# MODELLING EFFECTS OF METHADONE THERAPY FOR NARCOTIC WITHDRAWAL ON SEXUAL FUNCTION AMONG DRUG ADDICTS AT SELANGOR (MALAYSIA)

Noman D Salih\*, Abdul Rahman Azaman, Khairul Nizam M I, Hanan Kumar Gopalan

Universiti Kuala Lumpur, Institute of Medical Science Technology, Clinical Laboratory Science Section, A1-1 Jalan TKS 1, Taman Kajang Sentral, 43000 Kajang, Selangor, Malaysia.

Email: nomand@unikl.edu.my; Tel: +6012 319 0051

ABSTRACT: This study has been designed to evaluate the modelling effects of methadone treatment for narcotic withdrawal on sexual function among patients at different stages of drug addiction. A cross-sectional study has been applied, using AMOS software. 424 volunteers participated in this study, assessed through questionnaires regarding their demographic, addiction history and sexual functioning, as well as medical consultation session have been conducted to obtain their urine analysis results, current methadone dosage, the duration of methadone treatment, and type of previous drugs used. Reliability level for each variable was determined using Cronbach's Alpha. The correlation between duration, dose of treatment, and sexual functions were investigated. The independent variables were dosage and duration of methadone treatment while the dependent variables are global sexual dysfunction, libido dysfunction, erectile dysfunction, and orgasm dysfunction. The results showed a significant effect on the duration of methadone treatment taken by patients towards their orgasm, libido and erectile dysfunction (p<0.001). However, the effect of the duration, and the dose of methadone taken towards orgasm dysfunction, libido dysfunction, and erectile dysfunction found to be statistically insignificant, except for the effect of methadone dosage towards erectile dysfunction (p<0.05). This study indicated that duration of methadone taken significantly determined the sexual dysfunction among drug addicts', whilst the dose of methadone taken significantly determined the erectile dysfunction. However the duration of drugs taken does not poses enough evidences to show their importance towards sexual dysfunction among these patients.

**Keywords:** Drug addicts, Methadone treatment, Sexual dysfunction.

Corresponding: Dr. Noman D Salih, Clinical Laboratory Science Sec., Institute of Medical Science & Technology (MESTECH), Universiti Kuala Lumpur (UniKL).

# 1. INTRODUCTION

Addiction is a problem which is increasingly developed among the various populations throughout the world [1]. In Malaysia, the National Anti-Drug Agency (NADA) has reported throughout the period of 2000–2008 that the total of 126,153 new addicts were traced and on average 14,017 involved addicts each year [2]. Methadone has been used successfully to treat narcotic addiction throughout the world and it is the only approved agent in its class for the treatment maintenance of narcotic addiction. According to the Malaysian Ministry of Health (MOH), there are more than 10,000 opiate dependents receiving methadone substitution in Malaysia [3]. Methadone (also known as Methadose, Dolophine, Heptadon, Amidone, and many other names) is a synthetic opioid, which is also an acyclic analog of morphine, thus it acts on the same opioid receptors and has many of the same effects. Medically, it used as anti-addictive for patients with opioid dependency, and as analgesic for managing severe chronic pain, due to its extremely powerful effects, long duration of action, and very low cost [4]. Previous reports have indicated about the higher rates of sexual dysfunction in methadone-maintained populations than in the general population, and it appears to be associated with the alteration of serum levels of hormones related to normal sexual function [5]. Therefore, the present study has been designed to evaluate the modelling effects of methadone treatment for narcotic withdrawal on sexual function among different volunteers at different stages of addiction among Malaysians drug addicts.

### 2. MATERIALS AND METHODS

## 2.1 Descriptive Sampling

This research applies cross-sectional study, whereby the volunteers with inclusion criteria were prior informed about the study and the importance of their participation. There were 424 volunteers involved in this study, assessed through a set of questionnaires about their demographic, addiction history and sexual functioning, and at the same time, a medical consultation session has been conducted to obtain their urine analysis results, current methadone dosage, duration of methadone treatment, and the type of previous drug used. For the purpose of this study, correlation between duration, dose of treatment, and sexual functions were investigated. The independent variables were dose and duration of methadone treatment while the dependent variables are global sexual function, libido, erectile function and orgasm.

### 2.2 Research Session

All volunteers participated in a 15 minutes research session which prompted them to complete a set of questionnaires, related to their demographic, medication history, addiction history and sexual history (Using Sexual History Form (SHF) developed by Nowinski and Lopicollo [6].

# 2.3 Scoring the Sexual Functioning Score

In this study, questions of SHF were grouped into four axes; global sexual functioning score, desire dysfunction, orgasm dysfunction, and erectile dysfunction. The global sexual functioning score has been calculated on a 0-100 scale, with a normal range of 21 to 52, a higher score indicating a greater degree of dysfunction, while desire or libido dysfunction, arousal or erectile dysfunction and orgasm dysfunction were referred to as the subscales. Because there were no normative data for the subscales, the number of patients who scored

above 50 on a 0-100 scale has been considered as having dysfunction for the subscales.

## 2.4 Data Analysis

Data was analysed using descriptive analysis, factor analysis and structural equation modeling using AMOS 17.0

### 3. RESULTS

The results have indicated that the duration of methadone taken significantly determined the sexual dysfunction among drug addicts. Whilst the dose of methadone taken significantly determined the erectile dysfunction. However the duration of drugs taken does not have enough evidences to show their importance towards sexual dysfunction.

### 3.1 Reliability analysis

Reliability level for each variable was determined using Cronbach's Alpha. The alpha value for each variable exceeded 0.7 and this is considered acceptable for further analysis. The reliability analysis of the measurement model is presented in table 1& 2. The analysis revealed that the

measurement model adequately meet the reliability, validity, unidimensionality and discriminant validity.

### 3.2 Correlation

Correlation test was conducted for the purpose of this study, correlation between duration, dose of treatment, and sexual functions were investigated. The independent variables were dosage and duration of methadone treatment while the dependent variables are global sexual dysfunction, libido dysfunction, erectile dysfunction, and orgasm dysfunction (Table 2).

### 3.3 The Goodness of Fit Index

The structured model meets all the goodness of fit indices as required for the indexed values for RMSEA, CFI, TLI and Chisq/df, respectively [7,8,9].

# 3.4 The Structural Equation Modelling (SEM)

Results showed a significant effect for duration of methadone treatment taken by patients towards their orgasm, libido and erectile dysfunction (p<0.001). However,the effect of the duration, and the dose of methadone taken towards orgasm

Table 1: The Result of CFA for measurement model					
Construct Variable	Item	Factor Loading	Cronbach Alpha (Above 0.7)	<b>CR</b> (Above 0.6)	AVE (Above 0.5)
Orgasm Dysfunction	Org1	0.55	(110010 0.7)	(110016 0.0)	0.321
2 3	Org2	0.69			
	Org3	0.69	0.803	0.699	
	Org4	0.58			
	Org5	0.81			
Libido Dysfunction	Lib1	0.89		0.838	0.467
	Lib2	0.83			
	Lib3	0.69	0.875		
	Lib4	0.70	0.873	0.838	
	Lib5	0.69			
	Lib6	0.59			
Erectile Dysfunction	ED1	0.72			
	ED2	0.81			
	ED3	0.57	0.857	0.747	0.379
	ED4	0.91			
	ED5	0.57			

Table 2: Discriminant validity of constructs

Construct	OrgasmDysfunction	LibidoDysfunction	Erectile Dysfunction		
OrgasmDysfunction	0.57				
LibidoDysfunction	0.07	0.68			
<b>Erectile Dysfunction</b>	0.18	-0.04	0.62		

Table 3: Goodness of fit index

Name of category	Name of index	Index value	Comments
Absolute fit	RMSEA	0.069	The required level has achieved
Incremental fit	CFI	0.923	The required level has achieved
Incremental fit	TLI	0.905	The required level has achieved
Parsimonious fit	Chisq/df	2.055	The required level has achieved

Table 4: Regression Weights							
Variables	Path	Variables	Estimate (R <sup>2</sup> )	S.E.	C.R.	P value	Result
Orga	<	Methadone Duration	0.002	0.000	6.563	0.001	Significant
Lib	<	Methadone Duration	0.002	0.000	5.544	0.001	Significant
Erectile Dysfunction	<	Methadone Duration	0.002	0.000	5.819	0.001	Significant
Orga	<	DurationDrug	0.000	0.000	1.723	0.085	Insignificant
Lib	<	DurationDrug	0.000	0.000	0.089	0.929	Insignificant
Erectile Dysfunction	<	DurationDrug	0.000	0.000	-0.376	0.707	Insignificant
Orga	<	Methadone Dose	0.000	0.000	0.044	0.965	Insignificant
Lib	<	Methadone Dose	0.001	0.000	1.182	0.237	Insignificant
Erectile Dysfunction	<	Methadone Dose	0.001	0.000	2.831	0.005	Significant
Lib6	<	Lib	1.000				
Lib5	<	Lib	1.070	.103	10.382	***	Significant
Lib4	<	Lib	1.150	.137	8.369	***	Significant
Lib3	<	Lib	1.147	.140	8.220	***	Significant
Lib2	<	Lib	1.025	.112	9.181	***	Significant
Lib1	<	Lib	1.459	.153	9.547	***	Significant
ED5	<	Erectile Dysfunction	1.000				
ED4	<	Erectile Dysfunction	2.098	.227	9.225	***	Significant
ED3	<	Erectile Dysfunction	.996	.137	7.257	***	Significant
ED2	<	Erectile Dysfunction	2.243	.252	8.886	***	Significant
ED1	<	Erectile Dysfunction	1.762	.213	8.271	***	Significant
Org1	<	Orga	1.000				
Org2	<	Orga	1.324	.185	7.161	***	Significant
Org3	<	Orga	1.226	.182	6.744	***	Significant
Org4	<	Orga	1.411	.185	7.617	***	Significant
Org5	<	Orga	2.369	.280	8.455	***	Significant

dysfunction, libido dysfunction, and erectile dysfunction found to be statistically insignificant (p>0.05), except for the effect of methadone dosage towards erectile dysfunction (p<0.05)(Table 4).

These findings is in agreement with previous reports that the dose of methadone treatment were not associated with sexual dysfunction [10-14]. Moreover, other recent studies found no significant association between sexual dysfunction with duration of drug used [15,16]. However, there are still other publications which supported the fact that the duration of methadone treatment was the risk factor for sexual dysfunction among HIV patients [16,17].

# The Structural model

The structural equation model was estimated (Figure 1), using maximum likelihood estimation and confirmed the following hypothesis:

- H1: Duration of methadone taken has a positive and significant impact on sexual dysfunction (p<0.001). Thus, hypothesis is supported.
- H2: Duration of drug taken has a positive and significant impact on sexual dysfunction. Thus, hypothesis is not supported (p>0.05).
- H3: Dosage of methadone taken has a positive and significant impact on sexual dysfunction.

### 4. **DISCUSSION**

The positive effectiveness of methadone maintenance on patients have been referred by many previous researches which included its effects on the mortality reduction [18], the reduction of HIV prevalence and incidence rates [19-22], the reduction rates of viral hepatitis B and C transmission [23-26], the reduced frequency of opioid use [27], the reduced frequency of criminal behaviour [28] and improve employment status [29]. Many of these effects are strongly associated with higher daily methadone dose and with the increasing duration of treatment [30].

Another study claimed that higher rates of sexual dysfunction among methadone-maintained populations as compared to the general populations, considered sexual dysfunction status as a side effect of medication which is associated with alterations of serum levels of hormones. This was a critical issue because of the importance of fertility as a life conservative phenomenon to extend human generation [31]. Testosterone is a sex hormone which plays an important role in sexual functioning for males. Previous study has found that hypogonadal men whom undergo testosterone replacement therapy demonstrated an increase in their sexual interest and erectile function [32]. Lower-than-normal serum testosterone levels may manifest as reduced libido, erectile dysfunction, and with prolonged depression of serum testosterone, seminal emission may be inhibited as well. This scenario may support our findings and indicates the need for hormonal monitoring and replacement therapy especially those who ae on prolonged treatment with methadone to help them in maitaining normal sexual functioning.

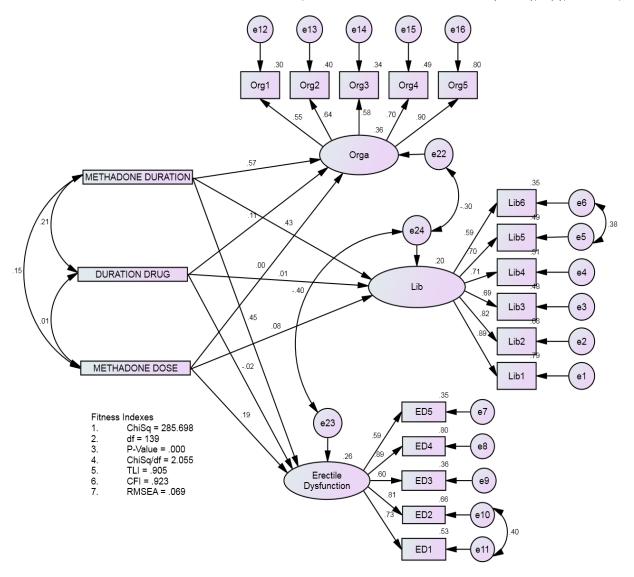


Figure 1: The Relationship between Methadone Therapy and Sexual Function among Drug Addicts

# CONCLUSION

This study has indicated that duration of methadone taken significantly determined the sexual dysfunction among drug addicts. Whilst the dose of methadone taken significantly determined the erectile dysfunction. However the duration of drugs taken does not poses enough evidences to show their importance towards the sexual dysfunction.

### **ACKNOWLEDGMENT**

The author is thankful to the Institute of Medical Science Technology (Mestech), Universiti Kuala Lumpur (UniKL) for providing necessary facilities and equipments.

### REFERENCES

- Hejazian, S. H., Dashti, M. H., and Rafati, A., "The effect of opium on serum LH, FSH and testosterone concentration in addicted men" Iranian J Reproductive *Med*, **1**(5):35-38(2007).
- 2. NADA, National Anti-Drug Agency, "Selected Social Statistic Series"12/10(2010).

- Mohamad, N., Abu Bakar, N. H., KC, S., Zulkafli, M. I., Razali, F., Talib, N. and Ismail, R., "Personalized Methadone Therapy: Clinically Stable Patients With High Dose Plasma Methadone And A Prolonged Qtc. A Safer Approach In Methadone Maintenance Therapy" Int J Addiction Sci1(1):1-4(2010).
- 4. Sepulveda, J. L., "Genetic Aspect of Opiate Metabolism and Addiction" Pharmacogenomics of Alcohol and Drugs of Abuse, 165-194(2012).DOI: 10.1201/b11879-9
- Teusch, L., Scherbaum, N., Bohme, H., Bender, S., Eschmann-Mehl, G. and Gastpar, M., "Different patterns of sexual dysfunctions associated with psychiatric disorders and psychopharmacological treatment. Results of an investigation by semistructured interview of schizophrenic and neurotic patients and methadone-substitutedopiate
  - addicts" Pharmacopsychiatry 28:84-92 (1995).
- 6. Creti, L., Fichten, C. S., Amsel, R., Brender, W., Schover, L. R., Kalogeropoulos, D., "Global sexual functioning: A single summary score for Nowinski and

- LoPiccolo's Sexual History Form (SHF). In C. M. Davis, W. L. Yarber, R. Bauserman, G. Schreer, and S. L. Davis (Ed.)" *Handbook of sexuality-related measures*, Thousand Oaks, CA,261-267(1998).
- Marsh, H. W., and Hocevar, D., "Application of confirmatory factor analysis to the study of selfconcept: First- and higher order factor models and their invariance across groups" Psychological Bulletin, 97:362-582(1985).
- 8. Browne, M. W., and Cudeck, R., "Alternative ways of assessing model fit. In: K. A. Bollen & J. S. Long (Ed.)", *Testing structural equation models*, Beverly Hills, CA,136-162(1993).
- 9. Bentler, P. M.,"Comparative fit indexes in structural models" *Psychological Bulletin*, **107**:238–246(1990).
- Minying, Z., Huifang, Z., Cynthia, X.S., Jennifer, McGoogan, M., Baohua, Z., Linglong Z., Mianzhi, Z., Keming, R., Zunyou, W.,"Sexual Dysfunction Improved in Heroin-Dependent Men after Methadone Maintenance Treatment in Tianjin, China"Plos One9(2):e88289(2014).
- 11. Hallinan, R., Byrne, A., Agho, K., McMahon, C., Tynan, P., Attia, J.,"Erectile dysfunction in men receiving methadone and buprenorphine maintenance treatment" *J Sexual Med*, 5:684–692 (2008).
- 12. Quaglio, G., Lugoboni, F., Pattaro, C., Melar, a B., Mezzelani, P., Des Jarlais, D.C., "Erectile dysfunction in male heroin users, receiving methadone and buprenorphine maintenance treatment, *Drug and Alcohol Depen*, **94**:12–18(2008).
- 13. Hanbury, R., Cohen, M. and Stimmel, B., "Adequacy of sexual performance in men maintained on methadone" *American J Drug Alcohol Abuse*, **4**:13-20(1977).
- 14. Cioe, P.A., Friedmann, P.D., Stein, M.D., Erectile Dysfunction in Opioid Users: Lack of Association with Serum Testosterone *J addictive dis*, **29**(4):455-460(2010).
- Bliesener, N., Albrecht, S., Schwager, A., Weckbecker, K., Lichtermann, D., and Klingmüller, D.,"Plasma testosterone and sexual function in men receiving buprenorphine maintenance for opioid dependence" *J* Clin Endocrinol Metabol, 90(1):203-206(2005).
- 16. Chen, W., Li, X., Li, X., Ling, L., Xia, Y., Chen, J., He, Q., "Erectile dysfunction among male heroin addicts receiving methadone maintenance treatment in Guangdong, China" *J Addict Med*, 6:212–218(2012).
- 17. Tatari, F., Farnia, V., Najafi, F., "Trazodone in methandone induced erectile dysfunction" *Iran J Psychiatry*, **5**:164–166(2010).
- 18. Langendam, M. W., Van Brussel, G. H., Coutinho, R. A., and Van Ameijden, E. J.,"The impact of harm-reduction-based methadone treatment on mortality among heroin users" *American J Pub Health*, **91**(5):774(2001).
- Byrne, A.,"Nine year follow-up of 86 consecutive patients treated with methadone in general practice, Sydney, Australia"Drug Alcohol Rev, 19:153-158(2000).
- 20. Shah, N.G., Celentano, D.D., Vlahov, D., Stambolis, V., Johnson, L., Nelson, K.E., Strathdee, S.A., "Correlates

- of enrollment in methadone maintenance treatment programs differ by HIV-serostatus" *AIDS*, **14**:2035-2043(2000).
- 21. Broers B., Junet, C., Bourquin, M., Deglon J.J., Perrin, L., Hirschel, B., "Prevalence and incidence rate of HIV, hepatitis B and C among drug users on methadone maintenance treatment in Geneva between 1988 and 1995" *AIDS*, 12(15):2059-2066(1998).
- 22. Gaughwin, M.D. and Ali, R.,"HIV infection among injecting drug users in the South Australian methadone program"*Med J Aust*, **162**:242-244(1995).
- 23. Carter, H., Robinson, G., Hanlon, C., Hailwood, C., Massarotto, A.,"Prevalence of hepatitis B and C infection in a methadone clinic population: implications for hepatitis B vaccination"*New Zealand Med J*,114(1136):324-326(2001).
- 24. Brunton, C., Kemp, R., Raynel, P., Harte, D., Baker, M., "Cumulative incidence of hepatitis C seroconversion in a cohort of seronegative injecting drug users" *New Zealand Med J*,**113**(1106):98-101(2000).
- 25. Smyth, B.P., Keenan, E., O'Connor, J.J., "Evaluation of the impact of Dublin's expanded harm reduction programme on prevalence of hepatitis C among short-term injecting drug users" *J Epidemiol Community Health*, **53**(7):434-435(1999).
- 26. Crofts, N., Nigro, L., Oman, K., Stevenson, E., Sherman, J.,"Methadone maintenance and hepatitis C virus infection among injecting drug users"*Addiction*, **92**(8):999-1005(1997).
- Yancovitz, S. R., Des Jarlais, D. C., Peyser, N. P., Drew, E., Friedmann, P., Trigg, H. L., and Robinson, J. W.,"A randomized trial of an interim methadone maintenance clinic" *American J Pub Health*, 81(9):1185-1191(1991).
- 28. Bell, J., Hall, W., and Byth, K., "Changes in criminal activity after entering methadone maintenance" *British j addiction*, **87**(2):251-258(1992).
- 29. Ward, J., Mattick, R. P., and Hall, W.,"The effectiveness of methadone maintenance treatment: an overview" *Drug and Alcohol Rev*, 13(3):327-336(1994).
- 30. Strain, E. C., Bigelow, G. E., Liebson, I. A., and Stitzer, M. L.," Moderate-vs high-dose methadone in the treatment of opioid dependence" *JAMA*, **281**(11):1000-1005(1999).
- 31. Moisey, R., Swinburne, J., and Orme, S.," Serum testosterone and bioavailable testosterone correlate with age and body size in hypogonadal men treated with testosterone undecanoate (1000 mg IM–Nebido®)" *Clin Endocrinol*, **64**(4):642-647(2008).
- 32. Bancroft, J.,"The endocrinology of Sexual Arousal"*J Endocrinol*,186:411-27(2005).