



# Comparison of YAZ to SSRIs in the Treatment of Premenstrual Dysphoric Disorder: Cost-Effectiveness Analysis

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## BACKGROUND

Four medications have been approved by the Food and Drug Administration (FDA) for treatment of premenstrual dysphoric disorder (PMDD), including three selective serotonin reuptake inhibitor (SSRI) agents (i.e., fluoxetine – Sarafem®, sertraline – Zoloft®, and paroxetine – Paxil CR®), and one oral contraceptive agent (i.e., DRSP/EE – YAZ®).

Although efficacy of SSRIs in alleviating PMDD symptoms has been shown in a meta-analysis of 15 trials (1), approximately 40% of women with PMDD reported no improvement under SSRI therapy (1,2) and only around 25% of those treated can be classified as remitters (2-4). In addition, antidepressant medications are usually not well perceived by patients (5,6).

Cost effectiveness of the SSRIs has been assessed in the treatment of depression (7-12). To our knowledge, no published studies have evaluated the cost-effectiveness of PMDD treatment.

## OBJECTIVE

To assess the cost-effectiveness of the four drugs with PMDD indication approved by the FDA.

## METHODOLOGY

### Analytical Model (Table 1, Figure 1)

**Intervention:** Initial treatment on one of three SSRIs or DRSP/EE for three cycles. Women who failed to achieve success, but did not drop out, at the end of the third cycle, switched to an alternative medication for three additional cycles.

**Time-frame:** 6 cycles

**Population:** Women of reproductive age who have been diagnosed with PMDD and for whom the treatments considered in the analysis are viable options.

**Perspective:** payer

### Sensitivity Analysis

#### Univariate

•Success rate, dropout rate and medication costs associated with three cycles of treatment were varied independently for each strategy.

•Success rate and dropout rate set at lower and upper bounds of 95% confidence interval.

•Medication costs set at 50% and 150% of base case value.

#### Multivariate

•10,000 Monte-Carlo simulation runs, varying clinical outcomes and medication costs using probability distributions.

•Outcome probabilities were varied according to Dirichlet prior distribution.

•Medication costs were varied according to Uniform defined between 50% and 150% of base case value.

Table 1 – Model Inputs and Parameters

| RESOURCE UTILIZATION   |   | Sources/Notes |            |
|--|---|---------------|------------|
| Medication – P(use)  | Proportion  |               |            |
| Fluoxetine   | .40   | (13)          |            |
| Paroxetine   | .21   | (13)          |            |
| Sertraline   | .39   | (13)          |            |
| Physician Specialty – P(phy)   |   | Fluoxetine    | Paroxetine |
| General practice   | .333  | .398          | .378       |
| Psychiatrist   | .141  | .116          | .094       |
| Other  | .526  | .486          | .578       |
|  |   | (13)          | (13)       |
| EFFECTIVENESS (based on CGI equal to 1 or 2)                               |   |               |            |
|  | Success   | Failure       | Dropout    |
| DRSP/EE  | .471  | .294          | .235       |
| Fluoxetine   | .736  | .113          | .151       |
| Paroxetine   | .478  | .259          | .263       |
| Sertraline   | .468  | .343          | .189       |
| SSRI class   | .577  | .234          | .189       |
|  |   |               | .834       |
|  | $P_{SSRI}(\text{Success}) = \sum_i P_i(\text{use}) \cdot P_i(\text{Success})$ |               |            |
|  | $i \in \{\text{fluoxetine, paroxetine, sertraline}\}$                         |               |            |
| COSTS  |   |               |            |
| Medication (\$ for 3 cycles) – MedCost                                     |   |               |            |
| DRSP/EE (3/20), YAZ Oral Tablet 0.02 mg x3                                 | 177.19  |               | (23)       |
| Fluoxetine: Sarafem Oral Tablet 20 mg                                      | 591.39  |               | (23)       |
| Paroxetine: Paxil CR Oral Tablet Extended Release 24 Hour 12.5 mg or 25 mg | 147.59  |               | (23)       |
| Sertraline: Zoloft Oral Tablet 50 or 100 mg                                | 313.62  |               | (23)       |
| SSRI class   | 398.22  |               |            |
|  | $MedCost_{SSRI} = \sum_i P_i(\text{use}) \cdot MedCost_i$                     |               |            |
|  | $i \in \{\text{fluoxetine, paroxetine, sertraline}\}$                         |               |            |
| Physician Specialty (\$) – SpecCost  |   |               |            |
| General practice   | 115.95  |               | (24)       |
| Psychiatrist   | 109.06  |               | (24)       |
| Other  | 177.94  |               | (24)       |
| Physician Visit (\$) – VisCost   |   |               |            |
| DRSP/EE  | 150.75  |               |            |
| Fluoxetine   | 147.59  |               |            |
| Paroxetine   | 145.28  |               |            |
| Sertraline   | 156.93  |               |            |
|  | $VisCost_{SSRI} = \sum_i P_i(\text{use}) \cdot VisCost_i$                     |               |            |
|  | $i \in \{\text{fluoxetine, paroxetine, sertraline}\}$                         |               |            |
|  | $i \in \{\text{general practice, psychiatrist, other}\}$                      |               |            |

\*Failure and dropout probabilities evaluated similarly. †Average of 12.5 and 25 mg cost.  
 CGI: Clinical Global Impression Improvement Scale

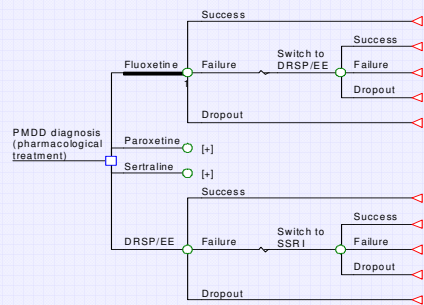


Figure 1 – Cost-Effectiveness Analysis Decision Tree for PMDD Treatment

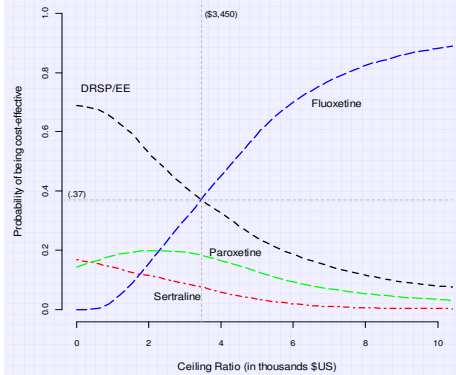


Figure 2 – Cost-effectiveness acceptability curves for the four treatment strategies.

## RESULTS

### Base Case

Starting therapy with DRSP/EE was the least costly and the most cost-effective alternative. Initiating therapy with paroxetine or sertraline was less effective and more costly. Starting therapy with fluoxetine was the most effective (78.9% achieved success by the end of 6<sup>th</sup> cycle) but also the most costly strategy. The cost of each additional patient successfully treated with fluoxetine was estimated to be \$4,385.

| Initial Treatment | CE Ratios     |                        |          | Incremental CE Ratios with DRSP/EE as reference |                           |                      |
|-------------------|---------------|------------------------|----------|---|---------------------------|----------------------|
|                   | Expected Cost | Expected Effectiveness | CE Ratio | Incremental Cost                                | Incremental Effectiveness | Incremental CE Ratio |
| DRSP/EE           | \$683         | 0.641                  | \$1,065  |   |                           |                      |
| Sertraline        | \$829         | 0.630                  | \$1,315  | \$146   | -0.011                    | Dominated            |
| Paroxetine        | \$844         | 0.600                  | \$1,406  | \$161   | -0.041                    | Dominated            |
| Fluoxetine        | \$1,332       | 0.789                  | \$1,688  | \$649   | 0.148                     | \$4,385              |

CE: cost-effectiveness.

### Sensitivity Analysis

#### Univariate

Changes in the choice of strategy occurred, conditional on ceiling values of \$3,000 or higher. For example, for a ceiling value of \$3,000, if the success rate of DRSP/EE was 31% or lower, or its discontinuation rate was 40% or higher, fluoxetine became the dominant strategy. At lower ceiling ratios (e.g., at \$2,500), starting with DRSP/EE remained the dominating strategy.

| DRSP/EE Parameter    | Base case | Range       | CE Ratio of DRSP/EE (US \$) | ICER: fluoxetine relative to DRSP/EE (US \$) | Ceiling ratio <sup>†</sup> (US \$) |       |       |
|----------------------|-----------|-------------|-----------------------------|--|------------------------------------|-------|-------|
|                      |           |             |                             |  | 3,000                              | 3,500 | 4,000 |
| Success rate         | .471      | .285 - .664 | 1,338 - 845                 | 2,818 - 8,142                                | .31                                | .38   | .44   |
| Cost                 | \$177     | \$90 - 266  |                             |  | --                                 | --    | .22   |
| Discontinuation rate | .235      | .11 - .44   |                             |  | .40                                | .33   | .27   |

CE: Cost-effectiveness; ICER: incremental cost-effectiveness ratio; <sup>†</sup>Ceiling value at which starting fluoxetine becomes the dominant strategy.

#### Multivariate (Figure 2)

At a ceiling value of \$3,450, initiating treatment with fluoxetine and DRSP/EE had equal probability (.37) of being the most cost-effective strategy. Ceiling values below \$3,450 gave preference to initiating treatment with DRSP/EE, while for higher values fluoxetine was the dominating strategy. At a ceiling value of zero, there was roughly a 70% probability that DRSP/EE was the most cost-effective strategy.

## LIMITATIONS

Brand name SSRIs were utilized to derive medication costs. At hypothetical rates of 100% and 50% (50% brand) for use of generic SSRIs, DRSP/EE (YAZ) was dominated by sertraline and fluoxetine in the former scenario, and had an ICER of \$803.12 relative to the most cost-effective option, sertraline, in the latter case.

Costs associated with side-effects and additional contraceptive medication use for women undergoing SSRI treatment were not considered. Difference in adherence to medication in relation to its efficacy were not taken into account. Given the much documented side effects and higher non-adherence rates of SSRIs, our results likely presented a conservative estimate in the cost-effectiveness of DRSP/EE for treatment of PMDD.

## CONCLUSIONS

DRSP/EE (YAZ) was shown to be the most cost-effective strategy, dominating both sertraline (Zoloft) and paroxetine (Paxil).

The ceiling ratio at which fluoxetine (Sarafem) became more cost-effective (\$3,450) than DRSP/EE (YAZ) was more than double the value associated with the most costly treatment (\$1,332).

For women who have been diagnosed with PMDD and who are willing to take an oral contraceptive, DRSP/EE (YAZ) provides a cost-effective alternative to SSRIs.

Women who are reluctant to take antidepressants and those that were not effectively treated with SSRIs can consider DRSP/EE (YAZ) for the treatment of PMDD.

List of references available as a separate document.



Presented at the ISPOR, 14<sup>th</sup> Annual International Meeting, May 16-20, Florida, FL. This study was supported by Bayer HealthCare Pharmaceuticals Inc. For additional information, please contact Min Yang, (401) 334-8800 or myang@qualitymetric.com.