# Switching to Sertraline or Venlafaxine after Failure of SSRIs Treatment in Major Depressive Disorder: An Economic Evaluation of the STAR*D Trial

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***Background:*** *Switching to another antidepressant is one of the alternative treatment strategies employed in major depressive disorder (MDD) patients who have no remission despite an adequate trial of an antidepressant. The aim of the present study was to present an economic evaluation of sertraline compared with venlafaxine after unsuccessful treatment for depression with citalopram.*

***Material and Method:*** *An economic model was constructed in line with the design of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) study. MDD patients who did not have a remission with or who had an intolerance to citalopram were randomly assigned to be switched to either sertraline or venlafaxine. Patients who had no remission at the end of the switching treatment phase still continued the antidepressants and received an adjunctive treatment with aripiprazole. The event probabilities were used to derive the transitional probabilities use in the model. The primary model outcome was remission of symptoms and the secondary outcome was quality-adjusted life-years (QALYs). Incremental cost-effectiveness ratios (ICEs) were estimated for the costs per unit of effectiveness. Sensitivity analyses were done to assess the effects of model assumptions.*

***Results:*** *The total direct costs per remission were 27,830 Baht for sertraline and 30,147 Baht for venlafaxine. Sertraline had lower total costs per QALY than venlafaxine (34,788 Baht vs. 37,683 Baht). The more cost-effectiveness of sertraline resulted in 7.68% of cost saving. The incremental cost of venlafaxine compared with sertraline was 2,316 Baht per remission gained and 2,895 Baht per QALY gained. By varying the remission rate of venlafaxine from 20% to 40%, the sensitivity analysis results in a decrease in total costs of venlafaxine from 31,926 Baht to 24,808 Baht. In addition, incremental cost per remission gained changed from 4,096 Baht in favour of sertraline to 3,023 Baht in favour of venlafaxine. Similarly, incremental cost per QALY gained changed from in favour of sertraline to in favour of venlafaxine.*

***Conclusion:*** *Based on the STAR*D trial, the results of the economic study indicate that a switch to sertraline is a cost-effectiveness treatment option compared with a switch to venlafaxine in MDD patients who have no remission or cannot tolerate citalopram.*

***Keywords:*** *Cost-effectiveness, Sertraline, Venlafaxine, Switching, Major depressive disorder*

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Remission, the virtual absence of depressive symptoms, is the desired goal of acute treatment of major depressive disorder (MDD)[1-4]. Regardless of the number of currently available antidepressants, they do not uniformly result in remission. For example, in the first level of the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial, only 35% to 40% of patients were in remission following up to 12 weeks of therapy with the selective serotonin reuptake inhibitor (SSRI) citalopram[5]. Compared with persistent depression, remission is associated with significantly lower subsequent utilization and costs across the full range of mental health and general medical services[6].

The major types of alternative treatment strategies employed after sufficiency of drug dosing and compliance in MDD patients, are (1) switching to another antidepressant within the same pharmacological class (*e.g.*, from an SSRI to another SSRI), (2) switching to another antidepressant from a different pharmacological class (*e.g.*, from an SSRI to a serotonin-norepinephrine reuptake inhibitor [SNRI]), (3)

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combining two antidepressants from different classes (*e.g.* a tricyclic antidepressant [TCA] plus an SSRI), and (4) augmenting the antidepressant with other agents (*e.g.*, lithium, thyroid hormone, or atypical antipsychotics)[2-4].

The advantage of switching strategy is that it minimizes polypharmacy, which helps prevent drug-drug interactions and can, therefore, improve patient compliance[7]. When switching antidepressants, the usual recommendation is to switch to another class of antidepressant. Nevertheless, there is evidence showing that a switch from on SSRI to another could be useful. In these studies, 42% to 63% of patients have presented a response after being switched from one SSRI to citalopram[8], from sertraline to fluoxetine[9], or from one SSRI to another[10].

Switching from one SSRI to another (a within-class switch) may be less effective than switching to a non-SSRI (an out-of-class switch) or to medications that inhibit the uptake of both serotonin and norepinephrine. A meta-analysis of the three randomized-controlled trials that compared switching to venlafaxine versus SSRIs showed that the weighted difference in remission rates was 8% (4% to 11%) in favour of venlafaxine and the weight differences in dropout rate due to side effects was 1% (-5% to 7%), with more dropouts for venlafaxine[11].

The purpose of the present study was to present an economic model and investigate the cost-effectiveness of sertraline (a within-class switch) compared with venlafaxine (a between class switch) for acute treatment of MDD after unsuccessful treatment with an SSRI. This analysis was based on the results of level 2 of the STAR*D trial comparing sertraline to venlafaxine[12].

## Material and Method

### *Model structure*

Cost-effectiveness analysis in depression generally requires modeling, as all the required data are seldom available from a single data set. For the present analysis, a model was developed in line with the design of the STAR*D study[12]. The structure of the model is shown in Fig. 1. In this model, outpatients with nonpsychotic MDD who did not have a remission with or who had an intolerance to citalopram alone were randomly assigned to receive one of the two switching medications for up to 14 weeks: sertraline at a maximal daily dose of 200 mg, or extended release venlafaxine at a maximal daily dose of 375 mg.

Patients who had no remission at the end of the prospective treatment phase continued the antidepressants and received an adjunctive treatment with aripiprazole (2-20 mg per day)[13], the approved medication as adjunctive treatment to antidepressant therapy in adults with MDD. Those with non-remission or intolerance after receiving aripiprazole augmentation will be hospitalized for electroconvulsive therapy (ECT). Patients who discontinued antidepressants due to intolerance were assumed to stop medications and to be hospitalized to receive ECT. Providing the serious adverse events (*e.g.*, suicidal ideation or attempt) occurred, those patients will be hospitalized for ECT and still remained on antidepressants.

The model was assumed that all patients will achieve remission of symptoms after receiving the given medication(s) and/or other interventions (hospitalization and ECT). The study protocol was reviewed and approved by the institutional review board of Phramongkutklao Hospital, Thailand.

### *Transitional probabilities*

The trials recorded the remission rate, the discontinuation rate due to intolerance, and the number of patients with serious events (*e.g.*, suicidal ideation or attempt) that required psychiatric hospitalization. The event probabilities of aripiprazole were assigned only on the non-remission event of the two antidepressants. These event probabilities were used to derive the transitional probabilities use in the model (Fig. 1 and Table 1). The path probabilities were applied to calculate the weighted cost of each health outcome.

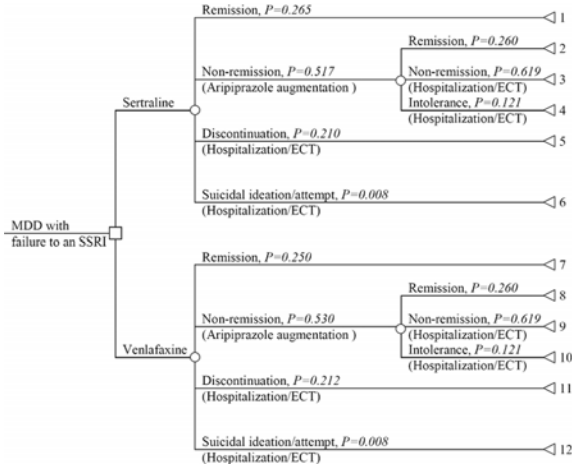


**Fig. 1** A Model Structure and Path Probabilities
MDD = major depressive disorder, ECT = electroconvulsive therapy

***Model outcomes***

The primary outcome-remission of symptoms -was defined as a score of 7 or less on the 17-item Hamilton Rating Scale for Depression (HRDS-17) at the end of the present study. The secondary health outcome was remission that was measured in terms of quality-adjusted life-years (QALYs). QALYs were estimated in the model in a similar way to costs, with a utility value being calculated for the remission state. Incremental cost-effectiveness ratios (ICERs) were estimated for the costs per unit of effectiveness of switching from one treatment to another. Consequently, the ICERs of the primary outcome examine the additional costs per remission gained and the ICERs of the secondary outcome estimate the additional costs per QALY gained.

***Resource-use estimates***

The resource-use data for different health states were obtained from the STAR*D trial[12] and Berman trial[13]. The model included: (1) drug acquisition costs for acute treatment, (2) hospitalization costs and (3) costs of ECT. All the resource-use assumptions and data sources are presented in Table 2. Cost data for drugs, hospitalization and ECT were obtained from Phramongkutklao Hospital, Thailand. Unit costs were taken form the fiscal year 2009 and expressed in Thai Baht (Table 3). The model did not include costs for physician monitoring, cost of adverse events, or indirect costs.

***Health state utilities***

Health state utility values were estimated from a report by Revicki and Wood[15]. The authors determined utility values using the 36-item Short Form (SF-36) data to examine differences in utilities in MDD patients. SF-36 values were compared as part of the STAR*D trial[12]. Hence, the present study assumed

**Table 1.** Transitional Probability Estimates

| Transitional probability | Sertraline (n = 238) | Venlafaxine (n = 250) | Aripiprazole (n = 182) |
|---|---|---|---|
| Remission | 0.265 | 0.250 | 0.260 |
| Non-remission | 0.517 | 0.530 | 0.619 |
| Discontinuation from treatment due to intolerance, adverse events or withdrawal of consent | 0.210 | 0.212 | 0.121 |
| Hospitalization for suicidal ideation or attempt | 0.008 | 0.008 | - |
| Source | Rush et al[12] | Rush et al[12] | Berman et al[13] |

**Table 2.** Resource Use Assumptions and Sources

| Resource use variable | Unit | Source |
|---|---|---|
| Dose (mg/d) | | |
| Sertraline | 135.5 | Rush et al[12] |
| Venlafaxine | 193.6 | Rush et al[12] |
| Aripiprazole | | |
| Added to sertraline | 14 | Berman et al[13] |
| Added to venlafaxine | 12 | Berman et al[13] |
| Time to receive drug (week) | | |
| Sertraline monotherapy | 6.3 | Rush et al[12] |
| Venlafaxine monotherapy | 6.4 | Rush et al[12] |
| Sertraline + Aripiprazole | 6.0 | Berman et al[13] |
| Venlafaxine + Aripiprazole | 6.0 | Berman et al[13] |
| Hospitalization/ECT | | |
| Days hospitalized for ECT | 20 | Survey |
| ECT (sessions) | 8 | Kennedy and Giacobbe[14] |

ECT = electroconvulsive therapy

utility values of 0.8 for remission state which is the primary outcome estimated by the model for each treatment arm.

***Sensitivity analyses***

Sensitivity analyses were done to assess the effects of various assumptions made in the analysis on the conclusion. Sensitivity analyses independently alter the value of each parameter across the range of plausible values for that parameter. Clinical input variables with influence on model results were remission rate of each antidepressant and drug cost. In the present study, one-way sensitivity analysis was undertaken for the probability of remission and unit cost of an antidepressant. The values of these two parameters were varied across the probable ranges. Other parameters that had a relatively small effect on the model outcome such as the discontinuation rate due to intolerance and an incidence of suicidal ideation/ attempt were not warranted for sensitivity analyses.

Threshold analysis, an extension of one-way sensitivity analysis, was performed to find the threshold point of one variable by varying the value until the alternative decision strategies are found to have an equal outcome. In the present analysis, two parameters (remission rate and drug costs) of an antidepressant with less cost-effective were varied until the other antidepressant was found to have equal cost-effectiveness.

## Results

***Base-case treatment analysis***

Remission rates over an up to 14-week period in the acute treatment of outpatients with non-psychotic MDD as assessed by HRDS-17, did not differ significantly between the group given sertraline (26.5%) and the group given venlafaxine (25.0%)[12]. However, when economic evaluation was evaluated, more cost-effectiveness was found with sertraline than venlafaxine on the basis of economic model (Table 4).

Table 5 shows the results of base-case analysis in the model that assessed the cost-effectiveness of sertraline compared with venlafaxine. The total direct costs per remission were 27,830 Baht for sertraline and 30,147 Baht for venlafaxine, respectively. Likewise, sertraline had lower total direct costs per QALY than venlafaxine (34,788 Baht vs. 37,683 Baht). The more cost-effectiveness of sertraline resulted in 7.68% of cost saving. The incremental cost of venlafaxine compared with sertraline was 2,316 Baht per remission gained and 2,895 Baht per QALY gained.

***Sensitivity analyses***

Since the more cost-effectiveness of sertraline, sensitivity analyses were performed for the probability of remission and unit cost of venlafaxine. The proportional change of remission rates (20%, 30% and 40%) and drug costs (10%, 20% and 30% discount) of venlafaxine were assessed. One-way sensitivity analysis to assess the sensitivity of sertraline-venlafaxine ICERs to the proportional change in remission rate and drug costs as mentioned previously were also undertaken.

Results of the sensitivity analysis are shown in Table 6. By varying the remission rate from 20% to

**Table 3.** Unit Cost (in Thai Baht)

| Cost | Unit resource/Cost | Source |
|---|---|---|
| Drug | | |
| Sertraline 50 mg/tab | 44 | Phramongkutklao Hospital |
| Venlafaxine 75 mg/tab | 62 | Phramongkutklao Hospital |
| Aripiprazole 10 mg/tab | 195.5 | Phramongkutklao Hospital |
| Cost per day | | |
| Sertraline | 119.24 | |
| Venlafaxine | 160.04 | |
| Aripiprazole | | |
| Added to sertraline | 273.7 | |
| Added to venlafaxine | 234.6 | |
| Hospitalization/ECT | | |
| Cost per inpatient bed day | 600 | Phramongkutklao Hospital |
| ECT per session | 1,700 | Phramongkutklao Hospital |

ECT=electroconvulsive therapy

40%, the analysis resulted in a decrease in total costs of venlafaxine from 31,926 Baht to 24,808 Baht. In addition, incremental cost per remission gained changed from 4,096 Baht in favour of sertraline to 3,023 Baht in favour of venlafaxine. Similarly, incremental cost per QALY gained changed from in favour of sertraline (5,120 Baht) to in favour of venlafaxine (3,778 Baht). Varying acquisition cost of venlafaxine by -10% to -30% resulted in a decrease of total costs per remission from 29,158 Baht to 27,181 Baht. Consequently, incremental cost per remission gained and incremental cost per QALY gained change from in favour of sertraline (1,328 Baht per remission gained and 1,660 Baht per QALY gained) to venlafaxine (649 Baht per remission gained and 811 Baht per QALY gained).

Table 6 also shows the results of a threshold analysis for the values of the two variables; probability of remission and unit cost of venlafaxine. For venlafaxine compared with sertraline, the threshold probability of remission is 0.32. This is the value of the probability for this variable at which the expected outcomes of sertraline and venlafaxine are equal. For the same comparison, the threshold value of unit cost of venlafaxine is 47.47 Baht (for the unit dose of 75 mg).

**Discussion**

This economic model evaluating the cost-effectiveness of switching to sertraline compared with switching to venlafaxine in the acute treatment of MDD patients who had no remission of symptoms or could not tolerate to the SSRI citalopram suggested that, based on the STAR*D data[12], a switch to sertraline is likely to be cost-effectiveness for additional health benefits in Thailand. Although both treatments did not differ significantly with respect to remission rate or

**Table 4.** Weighted Cost and Total cost (in Thai Baht)

| Health outcome | Medication | Hospitalization | ECT | Total cost | Path prob. | Weighted cost |
|---|---|---|---|---|---|---|
| Sertraline | | | | | | |
| 1 | 5,258.48 | | | 5,258.48 | 0.2650 | 1,393.50 |
| 2 | 21,761.96 | | | 21,761.96 | 0.1344 | 2,925.24 |
| 3 | 24,266.00 | 12,000.00 | 13,600.00 | 49,866.00 | 0.3200 | 15,958.27 |
| 4 | 5,258.48 | 12,000.00 | 13,600.00 | 30,858.48 | 0.0626 | 1,930.41 |
| 5 | 0.00 | 12,000.00 | 13,600.00 | 25,600.00 | 0.2100 | 5,376.00 |
| 6 | 5,258.48 | 12,000.00 | 13,600.00 | 30,858.48 | 0.0080 | 246.87 |
| | | | | Total | 1 | 27,830.29 |
| Venlafaxine | | | | | | |
| 7 | 7,169.91 | | | 7,169.91 | 0.2500 | 1,792.48 |
| 8 | 23,744.90 | | | 23,744.90 | 0.1378 | 3,272.05 |
| 9 | 27,105.80 | 12,000.00 | 13,600.00 | 52,705.80 | 0.3281 | 17,291.19 |
| 10 | 7,169.91 | 12,000.00 | 13,600.00 | 32,769.91 | 0.0641 | 2,101.53 |
| 11 | 0.00 | 12,000.00 | 13,600.00 | 25,600.00 | 0.2120 | 5,427.20 |
| 12 | 7,169.91 | 12,000.00 | 13,600.00 | 32,769.91 | 0.0080 | 262.16 |
| | | | | Total | 1 | 30,146.61 |

ECT = electroconvulsive therapy

**Table 5.** Cost-Effectiveness Analysis of Sertraline vs. Venlafaxine in Base-Case Analysis (in Thai Baht)

| Cost-effectiveness analysis | Sertraline | Venlafaxine |
|---|---|---|
| Total cost per remission | 27,830.29 | 30,146.61 |
| Incremental cost per remission gained | | -2,316.32 |
| Total cost per QALY | 34,787.86 | 37,683.26 |
| Incremental cost per QALY gained | | -2,895.40 |
| Cost saving (%) | 7.68 | |

QALYs = quality-adjusted life-years

**Table 6.** One-Way Sensitivity Analysis of the Influential Factors of Venlafaxine Compared with Sertraline

| Parameter range | Total cost | Incremental cost per remission gained | Incremental cost per QALY gained |
|---|---|---|---|
| Probability of remission | | | |
| 0.20 | 31,926.30 | -4,096.01 | -5120.01 |
| 0.30 | 28,366.92 | -536.63 | -670.786 |
| 0.3151* | 27,830.29 | 0.00 | 0.00 |
| 0.40 | 24,807.54 | 3,022.75 | 3778.441 |
| Unit cost of venlafaxine | | | |
| -10% (55.8 Baht/tab) | 29,158.21 | -1,327.92 | -1,659.90 |
| -20% (49.6 Baht/tab) | 28,169.81 | -339.52 | -424.40 |
| -23.44% (47.47 Baht/tab)* | 27,830.29 | 0.00 | 0.00 |
| -30% (43.4 Baht/tab) | 27,181.42 | 648.87 | 811.09 |

* = threshold value, QALYs=quality-adjusted life-years

drug efficacy, sertraline provides a lower cost per remission compared with venlafaxine. Hence, it is widely recognized that full remission is of high importance when treating an acute phase of MDD, both from clinical point of view[1-4], as well as from an economic point of view[16-18].

Recently, a meta-analysis[19] suggested a modest yet statistically significant advantage in remission rates when switching patients with SSRI-resistant depression to a non-SSRI rather than an SSRI antidepressant. Nevertheless, the present study reveals that a within-class switch (one SSRI to another SSRI) is more cost-effective than an across-class switch (one SSRI to venlafaxine). This analysis also indicates that the remission rate and the acquisition cost of each drug are important when assessing the economic benefits of treatment in this patient group.

Selecting a within-class switch SSRI may be warranted because of the differences in efficacy and safety between antidepressants. A recent meta-analysis of 117 randomized controlled trials (25,928 participants) revealed that clinically important differences exist between commonly prescribed antidepressants for both efficacy and acceptability in favour of escitalopram and sertraline. Sertraline might be the most favourable balance between benefits, acceptability and acquisition cost on MDD[20].

Few studies published to date have reported on the economic outcomes associated with pharmacological interventions for the acute treatment of MDD patients who had no remission despite an adequate treatment with an SSRI. One study evaluated the cost-effectiveness estimates of bupropion monotherapy compared with bupropion plus SSRI for treatment of patients who had MDD without remission of symptoms after receiving an adequate treatment of citalopram for up to 14 weeks[21]. The present economic study found that a switch to bupropion (an across-class switch) is a cost-effectiveness treatment option compared with a combination of SSRI with bupropion.

There are, however, a number of limitations with the current analysis, which should be considered when interpreting the results presented. First, the current analysis is based on effect data from a multicentre clinical trial in the US and there are several concerns when applying clinical effects of a treatment from one setting to another, specifically, from Western countries to Asian countries. Second, the health economic data employed in the present analysis was based partly on Phramongkutklao Hospital, a government general hospital in Thailand, which did not represent other hospitals in Thailand or other countries in Asia. For instance, there is no unit cost of staff time (*e.g.*, psychiatric consultants) during the monitoring visit in government hospitals. Compared with the US or European countries, cost for hospitalization in Thailand is relatively low whereas drug cost is one of the major concerns of the healthcare providers and the payers.

Third, indirect cost due to absenteeism or loss productive time that pose a substantial economic burden upon society[22-24], especially in MDD patients with partial or non-remission[18,24,25], is not accounted for the current study. Finally, the limitations of the equipoise stratified randomized design[26] used in the STAR*D study may have influenced on clinical output variables and inevitable economic outcomes of antidepressants.

## Conclusion

Based on the STAR*D trial, the results of this economic study indicate that switching to sertraline is a cost-effectiveness option compared with switching to venlafaxine in a treatment setting. Because of the limitations of the present study, future economic models are needed and should consider the inclusion of studies in Thai or Asian participants and a boarding costing perspective. Such models are likely to provide even more optimistic cost-effectiveness outputs for treatment options in nonremitting MDD in Thailand and other Asian countries.


## Potential conflicts of interest

Phramongkutklao Hospital's Foundation under Her Royal Highness Princess Maha Chakri Sirindhorn's Patronage.


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## *การเปลี่ยนการรักษาเป็น sertraline หรือ venlafaxine หลังจากล้มเหลวต่อการรักษาด้วย SSRIs ในโรคซึมเศร้า: การประเมินทางเศรษฐศาสตร์ของการศึกษา STAR*D*

***ธวัชชัย ลีฬหานาจ***

***ภูมิหลัง**: การเปลี่ยนการรักษาเป็นยาแก้ซึมเศร้าขนานอื่นเป็นทางเลือกหนึ่งในการรักษาผู้ป่วยโรคซึมเศร้าที่ไม่มีการสงบของโรคแม้จะได้รับการรักษาด้วยยาแก้ซึมเศร้าที่เพียงพอ*

***วัตถุประสงค์**: การประเมินทางเศรษฐศาสตร์ของการรักษาด้วยยา sertraline เทียบกับยา venlafaxine หลังจากที่ล้มเหลวต่อการรักษาโรคซึมเศร้าด้วยยา citalopram*

***วัสดุและวิธีการ**: สร้างแบบจำลองทางเศรษฐศาสตร์ตามรูปแบบของการศึกษา STAR*D ผู้ป่วยโรคซึมเศร้าที่อาการไม่สงบหรือไม่สามารถทนต่อการรักษาด้วย citalopram ได้จะถูกสุ่มให้ได้รับการเปลี่ยนยาเป็น sertraline หรือยา venlafaxine ผู้ป่วยที่อาการยังคงไม่สงบเมื่อสิ้นสุดการศึกษายังคงได้รับยาแก้ซึมเศร้าต่อไป แต่จะได้รับการเสริมการรักษาด้วย aripiprazole ใช้ความน่าจะเป็นของเหตุการณ์เพื่อหาการเปลี่ยนแปลง ความน่าจะเป็นที่มีการใช้ในแบบจำลอง ผลลัพธ์ปฐมภูมิคือ การสงบของอาการของโรค ผลลัพธ์ทุติยภูมิคือ QALYs ค่า incremental cost-effectiveness ratios จะถูกประเมินเพื่อหาต้นทุนต่อหน่วยประสิทธิผล การวิเคราะห์ความไวจะกระทำเพื่อประเมินผลของสมมติฐานของแบบจำลอง*

***ผลการศึกษา**: ค่าใช้จ่ายรวมต่อการสงบของโรคเท่ากับ 27,830 บาทสำหรับ sertraline และ 30,147 สำหรับ venlafaxine การรักษาด้วย sertraline มีค่าใช้จ่ายรวมต่อ QALY ต่ำกว่า venlafaxine (34,788 บาท เทียบกับ 37,683 บาท) การมีต้นทุน-ประสิทธิผลที่ดีกว่าของ sertraline ช่วยประหยัดต้นทุนลงได้ร้อยละ 7.68 ค่า incremental cost ของ venlafaxine เทียบกับ sertraline เท่ากับ 2,316 บาท ต่อการสงบของโรคที่เพิ่มขึ้นหนึ่งหน่วย และเท่ากับ 2,895 บาทต่อ QALY ที่เพิ่มขึ้นหนึ่งหน่วย การวิเคราะห์ความไวด้วยการเปลี่ยนค่าอัตราการสงบของโรคของ venlafaxine จากร้อยละ 20 เป็นร้อยละ 40 ทำให้การรักษาด้วย venlafaxine มีต้นทุนลดลงจาก 31,926 บาท เป็น 24,808 บาท และทำให้ incremental cost ต่อการสงบของโรคที่เพิ่มขึ้น เปลี่ยนจากเดิมที่ sertraline เหนือกว่า venlafaxine 4,096 บาท เป็น venlafaxine เหนือกว่า sertraline 3,026 บาท และ incremental cost ต่อ QALY ที่เพิ่มขึ้น เปลี่ยนจากเดิมที่ sertraline เหนือกว่าเป็น venlafaxine เหนือกว่า*

***สรุป**: จากผลการศึกษาของ STAR*D การศึกษาทางเศรษฐศาสตร์ครั้งนี้ชี้ให้เห็นว่า การเปลี่ยนการรักษาเป็น sertraline เป็นทางเลือกของการรักษาที่มีต้นทุน-ประสิทธิผลเหนือกว่าการเปลี่ยนการรักษาเป็น venlafaxine ในผู้ป่วยโรคซึมเศร้าที่ไม่มีการสงบของโรคหรือไม่สามารถทนต่อฤทธิ์ไม่พึงประสงค์ของยาได้รับการรักษาด้วยยา citalopram มาก่อน*