Erectile Dysfunction Among Patients on Methadone Maintenance Therapy and Its Association With Quality of Life

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Objectives: Erectile dysfunction (ED) is a problem commonly encountered by patients on methadone maintenance therapy (MMT). This study aimed to assess the prevalence of ED among this group of patients along with its risk factors and association with quality of life (QOL).

Methods: Male patients on MMT in a tertiary hospital in Malaysia were included in the study. A total of 134 patients with sexual partners were assessed for ED using the International Index of Erectile Function. Patients were assessed for substance use using Opiate Treatment Index (OTI) and depression using the Malay version of the self-rated Montgomery-Asberg Depression Rating Scale (MADRS-BM). QOL was evaluated using World Health Organisation Quality of Life (WHOQOL)-BREF.

Results: The prevalence of ED among patients on MMT was 67%, with 26.1% having mild ED, 30.4% having mild-to-moderate ED, 7.0% having moderate ED, and 17.2% having severe ED. Patients with depression were 4 times more likely to have ED compared with patients without depression, whereas increasing age significantly correlated with the severity of ED. Having ED predicted a poorer QOL in the social relationships domain.

Conclusion: Depression is highly associated with ED, which negatively influences the social aspect of QOL among patients on methadone maintenance therapy.

Key Words: erectile dysfunction, methadone, opioid use disorder, quality of life

(*J Addict Med* 2017;11: 40–46)

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Received for publication February 19, 2016; accepted August 26, 2016.

The authors report no conflicts of interest.

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ISSN: 1932-0620/16/1101-0040

DOI: 10.1097/ADM.0000000000000267

Sexual dysfunction is a common adverse effect associated with opioid use. Opioids have been reported to cause loss of libido and erectile dysfunction (ED) in men, as well as reduced fertility and amenorrhea in women (Deglon et al., 2004). As many as 75% of men and 67% of women reported worsening of sexual interest while using opiates, with 62% of men and 60% of women having affected orgasm (Palha and Esteves, 2002). Among patients with methadone maintenance therapy (MMT), the pooled prevalence of sexual dysfunction was found to be 52% in a meta-analysis (Yee et al., 2014).

ED is one of the sexual dysfunctions commonly encountered by patients on methadone. The prevalence of ED ranges from 50% to 93% (Hallinan et al., 2008; Quaglio et al., 2008; Tatari et al., 2013), higher than that found in the general population below the age of 65 years, which ranges from 5% to 34% (Brown et al., 2005). Among those who had ED, 19% to 37% reported severe ED (Quaglio et al., 2008; Zhang et al., 2014). Apart from ED, some patients experienced orgasm dysfunction, lack of intercourse satisfaction, lack of sexual desire, and lack of overall satisfaction after initiation of methadone treatment (Zhang et al., 2014).

Although sexual dysfunction may not be life-threatening, it has a potential impact on quality of life (QOL) and intimate relationships. Although evidence of the relationship between sexual dysfunction and QOL among patients on MMT is limited, studies among the general population have shown that ED is associated with a lower QOL (Jonler et al., 1995; Hwang et al., 2007). Meanwhile, it was found in a qualitative study among patients on MMT that sexual dysfunction reduced the quality of patients' sexual lives and affected relationships with their partners (Xia et al., 2013). Compared with the general population, patients on MMT also face other issues such as blood-borne infections, psychiatric comorbidities, and other social problems such as employment issues, relationship difficulties, and stigma, which may also contribute to a lower QOL (Carpentier et al., 2009; Earnshaw et al., 2013; Wang et al., 2015).

Despite the higher prevalence of sexual dysfunction among patients on MMT, sexual dysfunction still remains a taboo particularly in Asian countries and is considered as an embarrassing topic to discuss. It was found in a study that Chinese men were not likely to discuss issues of sexual

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dysfunction, and if they did so they were less likely to discuss them with a medical specialist (Sun and Liu, 2007). As much as patients do not express their sexual difficulties, it was found that clinicians do not adequately address this issue. In the study by Chekuri et al. (2012), only 3% of patients on methadone reported that they have been asked by the addiction services about their sex life. Xia et al. (2013) also observed that clinicians did not find this issue popular despite being important, and that they did not have any effective therapy strategy to solve this issue, while counseling about sexual problems was not actively conducted with patients and their partners.

In view of the limited evidence of the impact of sexual dysfunction among patients on MMT on QOL and the lack of adequate attention given to this problem by clinicians, this study aims to identify the prevalence of ED among patients on MMT, its risk factors, and the association between ED and QOL.

METHODS

Participants and Procedure

This study was carried out at the outpatient addiction psychiatric clinic in University Malaya Medical Centre (UMMC) between August 2014 and August 2015. UMMC is a university-affiliated tertiary referral centre with full psychiatric services including addiction psychiatry facilities. It is located in an urban and predominantly middle-class area. The MMT was implemented in UMMC since 2005. Patients who wish to seek methadone treatment are first assessed for suitability for methadone treatment in the general psychiatric clinic before being referred to the addiction psychiatric clinic for further management and follow-up. Patients who are started on MMT continue treatment at the addiction psychiatric clinic.

Male patients aged 18 years and above who were on MMT for a duration of at least 2 months, had a sexual partner, and fulfilled the criteria for opioid dependence based on the *Diagnostic and Statistical Manual, Fourth Edition* were included in the study. Patients had to be able to understand the Malay or English language. Patients were excluded from the study if they had severe behavioral disturbances, severe cognitive impairment, or intellectual disability.

This study was approved by the medical ethics committee of UMMC. Patients who fulfilled the inclusion criteria were informed about the study, the voluntary nature of participation, and confidentiality of information given by patients. Consent was obtained before commencement of the study. Patients who were found to have sexual dysfunction, depression, or suicidal tendency were referred to a psychiatrist for further investigation and management.

Measures

Sociodemographic data of patients who consented to the study were obtained, which included information regarding age, ethnicity, marital status, education level, and employment status. Clinical information such as human immunodeficiency virus, hepatitis B, hepatitis C, other comorbid medical illness, mean dose of methadone treatment, and duration of MMT was obtained from patients' medical records. Opiate Treatment Index (OTI) was used to assess substance use, HIV risk-taking behaviour, criminal behaviours and health in the past month as well as social functioning in the preceding 6 months.

The International Index of Erectile Function (IIEF) was used to assess for ED in the past 4 weeks before the interview. The IIEF is a valid and reliable measure of male sexual function (Rosen et al., 1997). It has been translated to the Malay language and validated, with good internal consistency (Quek et al., 2002). Each of the 15 items in IIEF is rated from 0 (or 1) to 15, and scores are calculated according to each domain. The score in the erectile function domain is classified into 5 categories according to Cappelleri et al. (1999), which include no ED (26–30), mild (22–25), mild-to-moderate (17–21), moderate (11–16), and severe ED (6–10). Only patients with sexual partners were included in this study as IIEF is neither designed nor validated for patients without sexual partners due to a number of questions that are intercourse-dependent.

The Malay version of the self-rated Montgomery-Asberg Depression Rating Scale (MADRS-BM) was used to assess for depression in this study. The self-rated MADRS has been found to demonstrate moderate-to-good correlation with the clinician-rated MADRS, with good concurrent validity (Fantino and Moore, 2009; Cunningham et al., 2011). The self-rated MADRS has been translated to the Malay language and validated, with promising psychometric properties (Yee et al., 2015). According to the study by Yee et al. (2015), a cutoff score of 4 was used to distinguish between individuals with and without depression.

The World Health Organization Quality of Life (WHOQOL)-BREF was used to assess QOL in the physical, psychological, social relationships and environment domains, as well as overall QOL and general health. The WHOQOL-BREF, which has good psychometric properties, has also been translated into the Malay language and validated (Hasanah et al., 2003).

Statistical Analysis

Data analysis was performed using the Statistical Package for the Social Sciences version 20 (SPSS, Inc, Chicago, IL). The prevalence of ED among patients on MMT was ascertained and categorized according to the severity of ED. Sociodemographic and clinical factors associated with ED were identified using χ^2 tests (for categorical variables) and independent t tests or Mann-Whitney U tests (for continuous variables). Logistic regression analysis was performed to determine the relationship between ED and significant variables. Variables were considered to be statistically significant at the level of $P < 0.05$ (2-sided). The WHOQOL-BREF scores in each domain were compared between patients with and without ED using independent t tests, whereas the association between other variables and quality-of-life scores was assessed using independent t tests (for categorical variables) and Pearson's or Spearman's correlation coefficient (for continuous variables), with Bonferroni adjustment. Statistically significant variables were included in the multiple regression analysis.

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TABLE 1. Sociodemographic and Clinical Characteristics of the Patients

Variable	Frequency (n) or Mean (SD)	Percent (%)
Mean age, y	43.0 (10.1)	
Ethnicity		
Malay	106	79.1
Chinese	18	13.4
Indian	9	6.7
Others	1	0.7
Marital status		
Single	9	6.7
Married	121	90.3
Divorced	4	3.0
Education level		
No formal education	2	1.5
Primary education	10	7.5
Secondary education	120	89.6
Tertiary education	2	1.5
Employment		
Employed	114	85.1
Unemployed	20	14.9
Medical illness		
HIV positive	4	3.0
Hepatitis B positive	5	3.7
Hepatitis C positive	46	34.3
Other medical illness	37	27.6
Mean dose of methadone, mg/d	72.1 (32.6)	
Duration of MMT, mo	48.8 (32.8)	

HIV, human immunodeficiency virus; MMT, methadone maintenance therapy.

RESULTS

Study Population Characteristics

A total of 134 male patients who fulfilled the inclusion criteria completed the study. The patients were of the mean age of 43 years (SD ± 10.1) and majority were of Malay ethnicity (79.1%), married (90.3%), had secondary education (89.6%), and were employed (85.1%) (Table 1). Slightly more than one-third of patients had hepatitis C (34.3%), 3.7% had hepatitis B, 3% had human immunodeficiency virus, while 27.6% had other medical conditions such as liver dysfunction, hypertension, and diabetes mellitus. The patients had been on MMT for a mean duration of 48.8 months (SD ± 32.8), at a mean daily dose of 72.1 mg (SD ± 32.6).

Erectile Dysfunction

Almost two-thirds of patients had ED (67%), with 26.1% having mild ED, 30.4% having mild-to-moderate ED, 7.0% having moderate ED, and 17.2% having severe ED (Table 2). The only factor found to be significantly associated with ED was depression (odds ratio 3.98, 95% confidence interval 1.52–10.40, $P = 0.006$) (Table 3). There was no significant association between age and the presence of ED using the cutoff score by Cappelleri et al. (1999), but there was a significant negative correlation between age and ED score ($r = -0.27$, $P = 0.002$), indicating that increasing age correlated with the severity of ED.

Quality of Life

The mean quality-of-life scores for all patients were 26.22 (SD ± 2.49) for physical health domain, 22.70 (SD ± 3.73) for psychological domain, 10.98 (SD ± 2.25) for social relationships domain, 29.02 (SD ± 4.56) for environment domain, and 7.29 (SD ± 1.65) for combined overall QOL and general health. On univariate analysis, ED was significantly associated with a lower QOL in the social relationships domain after Bonferroni adjustment (mean difference 1.24, 95% confidence interval 0.52–1.97, $P = 0.001$). The association between the different variables and quality-of-life scores is shown in Table 4. All variables that were associated with significant differences in quality-of-life scores at the level of $P < 0.003$ (Bonferroni-adjusted) in the univariate analysis were included in the multiple linear regression analysis.

Multiple Linear Regression Analysis for QOL

On multiple linear regression analysis, having depression ($P < 0.001$) and being on methadone treatment for a longer duration ($P < 0.001$) were significantly associated with a lower QOL in the physical health domain (Table 5). Patients with ED ($P < 0.05$) and depression ($P < 0.001$) had a significantly poorer QOL in the social relationships domain. Meanwhile, patients with depression ($P < 0.01$) and those who were on methadone for a longer duration had a significantly lower QOL in the environment domain. In the psychological domain and overall QOL and general health, the only factor associated with a lower QOL was depression in the univariate analysis, thus multiple linear regression analysis was not performed.

DISCUSSION

This study found that up to two-third of patients on MMT with sexual partners experienced ED. Depression was associated with having ED, while increasing age correlated with the severity of ED. Having ED was significantly associated with a lower QOL in the social relationships domain.

The prevalence of ED found in our study was in concordance with the prevalence of ED among patients on MMT reported in other studies, which ranged from 50% to 93% (Hallinan et al., 2008; Quaglio et al., 2008; Tatari et al.,

TABLE 2. Prevalence of ED and Its Severity Among Patients on MMT

	No ED n (%)	Mild ED n (%)	Mild-to-Moderate ED n (%)	Moderate ED n (%)	Severe ED n (%)
Number of patients	38 (33.0)	30 (26.1)	35 (30.4)	8 (7.0)	23 (17.2)
Age group, y					
18–30	3 (33.3)	2 (22.2)	2 (22.2)	2 (22.2)	0 (0.0)
31–40	16 (29.6)	12 (22.2)	17 (31.5)	4 (7.4)	5 (9.3)
41–50	12 (31.6)	10 (26.3)	10 (26.3)	1 (2.6)	5 (13.2)
Above 50	7 (21.2)	6 (18.2)	6 (18.2)	1 (3.0)	13 (39.4)

ED, erectile dysfunction; MMT, methadone maintenance therapy.

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TABLE 3. Factors Associated With ED Among Patients on MMT

Variables	ED n (%), Mean (SD) or Median		t, r, χ^2, or U	P	OR	95% CI for OR
	Yes (n = 96)	No (n = 38)				
Age, y						
Independent t test	43.4 (10.60)	42.2 (8.85)	0.63†	0.532		
Correlation between age and IIEF score			−0.27‡	0.002*		
Ethnicity						
Malay	77 (72.6)	29 (27.4)	0.25	0.641	1.26	0.51–3.10
Non-Malay	19 (67.9)	9 (32.1)				
Marital status						
Married	88 (72.7)	33 (27.3)	0.72	0.517	1.67	0.51–5.46
Not married	8 (61.5)	5 (38.5)				
Education level, y						
≤6	10 (83.3)	2 (5.3)	0.88	0.508§	0.48	0.10–2.29
>6	86 (70.5)	36 (29.5)				
Employment status						
Employed	78 (68.4)	36 (31.6)	3.90	0.060	0.24	0.05–1.09
Unemployed	18 (90.0)	2 (10.0)				
Medical illness						
Yes	44 (66.7)	22 (33.3)	1.59	0.208	0.62	0.29–1.31
No	52 (76.5)	16 (23.5)				
Depression						
Yes	41 (87.2%)	6 (12.8%)	7.52	0.006*	3.98	1.52–10.40
No	55 (63.2%)	32 (36.8%)				
Psychiatric medications						
Yes	5 (55.6)	4 (44.4)	1.23	0.272§	0.47	0.12–1.84
No	91 (72.8)	34 (27.2)				
Comorbid substance use						
Yes	88 (71.5)	35 (28.5)	0.007	1.000§	0.94	0.24–3.76
No	8 (72.7)	3 (27.3)				
OTI scores						
Heroin Q score	0.0	0.0	1679.0‖	0.133		
HIV risk-taking behavior	6.0	6.0	1804.5‖	0.911		
Social functioning	6.0	5.0	1431.5‖	0.052		
Criminality	0.0	0.0	1805.0‖	0.529		
Health	0.0	0.0	1570.0‖	0.114		
Daily methadone dose, mg	71.8 (31.86)	72.6 (34.89)	−0.13†	0.898		
Duration of methadone, mo	47.7 (33.92)	51.4 (29.95)	−0.60†	0.552		

CI, confidence interval; ED, erectile dysfunction; HIV, human immunodeficiency virus; IIEF, International Index of Erectile Function; MMT, methadone maintenance therapy; OR, odds ratio; OTI, Opiate Treatment Index.

*Significant when $P < 0.05$.

†Independent t test.

‡Pearson's correlation coefficient.

§Fisher's exact test.

‖Mann-Whitney U test.

2013), and comparable with that of another local study, which found that 68.5% of Malaysian male patients on MMT with sexual partners had ED (Nik Jaafar et al., 2013). However, our study had higher proportions of patients with mild-to-moderate, moderate, and severe ED as compared to the study by Nik Jaafar et al. (2013). Among Malaysian men aged 40 and above, patients in our study had a slightly higher prevalence of ED (73.2%) than the general population (ranging from 60% to 69.5%) but a notably higher prevalence of severe ED (25.4%) compared with the general population (9.8%) (Thambi, 1998; Ab Rahman et al., 2011). The fact that our prevalence was based on a self-reported questionnaire showed that patients may be willing to express their issues with sexual health if asked by clinicians, thus sexual dysfunction is an issue that should be addressed among patients undergoing methadone treatment, despite the perception of the issue as a taboo.

In our study, patients with depression were 4 times more likely to have ED than patients without depression. Other studies have also found an association between depression and both ED and global sexual dysfunction (Brown et al., 2005; Quaglio et al., 2008). The relationship between depression and ED is postulated to be a bidirectional one, in which sexual dysfunction may be due to depression, and depression may be a consequence of sexual dysfunction forming a vicious cycle (Seidman and Roose, 2000). A similar association between ED and depressive symptoms was observed in the Massachusetts Male Aging Study (Araujo et al., 1998), and it has even been suggested that sexual dysfunction among patients on MMT may be due to psychiatric problems rather than opioids (Spring et al., 1992). Although the relationship between depression and sexual dysfunction has been well-established, the findings of our study that depression was the only factor associated with ED apart from the association between age and severity of ED demonstrated the importance of detecting and treating both depression and ED among patients on MMT in view of its possible bidirectional relationship. In addition, psychiatric comorbidities such as depression has been found

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TABLE 4. Univariate Analysis: Association Between Different Variables and Quality-of-Life Scores Among Patients on MMT

	WHOQOL-BREF Domains				
	Physical Health	**Psychological**	**Social Relationships**	**Environment**	**Overall QOL and General Health**
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**
ED	$t=-1.411$	$t=-2.759$	$t=-3.420$	$t=-2.851$	$t=-0.687$
	$P=0.161$	$P=0.007$	$P=0.001^*$	$P=0.005$	$P=0.493$
Yes	25.05 (3.88)	22.16 (3.93)	10.63 (2.36)	28.33 (4.63)	7.23 (1.59)
No	27.05 (3.88)	24.08 (2.73)	11.87 (1.68)	30.76 (3.93)	7.45 (1.81)
Age†	$r=-0.109$	$r=-0.158$	$r=0.190$	$r=-0.188$	$r=-0.030$
	$P=0.210$	$P=0.069$	$P=0.028$	$P=0.029$	$P=0.729$
Ethnicity	$t=0.381$	$t=-0.161$	$t=-0.223$	$t=0.203$	$t=2.399$
	$P=0.704$	$P=0.873$	$P=0.824$	$P=0.840$	$P=0.164$
Malay	26.15 (4.29)	22.74 (3.28)	11.00 (2.27)	28.98 (4.42)	7.19 (1.69)
Non-Malay	26.50 (4.36)	22.57 (5.15)	10.89 (2.23)	29.18 (5.17)	7.68 (1.49)
Married	$t=0.821$	$t=-0.322$	$t=-0.479$	$t=-0.146$	$t=1.456$
	$P=0.413$	$P=0.748$	$P=0.633$	$P=0.884$	$P=0.148$
Yes	26.12 (4.32)	22.74 (3.67)	11.01 (2.20)	29.04 (4.52)	7.22 (1.66)
No	27.15 (4.06)	22.38 (4.33)	10.69 (2.75)	28.85 (5.19)	7.92 (1.50)
Education level, y	$t=-0.444$	$t=0.277$	$t=-0.170$	$t=-0.379$	$t=0.272$
	$P=0.658$	$P=0.783$	$P=0.865$	$P=0.706$	$P=0.786$
≤6	26.75 (3.55)	22.42 (4.23)	11.08 (2.02)	29.50 (4.52)	7.17 (1.85)
>6	26.17 (4.37)	22.73 (3.69)	10.97 (2.28)	28.98 (4.58)	7.30 (1.64)
Employed	$t=-0.156$	$t=-1.773$	$t=0.048$	$t=-0.926$	$t=-0.705$
	$P=0.121$	$P=0.079$	$P=0.962$	$P=0.356$	$P=0.482$
Yes	26.46 (4.13)	22.94 (3.71)	10.97 (2.16)	29.18 (4.33)	7.33 (1.59)
No	24.85 (5.03)	21.35 (3.60)	11.00 (2.81)	28.15 (5.78)	7.05 (2.01)
Medical illness	$t=1.693$	$t=2.422$	$t=-0.189$	$t=1.347$	$t=0.126$
	$P=0.093$	$P=0.017$	$P=0.850$	$P=0.181$	$P=0.900$
Yes	25.59 (4.26)	21.92 (3.74)	10.94 (2.18)	28.48 (4.69)	7.27 (1.59)
No	26.84 (4.27)	23.46 (3.58)	11.02 (2.35)	29.54 (4.41)	7.31 (1.59)
Depression	$t=4.385$	$t=5.466$	$t=4.561$	$t=3.514$	$t=3.374$
	$P<0.001^*$	$P<0.001^*$	$P<0.001^*$	$P=0.001^*$	$P=0.001^*$
Yes	24.15 (4.03)	20.53 (3.24)	9.85 (2.11)	27.21 (3.84)	6.66 (1.31)
No	27.34 (4.03)	23.87 (3.45)	11.59 (2.10)	30.00 (4.64)	7.63 (1.73)
Psychiatric medications	$t=-0.159$	$t=-0.804$	$t=-1.104$	$t=-1.044$	$t=-1.336$
Yes	$P=0.874$	$P=0.423$	$P=0.272$	$P=0.299$	$P=0.184$
No	26.44 (4.77)	23.67 (4.42)	11.78 (1.56)	30.56 (4.64)	8.00 (1.41)
	26.21 (4.28)	22.63 (3.68)	10.92 (2.29)	28.91 (4.46)	7.24 (1.66)
Comorbid substance use	$t=0.258$	$t=1.038$	$t=-0.244$	$t=0.258$	$t=-0.799$
	$P=0.797$	$P=0.301$	$P=0.808$	$P=0.797$	$P=0.426$
Yes	26.20 (4.12)	22.60 (3.74)	10.99 (2.25)	28.99 (4.47)	7.33 (1.58)
No	26.55 (6.14)	23.82 (3.52)	10.82 (2.40)	29.36 (5.78)	6.91 (2.39)
Daily methadone dose†	$r=-0.159$	$r=-0.051$	$r=-0.072$	$r=-0.008$	$r=-0.031$
	$P=0.067$	$P=0.561$	$P=0.412$	$P=0.928$	$P=0.719$
Duration of methadone†	$r=-0.306$	$r=-0.131$	$r=-0.177$	$r=-0.259$	$r=-0.186$
	$P<0.001^*$	$P=0.130$	$P=0.040$	$P=0.003^*$	$P=0.032$
OTI heroin Q score‡	$r=0.003$	$r=0.026$	$r=-0.074$	$r=-0.046$	$r=0.019$
	$P=0.972$	$P=0.763$	$P=0.393$	$P=0.600$	$P=0.825$
OTI HIV risk-taking behavior score‡	$r=0.005$	$r=0.035$	$r=0.077$	$r=0.032$	$r=-0.089$
	$P=0.957$	$P=0.689$	$P=0.379$	$P=0.717$	$P=0.308$
OTI social functioning score‡	$r=-0.145$	$r=-0.176$	$r=-0.151$	$r=-0.162$	$r=-0.059$
	$P=0.094$	$P=0.042$	$P=0.081$	$P=0.061$	$P=0.496$
OTI crime score‡	$r=-0.076$	$r=-0.019$	$r=0.050$	$r=-0.049$	$r=-0.032$
	$P=0.389$	$P=0.826$	$P=0.564$	$P=0.579$	$P=0.711$
OTI health score‡	$r=-0.230$	$r=-0.182$	$r=-0.105$	$r=-0.204$	$r=-0.213$
	$P=0.007$	$P=0.035$	$P=0.229$	$P=0.018$	$P=0.013$

MMT, methadone maintenance therapy; OTI, Opiate Treatment Index; QOL, quality of life; WHOQOL, World Health Organization Quality of Life.
*Significant when $P<0.003$ (Bonferroni-adjusted).
†Pearson's correlation coefficient.
‡Spearman's correlation coefficient; r = correlation coefficient.

to be more prevalent among patients on MMT, and thus may further worsen ED in this group of individuals (Callaly et al., 2001; Chen et al., 2013).

Our study did not find any association between age and having ED using the recommended cut-off score; however, there was a significant correlation between increasing age and severity of ED. Although the association between age and ED has been demonstrated (Johannes et al., 2000; Selvin et al., 2007), there were some studies among patients on MMT that did not find any significant association between these 2

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TABLE 5. Multiple Linear Regression: Factors Associated With Significant Differences in Quality-of-Life Scores

	Physical Health	Social Relationships	Environment
	$R^2 = 0.211$	$R^2 = 0.162$	$R^2 = 0.145$
ED		-0.167^{*}	
Depression	-0.343^{***}	-0.327^{***}	-0.281^{**}
Duration of MMT	-0.290^{***}		-0.245^{**}

ED, erectile dysfunction; MMT, methadone maintenance therapy.
$^{*}P < 0.05$.
$^{**}P < 0.01$.
$^{***}P < 0.001$.

variables (Quaglio et al., 2008; Tatari et al., 2010). Nevertheless, evidence has shown increasing severity of ED with advancing age (Feldman et al., 1994; Shiri et al., 2003). Results from the Massachusetts Male Aging Study showed that the likelihood of complete ED at age 70 was 3-fold and the likelihood of moderate ED was 2-fold that at age 40, whereas the likelihood of minimal ED was constant across all age groups (Feldman et al., 1994). Our study showed a similar trend in which the prevalence of severe ED among patients above 50 years old was more than 4-fold higher compared with those 40 years aged and below, and 3-fold higher than those aged between 41 and 50 years old, whereas the prevalence of mild ED did not differ much across the age groups. This finding is further supported by the study by Nik Jaafar et al. (2013), which found that the prevalence of severe ED among Malaysian methadone patients aged above 51 was 14.3% whereas none of the patients aged 50 and below had severe ED. This may suggest that ED may occur in any age groups among patients who are on methadone; however, the severity of the ED worsens with increasing age.

Having ED predicted a lower QOL in the social relationships domain. Although evidence of the relationship between sexual dysfunction and QOL among patients on MMT is limited, studies among the general population have shown that ED is associated with a lower QOL (Jonler et al., 1995; Hwang et al., 2007). Other studies have also found similar findings that social relationships were impaired in individuals with EDs, suggesting that sexual function affects interpersonal relationships (Tsai et al., 2008; Idung et al., 2012). Relationship problems and marital tension may arise as a result of ED, as evidenced by a study, which showed that approximately 12% to 28% of men with ED believed that the ED was one of the main factors that affected their relationship (Guest and Das Gupta, 2002). In our study, ED and depression were both independently associated with a lower QOL in the social relationships domain. The additional stigma of having depression and sexual dysfunction on top of being on MMT and their influence on QOL further emphasizes the importance of adequate assessment and management of these issues particularly among patients on MMT.

Although ED appeared to affect the social aspects of QOL more than the physical health and psychological aspects in our study, it is nevertheless important to address and adequately treat ED considering the advancement and increase in the number of treatment options available. Among the treatment options that have been studied include testosterone patch therapy, bromocriptine treatment, and bupropion (Shinderman and Maxwell, 2000; Daniell et al., 2006). Other treatment strategies, which may benefit patients with sexual dysfunction include reduction of their daily methadone dose as some studies, have demonstrated an association between methadone dose and severity of sexual dysfunction (Brown et al., 2005; Tatari et al., 2010). Another option that can be considered is a switch from methadone to buprenorphine, as Yee et al. (2014) observed in a meta-analysis that the combined odds of sexual dysfunction were 4 times higher in patients on methadone as compared with those on buprenorphine.

Our study, however, only evaluated the sexual health of patients with sexual partners due to the use of IIEF questionnaire, which was not validated for men without sexual partners. This may not represent the prevalence of sexual dysfunction among patients without sexual partners. For patients without sexual partners, the use of modified IIEF questionnaire is proposed to improve the accuracy of the prevalence of ED (Yule et al., 2011). However, further research is needed to establish the psychometric properties of this modified questionnaire. The characteristics of sexual partners were also not assessed in this study. This limits the findings of the factors associated with ED as certain characteristics of sexual partners such as having a sexual partner with a history of drug use may be associated with a greater risk of ED (Quaglio et al., 2008).

Secondly, our study did not examine alcohol use disorder or alcoholic liver disease in particular as a risk factor for ED. The association between alcohol use and sexual dysfunction has been well-documented, with evidence showing that patients with alcoholic cirrhosis having a more severe impotence compared to nonalcoholic liver cirrhosis (Cornely et al., 1984). In addition, alcohol use is common among patients on methadone treatment and is also known to be associated with depression, and thus may be a potential confounding factor in our study (Grant and Harford, 1995; Ryder et al., 2009). However, the prevalence of alcohol use in the preceding month before interview in our study is considerably low (0.03%), possibly due to a majority of the patients being Muslims (81.3%), and Islam prohibits alcohol consumption. It is therefore recommended that future studies further explore the role of alcohol use disorder and liver disease on sexual dysfunction among patients on methadone treatment.

Another limitation is that hormonal levels of patients were not measured in this study. Assessment of the correlation between sexual dysfunction and hormonal levels may further explain the etiological relationship between methadone and sexual dysfunction. In addition, the questionnaires used were self-rated and collateral information from a partner was not obtained. Finally, other limitations include the small sample size of the study and the recruitment of patients from 1 centre in a single geographic area, which limits its generalizability.

Despite these weaknesses, this study is one of the few studies that provided insight into the impact of ED on QOL among patients on MMT. Although the relationship between depression, ED, and QOL remains complex and interconnected, sexual health nevertheless plays an important role in patients' lives and needs to be addressed as part of managing patients on MMT.

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CONCLUSION

ED is prevalent among patients on MMT, which is more likely to occur in the presence of depression, and predicts a lower QOL in the social relationships domain. This stresses the need not only to detect, address, and adequately treat ED as part of the management for patients on methadone treatment, but also to treat underlying depression that poses as a risk factor for ED.

ACKNOWLEDGMENTS

The authors thank Ernie Azwa Binti Yusop for her valuable assistance in data collection during the study.

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