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# Prevalence and associated factors of female sexual dysfunction among type 2 diabetes patients in Indonesia: A systematic review and meta-analysis



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#### ABSTRACT

Background and aims: Female sexual dysfunction (FSD) is a neglected chronic complication of diabetes. However, there is a scarcity of data in Indonesia, which is currently ranked as the 5th in the world for the number of people with Type 2 Diabetes (T2D). Our study aims to analyze the prevalence and factors of FSD among T2D patients in Indonesia.

*Method:* Literature searching was performed in PubMed/Medline®, CINAHL®, Embase®, Proquest®, Scopus®, local journals and libraries. All studies in searching keywords "sexual", "diabetes" and "Indonesia" with Medical Subject Headings (MeSH) terms were included, without time or language restriction. Pooled prevalence and odds ratio of associated factors of FSD were analyzed using STATA.

*Results:* Ten studies comprised 572 females with T2D were included in this review. The pooled prevalence of FSD reached 52% (95% CI = 0.49–0.56; I<sup>2</sup> 93.9%, p < 0.001). After removing one study that was conducted with an unstandardized questionnaire cut-off value, the pooled prevalence of FSD was 62% (95% CI = 0.58–0.66; I<sup>2</sup> 68.7%, p = 0.001). Age more than 45 years old and or menopause, and the use of antihypertensives were associated with FSD. While Hemoglobin A1c (HbA1c) is only correlated with a desire for sexual dysfunction. *Conclusion:* FSD was prevalent among T2D patients in Indonesia and was associated with age more than 45 years old, menopause, and the use of antihypertensive medications.

#### 1. Introduction

The prevalence of diabetes mellitus, a chronic progressive hyperglycemic state, is consistently increasing worldwide. According to the International Diabetes Federation (IDF), Indonesia is the fifth most prevalent country with diabetes, which corresponds with its complications [1]. Sexual dysfunction is one of the chronic complications of diabetes that may affect both males and females. Moreover, female sexual dysfunction (FSD) among patients with diabetes is often neglected, with doubled risk and relatively high prevalence, ranging from 20 to 80% [2–5]. Malaysia, the majority of the population similar to Indonesians, has a prevalence of FSD of 26.4% [6] while Poland, a European country, has a prevalence of 68.4% [7]. However, within the

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Abbreviations		IDF	International Diabetes Federation
		IQR	Interquartile Range
ARE	Arylesterase	ISSWSH	International Society for the Study of Women's Sexual
BISF-W	Brief Index of Sexual Functioning for women		Health
CI	Confidence Interval	JBI	Joanna Briggs Institute
DHEA	Dehydroepiandrosterone	MSD	Male Sexual Dysfunction
DHEAS	Dehydroepiandrosterone sulfate	MeSH	Medical Subject Headings
DSM-5	Diagnostic and Statistical Manual of Mental Disorders,	OR	Odds Ratio
	Fifth Edition	PON-1	Paraoxonase-1
FSD	Female Sexual Dysfunction	PRISMA	The Preferred Reporting Items for Systematic Review and
FSFI	Female Sexual Function Index		Meta-analyses
GRADE	Grading of Recommendations Assessment, Development	PROSPE	RO Prospective Register of Systematic Reviews
	and Evaluation	SAGE	Survey Study on Global Ageing and Adult Health
HADS	Hospital Anxiety and Depression Scale	SD	Standard Deviation
HbA1c	Hemoglobin A1c	T1D	Type 1 Diabetes
$I^2$	I-square	T2D	Type 2 Diabetes
ICD-10	International Classification of Diseases 10		

Indonesian population itself, which has a variety of ethnicities, languages and beliefs, it certainly has different characteristics, so this research is very important.

Sexual health is a state of complete physical, emotional, psychological, and social well-being in sexual function [8]. The diagnosis of FSD is established based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), International Classification of Diseases 10 (ICD-10), and the International Society for the Study of Women's Sexual Health (ISSWSH) diagnostic criteria for FSD. In addition, standardized questionnaires such as the Female Sexual Function Index (FSFI) are often practically used in community-based studies that may identify the desire, arousal, lubrication, orgasm, satisfaction, and pain dysfunction [9,10]. Even though the diagnostic criteria of FSD is clear, FSD is often unrecognized due to a lack of complaints from female diabetes patients or rarely asked in between routine physician examination sessions.

Unlike male sexual dysfunction (MSD), FSD is not only associated with metabolic factors but also with psychological, social, and cultural backgrounds [11]. Esposito et al. [12] which analyzed female patients without severe diabetes complications revealed depression and marital status as the main causes of FSD among the study population. A study in Iran found approximately 58.7% of female diabetes patients with FSD had depression, and 96.7% had anxiety assessed by Hospital Anxiety and Depression Scale (HADS) [13]. Hence, FSD resulted from a complex metabolic, psychosocial, and cultural interaction. Previous studies also identified several factors associated with increasing FSD in T2D, such as older age, menopause, longer duration of diabetes, obesity, dyslipidemia, smoking, hypertension, diabetes comorbid and complications, hyperglycemia, medication, depression, and anxiety [2,7,12–14]. Nevertheless, there were conflicting findings regarding associated factors among these studies.

Asian populations have different metabolic characteristics, beliefs, and sociocultural background compared to the Caucasian population. Particularly Indonesians, a population with diverse cultural and ethnicity backgrounds, are generally more sexually conservative than European or the majority of Asians. Most of these people rarely complained about their sexual matters, either because of lack of health access or fear of taboo stigma from the society [15]. Previous systematic review in Italy [16] and a meta-analysis in Iran [3] have summarized the prevalence and several associated factors of FSD among diabetes population. However, these reviews did not include the Indonesian population whose characteristics were distinctive to other Asian or Caucasian population [3,16]. In addition, microvascular complication prevalence in Indonesia (56%) was higher than global data (18.8%), thus portraying the increasing risk of FSD as a part of microvascular complication compared to other countries [17,18]. In a nutshell, specific data on FSD in Indonesia was needed. This systematic review aims to investigate the prevalence and associated factors of FSD among T2D patients in Indonesia.

# 2. Methods

This meta-analysis was conducted based on The Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA) recommendation. The protocol of this review was registered at the Prospective Register of Systematic Reviews (PROSPERO), code number CRD42020189630. The inclusion criteria were articles on adult females (age >19 years old) with T2D that studied FSD and were conducted among the Indonesian population. Studies on animals or without FSD prevalence data were excluded. The primary outcome of this metaanalysis was the pooled prevalence and associated factors of FSD in Indonesia.

# 2.1. Searching strategies

Literature searching was performed in September 2020 from various databases, including PubMed/Medline®, CINAHL®, Embase®, EBSCO-host®, ProQuest®, and Scopus®, along with Indonesian local journals or databases and libraries. All observational and experimental studies were included in this review. The keywords that were used in the searching strategies include "sexual", "diabetes" and "Indonesia". MeSH terms in English and Bahasa were also applied without time of study or language restriction. Grey literature such as abstract, proceeding and thesis were included in the literature searching. The list of keywords from respective databases were shown in Table S1.

Female sexual dysfunction was defined as a diagnosis made by clinical physician from validated questionnaires such as FSFI, Survey Study on Global Ageing and Adult Health (SAGE), Brief Index of Sexual Functioning for Women (BISF-W), and Sexual Function Questionnaire (SFQ). T2D was defined by a clinical physician based on the American Diabetes Association criteria for T2D. Literature searching was accomplished by one author, whereas both title or abstract screening and fulltext reading were reviewed by two independent investigators (AP and CA), with the help of Covidence® online software. Any disagreements were discussed and resolved by a third independent investigator (DLT).

## 2.2. Data extraction

Data extraction comprised of author, year of publication, city, study design, sample size, clinical setting, diagnostic criteria, and number of participants. When available, factors in FSD were also identified in percentage, mean (standard deviation; SD), or median (interquartile range; IQR), including duration of diabetes, obesity, medication, age, menopause, anxiety, depression, HbA1c, occupation, parity, physical activity, education, types of diabetes treatment, contraception, and lipid profile. The prevalence of FSD in proportion or percentage and associated factors in odds ratio (OR) were extracted as the primary outcome of this review.

#### 2.3. Quality assessment

Selected studies were critically reviewed for risk of bias with the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence study [19]. Studies with a score of more than five were assessed as good quality studies. We also evaluated the quality of outcomes with the Grading of Recommendations Assessment, Development and Evaluation (GRADE) [20].

# 2.4. Statistical analysis

Meta-analysis was performed using STATA version 13. We used a random-effect model to analyze the pooled prevalence of FSD and identify the 95% confidence interval (CI). Sensitivity analysis was conducted by removing one study by Fitrika et al. [21] that used an

unstandardized FSFI score cut-off value. The heterogeneity of studies was analyzed by using I-square (I<sup>2</sup>) test which was grouped into low (<25%), moderate (25–75%), and high heterogeneity (>75%). Analysis for OR of the associated factors in FSD, pooled OR, 95% confidence interval and p-value were identified. P-value of <0.05 was considered significant.

#### 3. Results

A total of 975 studies were obtained through the searching strategy (Fig. 1). After removing duplicates, followed by abstract or title screening and full-text reading of a total of 38 studies, we obtained a total of 11 studies. However, we did not find the full text of a study by Asmalinda et al. [22], therefore, only ten studies were included in the analysis (Table 1). The baseline characteristic of ten studies is shown in Table S2.

Based on the quality assessment with the JBI Critical Appraisal Checklist, only five studies had good quality (Table S3). All included articles were cross-sectional studies that comprised 572 females with T2D. Five studies [14,23–26] were performed in the community setting, whereas the others [21,27–30] were in hospital settings. Nine studies [14,21,23–25,27–30] applied FSFI questionnaire to diagnose FSD. Only one study by Hastuti et al. [26] used the SAGE questionnaire for the diagnosis of FSD. Half of the studies were held in Java while the others

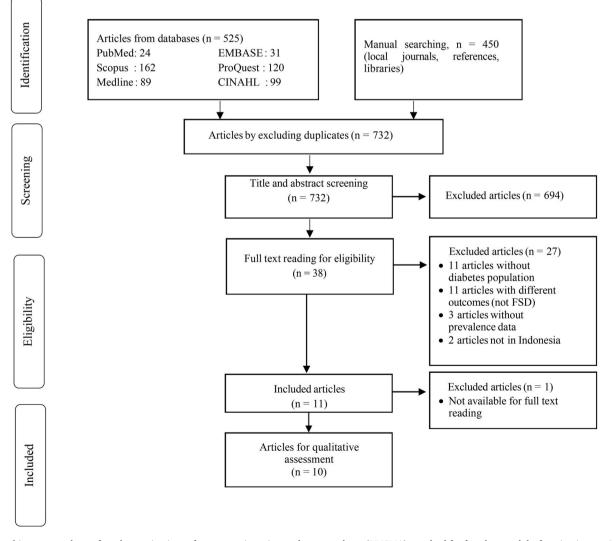


Fig. 1. Searching strategy by preferred reporting items for systematic review and meta-analyses (PRISMA) standard for female sexual dysfunction in type 2 diabetes in Indonesia. FSD = female sexual dysfunction.

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## Table 1

Description of selected studies.

No	Author (years)	City/Clinical Setting	Ν	Diagnostic Tool	Prevalence of FSD	Odds Ratio of The Associated Factors
1.	Amelia et al. [27] (2015)	Banjarmasin/ Hospital	30	FSFI	63.3%	N/A
2.	Saraswati et al. [14] (2019)	Semarang/ Community	103	FSFI	74.8%	Age >45 years old: OR 4.4 (95% CI 1.2, 14.5; p = 0.02) Menopause: OR 3.3 (95% CI 1.3, 8.4; p = 0.012) Antihypertensives: OR 8.08 (95% CI 1.78,36.7; p = 0.007)
3.	Insiyah et al. [23] (2018)	Surakarta/ Community	60	FSFI	53.3%	Depression: OR 7.7 (95% CI 2.3,25.5; $p=0<001$ ) Anxiety: 7.7 (95% CI 2.17,27.4; $p=0.002$ )
4.	Lamuhammad et al. [28] (2017)	Lampung/Hospital	42	FSFI	54.8%	Duration diabetes: OR 8.6 (95% CI 2.1,35.3; $p = 0.0029$ )
5.	Tatiana et al. [24] (2017)	Medan/Hospital	85	FSFI	63.5%	Duration diabetes: OR 10.1 (95% CI 3.6,28.2; p < 0.001) Obesity: OR 5.7 (95% CI 2.2,15; p < 0.001) Consumption of drugs: OR 6.1 (95% CI 2.3,16.4; p < 0.001) Depression: OR 1.4 (95% CI 0.59,3.49; p = 0.423)
6.	Rahayu et al. [29] (2015)	Blitar/Hospital	20	FSFI	75%	N/A
7.	Djailani et al. [25] (2019)	Banjarmasin/ Hospital	27	FSFI	70.3%	Obesity: OR 5.6 (95% CI 3.0,10.4; $p < 0.001)$
8.	Fitrika et al. [21] (2014)	Aceh/Hospital	51	FSFI	9.8%	N/A
9.	Djusad et al. [30] (2016)	Jakarta/Hospital	14	FSFI	64.3%	N/A
10.	Hastuti et al. [26] (2008)	Purworejo/ Community	140	SAGE	48.5%	Anxiety: OR 1.3 (95% CI 0.8,2.2; $p < 0.05)$

All studies were cross-sectional study. N: number of participants, FSFI: Female Sexual Function Index, FSD: Female Sexual Dysfunction, SAGE: Survey Study on Global Ageing and Adult, OR: odd ratio, CI: confidence interval, N/A: not available, OR: Odds Ratio, CI: Confidence Interval.

were in Kalimantan and Sumatera.

#### 3.1. Prevalence of FSD in Indonesia

The pooled prevalence of FSD in ten studies was 52% (95% CI 0.49,

0.56; I<sup>2</sup> 93.9%, p < 0.001) (Fig. S1). In the sensitivity analysis, we excluded a study by Fitrika et al. [21] due to unstandardized measurement of FSFI, and the determined the pooled prevalence of FSD was 62% (95% CI 0.58, 0.66; I<sup>2</sup> 68.7%, p = 0.001) (Fig. 2). There was no significant difference between pooled prevalence in the community and

■ 0.70 (0.52, 0.84)	5.90
0.49 (0.40, 0.57)	23.54
0.53 (0.41, 0.65)	10.49
0.75 (0.66, 0.82)	22.90
0.64 (0.53, 0.73)	15.64
0.61 (0.57, 0.66)	78.47
0.63 (0.46, 0.78)	5.91
- 0.55 (0.40, 0.69)	7.56
0.64 (0.39, 0.84)	3.12
0.75 (0.53, 0.89)	4.94
> 0.63 (0.55, 0.72)	21.53
0.62 (0.58, 0.66)	100.00
	0.53 (0.41, 0.65) 0.75 (0.66, 0.82) 0.64 (0.53, 0.73) 0.61 (0.57, 0.66) 0.63 (0.46, 0.78) 0.55 (0.40, 0.69) 0.64 (0.39, 0.84) 0.75 (0.53, 0.89)

Fig. 2. Pooled Prevalence of Female Sexual Dysfunction in Female with Type 2 Diabetes in Indonesia (9 studies). Data of effect estimates was presented as percentage and 95% confidence interval of Female Sexual Dysfunction prevalence. There are five studies in the community setting and four studies in hospital setting, in which respective pooled prevalence values are represented in the figure (subtotal effect estimates). The pooled prevalence of both setting is depicted as overall effect estimates.

Descargado para Anonymous User (n/a) en National Library of Health and Social Security de ClinicalKey.es por Elsevier en noviembre 16, 2023. Para uso personal exclusivamente. No se permiten otros usos sin autorización. Copyright ©2023. Elsevier Inc. Todos los derechos reservados. hospital settings (Fig. 2). Furthermore, we measured pooled prevalence in five good-quality studies. We found no significant difference compared to analysis of other nine studies.

When comparing the FSD domain in FSFI, two studies by Lamuhammad et al. [28] and Saraswati et al. [14] discovered that desire and arousal were the most frequent sexual dysfunction with the lowest FSFI score.

## 3.2. Risk factors of FSD

There were six studies in this review that identified risk factors for FSD. Fig. 3 showed the pooled OR of depression, anxiety, obesity, and duration of diabetes towards FSD, which were not statistically significant. A study by Saraswati et al. [14] claimed that age more than 45 years old and or menopause and the use of antihypertensives increased the risk of FSD. However, the author did not further elaborate whether the population aged more than 45 years old was mutually included in the menopause population or vice versa. Another study by Tatiana et al. [24] stated that the consumption of antidepressants, analgesics, antihypertensives, antihistamines, and cholesterol-lowering drugs likewise increased the risk of FSD.

In the study by Fitriaka et al. [21] although the correlation of HbA1c to desire sexual dysfunction is only around 28%, it could be considered that poor glycemic control could be one of the risk factors for FSD.

According to the GRADE evaluation, anxiety, depression, duration of diabetes, and obesity had very low quality, whereas the prevalence of FSD, medication use, age, menopause and HbA1C level were graded low quality (Table 2). Publication bias was rated by funnel plot and depicted asymmetric distribution of dots (Fig. S2)

#### 4. Discussion

The prevalence of FSD among T2D patients in this meta-analysis of ten studies among the Indonesian population ranged from 9.8% to 78.4%, with a pooled prevalence of 52%. The proportion of FSD in Indonesia was similar to other countries in the world, which ranges from 18.2% to 88.7% [13,31,32]. In addition, the proportion of FSD was also similar, both in western and eastern countries (Table 3). However, our study inferred to use data from the analysis of 9 studies by excluding one study that performed unstandardized measurement to diagnose FSD. The pooled prevalence of nine studies was 62%, with no significant difference between the community and hospital settings. The sensitivity analysis of five high-quality studies also showed no significant difference in FSD prevalence (63%).

Studies from Amelia et al. [27], Tatiana et al. [24] and Djusad et al. [30] had the closest prevalence proximity with the pooled prevalence. However, there was no significant distinctive characteristic among those studies that might explain the similarity in terms of social background, age, duration of diabetes, or setting of the study. Other studies by Lamuhammad et al. [28] and Insiyah et al. [23] reported lower prevalence of FSD which was 54.8% and 53.3%, respectively that resembled the FSD proportion in other countries [12,33-35]. These two studies had similar baseline characteristics, such as productive age, non-menopause, diabetes duration less than five years, and similar ethnic groups. The other three studies by Saraswati et al. [14], Djailani et al. [25] and Rahayu et al. [29] had a higher prevalence of FSD compared to the others with percentage of 74.8%, 70.35%, and 75%, respectively. These studies were similar in educational, occupational, parity, and obesity background, with a higher proportion of older respondents with menopause status. More than half of the respondents in the study from Saraswati et al. [14] and Djailani et al. [25] were housewives and almost half of them had lower than senior high school educational background. The latter characteristics might explain why these studies reported a higher FSD prevalence. In addition, a study by Fitrika et al. [21] was performed using unstandardized cut-off measurement of FSFI, whereas Hastuti et al. [26] used SAGE in diagnosing FSD. These conditions

accounted for the reason why these articles had distinct FSD prevalence compared to the pooled prevalence.

The pooled prevalence of FSD in our study was consistent with findings in other observational studies abroad [3,36–38]. Even though Indonesia is constantly compared to Malaysia for its cultural similarity, the rate of FSD in Malaysia is much lower, ranging from 18 to 34%. As dissimilar to studies in Indonesia, three studies in Malaysia applied Malay Version FSFI with different cut-off to standard values, investigated a smaller number of patients with T2D (in two articles, the number of samples was respectively 29 and 22 females), with lesser comorbid and complication, and also only included patients who had performed sexual activity within 4 weeks [31,39,40].

When comparing the FSD domains in FSFI, two studies by Lamuhammad et al. [28] and Saraswati et al. [14] discovered that desire and arousal were the most frequent sexual dysfunction with the lowest FSFI score. This finding corresponded with results in several countries [7,31, 38,41–44]. Hyperglycemia in diabetes is responsible to cause dehydration of vaginal mucosa and disturb lubrication. These conditions may lead to dyspareunia and eventually cause desire and arousal dysfunction. Females with T2D also often experience psychosocial discomfort due to complications of diabetes, comorbid, low self-esteem, poor body image, interpersonal and cultural background diversity, hence rendering the sexual inaptitude [9,45].

Duration of diabetes, obesity, anxiety and depression were not associated with an increasing prevalence of FSD in females with T2D. These results differed from previous studies from other countries [12,46, 47]. The prevalence of undiagnosed diabetes in adults has reached 50.1% worldwide and 73.7% in Indonesia [1]. The unawareness of this condition led to ignorance toward the duration of the disease, therefore making the actual data on the duration of diabetes might be inaccurate. Furthermore, instead of solely due to the longer duration of diabetes, specific pathological processes, such as hyperglycemia, atherosclerosis, hormonal imbalance, and neuropathy, were believed to weigh the risk of FSD even more [11].

Our study found that obesity did not increase the risk of FSD, whereas two cross-sectional studies in Italy stated that metabolic syndrome was the main risk factor for FSD [12,48]. This discrepancy notified us that FSD was not only affected by obesity alone but also by other components in metabolic syndromes, such as higher hip circumference, high levels of triglyceride, hypertension, and microalbuminuria. Furthermore, three articles [23,24,26] in this systematic review had different diagnostic measurements to diagnose anxiety and depression. Thus, an assured relationship between FSD, anxiety, and depression relation cannot be established yet.

Over 45-year-old and or menopausal females with T2D were associated with a higher risk of FSD. These conditions were consistent with results from other studies [40,41]. Older age and or menopause intensify the risk of FSD by the accumulation of molecular damages, micro-and macro-complication of diabetes, hormonal imbalance, and hot flush symptoms [1,49].

Based on a study by Fitrika et al. [21], there is a correlation between HbA1C level and decreased sexual desire, although it is not high (28%). This study's result was in line with another study by Bal et al. [50]. Higher HbA1C level indicated poor glycemic control which led to dehydration of mucus membrane, worsened inflammation, diabetes complication, and endothelial dysfunction, therefore resulting in sexual dysfunction [2]. Sexual desire and arousal are also activated by the central nervous system and its related limbic-hippocampal structures, which leads to the defect in parasympathetic and sympathetic nervous system signaling [51]. Chronic hyperglycemia in diabetes mellitus leads to the accumulation of advanced glycation end products and damage in bioavailability of neurotransmitters, thus also causing endothelial dysfunction [2]. The neurovascular imbalance in diabetes mellitus may contribute to the pathogenesis of FSD by altering both the normal transduction of sexual stimuli and the triggered sexual response [52].

Tatiana et al. [24] found that some medications increased the risk of

Author, year F	Risk Factor: Depression and FSI	Odds ratio (95% CI) % Weight
Insiyah, 2018 [23]		7.66 (2.30, 25.53) 1.45
Tatiana, 2017 [24]	-	1.44 (0.59, 12.68) 92.88
Saraswati, 2019 [14]		3.47 (0.95, 12.68) 5.68
Overall (I-squared = 0.0%, p	0 = 0.477)	1.65 (0.25, 3.04) 100.00
-25.5	0	25.5
Author, year	Risk Factor: Anxiety and FSD	Odds ratio (95% CI) % Weight
Insiyah, 2018 [23]		7.71 (2.17, 27.41) 0.31
Hastuti, 2008 [26]	-	1.30 (0.80, 2.20) 99.69
Overall (I-squared = 0.0%, p	= 0.320)	1.32 (0.62, 2.02) 100.00
-27.4	0	27.4
Author, year	Risk Factor: Obesity and FSD	Odds ratio (95% CI) % Weight
Tatiana, 2017 [24]		5.73 (2.18, 15.04) 1.62
Djailani, 2019 [25]		- 5.60 (3.01, 10.41) 4.90
Saraswati, 2019 [14]	-	0.83 (0.34, 2.04) 93.48
Overall (I-squared = 75.2%, J	p = 0.018)	1.14 (0.32, 1.96) 100.00
-15	0	15
Author, year Risl	k Factor: Duration of T2D and F	SD Odds ratio (95% CI) % Weight
Lamuhammad, 2017 [28]	•	8.57 (2.08, 35.32) 0.65
Tatiana, 2017 [24]		10.06 (3.59, 28.15) 1.18
Saraswati, 2019 [14]	-	1.21 (0.46, 3.16) 98.17
Overall (I-squared = 25.9%, p	o = 0.259)	1.36 (0.03, 2.70) 100.00
-35.3	0	35.3

Fig. 3. Pooled Odd Ratio of Risk Factors that Contribute in Female Sexual Dysfunction with Type 2 Diabetes in Indonesia. Data was presented as odds ratio of risk factors and 95% confidence interval of Female Sexual Dysfunction FSD = Female Sexual Dysfunction; T2D = type 2 diabetes.

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#### Table 2

Assessment of study outcomes by Grading of Recommendations Assessment, Development, and Evaluation (GRADE).

Outcome	No. of subject (study)	GRADE
Prevalence FSD	572 (10	<b>@@</b> OO
A	studies)	Due to inconsistency & publication bias $\Phi$
Anxiety and	388 (4 studies)	$\oplus O O O$
depression		Due to indirectness, imprecision, & publication bias
Duration of T2D	230 (3 studies)	$\Phi \cap \cap \cap$
		Due to indirectness, imprecision, &
		publication bias
Obesity	188 (2 studies)	<b>⊕</b> ∩∩∩
		Due to inconsistency, indirectness,
		imprecision, & publication bias
Age	103 (1 study)	$\oplus \oplus \bigcirc \bigcirc$
		Due to indirectness & publication bias
Menopause	103 (1 study)	$\oplus \oplus \bigcirc \bigcirc$
		Due to indirectness & publication bias
The use of	188 (2 studies)	$\oplus \oplus \bigcirc \bigcirc$
medications		Due to indirectness & publication bias
HbA1C level	51 (1 study)	$\oplus \oplus \bigcirc \bigcirc$
		Due to imprecision & publication bias

 $\bigoplus$  ) : very low quality,  $\bigoplus$  ): low quality, T2D: type 2 diabetes mellitus, HbA1C: Hemoglobin A1C.

FSD but did not perform subgroup analysis according to the drug classes. On the other hand, Saraswati et al. [14] showed that antihypertensives were associated with FSD, although they also did not specify the names of the drugs. Studies concerning antihypertensives and FSD are still limited. It is hypothesized that consuming thiazide and beta-blocker (except nebivolol) led to penile vascular smooth muscle vasoconstriction, catecholamine disruption, and hormone reduction in male erectile dysfunction [53]. However, the exact mechanism in FSD is not known yet. Hence, further research needs to be conducted. Other studies in this systematic review did not deliver background characteristic data on medication that might predispose to FSD.

Other than above-mentioned possible risk factors of FSD, thyroid disease is known as an independent predictor of sexual activities in females, in association with lower paraoxonase-1 (PON-1) and arylesterase (ARE) enzyme activity, which is a strong cholinesterase inhibitor [54]. Another cause of FSD is psychotic disorders. Sexual impairment is also more commonly observed in type 1 diabetes (T1D) due to the longer duration of pathological complications of the disease compared to T2D [55]. The decreased level of dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS) in underlying adrenal failure is also known as one of the causes of FSD [56].

The limitation of this study were the high heterogeneity among

Table 3					
List of studies with	prevalence	of female	sexual	dysfunction	in diabetes.

studies and inability to establish cause and effect relationship. Moreover, among ten studies, there were five studies classified as high risk of bias. Those conditions explained why the heterogeneity was high, as also described in  $I^2$  value in the pooled prevalence of FSD. The funnel plot showed an asymmetric distribution of dots, which denoted publication bias. This matter was caused by the lack of publication on studies regarding FSD and T2D in Indonesia, which caused difficulty in obtaining articles. This review did not compare the prevalence or associated factors between type 1 and type 2 diabetes. Besides, there was limited data on socioeconomic, education, and relationship with partner in this review that might potentially affect the prevalence of FSD among the population. Hence, further larger and well-designed studies on these factors need to be conducted.

Despite of some limitations, our study was the first systematic review in Indonesia that analyzed FSD among T2D patients. This study also explored factors associated with FSD and assessed the quality of evidence by using GRADE. Moreover, this study result demonstrates the importance of FSD as a common complication of chronic T2D. As portrayed in the high prevalence of FSD in all studies, physicians need to actively investigate FSD toward all females with T2D in Indonesia, particularly ones who are older than 45 years old, in a menopausal state, have a high level of HbA1C and are under medications, by using an alike criteria or questionnaire to diagnose FSD.

The findings of this study demonstrate the importance of research on FSD in Indonesia. Especially as the number of diabetes rises, with a higher number of female diabetes patients, it is hoped that it can increase awareness of the incidence of FSD to improve the quality of life of patients with diabetes.

# 5. Conclusion

The prevalence of FSD among T2D patients in Indonesia was 62% and notably affected the desire and arousal domain of FSD. Older age over 45-year-old and or menopause, and usage of antihypertensive medications, were associated with FSD.

# Author contributions

Idea and study design: EY, DLT, AP and PS; Data collection and analysis: AP, DLT, CA, MK; Article draft writing: AP; Draft revision: EY, DLT, CA, HS, PS, and TJET; Writing supervision: EY, TJET, DLT, and HS. EY, DLT and HS had contributed equally in supervising the writing of this article.

No	Author, year	No. of subjects	Design of study	Country	Population	Measurement of FSD	Prevalence (%)
1	Valverde, 2016 [57]	136	Cross sectional	Spain	Female T2D	FSFI	66.9%
2	Nowosielski, 2010 [58]	544	Cross sectional	Polandia	Female T1D & T2D	FSFI	T1D = 26.5%
							T2D=42.2%
3	Bak, 2017 [7]	114	Cross sectional	Polandia	Female T2D	FSFI	68%
4	Esposito, 2010 [12]	595	Cross sectional	Italy	Female T2D	FSFI	53.4%
5	Enzlin, 2009 [59]	424	Cross sectional	USA	Female T1D	FSFI	35.4%
6	Elyasi, 2015 [13]	150	Cross sectional	Iran	Female T2D	FSFI	78.7%
7	Duman, 2014 [60]	200	Cross sectional	Turkey	Female T1D & T2D	FSFI	26.2%
8	Celik, 2015 [41]	423	Cross sectional	Turkey	Diabetes	FSFI	80.4%
9	Al-Mogbel, 2017 [32]	275	Cross sectional	Saudi Arabia	Female T2D	FSFI	88.7%
10	Fang, 2012 [61]	115	Cross sectional	China	Female T2D	FSFI	79.2%
11	Kamaralzaman, 2010 [31]	22	Cross sectional	Malaysia	Female T2D	MVFSFI	18.2%
12	Bau, 2010 [62]	178	Cross sectional	Malaysia	Female T2D	MVFSFI	26.4%
13	Nagpal, 2016 [38]	100	Cross sectional	India	Female T2D	FSFI	64.5%
14	Paningbatan, 2018 [6]	75	Cross sectional	Philippines	Female T2D	FSFI	72%

T1D: type 1 diabetes; T2D: type 2 diabetes; USA: United States of America; FSD: Female Sexual Dysfunction; FSFI: Female Sexual Function Index; MVFSFI: Malaysia Version Female Sexual Function Index.

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#### Declaration of conflicting interests

The authors declared no conflict of interest.

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.dsx.2023.102878.

#### References

- [1] International Diabetes Federation. IDF diabetes atlas ninth edition 2019. International diabetes federation; 2019.
- [2] Maiorino M, Bellastella G, Esposito K. Diabetes and sexual dysfunction : current perspectives. Diabetes Metab Syndr Obes 2014;7:95–105.
- [3] Rahmanian E, Salari N, Mohammadi M, Jalali R. Evaluation of sexual dysfunction and female sexual dysfunction indicators in women with type 2 diabetes : a systematic review and meta - analysis. Diabetol Metab Syndrome 2019:1–17.
- [4] Laumann EO, Paik A, Rosen RC. Sexual dysfunction in the United States: prevalence and predictors. J Am Med Assoc 1999;281(6):537–44.
- [5] Kouidrat Y, Pizzol D, Cosco T, Thompson T, Carnaghi M, Bertoldo A. High prevalence of erectile dysfunction in diabetes : a systematic review and metaanalysis of 145 studies. Diabet Med 2017:1185–92.
- [6] Paningbatan J, Aragon J, Landicho-Kanapi MP, Rodriguez-Asuncion K. Prevalence of sexual dysfunction and its associated factors among women with diabetes mellitus type 2 at makati medical center outpatient department. J ASEAN Fed Endocr Soc 2018;33(2):165–71.
- [7] Bąk E, Marcisz C, Krzemińska S, Dobrzyn-Matusiak D, Foltyn A, Drosdzol-Cop A. Relationships of sexual dysfunction with depression and acceptance of illness in women and men with type 2 diabetes mellitus. Int J Environ Res Publ Health 2017: 1–14.
- [8] Ishak WW, Tobia G. DSM-5 changes in diagnostic criteria of sexual dysfunctions. Reprod Syst Sex Disord Curr Res 2013;2(2):1185–92.
- [9] Bargiota A, Dimitropoulos K, Tzortzis V, Koukoulis GN. Sexual dysfunction in diabetic women. Hormones (Basel) 2011;10(3):196–206.
- [10] DeRogatis LR. Assessment of sexual function/dysfunction via patient reported outcomes. Int J Impot Res 2008;20(1):35–44.
- [11] Gupta L, Prakash S, Khandelwal D, Kalra B, Kalra S. Diabetes and female sexual dysfunction. US Endocrinol 2018:35–8.
- [12] Esposito K, Maiorino MI, Bellastella G, Giugliano F, Romano M, Giugliano D. Determinants of female sexual dysfunction in type 2 diabetes. Int J Impot Res 2010: 179–84.
- [13] Elyasi F, Kashi Z, Tasfieh B, Bahar A, Khademloo M. Sexual dysfunction in women with type 2 diabetes mellitus. Iran J Med Sci 2015;40(3):206–13.
- [14] Saraswati LD, Udiyono A, Sutrisni D, Fauzi M. Sexual dysfunction among women with diabetes in a primary health care at semarang, central Java province, Indonesia. Kesmas 2019;14(2):95–102.
- [15] Nicolosi A, Glasser DB, Kim SC, Marumo K, Laumann EO. Sexual behaviour and dysfunction and help-seeking patterns in adults aged 40-80 years in the urban population of Asian countries. BJU Int 2005;95(4):609–14.
- [16] Pontiroli AE, Cortelazzi D, Morabito A. Female sexual dysfunction and diabetes : a systematic review. J Sex Med 2013;10(4):1044–51.
- [17] Tarigan TJE, Yunir E, Subekti I, Pramono LA, Martina D. Profile and analysis of diabetes chronic complications in outpatient diabetes clinic of Cipto Mangunkusumo Hospital, Jakarta. Med J Indones 2015;24:156–62.
- [18] Kosiborod M, Gomes MB, Nicolucci A, Pocock S, Rathmann W, Shestakova MV, et al. Vascular complications in patients with type 2 diabetes: prevalence and associated factors in 38 countries (the DISCOVER study program). Cardiovasc Diabetol 2018;17(1):1–13.
- [19] Zachary M, Moola S, Lisy K, Dagmara, Riitano, Tufanaru C. Systematic reviews of prevalence and incidence. In: Aromataris E MZ (Editors)., editor. JBI manual for evidence synthesis. 2020. p. Aromataris E, Munn Z (Editors).
- [20] Schünemann H, Brożek, Guyatt G. Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach..
- [21] Fitrika Y. Hubungan disfungsi seksual pada wanita penderita diabetes melitus tipe 2 dengan tingkat pengontrolan glukosa darah. Syiah Kuala University; 2014.
  [22] Asmalinda D, Nursiswati, Priambodo AP. Gambaran fungsi seksual pada wanita
- penderita diabetes melitus tipe 2. 2018.
   [23] Insiyah Hastuti R. Kecemasan dan depresi pada penderita diabetes melitus tipe 2
- [20] Insyah Hasturi R. Keelmasan dan depresi pada penderna diabetes mentus upe a yang mengalami disfungsi seksual di Puskesmas Sibela Kota Surakarta. J Keperawatan Glob 2018;3:58–65.
- [24] Tatiana M, Santosa H, Ashar T. Hubungan IMT DM tipe II dengan kejadian disfungsi sekdual pada wanita usia subur (15-49 tahun) di Puskesmas bromo medan tahun 2017. J muara sains. Teknol Kedokt dan Ilmu Kesehat 2018;1(2): 74-9.

- [25] Djailani A, Dasuki D. Hubungan obesitas dengan disfungsi seksual pada perempuan di Kota Banjarmasin. Gadjah Mada University; 2019.
- [26] Hastuti L, Hakimi M. Hubungan antara kecemasan dengan aktifitas dan fungsi seksual pada wanita usia lanjut di Kabupaten Purworejo. Ber Kedokt Masy 2008;24 (4):176–90.
- [27] Amelia H, Khatimah H, Istiana I. Perbedaan kejadian disfungsi seksual pada wanita dengan diabetes melitus dan tanpa diabetes melitus. Berk Kedokt 2016;12(2): 133–8.
- [28] Lamuhammad FH, Rahmanisa S, Yonata A, Kurniawaty E. Hubungan durasi diabetes melitus tipe 2 dengan kejadian disfungsi seksual pada wanita di Rumah Sakit Natar Medika Lampung. J Agromed Unila 2017;4(2):191–5.
- [29] Rahayu SP, Sepdianto TC, Mulyadi A. The description of sexual dysfunction in patients of type II diabetes mellitus in poly disease in mardi hospital waluyo city blitar. J Ners dan Kebidanan (Journal Ners Midwifery) 2015;2(3):216–21.
- [30] Djusad S, Lestari K. Faktor-faktor yang terkait Disfungsi Seksual pada Pasien Prolaps Organ Panggul di RSUPN Cipto Mangunkusumo dan RSUP Fatmawati Jakarta 2016. University of Indonesia; 2016.
- [31] Kamaralzaman S, Sidi H, Yau M, Budin S, Sani A, Mohamed J. Sexual function of Malay women with type 2 diabetes mellitus: a preliminary study. ASEAN J Psychiatry 2010;11(May 2014):1–8.
- [32] AlMogbel TA, Amin HS, AlSaad SM, AlMigbal TH. Prevalence of sexual dysfunction in saudi women with Type 2 diabetes: is it affected by age, glycemic control or obesity? Pakistan J Med Sci 2017;33(3):732–7.
- [33] Vafaeimanesh J, Raei M, Hosseinzadeh F, Parham M. Evaluation of sexual dysfunction in women with type 2 diabetes. Indian J Endocrinol Metab 2014;18(2): 175–9.
- [34] Tuncel E, Durgun O, Peynirci H, Ersoy C. Sexual dysfunction in female patients with type 2 diabetes mellitus: a cross-sectional single-centre study among Turkish patients. Hum Fertil 2017;20(3):192–9.
- [35] Wing RR, Bond DS, Gendrano IN, Wadden T, Bahnson J, Lewis CE, et al. Effect of intensive lifestyle intervention on sexual dysfunction inwomen with type 2 diabetes: results from an ancillary look ahead study. Diabetes Care 2013;36(10): 2937–44.
- [36] Owiredu WKBA, Alidu H, Amidu N, Obirikorang C, Gyasi-Sarpong CK, Bawah AT, et al. Sexual dysfunction among diabetics and its impact on the SQoL of their partners. Int J Impot Res 2017;29(6):250–7.
- [37] Hintistan S, Cilingir D. Sexual dysfunction in Turkish men and women with type 2 diabetes mellitus. Sex Disabil 2013;3(1):31–41.
- [38] Nagpal M, Jangid R. A study of sexual function in women with type 2 diabetes mellitus in a tertiary care centre in India. JAMA Psychiatr 2016;19(6):1–5.
- [39] Husin H, Sidi H, Baharudin A. Depression, anxiety and sexual dysfunction in patients with diabetes mellitus with and without foot ulcer. Int Med J Malaysia 2017;16(1):53–66.
- [40] Rawa B, Adibah HI, Norhayati MN, Hatta S. Prevalence and associated factors of female sexual dysfunction among diabetics in Kelantan. Int Med J 2010;17(3): 179–85.
- [41] Celik S, Golbasi Z, Kelleci M, Satman I. Sexual dysfunction and sexual quality of life in women with diabetes: the study based on a diabetic center. Sex Disabil 2015;33 (2):233–41.
- [42] Omidvar S, Niaki MT, Amiri FN, Kheyrkhah F. Sexual dysfunction among women with diabetes mellitus in a diabetic center in Amol. J Nat Sci Biol Med 2013;4(2): 321–4.
- [43] Shi YF, Shao XY, Lou QQ, Chen YJ, Zhou HJ, Zou JY. Study on female sexual dysfunction in type 2 diabetic Chinese women. Biomed Environ Sci 2012;25(5): 557–61.
- [44] Li F, Wang Y, Xiao L, Lou Q, Fish AF. Frequency, severity, and risk factors related to sexual dysfunction in Chinese women with T2D. J Diabetes 2016;8(4):544–51.
- [45] Rochester-Eyeguokan C, Meade L. A practical approach to managing hypoactive sexual desire disorder in women with diabetes. Diabetes Ther 2017;8(5):991–8.
- [46] Wang GL, Wang I, Wang YL, Li ML. Risk factors for sexual dysfunction among Chinese women with type 2 diabetes. Int J Diabetes Dev Ctries 2015;35(3):219–24.
  [47] Nowosielski K, Skrzypulec-Plinta V. Mediators of sexual functions in women with
- [47] Nowosielski K, Skrzypulec-Plinta V. Mediators of sexual functions in women with diabetes. J Sex Med 2011;8(9):2532–45.
- [48] Martelli V, Valisella S, Moscatiello S, Matteucci C, Lantadilla C, Costantino A, et al. Prevalence of sexual dysfunction among postmenopausal women with and without metabolic syndrome. J Sex Med 2012;9(2):434–41.
- [49] Kirkman MS, Briscoe VJ, Clark N, Florez H, Haas LB, Halter JB, et al. Diabetes in older adults. Diabetes Care 2012;30(4):383–90.
- [50] Bal MD, Yilmaz SD, Çelik SG, Dinçal N, Beji NK, Yalçin Ö. Does the diabetes of type 2 affect the sexual functions of women? J Sex Marital Ther 2015;41(1):107–13.
- [51] Berman J. Physiology of female sexual function and dysfunction. Int J Impot Res 2005;17:S44–51.
- [52] Duby J, Campbell R, Setter S, White J, Rasmussen KA. Diabetic neuropathy: an intensive review. Am J Health Syst Pharm 2004;61:160–73.
- [53] Chrysant SG. Antihypertensive therapy causes erectile dysfunction. Curr Opin Cardiol 2015;30(4):383–90.
- [54] Yenice MG, Danacioğlu YO, Mert M, Karakaya P, Seker KG, Akkaş F, et al. Evaluation of factors affecting sexual dysfunction in female patients with diabetes mellitus. Arch Endocrinol Metab 2020:319–25.
- [55] Das J, Yadav S, Arora B. Comorbidities of female patients with sexual dysfunction in a psychiatry clinic: a cross-sectional study. J Psychosexual Heal 2022;4(3): 162–70.
- [56] Carosa E, Sansone A, Jannin E. Female sexual dysfunction for the endocrinologist. Eur Soc Endocrinol 2020;182(6):101–16.

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- [57] Valverde JMG, Portillo PF, Guevara-Valtier MC, Mendoza-Catalán GS, Ramos-Vázquez G, Pimentel-Jaimes JA, et al. Sexual dysfunction, depression and quality of life in individuals with diabetes mellitus type 2. Int J Nurs 2016;3(2):9–19.
- [58] Nowosielski K, Drosdzol A, Sipiński A, Kowalczyk R, Skrzypulec V. Diabetes mellitus and sexuality—does it really Matter?jsm\_1561 723.73. J Sex Med 2010;7: 723–35.
- [59] Enzlin P, Rosen R, Wiegel M, Brown J, Wessells H, Gatcomb P, et al. Sexual dysfunction in women with type 1 diabetes. Diabetes Care 2009;32(5):780–5.
- [60] Duman NB. Frequency of sexual dysfunction and its causative factors among diabetic women in Turkey. Pakistan J Med Sci 2014;30(3):558–63.
- [61] Fang SY, Yu SX, Qing LQ, Juan CY, Juan ZH, Ying ZJ. Study on female sexual dysfunction in type 2 diabetic Chinese women. Biomed Env Sci 2012;25(5): 557–61.
- [62] Bau R, Ismail AH, Noor NM, Sidi H. Comparison of prevalence and female sexual dysfunction between diabetic and non-diabetic in kelantan. Int Med J 2010;17(4): 261–6.