

The Early Cost-Effectiveness of a Novel Scalp Cooling Device to Alleviate Chemotherapy-Induced Alopecia in Patients with Early Breast Cancer

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Background: Chemotherapy-induced alopecia is a common side effect with psychological impacts that affect quality of life. Up to 14% of patients may decline chemotherapy due to concerns over hair loss. While existing scalp cooling therapies can reduce alopecia, constraints including space, staffing, and extended chair time limit their use in health services. Hence, a novel scalp cooling cap ("Product X") was developed to address this gap. Product X is cordless and portable and does not require patients to remain in treatment chairs post-chemotherapy. This early-stage cost-effectiveness analysis addresses the potential economic value of adopting Product X versus current practice (no scalp cooling).

Methods: We developed a decision tree and a lifetime Markov model to estimate change to total costs and health benefits for female patients with early breast cancer, from a health system perspective in a Singapore tertiary cancer care setting. The model incorporated costs related to scalp cooling equipment and administration, chemotherapy, and treatment for cancer recurrence. Assumptions regarding Product X's efficacy and its potential impact on chemotherapy compliance were tested in nine scenario analyses (efficacy: 50%, 75%, 100%; compliance improvement: 0, 1%, 5%). Probabilistic scenario analysis was conducted using Monte Carlo simulation with 1000 iterations from appropriate parameter distributions.

Results: In the base case (1% improvement in compliance and 100% efficacy), Product X yielded an incremental cost of S\$265 per patient (95% UI: S\$251–S\$281) and incremental quality-adjusted life years (QALY) of 0.0717 (95% UI: 0.0705–0.0729). At a willingness-to-pay of S\$45,000 per QALY, incremental net monetary benefits (INMB) was S\$2961 (95% UI: S\$2906–S\$3015), with >99.9% probability of cost-effectiveness. Across all scenarios, INMB ranged from S\$1158 to S\$3330.

Conclusion: Scenario and probabilistic analyses suggest that Product X is a cost-effective solution for chemotherapy-induced alopecia, supporting its adoption from a health system perspective.

Keywords: scalp cooling, hair loss, breast cancer, chemotherapy side effect, cost-effectiveness

Background

Chemotherapy-induced alopecia is the thinning or loss of hair caused by the cytotoxic effects of chemotherapy and is a distressing side effects of cancer treatment.^{1,2} Depending on the drug administered, it typically occurs within one to three weeks after the start of treatment, and can result in partial or complete hair loss in up to 65% of patients.³ Due to the visibility of hair loss and its association with the cancer illness, affected patients often experience fear of stigmatization, anxiety, low self-esteem, and a marked reduction in quality of life.^{4–7} Notably, up to 14% of patients have declined curative chemotherapy to avoid alopecia.⁸ Interventions that mitigate hair loss may therefore enhance patients' quality of life and improve patients' clinical outcomes by supporting adherence to curative chemotherapy.

Scalp cooling therapy has been acknowledged as an effective method of mitigating chemotherapy-induced alopecia.^{9–15} Lowering the scalp temperature before, during and after chemotherapy induces local vasoconstriction, reducing blood flow and drug uptake by hair follicles, while also lowering cellular metabolism in hair follicles, making them less vulnerable to chemotherapy.¹⁶ Presently, scalp cooling is mainly achieved through cold caps or automated systems. Commercially available cold caps, such as the Penguin cold caps, are gel caps that are pre-cooled and applied to the head during chemotherapy. Because they warm quickly, these caps must be manually changed every 20–30 minutes during and after chemotherapy to remain effective.¹⁷ In contrast, automated systems such as the Paxman or Dignicap are bulky processor-controlled systems operated by healthcare personnel before, during and after chemotherapy. Unlike manual cold caps, these systems use temperature-regulating sensors to maintain a consistent temperature, thus eliminating the need for repeated cap change.¹⁸ However, their main drawbacks are longer infusion chair time, additional space required for the bulky machines and high costs.¹⁹ In addition, evidence on the cost-effectiveness of scalp cooling technologies remains extremely limited, with only one study published in 2014.²⁰ This highlights the need for new, effective devices supported by robust, evidence-based cost-effectiveness evaluations.

In Singapore, automated scalp cooling systems remain limited in public cancer care centres despite increasing patient demand. Currently, scalp cooling therapy is routinely offered at only one public hospital, the National University Cancer Institute Singapore.²¹ High patient volumes make it difficult for centres to accommodate the additional resources required, such as manpower, extended treatment chair time, and space. Since each machine serves a maximum of two patients at a time, large quantities would be needed. To address these barriers, a Singapore-based medical technology company, in collaboration with the National Cancer Centre Singapore, is developing a novel low-cost, self-administered scalp cooling device, termed Product X. Product X was specifically designed to overcome the limitations of current technologies. It is portable, allows patients to continue cooling after leaving the infusion chair, and incorporates a long-lasting coolant that maintains a consistent low temperature, eliminating the need for repeated cap changes.

This early stage study aimed to evaluate the potential cost-effectiveness of adopting Product X compared to current practice, in female patients with early breast cancer receiving cytotoxic chemotherapy at a Singapore tertiary cancer centre, from a health system perspective. Rather than claim definitive evidence, our goal was to offer preliminary insights into the likelihood of cost-effectiveness under varying clinical scenarios and to inform decision-makers regarding potential adoption and reimbursement considerations, providing context for local policy and clinical practice.

Methods

Study Setting

The National Cancer Centre Singapore (NCCS) is the leading outpatient cancer centre in Singapore, managing approximately 70% of all new cancer cases in the public healthcare system.²² It operates a total of 109 chairs in the Ambulatory Treatment Unit for outpatient chemotherapy treatment, and receives approximately 160,000 clinic attendances every year.^{23,24} At present, NCCS does not offer scalp cooling with automated cooling systems for cancer patients. Although patients may bring their own manual cooling caps, few choose to do so because of the cost and the practical challenges of using them during and after chemotherapy.

Target Population

Breast cancer is the most common female malignancy in Singapore, accounting for 29.6% of all female cancers.²⁵ Approximately 89% of cases are non-metastatic at diagnosis.²⁶ The mainstay treatment of non-metastatic breast cancer is surgical resection (eg total mastectomy or breast-conserving surgery), followed by adjuvant systemic therapy, which may include radiotherapy, chemotherapy, hormonal therapy, or targeted therapy.²⁷ While the choice of adjuvant systemic therapy depends on multiple factors, chemotherapy is commonly prescribed for early breast cancer. Reportedly, patients who did not undergo chemotherapy after primary surgery are more likely to perceive a lower risk of cancer recurrence.²⁸ The fear of hair loss may further reduce adherence to adjuvant chemotherapy. Therefore, the target population for our study is female patients with non-metastatic breast cancer, who are recommended adjuvant chemotherapy following surgical resection for curative intent.

We excluded male patients with breast cancer, as we believe that the impact of hair loss on patient's quality of life will differ substantially between male and female. We also excluded female patients with metastatic breast cancer who are offered chemotherapy with palliative intent, as their treatment outcomes will be substantially different from the target population. Lastly, we excluded female patients receiving neo-adjuvant chemotherapy prior to surgical resection, as their subsequent adherence to surgery affects outcomes.

Innovation

Product X is a portable cold cap which uses an innovative long-lasting coolant to maintain stable low scalp temperatures during scalp cooling therapy, while eliminating the need for regular cap changes. It is designed to be cordless and portable and does not require patients to remain in the treatment chair after chemotherapy for administration of scalp cooling.

Model Structure

The reporting of this study follows the CHEERS guidelines ([Appendix Table A](#)).²⁹ We developed a decision-analytic model consisting of a decision tree followed by a lifetime Markov model, to estimate the costs and health outcomes associated with the adoption of Product X compared to no scalp cooling, from a health system perspective (see [Figure 1](#)).

The decision tree models the impact of scalp cooling on adjuvant chemotherapy uptake and its effectiveness in preventing hair loss during the first year after diagnosis, based on the reported average diagnosis age of 54 years.²⁶ We assumed that the availability of scalp cooling influences adherence to chemotherapy, but only at the initial treatment decision point. Patients undergoing adjuvant chemotherapy are at risk of developing alopecia, which can be mitigated by scalp cooling. Since hair loss severity can range from mild thinning to complete baldness, we categorised the patients into two groups using the Dean's scale: successful hair preservation, defined as Dean's scale of grade 0 (no hair loss), grade 1 (<25%) or grade 2 (25–50%); and failure of hair preservation, defined as Dean's scale of grade 3 (50–75%), and grade 4 (>75%).³⁰

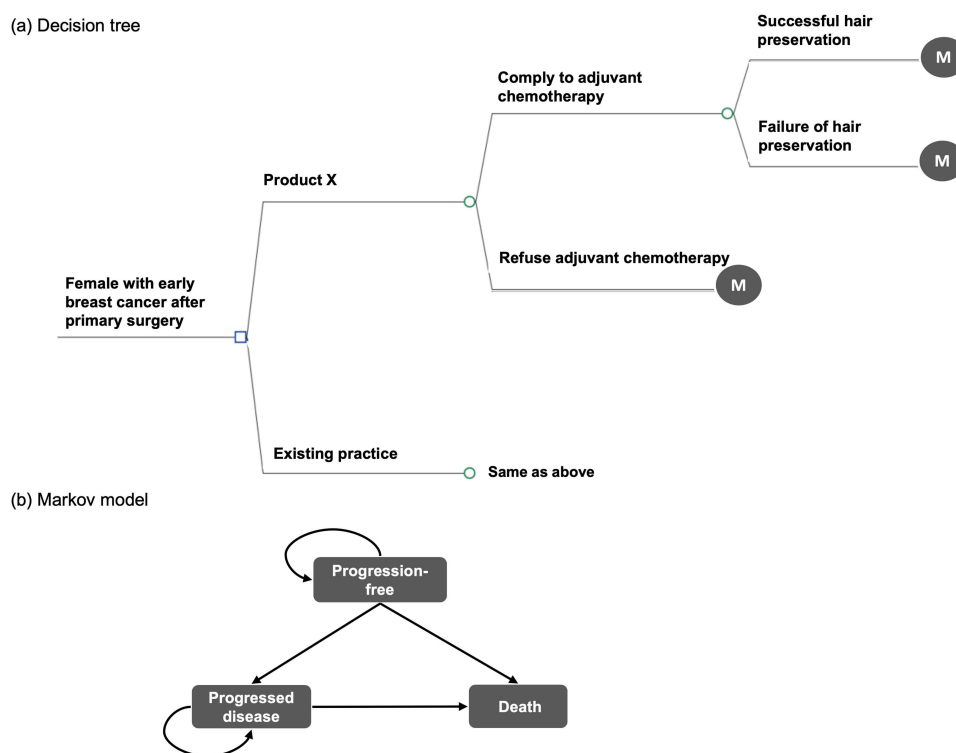


Figure 1 Hybrid decision-analytic model structure.

The Markov model describes disease progression after one year since diagnosis, with three states: “progression-free”, “progressed disease” and “death”. The model used one-year cycle length over a 32-year time horizon, corresponding to the remaining life expectancy of females in Singapore.³¹ “Progression-free” was defined as the period following initial treatment during which the disease remains stable without signs of advancement. All patients were assumed to enter the model via this state at the end of the decision tree. “Progressed disease” referred to the state in which the cancer has advanced, indicating either relapse or metastasis. For all patients with disease progression, they are assumed to undergo one additional round of scalp cooling alongside with chemotherapy as part of their cancer recurrence treatment. Patients can only transit unidirectionally from “progression-free” to “progressed disease” or to “death”, or from “progressed disease” to “death”.

Model Inputs

Probabilities and Transition Probabilities

The probabilities in the decision tree and the transitional probabilities used in the Markov model are shown in Table 1. We obtained the probabilities for adherence to adjuvant chemotherapy under existing practice from a local retrospective

Table 1 Major Model Parameters

Variables	Estimate (Standard Deviation)	Distribution	Reference
Costs			
Product X per year, S\$ (± 20%)	400–600	Uniform	Estimation from manufacturer
Nurse gross wage per hour, S\$	39.6 (28.0)	Gamma (2, 19.8)	Hospital administrative database
Chemotherapy per cycle	2798 (1978)	Gamma (2, 1399)	[35]
Total treatment cost in recurrent breast cancer, S\$	48,222 (34,098)	Gamma (2, 24,111)	[36]
Resource utilization			
Product X: waiting time due to scalp cooling, mins	96–144	Uniform	Assumed to be the same as Paxman, which is the benchmark ¹¹
Active nurse time per scalp cooling session for briefing, cap fitting and cleaning, mins	36 (12)	Normal	[20]
Probability			
Non-compliance to recommended chemotherapy	31.6%	Beta (3482, 7552)	[32]
Efficacy of scalp cooling services	61.0%	Beta (38, 24)	[11]
Proportion of patients suffered from alopecia without scalp cooling	94.7%	Beta (1385, 78)	[37]
Transition Probability			
Annual probability of progression in early breast cancer (age 40–60)	13.3%	Beta (12636, 764)	[26]
Annual probability of progression in early breast cancer (age 60 above)	20.1%	Beta (6693, 76)	[26]
Hazard ratio, relative risk			
Hazard ratio of mortality of non-compliant breast cancer patient	1.25	Log-normal (0.223, 0.061)	[32]
Hazard ratio of progression-free survival of patient without adjuvant chemotherapy	1.71	Log-normal (0.536, 0.105)	[33]
Relative risk of mortality in patient with cancer recurrence	4.20	Log-normal (1.44, 0.155)	[34]

(Continued)

Table 1 (Continued).

Variables	Estimate (Standard Deviation)	Distribution	Reference
Utility			
Patient with invasive breast cancer undergoing surgery, radiation therapy and/or chemotherapy (first year)	0.731	Beta (1124, 414)	[38]
Progression free (no recurrence with no adverse effects)	0.800	Beta (92, 23)	[39]
Progressed disease (Loco-regional recurrent with adverse effect)	0.460	Beta (44, 52)	
Experienced alopecia	-0.114–0.0500	Uniform	[40,41]
Others			
Age at diagnosis	54	Fixed	[26]
Survival time of local recurrence in breast cancer patients, years	2.60 (1.64)	Gamma (2.53, 1.03)	[42]

study.³² While we expected scalp cooling to reduce non-adherence, we were unable to find estimates in published literature. Hence, we sought expert opinion from clinical oncologists, who estimated the introduction of scalp cooling services could reduce non-adherence to adjuvant chemotherapy at least 1%. Given this information, we assumed the most conservative estimate of 1% improvement in adherence for our model. The transition probability for disease progression was derived from the Singapore Joint Breast Cancer Registry Report 2022.²⁶ For non-adherent patients, this probability was adjusted by multiplying the above transition probability with the hazard of disease progression in those that did not receive recommended chemotherapy.³³ The transition probability to death for patients in the progression-free state was assumed to be equivalent to that of the general population, based on the Singapore Life Table 2022.³¹ For those non-adherent patients, we multiplied the above transition probability by the hazard of death of non-compliance to chemotherapy.³² To estimate the transition probability to death in patients with progressed disease, the transition probability to death for the general population was multiplied by the hazard of death in patients with cancer recurrence.³⁴

Costs

We included health resource costing items relevant to uptake of scalp cooling, consistent with a health system perspective: equipment for scalp cooling, nursing time incurred, initial chemotherapy, and treatment for cancer recurrence. Detailed calculations are provided in the [Appendix Table B](#). Using national cancer incidence data²⁵ and published chemotherapy utilization rates,⁴³ we estimated that approximately 16.1% of patients receiving chemotherapy at NCCS ATU would be eligible for scalp cooling. Based on this target population, we estimated that 53 Product X devices would be needed. The acquisition cost of Product X was converted into an hourly cost, assuming 90% utilization of available caps and full operating capacity. To calculate nursing time, the average duration required for cap fitting and cleaning per session was multiplied by the weighted average number of cycles across the four most common regimens. Costs were calculated by multiplying hourly salary with the total nursing time. Due to the heterogeneity of chemotherapy regimens used in breast cancer treatment, the cost per cycle was estimated using publicly available data from the website of a local tertiary hospital.³⁵ The costs associated with cancer recurrence were derived from stage- and phase-of-care-specific treatment costs reported in a Singapore breast cancer screening modelling study.³⁶ All costs were reported in 2023 Singapore dollars. A discount rate of 3% per year was applied to all costs as recommended by US Panel on Cost-Effectiveness in Health and Medicine.⁴⁴

Outcomes

Patients' outcome is measured by quality adjusted life-years (QALYs) in which the health states were adjusted for health utility, multiplied by the duration in the state. In the decision tree, patients in the first year of diagnosis were assigned utility value obtained from a Korean general population study.³⁸ We assume that Korean population's economic wealth and culture are more comparable to Singapore's than those of Western countries. Health state utilities for breast cancer

patients in the “progression-free” and “progressed disease” state within Markov Model were derived from Singaporean breast cancer population.³⁹ The utility weight of chemotherapy-induced alopecia was based on published studies.^{40,41} A discount rate of 3% per year was applied to all QALYs.⁴⁴

Key model parameters are summarized in [Table 1](#). Full list for all parameters is reported in [Appendix Table C](#).

Data Analysis

All statistical analyses were performed using Microsoft Excel 2019 (Microsoft Corporate, US). For probabilistic sensitivity analysis, parameter uncertainties based on prior distributions were considered using Monte Carlo simulation with 1000 iterations. This output summarized the probability of each option (Product X and existing practice) being cost-effective as a percentage and plotted in the cost-effectiveness acceptability curve. We reported the incremental costs and QALYs, incremental cost-effectiveness ratios (ICERs), and incremental net monetary benefits (INMB) with 95% uncertainty interval (UI), compared to existing practice. The willingness-to-pay (WTP) threshold was set at \$45,000 per QALY gained at base case, as recommended in the Medical Technologies Evaluation Methods and Process Guide by the Ministry of Health Singapore.⁴⁵

A two-way scenario analysis was conducted by varying two key assumptions: (1) the improvement in chemotherapy adherence (0%, 1%, 5%) and (2) the efficacy of Product X relative to reported efficacy of existing scalp cooling therapies (50%, 75%, and 100%). This resulted in a matrix of nine scenarios exploring the combined effects of these assumptions on cost-effectiveness. The base-case assumed 1% reduction in non-compliance and 100% relative efficacy. The worst- and best-case scenarios corresponded to the lowest and highest values for both parameters, respectively.

Results

In 1000 Monte Carlo simulations, the mean change in cost was S\$265 (95% UI: S\$251–S\$281) and mean change in QALYs was 0.0717 (95% UI: 0.0705–0.0729) when compared to existing practice ([Figure 2](#)). The cost-effectiveness acceptability curve with WTP ranging from S\$0 to S\$100,000 was presented in [Figure 3](#). When WTP threshold exceeded \$4000 per QALY, probability of cost-effectiveness of Product X began to outweigh that of existing practice (57.9% vs 42.1%). At WTP of S\$45,000 per QALY, INMB was estimated at S\$2961 (95% UI: S\$2906–S\$3015) with >99.9% likelihood that adoption of Product X is cost-effective.

Scenario Analysis

As illustrated in [Figure 4](#), all scenarios estimated that adoption of Product X is cost-effective with positive incremental net monetary benefits. In the worst case scenario (Scenario 2), INMB was approximately S\$1158 (95% UI: S\$1132–S\$1184) with 99.9% likelihood of cost-effectiveness whereas in the best case scenario (Scenario 9), INMB was

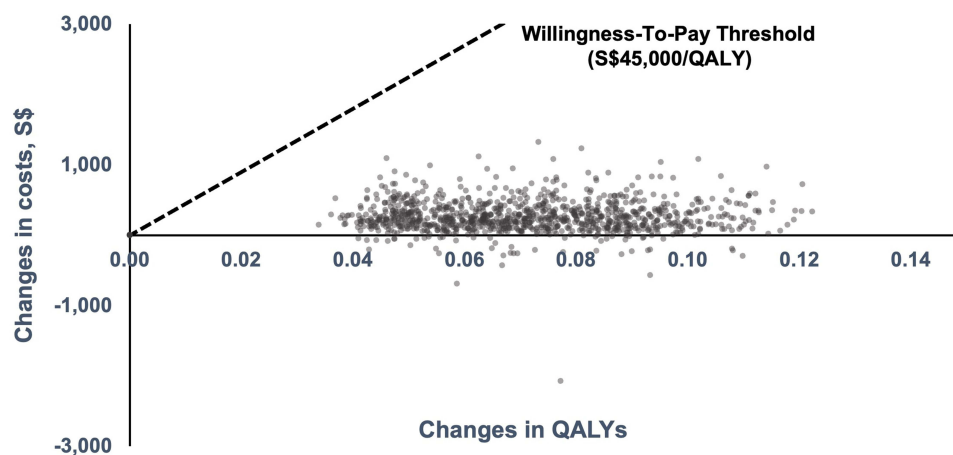


Figure 2 Cost-effectiveness plane of base-case analysis.

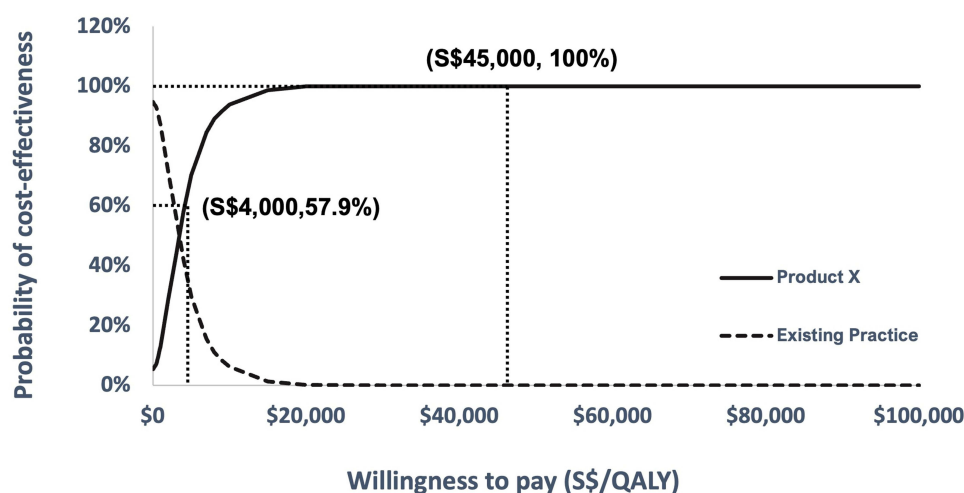


Figure 3 Cost-effectiveness acceptability curve.

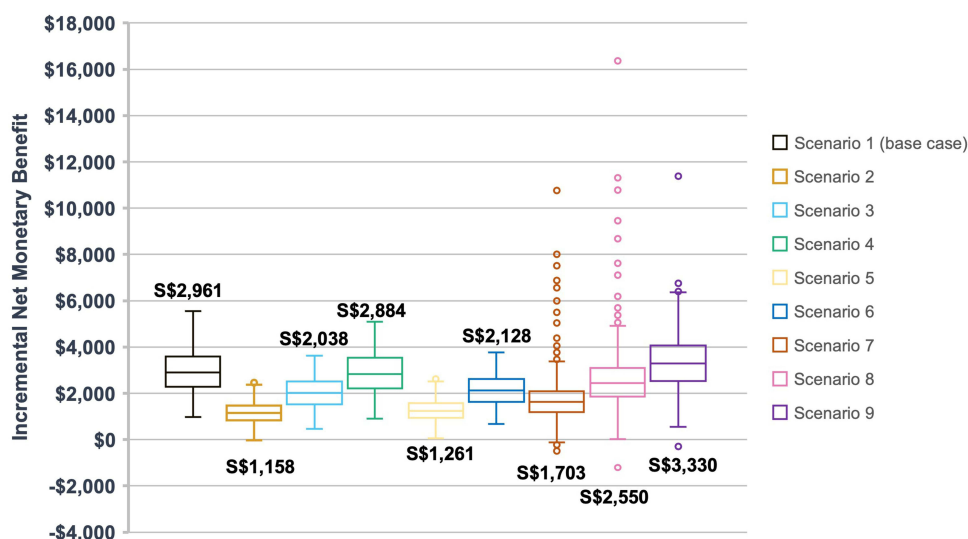


Figure 4 Results of Monte Carlo simulations in nine scenarios. Box-and-whisker plots display the mean (indicated), median with interquartile range (boxes), range (whiskers), and outliers (dots). Nine scenarios were modeled, combining different assumptions on compliance improvement and scalp cooling efficacy: Scenario 1 (base case): 1% improvement, 100% efficacy; Scenario 2: 0% improvement, 50% efficacy; Scenario 3: 0% improvement, 75% efficacy; Scenario 4: 0% improvement, 100% efficacy; Scenario 5: 1% improvement, 50% efficacy; Scenario 6: 1% improvement, 75% efficacy; Scenario 7: 5% improvement, 50% efficacy; Scenario 8: 5% improvement, 75% efficacy; Scenario 9: 5% improvement, 100% efficacy.

approximately S\$3330 (95% UI: S\$3261–S\$3398) with 99.9% likelihood of cost-effectiveness. Detailed results for probabilistic sensitivity analysis are reported in [Appendix Table D](#).

Discussion

This early cost-effectiveness modelling study suggests that the adoption of a novel cold cap, Product X, is likely to be >99.9% cost-effective in a Singapore tertiary cancer centre, from a health system perspective. The incremental net monetary benefits are approximately S\$2961 per patient at willingness-to-pay of S\$45,000/QALY.

Our scenario analysis suggests that the model is robust in estimating the net benefits that Product X could offer to patients, with incremental net monetary benefit ranging from S\$1158 per patient in the worst-case scenario to S\$3330 per patient in the best-case scenario. Even under the most pessimistic assumptions where Product X achieves only 50% of the

efficacy of commercially available scalp cooling therapies and does not impact on treatment adherence, the probability of an adoption decision being cost-effective compared to current practice is almost 100%. Of course, the clinical effectiveness of Product X has yet to be established. Yet, our findings provide a useful benchmark for further development of the coolant technology, indicating that achieving even half the efficacy of existing commercial products would likely result in cost-effective adoption.

To the best of our knowledge, this is the first modelling analysis to investigate the cost-effectiveness of scalp cooling in breast cancer patients in the Asia context. van Den Hurk et al published the first cost-effectiveness analysis of scalp cooling using the Paxman automated system compared with usual care, in the hospital setting in Netherlands.²⁰ The analysis was based on the findings from a non-randomised prospective study that captured the reported short-term medical and non-medical costs, eg cost of wigs and head covers. They found that scalp cooling was cost-effective at low WTP (up to €34,000) in the Dutch society. In our study, we evaluated the long-term economic impacts of scalp cooling using the best available data. We made conservative assumptions about Product X's hair preservation efficacy and its potential to improve treatment compliance among patients concerned about chemotherapy-induced alopecia. Despite this, our simulation results indicate that Product X has nearly 100% probabilities of being cost-effective across the various scenarios.

Strengths

The strength of our hybrid model lies in its ability to capture both short- and long-term benefits of scalp cooling. In the short term, it preserves hair during chemotherapy, improving patient quality of life. In the long term, it may indirectly enhance survival by addressing factors that influence adherence to adjuvant chemotherapy. The model also provides a realistic estimation of scalp cooling duration and associated costs by incorporating weighted regimen-specific parameters (eg infusion durations and number of treatment cycles) across four commonly used breast cancer regimens: Taxane-based, Anthracycline-based, combined Anthracycline and Taxane, and Taxane with cyclophosphamide. This approach maintains model simplicity while producing estimates that are representative of real-world practice.

Limitations

Our study has several limitations. First, as this is an early-stage cost-effectiveness analysis model, some of the input data were derived from overseas studies, which may not accurately represent the epidemiology or patient preferences in Singapore. We partially addressed this by applying appropriate distributions in the probabilistic sensitivity analysis. The model's symmetric structure further mitigates potential bias. Assumptions regarding the clinical and technical performance of Product X should be validated as soon as the device becomes available. As published evidence on the impact of similar innovations on adherence is limited, we consulted local oncology experts for their opinions. The lack of published evidence underscores the need for future research to better understand and quantify the determinants of treatment adherence, through the conduct of focus group discussions and expert elicitation studies. As new evidence emerges, the model can be easily updated to support future decision-making. Second, our model does not account for the impact of time from initial diagnosis to recurrence, which has been shown to be a strong predictor of mortality in cancer recurrence.^{34,42,46} This limitation arises from the memoryless property of the Markov model, meaning that future transitions are independent of the model's history. Future work could address this structural uncertainty using tunnel states or time-dependent transitions. Lastly, the model did not include potential societal benefits, such as reduced out-of-pocket costs or productivity gains, which may lead to underestimation of the overall value of scalp cooling.

Conclusions

This early-stage analysis provides supportive evidence that the novel scalp cooling cap is likely to be cost-effective for early breast cancer patients in a tertiary outpatient setting in Singapore. Future work should focus on validating the performance of Product X and collecting data on its impact on adherence and alopecia-related quality of life. As new evidence emerges, the model should be updated to guide decision-making.

Data Sharing Statement

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical Approval and Consent to Participate

This is a Review-Not-Required study as no identifiable individual data were used in this analysis.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests.

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