

## EDUCATION SECTION

# MOCK MODEL ANSWER FOR CRITICAL REVIEW PAPER: CONJOINT EXAMINATION FOR MASTER OF MEDICINE (PSYCHIATRY) AND MPM, NOVEMBER 2011

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### Abstract

**Objective:** This paper aims to highlights the answer for Review Paper Mock Exam for the Malaysian Master of Medicine (Psychiatry) theory examination. The paper compared the risk of sexual dysfunction associated with the use of two antidepressants in patients attending a university hospital. **Methods:** One of the papers presented during the journal club presentation was picked-up for evaluation of student's critical appraisal. **Results:** Model answer was given at the end of the Mock Critical Review Paper. **Conclusion:** This review paper is an important method of evaluating the student's understanding and critical thinking on the topic of risk of sexual dysfunction associated with escitalopram and fluoxetine in female patients. This paper may serve as a guideline for nurturing young talents at the postgraduate level to critically appraise topic related to Psychiatry and sexuality. *ASEAN Journal of Psychiatry, Vol. 13 (2): July – December 2012: XX XX.*

**TITLE OF PAPER: FEMALE SEXUAL DYSFUNCTION IN PATIENTS TREATED WITH ANTIDEPRESSANT – COMPARISON BETWEEN ESCITALOPRAM AND FLUOXETINE (Published in the International Journal of Clinical Practice in Psychiatry, 2012: 41 – 47)**

### Objective

Escitalopram and fluoxetine are the two most commonly prescribed antidepressants in our local setting. As a result, this study aims to compare the risk of sexual dysfunction associated with escitalopram and fluoxetine in female patients from a university hospital setting.

### Methods

This is a cross-sectional study to assess and compare the prevalence of female sexual dysfunction associated with fluoxetine and escitalopram. Data was collected over a period

of six months, from 1<sup>st</sup> June 2009 until 30<sup>th</sup> November 2009. The study subjects were female patients on fluoxetine and escitalopram who fulfilled the inclusion criteria and attended the Psychiatric Clinic UKMMC during the study period. **Inclusion criteria** include: (i) female outpatients who were diagnosed with major depressive disorder (MDD) based on DSM-IV by the treating Psychiatrists in UKMMC using Structured Clinical Interview for DSM-IV Disorders (SCID); (ii) patients who were in full remission (defined by DSM-IV as during the past 2 months had no significant signs or symptoms of the disturbance and Montgomery-Asberg depression rating scale (MADRS) score of = 10), (iii) patients aged between 18 and 65

years old; (iv) patients who were married and with a sexually active partner, (v) Patients who were able to read and understand Malay Language (the national language); (vi) patients who consented. **Exclusion criteria** include: (i) patients who were suffering from chronic and severe medical illness (based on history taking and physical examination); (ii) patients who were pregnant or within 2 months postpartum period. The estimated prevalence of sexual dysfunction associated with escitalopram was 30% (Clayton and Montejo, 2006) and fluoxetine was 57.7% (Montejo et al., 2001). A total sample of 112 subjects with 56 per group will give the power of 80% with the precision of 5% for the study.

Subjects of this study were identified from the psychiatric outpatient clinic, UKMMC. Written consent was obtained. Subjects were then interviewed by using the Structured Clinical Interview for DSM-IV Disorders (SCID) Interview and the depressive symptoms were assessed with MADRS and sexual dysfunction with the Malay Version of the Female Sexual Function Index (MVFSFI). The basic socio-demographic data of the subjects was collected using a predesigned questionnaire.

Open-ended questions encourage subjects to expand their answers. Both required and optional probes are provided, and allowing the interviewer to skip unnecessary questions and moves on the next session and module. Therefore interview time can be shortened and quickened.

Montgomery-Asberg Depression Rating Scale (MADRS) was used. The original author found that a cutoff of = 10 maximized the level of agreement with the Hamilton rating scale for depression (HRSD) definition of remission (Montgomery and Asberg, 1979; Zimmerman et al., 2004). Malay Version of the Female Sexual Function Index (MVFSFI) (Hatta Sidi et al., 2007) was used to assess female sexual function. MVFSFI is a validated and locally accepted questionnaire for use in the assessment of female sexual dysfunction in the Malaysian population. A total score of 55 was taken as the cut-off point for the MVFSFI to distinguish between women with and without sexual dysfunction (sensitivity = 99%, specificity = 97%). Previously published dosing classification as described by Gartlehner et al. (2007) was used in this study. This classification is used to detect inequalities in dosing, and does not indicate dosing equivalence (Cipriani et al., 2009).

#### **Dosing classification**

	<b>Low</b>	<b>Medium</b>	<b>High</b>
<b>Fluoxetine</b>	< 30 mg/day	30-50 mg/day	> 50 mg/day
<b>Escitalopram</b>	< 15 mg/day	15-25 mg/day	> 25 mg/day

The data collected was analyzed using the Statistical Package for Social Science (SPSS) version 12 (Chicago, IL, USA). Chi-Square test was used to compare categorical variables. Further analysis was used to examine the association between independent variables and dependent variable. Instead of choosing the variables for multivariate model based on the conventional method ie., significant variables from univariate analysis, the authors included clinical important associated variables into the final multivariate analysis.

#### **Results**

A total of 112 female outpatients, with 56 patients on fluoxetine and 56 patients on escitalopram who attended the Psychiatric Clinic UKMMC during the study period were included in the study. The mean age of the subjects was about 40 years old with average 15 years of marriage. Majority of patients were Malay (49.1%) followed by Chinese (38.4%) and Indian (12.5%). Academically, most patients had

their education until secondary level (37.5%) and tertiary level (40.2%). Majority of patients were employed (63.4%). More than half of the subjects had monthly family income of more than RM3000 (54.5%). Majority of the subjects had child(ren) (80.4%). Most patients had one to

two children (42.9%). In term of frequency of sexual intercourse in the last 4 weeks, it was higher in subjects on escitalopram than those on fluoxetine. 33.9% of the subjects were using contraceptive methods. 22.3% experienced dysmenorrhoea.

**Table 1. Dosage and duration of antidepressant usage of the subjects**

	Treatment group	
	Fluoxetine	Escitalopram
Dosage, mean (sd)	30.71 (10.76)	12.32 (4.15)
Duration in months, mean (sd)	50.04 (34.37)	22.70 (11.87)
Dosing classification*		
Low	27 (48.2)	38 (67.9)
High	29 (51.8)	18 (32.1)

\*Low = (=30mg for fluoxetine or = 15mg for escitalopram); High = (> 30mg for fluoxetine or > 15mg for escitalopram); Based on classification described by Gartlehner and colleagues (2007), there were more subjects in the escitalopram group (67.9%) in the low dosing class compared to fluoxetine (48.2%).

**Table 2. Comparison of overall and each domain of female sexual dysfunction associated with fluoxetine and escitalopram based on MVFSFI**

	Female sexual dysfunction	Chi-Square	OR (95% CI)	
	Present N (%)	Absent N (%)		
<b>Overall Sexual Function</b>				
Fluoxetine	31 (55.4)	25 (44.6)	5.203	2.415 (1.125-5.184)
Escitalopram	19 (33.9)	37 (66.1)		
<b>Desire Domain</b>				
Fluoxetine	36 (64.3)	20 (35.7)	8.038	3.000 (1.390-6.473)
Escitalopram	21 (37.5)	35 (62.5)		
<b>Arousal Domain</b>				

Fluoxetine	28 (50.0)	28 (50.0)	3.689	2.111 (0.980- 4.548)
Escitalopram	18 (32.1)	38 (67.9)		
<b>Lubrication Domain</b>				
Fluoxetine	26 (46.4)	30 (53.6)	3.058	1.988 (0.916- 4.315)
Escitalopram	17 (30.4)	39 (69.6)		
<b>Orgasm Domain</b>				
Fluoxetine	33 (58.9)	23 (41.1)	3.571	2.059 (0.970- 4.371)
Escitalopram	23 (41.1)	33 (58.9)		
<b>Satisfaction Domain</b>				
Fluoxetine	15 (26.8)	41 (73.2)	1.287	1.683 (0.681- 4.156)
Escitalopram	10 (17.9)	46 (82.1)		
<b>Pain Domain</b>				
Fluoxetine	10 (17.9)	46 (82.1)	0.265	1.304 (0.473- 3.595)
Escitalopram	8 (14.3)	48 (85.7)		

\*p<0.05, \*\* Sexual dysfunction = (= 55 in MVFSFI score), OR = Odds Ratio, CI = Confidence Interval

**Table 3 Analysis of the determinant for female sexual dysfunction**

Variable	$\beta$	SE	p value	Adjusted Odds Ratio	95% CI
<b>Antidepressant</b> Fluoxetine Escitalopram	0.955	0.558	0.087	2.599	0.870-7.764
<b>Dosing classification</b> Moderate to high Low	1.588	0.472	0.001	4.892	1.941-12.331
Duration of usage	0.001	0.010	0.921	1.001	0.982-1.020
Age	-0.015	0.060	0.801	0.985	0.875-1.109
<b>Smoking</b> Yes No	1.771	0.903	0.050	5.878	1.002-34.473
<b>Alcohol</b> Yes No	-1.585	1.080	0.142	0.205	0.025-1.703
Years of marriage	0.087	0.058	0.134	1.091	0.974-1.222
Menopause Yes No	-0.164	0.797	0.837	0.849	0.178-4.046

## Questions

**1. In the exclusion criteria, women within 2 months postpartum period were excluded. What is the most likely reason why they were excluded in this research? (1 mark).**

*Sexual activity is less practised during confinement period*

**2. The statistical power was determined at 80% with the precision of 5% for the study.**

**(a) Define the meaning of statistical power (2 marks).**

*The **power** (P) of a statistical test is the probability that the test will reject a false null hypothesis (i.e. that it will not make a Type II error). As power increases, the chances of a Type II error decrease.*

**(b) Besides increasing the sample size, name two other ways to increase the statistical power for a study (2 marks).**

*i. Using parametric rather than non-parametric statistical test*

*ii. Increase the level of significant ( $\alpha$ ) to 0.001 from 0.05*

**3. Outline one significant finding on the sexual domain in Table 2 (1 mark). Explain the meaning of the significant finding (2 marks).**

*The only domain of sexual dysfunction that showed statistically significant difference between the two groups was desire (1 mark).*

*Patients on fluoxetine were found to be 3 times (95% CI: 1.39-6.47) more likely to suffer from desire problems as compared to patients on escitalopram, and it is significant statistically because the OR do not cross 1. (2 marks).*

**4. (a) Name the type of statistic used in Table 3? (1 mark).**

*Multivariate logistic regression analysis / logistic regression / regression analysis*

**(b) Describe 3 assumptions that were made in the statistical analysis for (a).(3 marks)**

*i. Samples are taken at random*

*ii. The relationship between X and Y is linear*

*iii. Samples are independent, eg. one sample with one scores for each independent variable*

- iv. *Equal variation of Y values in relation to X*
- v. *Y values are normally distributed in relation to X*

**(c) Describe and discuss the significant findings found in Table 3 (3 marks).**

*Patients on medium to high dose of fluoxetine and escitalopram were found to be significantly more likely (almost 5 x risk) to suffer from FSD as compared to patients on low dose, ie. OR=4.89, with OR values does not cross 1.*

**5. Outline 4 limitations of this study (4 marks).**

- (i) *The treatment duration of the two groups were different (fluoxetine = 50.04 months; escitalopram = 22.70 months). This could bias the results as patients with poor tolerability of sexual dysfunction could have abandoned the treatment.*
- (ii) *The dosage was clearly higher than the recommended dosage in fluoxetine group as compared to escitalopram group. Higher dosage could be the main factor for higher rate of sexual dysfunction in the fluoxetine group and bias the result.*
- (iii) *Axis II (personality) diagnosis could be a pertinent factor for sexual dysfunction and not measured in the present study.*
- (iv) *This is a comparative cross-sectional study and was conducted at only one particular urban centre. These may limit the generalizability of the findings from this study.*
- (v) *This is a cross-sectional study in nature, only an association could be determined and not a causal effect.*
- (vi) *The relationship of the subjects with their husband as well as the cultural influences on sexual functioning was not investigated in this study. Female sexual dysfunction can actually reflect problems in intimacy and eroticism between couples (Sidi et al. 2007).*

**6. What is the clinical implication of the research? (2 marks)**

*Patients on medium to high dose of antidepressants had higher risk of FSD. Therefore, it is important to advise the sexual side-effects of SSRI to our patients.*

*Clinician has to be concerned about the dosage of antidepressants prescribed*

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