

Cost Effectiveness of Fluvoxamine versus Desvenlafaxine among the Patients with Major Depressive Disorder in China

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How to cite this paper: Ahn, J., Noh, S., Yang, X.Q. and Kim, K. (2024) Cost Effectiveness of Fluvoxamine versus Desvenlafaxine among the Patients with Major Depressive Disorder in China. *Health*, 16, 1050-1056. <https://doi.org/10.4236/health.2024.1611072>

Received: October 8, 2024

Accepted: November 19, 2024

Published: November 22, 2024

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Abstract

Objectives: To estimate the cost effectiveness of fluvoxamine against desvenlafaxine in Chinese patients with major depressive disorder (MDD). **Methods:** A cost effectiveness of treating Chinese patients with MDD for 6 months maintenance period has been estimated by a decision tree model. The relative effectiveness on relapse rates came from a recent network meta analysis by Kishi *et al.* (2023) along with local drug cost data based on WHO defined daily dose (DDD) and relapse cost for the 6 months estimated from various sources were used in the model. Based on the Quality Adjusted Life Years (QALY) gain reported by Sobocki *et al.* (2007), QALY loss from a relapse was estimated. Univariate sensitivity analyses were presented by a Tornado diagram and extensive probabilistic sensitivity analysis based on 10,000 simulations was performed. The most recent cost effectiveness threshold of 1.5 times GDP suggested by Cai *et al.* (2022) was applied. **Results:** Fluvoxamine dominated desvenlafaxine (cost savings of 4003 CNY and 0.01 QALY higher in 6 months). The most sensitive parameters were relapse rates followed by desvenlafaxine cost and utility loss of relapse. However, the default result of fluvoxamine dominance was not changed for any univariate sensitivity analysis. The probabilistic sensitivity result showed the cost effectiveness acceptability at 1.5 times GDP as 99.93%. **Conclusions:** The cost effectiveness of fluvoxamine against desvenlafaxine among Chinese patients with MDD in a 6-month maintenance period was cost saving with better effectiveness (*i.e.*, dominating) with low uncertainty.

Keywords

Cost-Effectiveness Analysis (CEA), Fluvoxamine, Desvenlafaxine, Major Depressive Disorder (MDD), Chinese Healthcare

1. Introduction

Major depressive disorder (MDD) is a psychiatric disorder characterized by at least two weeks duration of depressed mood [1]. MDD is a prevalent mental health condition, affecting 4.4% of the global population annually [2]. During the acute phase of MDD, individuals receive either pharmacological treatment, such as selective serotonin reuptake inhibitor (SSRI), or non-pharmacological interventions, including psychotherapy and electroconvulsive therapy [3] [4]. The risk of relapse or recurrence, chronicity (as indicated by the length of depressive episodes), and treatment resistance rises with each new major depressive episode [5]. Therefore, achieving full remission (typically defined as a score of 7 or lower on the 17-item Hamilton Depression Scale or a 50% - 80% reduction from the initial score) and maintaining ongoing treatment to prevent relapse or recurrence are top priorities in managing MDD [5].

A systematic review by Gu *et al.* [6] reported that the lifetime prevalence of MDD in China is 3.3%, and it is more prevalent in rural areas than in urban areas (2.0% vs. 1.7%) and among females than males (2.1% vs. 1.3%). The relatively low prevalence of MDD in China, estimated at 3.02%, may be attributed to the high incidence of somatic symptoms, such as headaches or stomach pain, among depressed patients [7]. These symptoms often lead to underdiagnosis, as the current diagnostic criteria primarily emphasize psychological symptoms like sadness and diminished interest and energy [6] [8].

For antidepressants, limited evidence is available among the Chinese population [9]. Hu *et al.* [10] projected that the total estimated cost of depression in China is 51,370 million RMB (6264 million USD) at 2002 prices. The direct cost of MDD in China was 8090 million RMB (986 million USD), while the indirect cost was 43,280 million RMB (5278 million USD). Hsieh and Qin [11] estimated that patients with depression spend annually 1836.52 CNY more on healthcare services and 3773.92 CNY more on hospital care than patients without symptoms.

While some studies have examined healthcare costs for MDD patients in China, there is a paucity of research on the cost and cost-effectiveness of treating MDD with specific pharmacological interventions. This study was conducted to estimate the cost-effectiveness between a well-established SSRI (fluvoxamine) [12] and a new serotonin-norepinephrine reuptake inhibitor (SNRI: desvenlafaxine) in Chinese patients with MDD.

2. Methods

A simple decision tree model comparing two antidepressants for cost effectiveness of treating Chinese patients with major depressive disorder (MDD) for 6 months maintenance period was developed (**Figure 1**).

This model encompasses pharmacotherapy for the treatment of major depressive disorder (MDD) and the occurrence of relapse events based on the type of medication. In the initial stage of the model, pathways are divided according to the choice of fluvoxamine or desvenlafaxine, for Chinese patients with major

depressive disorder.

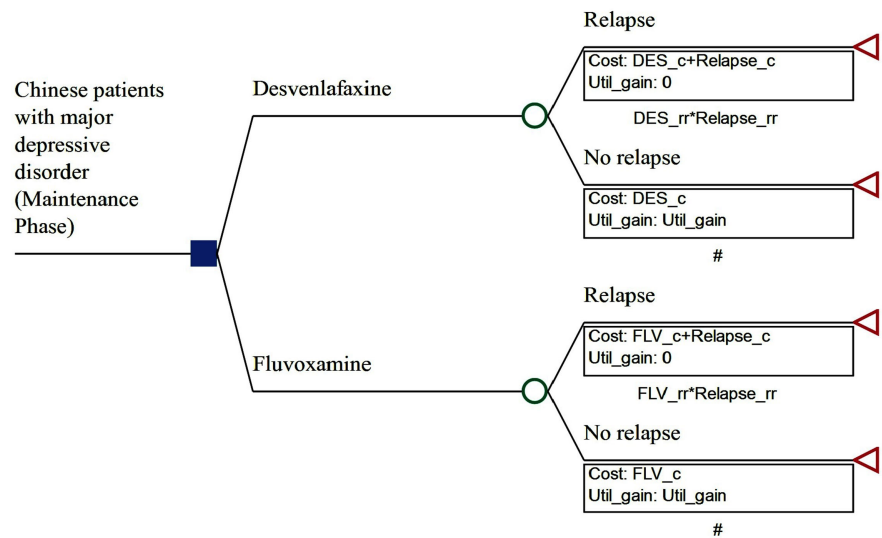


Figure 1. Decision tree model.

After the pathways are divided according to each medication, the model progresses based on the occurrence of relapse events. The relapse rates vary depending on the medication, and the relative effectiveness on relapse rates was obtained from a recent network meta-analysis by Kishi *et al.* (2023). Kishi *et al.* [3] showed risk ratio of relapse during the maintenance phase as 0.298 (95% CI = [0.114, 0.686]) and 0.527 (95% CI = [0.347, 0.787]), for fluvoxamine and desvenlafaxine, respectively. Local drug cost was collected from various sources and defined daily dose (DDD) from WHO ATC/DDD index (ATC = N06A antidepressants) was used to estimate the median antidepressant cost for the 180-day maintenance phase: fluvoxamine for 1080 CNY versus desvenlafaxine for 5008 CNY. Since the local cost for relapse could not be found, the following method was applied to estimate the relapse cost in China. Using the relapse costs reported by Gauthier *et al.* [13], we determined that 2015 USD 7037 per patient per year (PPPY) out of 2015 USD 14416.84 translates to 24.4% of the annual treatment cost of depression for six months. Additionally, Hu *et al.* [10] estimated the annual treatment cost of depression per patient in China to be 2957 CNY in 2006 (equivalent to 360 USD in 2006). Due to the unavailability of the Chinese Medical Consumer Price Index (MCPI) from 2006 to 2015, we used the U.S. Medical CPI data to estimate the 2015 annual treatment cost, which resulted in 3929.34 CNY. Consequently, 24.4% of 3929.34 CNY is calculated as 958.98 CNY. Thus, we assumed 1000 CNY as the six-month relapse cost in China and conducted extensive sensitivity analyses. These costs were incorporated into the model to compare the economic impact of each treatment.

For disutility from a relapse, again there was no local data available, a Swedish study by Sobocki *et al.* [14] was used as follows: Swedish patients with MDD in remission showed a 0.2635 improvement in health related utility measured by EQ-5D instrument. Hence, a utility loss of 0.13 for relapse period during 180-day

maintenance phase was assumed.

The input parameters used in the model are summarized in **Table 1**.

Table 1. Input parameters for the model.

Variable Name	Variable Description	Parameter values (costs in CNY)	Probabilistic Distribution Used [Univariate Sensitivity range]	Source
Relapse_rr	Underlying risk of Relapse (Placebo)	0.4	Triangular [0.1, 0.7]	Assumption
DES_rr	Risk Ratio of Desvenlafaxine compared to Placebo	0.527	Triangular [0.347, 0.787]	Kishi <i>et al.</i> (2023)
FLV_rr	Risk Ratio of Fluvoxamine compared to Placebo	0.298	Triangular [0.114, 0.686]	Kishi <i>et al.</i> (2023)
DES_c	180 day cost of Desvenlafaxine	5008	Gamma [4006.4, 6009.6]	DDD based drug cost
Util_gain	Estimated utility gain for avoiding relapse	0.13	Triangular [0.104, 0.156]	Sobocki <i>et al.</i> (2007)
FLV_c	180 day cost of fluvoxamine	1080	Gamma [864, 1296]	DDD based drug cost
Relapse_c	Cost of treating relapse	CNY 1000	Gamma [800, 1200]	Gauthier <i>et al.</i> (2019) applied to Hu <i>et al.</i> (2007) after inflation adjustment

In this model, the incremental cost effectiveness ratio (ICER) between fluvoxamine and desvenlafaxine was used to assess the cost-effectiveness during the maintenance phase for Chinese patients with major depressive disorder (MDD). The ICER is defined as the ratio of the difference in costs over effectiveness measured by health related utility between two antidepressant interventions. To judge the cost effectiveness, the estimated ICER is compared to the cost effectiveness threshold value in China, or the value of one additional quality-adjusted life year (QALY) in China. According to Cai *et al.* [15], the cost effectiveness threshold value in China was estimated as 1.5 times gross domestic product (GDP) which corresponds to CNY 138,332 in 2023.

Since many assumed input parameters were inevitably used, extensive sensitivity analyses was employed to examine uncertainties from these parameters. A tornado diagram was used to summarize univariate sensitivity analyses. Probabilistic sensitivity analyses with 10,000 simulations using the probabilistic distributions of input parameters and cost effectiveness acceptability curve were used to summarize the results of probabilistic sensitivity analyses.

3. Results

Fluvoxamine was found to be dominating over desvenlafaxine, with cost savings of 4003 CNY and 0.0098 QALY higher over 180-day maintenance phase. The analysis demonstrated that fluvoxamine dominates desvenlafaxine in terms of both costs and effectiveness in China, indicating a strong economic advantage in China.

Univariate sensitivity analyses were presented by a Tornado diagram in **Figure 2**.

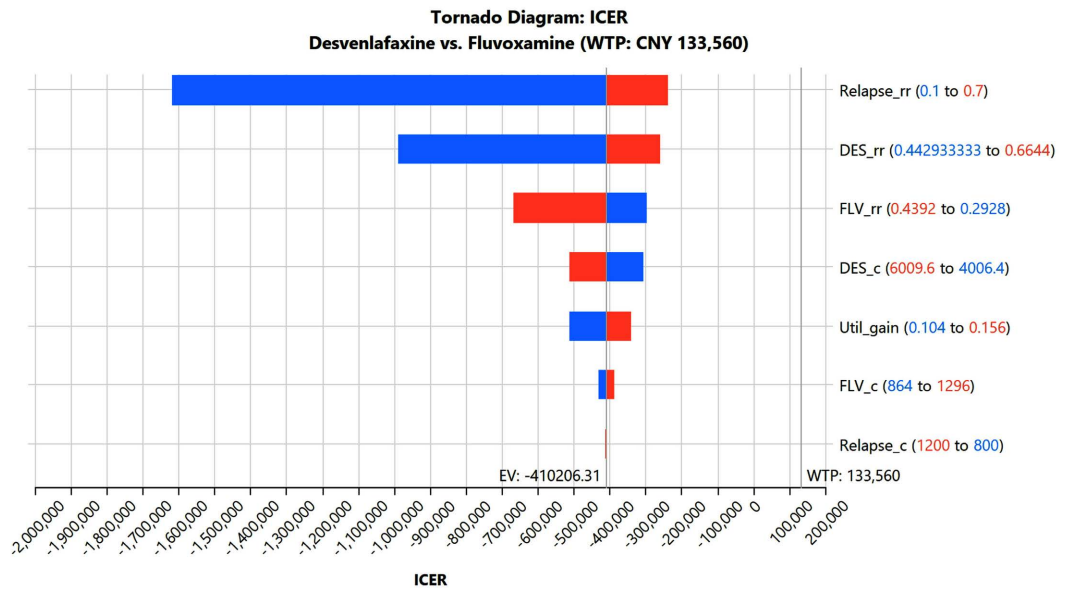


Figure 2. Tornado diagram.

The most sensitive parameters in the univariate sensitivity analyses were the relapse rates, followed by the cost of desvenlafaxine and the utility loss due to relapse. However, the default result of the dominance of fluvoxamine over desvenlafaxine was not changed by any univariate sensitivity analysis.

Extensive probabilistic sensitivity analyses based on 10,000 simulations were performed and the results are shown in **Figure 3**.

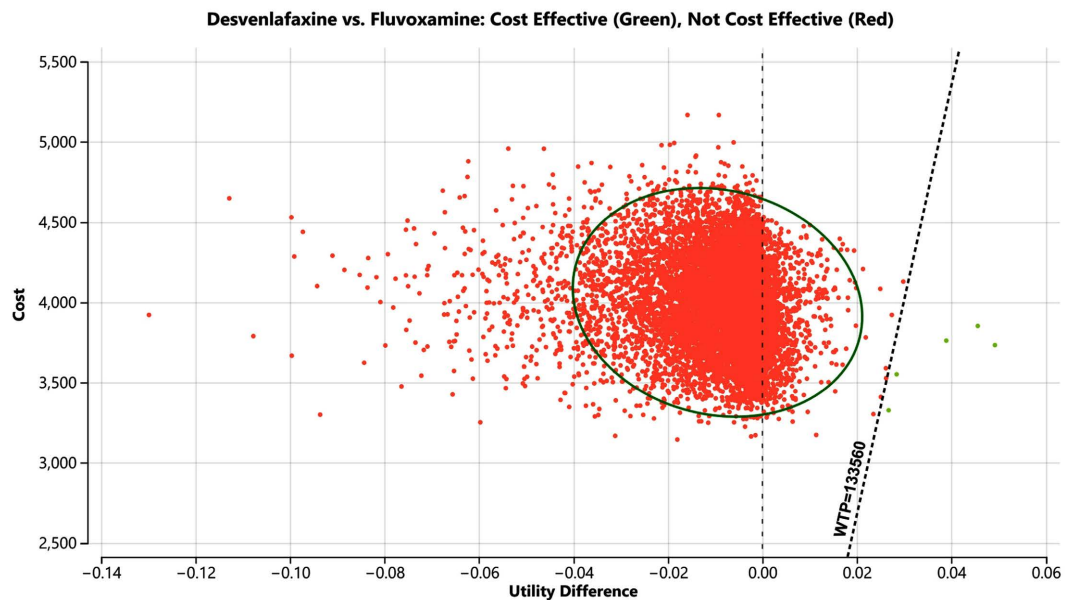


Figure 3. Probabilistic sensitivity analysis.

Probabilistic sensitivity analyses demonstrated almost certain results, the probability of being more cost-effective than the comparator was 99.93% for fluvoxamine at 1.5 times the GDP cost effectiveness threshold.

4. Concluding Remarks

This study evaluated the cost-effectiveness of fluvoxamine compared to desvenlafaxine for treating Chinese patients with major depressive disorder (MDD) over a six-month maintenance period. The analysis demonstrated that fluvoxamine is more cost-effective than desvenlafaxine, with a particularly strong cost-effectiveness profile and low uncertainty during this period. These findings highlight fluvoxamine as a viable treatment option for MDD due to its economic advantages. However, the study's reliance on assumptions and the lack of localized cost data are limitations, suggesting that future research should incorporate more specific regional data. Also disutilities from side effects were not included in the analysis because of lack of local data. Kishi *et al.* [3] reported desvenlafaxine showed significantly higher risk ratio of nausea/vomiting during the maintenance phase than fluvoxamine (RR = 3.011 vs 0.840) in their network meta-analysis. Overall, fluvoxamine offers a cost-effective alternative for managing MDD, especially when balancing treatment outcomes with economic considerations.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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