remain throughout his lifetime (6).

Results from in vivo animal research, human neurobiological, genetic as well as pharmacological research in the last two decades has contributed to our better understanding of the role of the central and peripheral nervous system in lifelong PE.

It is postulated so far, that neurobiological and genetic predisposing are two main contributing factor in lifelong PE, but still partly understood and a lot need to prove.

The introduction of SSRI's and its application to delay ejaculation in men with PE has catalysed the research in neurophysiological aspect of PE. Serotonin is the neurotransmitter of greatest interest in the control of ejaculation and has the most evidence based data in animal and human models. Animal and human psychopharmacological studies had shown that lifelong PE is related to dysfunctional of some central serotonergic neurotransmission (5-hydroxytryptamine (HT)-2C and/or 5-HT-1A receptor) and as serotonin tends to delay ejaculation, serotonin dysregulation may have intrinsically lower ejaculatory thresholds among men with LPE (7).

On the other hand, genetic variations have been suggest to result in significant differences in the neurobiological factors associated with PE. A survey of family members of 14 men with a lifelong IELT less than 1 minute has shown that IELT of less than 1 minute was found in 88% of these first-degree male relatives of men with LPE. However, the author stressed that lifelong PE is not a classical Mendelian inheritable disorder affecting all the male family member. This was later confirm by a Finnish twin research where Jern et al. it is reported a moderate genetic influence of 28% on PE. The first DNA-based study on PE was performed by Janssen et al. in 89 Dutch men with LPE compared with a cohort of mentally and physically healthy Dutch Caucasian men which this study concluded that there is a specific genotype of polymorphism of the 5-HT-1A receptor that associated with faster ejaculatory time (22).

The latest postulation suggested that, in related to the role of oxytocin release, despite LPE men suffer from diminished controlled of ejaculation, these men also suffer from early erection (erectio praecox), and an immediately detumescence of the penis after ejaculation (detumescence praecox)(7).

## 2.6 Associated factor of premature ejaculation

Recent evidences have suggested that pathophysiology of lifelong PE may be contributed by neurobiological and genetic variations in some men. Meanwhile, acquired PE is understood to be contributed by either psychological (sexual performance anxiety, psychological or relationship problem) or organic where commonly it is being associated with other comorbid disease such erectile dysfunction, hyperthyroidism and occasionally prostatitis and cardiovascular disease (18).

### 2.6.1 Socio-demographic factors in premature ejaculation

Advancing age is proven as not to be a risk factor for PE and this has been documented by several studies (2, 27, 40-42). Traditionally, PE was postulated to be closely related to younger age group. Several explanation has been given for example, lack of sexual experience, as well as there was possibilities that younger men with short latencies may have higher threshold for defining rapid ejaculation as a lack of ejaculatory control but this theory was never proven. Contrary to this understandings, a study involving 1410 men showed that younger individuals (18-29 years old) do not appear to be at any greater risk for PE as compared to older population. This study reported the prevalence of PE appeared constant over all age group from 18 to 59 years old (41). Similarly, a large internet-based survey among 12133 men has showed that there was no significant relationship between age (24 to 70 years old) and the

prevalence of PE which was contradict with ED where the prevalence dramatically increase with age (27). It is believed that public may seem to be more aware of ED (much popular sexual disorder) exclusively in older group, leading the younger group a perception that PE is the only major sexual dysfunction to manifest in their age group despite the fact that PE is constantly prevalent across at all age group leading to inaccurately concordance believes with the traditional theory (41).

However, in regards of recent introduction of new PE subtypes, along with more specific operational definition of PE, few data has suggested that older men are actually seen as higher risk in developing only in acquired PE (9, 10, 17). Consistent with the predominant organic aetiology (underlying comorbidities) among them, these studies also have reported that men with acquired PE were significantly older than men with other PE subtypes. Similarly in a study that measures IELT as baseline epidemiological characteristic among men with PE, acquired PE group reported slight older age than other subtypes, as they were also associated with mild ED (17). This was later also has been proven that the increase incidence of ED in acquired PE and the epidemiology of ED.

There were several studies that investigates the relation between PE and men's educational and occupational/ social status background. Interestingly, the data showed mixed preference. In 1999, Lauman et al. has reported the findings from her study of sexual behaviour in a cohort of U.S adults that men with PE were from the less educated group of people. Specifically, the college graduate group were less likely to report early climax then the group without college experience or not completing school (41). This is explained by the author that, health status is considered as part of a function of one's educational status. In other words, individuals with more education

are likely to have greater quality of life, including improved emotional and physical health and thus less likely to experience PE.

Interestingly, in 2005 Basile Fasolo et al. on their observation among 569 men with PE showed the other way round with higher educational and economic status showed a positive correlation to PE. They postulated the possibility of higher socioeconomic status leading to a greater attention to health issue rather than a true contributory risk of developing PE (43). These results, although contradicting each other, corroborate the conclusion that perhaps health status is a more direct predictor of the prevalence of PE rather than educational or social status per se. Similarly, a study has shown that there was no significant differences in prevalence of PE recognizable in men with different household income, as well as the factor of 'current employment status' and 'financial problems' including them in Southeast Asia (1).

In 1974, Kaplan et al. has suggested that PE was associated with low sexual frequency. The possible reason behind this theory was that men who experienced low sexual frequency resulted them fewer opportunities to learn and practice on how to control their ejaculation, as well as there is possibilities of sexual-novelty lead anxiety performance. However, towards recently epidemiological study has showed conflicting data. An observational study done by Laumann et al on 1039 men regarding their low sexual frequency (defined as not more than once per month) was not significantly related to PE. Although the author could not explain this findings, they also found similar pattern of no dissociation of PE with 'less thinking about sex in a week' and 'masturbation at least once per month' (41). However, in more recent study among larger group of men with PE done in 2005, has shown that infrequent sex tended to be associated with PE (1). However, this large epidemiological studies involved multiple continental and variety of sampling method reported the association between

low sexual frequency (less than once per month) and PE was only at several region such as East Asia [OR 2.1, 95%CI (1.0,4.1)] where the same region they reported the highest PE prevalence among other participant from other continental. Overall, despite what would seem to be reasonable assumption, the link of frequency of sexual intercourse and PE still cannot be explain with certainty (42).

On the other hand, PE also has been long linked with sexual anxiety and the novelty of sexual experience, hence produce the postulation that married men would seem to be less likely to report PE if one assumes that they are more comfortable and less anxious about sexual encounter with their long-term spouse, compare to the non-married men who might report higher rates of PE in view of less-secure relationship. However, a study showed that the prevalence of PE does not related significantly among married, never married or divorced, separated or widowed men (1). Interestingly, the non-married men reported higher rates of all kind of sexual dysfunction than married men in this particular study. The author concluded that there might be no difference in anxiety to perform between married and non-married men. Related to this matter, duration of marriages showed mixed data in term of relationship with PE. A prevalence study of PE and its associated factor among 2593 men showed significant relationship in duration of marriages and PE (9). However, a similar study done in different region among 3016 men reported contradictory where there was no significant relationship found (10). Having said that, the later study did showed significant correlation of PE and frequency of sexual frequency in month. Despite the inconsistent results between the studies (in pertaining duration of marriages), this was done in total different continental population and the method of sampling was totally different between these two.