Cost-Effectiveness of Obstructive Sleep Apnea Screening and Treatment Before Catheter Ablation for Symptomatic Atrial Fibrillation

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SUPPLEMENTAL MATERIAL

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Abbreviations list
AF = atrial fibrillation
CPAP = continuous positive airway pressure
IC = incremental cost
ICER = incremental cost-effectiveness ratio
IE = incremental effectiveness
JPY = Japanese yen
NMB = net monetary benefits
NSR = Normal sinus rhythm
OAC = oral anticoagulation
OSA = obstructive sleep apnea
PM = portable monitor
PSA = probability sensitivity analysis
PSG = polysomnography
QALY = quality-adjusted life-year
RDI = respiratory disturbance index
WTP = willingness-to-pay

Supplementary Table 1. Unit cost of each test and drug in this study.

| Test / Drug                          | Unit cost (JPY)   | Notes                           |
|--------------------------------------|-------------------|---------------------------------|
| Holter electrocardiogram (ECG)       | 15,000/test       |                                 |
| 12-lead ECG                          | 1,300/test        |                                 |
| Transthoracic echocardiogram         | 8,800/test        |                                 |
| Type-3 PM                            | 7,200/test        |                                 |
| PSG                                  | 110,000/test      |                                 |
| First visit fee                      | 2,820/visit       | Outpatient clinic fee           |
| Revisit fee                          | 730/visit         | Outpatient clinic fee           |
| Direct oral anticoagulation          | 546/day           | Standard dose/day               |
| Bisoprolol                           | 29/day            | 2.5mg /day                      |
| Flecaainide                          | 119/day           | 100mg/day                       |
| CPAP                                 | 13,500/month      | Including management fee        |
Supplementary Figure 1. One-way sensitivity analysis for probability of type-3 PM false negative in patients who had RDI < 10.

PM-guided screening vs. PSG-guided screening

WTP = 5,000,000

ICER (JPY/QALY)

Probability of type-3 PM false negative
Supplementary Figure 2. Results of deterministic sensitivity analyses in the scenario analyses. Tornado diagram demonstrating influence of cost, utilities and transition probabilities on expected value, assuming a WTP value of 5,000,000 JPY. Variables and ranges used in the analysis are described in Table 1. A) and D) no screening vs. PM-guided screening. B) and E) no screening vs. PSG-guided screening. C) and F) PM-guided screening vs. PSG-guided screening.
Supplementary Figure 3. Cost-effectiveness acceptability curves representing the probability that each OSA screening is cost-effective for a given maximum willingness-to-pay threshold per QALY gained in the scenario analyses. A) Results in low OSA risk cohort (OSA prevalence 30%). B) Results in high OSA risk cohort (OSA prevalence 70%).
Supplementary Figure 4. Incremental cost-effectiveness boot strap scatter plots in scenario analyses. A) and D) PM-guided screening vs. no screening. B) and D) PSG-guided screening vs. no screening. C) and F) PSG-guided screening vs. PM-guided screening. Red triangles stand for the result of base case and ellipses mean 95% CI.

Low risk cohort (OSA30%)

A) PM-guided screening vs. No screening

B) PSG-guided screening vs. No screening

C) PSG-guided screening vs. PM-guided screening

High risk cohort (OSA70%)

D) PM-guided screening vs. No screening

E) PSG-guided screening vs. No screening

F) PSG-guided screening vs. PM-guided screening
**Supplementary Figure 5.** Decision model for comparing three approaches to OSA screening in the first supplementary analysis.
**Supplementary Table 2.** Deterministic cost-effectiveness results in the first supplementary analyses using the modified Markov model.

| Strategy               | Total costs (JPY) | Total QALYs | ICER (JPY/QALY) vs. No screening | ICER (JPY/QALY) vs. PM-guided screening |
|------------------------|-------------------|-------------|-----------------------------------|----------------------------------------|
| No screening           | 3,901,154         | 6.55506     |                                   |                                        |
| PM-guided screening    | 4,183,084         | 6.74680     | 1,470,405                         |                                        |
| PSG-guided screening   | 4,213,428         | 6.74924     | 1,608,199                         | 12,436,893                             |
Supplementary Figure 6. Deterministic sensitivity analyses in the first supplementary analyses using the modified Markov model. Tornado diagram demonstrating influence of cost, utilities and transition probabilities on expected value, assuming a WTP value of 5,000,000 JPY. Variables and ranges used in the analysis are described in Table 1. A) no screening vs. PM-guided screening. B) no screening vs. PSG-guided screening.
Supplementary Figure 7. Cost-effectiveness acceptability curves representing the probability that each OSA screening is cost-effective for a given maximum willingness-to-pay threshold per QALY gained in the first supplementary analyses using the modified Markov model.
Supplementary Figure 8. Incremental cost-effectiveness boot strap scatter plots in the supplementary analyses excluding the effect of CPAP on QOL scores using the modified Markov model. A) PM-guided screening vs. no screening. B) PSG-guided screening vs. no screening. C) PSG-guided screening vs. PM-guided screening. Red triangles stand for the result of base case and ellipses mean 95% CI.

Supplementary Table 3. Deterministic cost-effectiveness results in the supplementary analyses excluding the effect of CPAP on QOL scores using the same Markov model.

| Strategy                  | Total costs (JPY) | Total QALYs | ICER (JPY/QALY) vs. No screening | ICER (JPY/QALY) vs. PM-guided screening |
|---------------------------|-------------------|-------------|----------------------------------|----------------------------------------|
| No screening              | 3,959,246         | 6.98763     |                                   |                                        |
| PM-guided screening       | 3,702,510         | 7.00833     | Dominant                          |                                        |
| PSG-guided screening      | 3,725,999         | 7.00860     | Dominant                          | 89,147,728                            |
**Supplementary Figure 9.** Deterministic sensitivity analyses in the second supplementary analyses excluding the effect of CPAP on QOL scores using the same Markov model. Tornado diagram demonstrating influence of cost, utilities and transition probabilities on expected value, assuming a WTP value of 5,000,000 JPY. Variables and ranges used in the analysis are described in Table 1. A) no screening vs. PM-guided screening. B) no screening vs. PSG-guided screening. C) PM-guided screening vs. PSG-guided screening.
Supplementary Figure 10. Cost-effectiveness acceptability curves representing the probability that each OSA screening is cost-effective for a given maximum willingness-to-pay threshold per QALY gained in the second supplementary analyses excluding the effect of CPAP on QOL scores using the same Markov model.
Supplementary Figure 11. Incremental cost-effectiveness boot strap scatter plots in the second supplementary analyses excluding the effect of CPAP on QOL scores using the same Markov model. A) PM-guided screening vs. no screening. B) PSG-guided screening vs. no screening. C) PSG-guided screening vs. PM-guided screening. Red triangles stand for the result of base case and ellipses mean 95% CI.
Supplementary Figure 12. One-way sensitivity analysis evaluating total net monetary benefits across a range of relative risk of AF recurrence comparing CPAP and medication therapy with CA.
CHEERS Checklist

Items to include when reporting economic evaluations of health interventions

The ISPOR CHEERS Task Force Report, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

| Section/item | Item No | Recommendation | Reported on page No/line No |
|---------------|---------|----------------|-------------------------------|
| **Title and abstract** | | | |
| Title | 1 | Identify the study as an economic evaluation or use more specific terms such as “cost-effectiveness analysis”, and describe the interventions compared. | Page 1, line 1 |
| Abstract | 2 | Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions. | Page 3, line 1 |
| **Introduction** | | | |
| Background and objectives | 3 | Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions. | Page 5, line 1 |
| **Methods** | | | |
| Target population and subgroups | 4 | Describe characteristics of the base case population and subgroups analysed, including why they were chosen. | Page 6, line 15 |
| Setting and location | 5 | State relevant aspects of the system(s) in which the decision(s) need(s) to be made. | Page 6, line 1 |
| Study perspective | 6 | Describe the perspective of the study and relate this to the costs being evaluated. | Page 9, line 14 |
| Comparators | 7 | Describe the interventions or strategies being compared and state why they were chosen. | Page 5, line 9 |
| Time horizon | 8 | State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate. | Page 6, line 5 |
| Discount rate | 9 | Report the choice of discount rate(s) used for costs and outcomes and say why appropriate. | Page 6, line 6 |
| Choice of health outcomes | 10 | Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed. | Page 6, line 4 |
| Measurement of effectiveness | 11a | *Single study-based estimates*: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data. | NA |
| Section | Description |
|---------|-------------|
| 11b Synthesis-based estimates | Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data. |
| 12 Measurement and valuation of preference based outcomes | If applicable, describe the population and methods used to elicit preferences for outcomes. |
| 13a Estimating resources and costs | Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. |
| 13b Model-based economic evaluation | Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs. |
| 14 Currency, price date, and conversion | Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate. |
| 15 Choice of model | Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended. |
| 16 Assumptions | Describe all structural or other assumptions underpinning the decision-analytical model. |
| 17 Analytical methods | Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty. |
| Results Study parameters | Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended. |
| Incremental costs and outcomes | For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios. |
| Characterising uncertainty | Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact |
of methodological assumptions (such as discount rate, study perspective).

20b \textit{Model-based economic evaluation:} Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.

Characterising heterogeneity

21 If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.

\textbf{Discussion}

22 Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.

\textbf{Other}

23 Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.

24 Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The ISPOR CHEERS Task Force Report provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the \textit{Value in Health} link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: \url{http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp}

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