Cost-effectiveness of different surgical treatment approaches for early breast cancer: a retrospective matched cohort study from China

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Abstract

Background

Both breast-conserving surgery and breast reconstruction surgery are less popular in China, although they can improve patients' quality of life. The main reason comes from the economy. There is currently no economic evaluation of different surgical treatment options for early breast cancer. Our study aimed to evaluate the long-term cost-utilities of different surgical treatment approaches for early breast cancer. The surgical approaches are including mastectomy(MAST), breast-conserving therapy(BCT), and mastectomy with reconstruction (MAST+RECON).

Methods

We applied the propensity score matching method to perform a 1: 1 match on patients undergoing these three types of surgery in a tertiary academic medical center from 2011 to 2017 to obtain a balanced sample of covariates between groups. A Markov model was established. Clinical data and cost data were obtained from the medical records. Health utility values were derived from clinical investigations. Strategies were compared using an incremental cost-effectiveness ratio (ICER).

Results

The total cost of MAST, MAST+RECON and BCT was $35,282.24, $69,428.82 and $73,661.08, respectively. The discounted quality-adjusted life year(QALYs) were 17.94, 18.71 and 20.49, respectively. Compared with MAST, MAST+RECON and BCT have an ICER of $106708.06/QALY and $15050.53/QALY, respectively. The ICER of BCT vs. MAST was less than the threshold of $27,931.04. The reliability and stability of the results were confirmed by Monte Carlo simulation and sensitivity analysis.

Conclusions

We believe that in the context of the limited resources in China, after comparing the three surgical approaches, BCT is the more cost-effective and preferred solution.

Background

Breast cancer is the most common cancer in the world, ranking as the leading cancer among women and as the second leading cause of cancer death among women after lung cancer[1]. Breast cancer is also one of the most important malignancies in China. According to data from the National Cancer Registry Annual Report 2018[2], the number of women with breast cancer in China in 2014 was approximately 279,000, with an incidence rate of 41. 82 per 100,000. The incidence rate has been increasing over the past 10 years. The increasing morbidity and mortality of breast cancer, which lead to high medical costs, has placed a huge burden on both families and society[3].

In recent years, under the background of increasing B-resolution and X-ray mammography, the early diagnosis rate of breast cancer has increased significantly[4]. Surgery is the main method of treating early breast cancer. The traditional surgical method is mastectomy. With the increasing emphasis on quality of life, breast-conserving surgery has begun to mature. A number of studies have shown that for early breast cancer, there is no statistically significant difference in disease-free survival and overall survival between the breast-conserving surgery plus radiotherapy group and the mastectomy group[5–7]. For patients undergoing mastectomy, breast reconstruction offers them the possibility to reshape their breasts[8]. However, breast-conserving therapy and breast reconstruction have increased the costs of treatment while improving the quality of life[9, 10]. Studies by Barlow et al. [11] have found that breast-conserving therapy may have higher short-term costs but lower long-term costs compared to mastectomy. Although most studies believe that breast-conserving therapy and breast reconstruction have higher costs, some studies have reached inconsistent conclusions, and evidence from China is lacking.

In China, breast-conserving surgeries account for only 6% of all breast cancer surgeries[12], and breast reconstruction only accounts for less than 10%[13]. Both breast-conserving surgery and breast reconstruction surgery are less popular in China, although they have increased in the past few decades[14]. Most stage □ and □ breast cancer cases still undergo modified radical surgery. Several studies have confirmed that the socioeconomic status of breast cancer patients, rather than their clinical status, is the main factor that determines the surgical treatment options for breast cancer patients[15, 16]. The trade-off between cost and quality of life benefits has become a decision that breast cancer patients must face. Cost-effectiveness analysis often uses data from clinical trials, but these patient populations may not always truly represent the patient population encountered in routine clinical practice[17]. Therefore, health economic evaluation of cancer using real-world research has become a research hotspot and trend[17, 18].

There is currently no economic evaluation of different surgical treatment options for early breast cancer. Therefore, the purpose of this study is to establish an economic model to evaluate the long-term cost-effectiveness of different surgical treatment approaches for early breast cancer from a social perspective. The research results can provide a basis for clinical treatment decisions and the formulation of medical insurance policies.

Methods

Patients and treatment options

Breast cancer patients were registered in the Breast Cancer Information Management System of West China Hospital, Sichuan University (Sichuan, China) since 1989. Their medical history, pathological diagnosis, and treatment information were prospectively collected by oncologists. Each patient was followed by outpatient visit or telephone at 3 to 4-month intervals within 2 years after diagnosis, 6-month intervals within 3 ~ 5 years, and then annually. Written informed consent was provided by all the patients.

Ethical permission was granted by the Ethics Committee, West China School of Medicine/West China Hospital, Sichuan University(approval number 2017 – 255).

From 2011 to 2017, a total of 5,070 early breast cancer patients were diagnosed in the West China Hospital of Sichuan University, of which 4,408 were treated with three main types of surgery. There were 206 cases of MAST + RECON, 425 cases of BCT and 3777 cases of MAST.

Because the baselines of the three groups were not consistent, we used R software to match the propensity scores. Based on the MAST + RECON group, the nearest-neighbor method was used for 1:1 matching. The rest of the statistics were performed using SPSS 25.0 software. The measurement data were analyzed by analysis of variance, the unordered counting data were tested by row × list chi-square tests, and the ordered counting data were tested by rank sum. All the tests were two-sided, and $p < 0.05$ indicated statistical significance. There was no statistically significant difference in breast lesion location before propensity score matching. The variables of age, medical insurance type, histology type, TNM stage, BMI, HR, patient source, whether to use neoadjuvant chemotherapy, and whether to use targeted therapy were statistically significant ($p < 0.05$). After matching, there were 206 cases in each of the three groups. There was no significant differences in the general information orclinical characteristics, indicating that the data of the three groups were balanced after matching (Table 1). We conducted survival follow-up for the 3 groups of patients, and the deadline was April 2019.

Table 1
Comparison of general information after matching of propensity scores of early breast cancer patients with different surgical treatment approaches

		MAST + RECON	BCT	MAST	Statistics	p value
Age,year		38.63 ± 6.94	38.60 ± 7.58	39.03 ± 7.21	0.222	0.801
Health-care insurance	Provincial medical insurance	13	12	11	4.367	0.359
	City medical insurance	102	100	119		
	Other	90	93	75		
Lesion location	Left breast	110	112	109	2.268	0.687
	Right breast	95	93	95		
	Double breast	0	0	1		
Histology type	Ductal carcinoma in situ	10	5	6	3.888	0.692
	Invasive ductal carcinoma	158	168	164		
	Invasive lobular carcinoma	5	3	2		
	Other	32	29	33		
TNM	0	4	3	7	1.336	0.513
	[illegible]	6	5	6		
	[illegible]	195	197	192		
BMI,Kg/m^2	[illegible]18.5	21	15	15	2.687	0.261
	18.5～23.9	144	164	148		
	[illegible]23.9	40	26	42		
HR	Positive	105	106	195	0.749	0.993
	Negative	19	17	21		
	Mixed	73	75	73		
	Unkonwn / missing	8	7	6		

		MAST + RECON	BCT	MAST	Statistics	p value
Patient source	In this city	126	129	131	1.072	0.899
	In this province	71	65	66		
	Other	8	11	8		
Neoadjuvant chemotherapy	No	165	169	169	0.349	0.840
	Yes	40	36	36		
Targeted therapy	No	167	172	11	0.482	0.786
	Yes	38	33	34		

Model Structure

The Markov model of early breast cancer identified in this study has four states: disease-free survival, local recurrence, distant metastasis, and death. Patients with disease-free survival can develop local recurrence and distant metastases, patients with local recurrence can develop distant metastases, and only patients with distant metastases may have breast cancer-related deaths. All of the states can result in death from other causes. Once a patient has died, they cannot transition to other states, so death is also an absorbed state (Fig. 1).

There are three alternative surgical options for confirmed early breast cancer patients: MAST + RECON, BCT, and MAST. The initial age of the cohort after the propensity score in this study was 39 years. Therefore, the Markov model simulates the 60-year outcome of patients after receiving the three surgical routes. The status of all the patients entering the model was the disease-free survival status.

This study analyzed the costs and effectiveness of the three surgical treatment paths from the perspective of society as a whole. The utility analysis used quality-adjusted life years (QALYs) and then weighed the advantages and disadvantages of the three surgical treatment paths. The evaluation index of this method was the ICER, which was the incremental cost-effectiveness ratio, that is, the ratio of the difference between the relative costs and effects of the intervention plan and those of the control plan. In this study, it was necessary to calculate the cost of each additional quality-adjusted life year compared to different treatment strategies. When comparing the ICER with the threshold, if the ICER is less than the threshold, it means that the solution is cost-effective; if the ICER is greater than the threshold, then the solution does not have cost-utility. The threshold for this study, which was WTP, used 3 times China's GDP per capita in 2018[19, 20], which was $27,931.04.

TreeAge Pro 2011 (TreeAge Software, Inc., Williamstown, MA, USA) was used to build and analyze the Markov model. This software is professional software for decision trees and Markov models. This study used a 3% discount rate to discount costs and utility values and applied a half-cycle correction.

Transition Probability

In this study, the transition probability was determined by survival analysis to obtain the time to transition from one state to another state, and then the transition probability was calculated by the formula. The survival analysis curve for each state transition in the study cohort is shown in Fig. 2. If a patient had both recurrence and metastasis, it was counted as metastasis. According to the calculation formula of transition probability, i.e., $r=-[\ln(1-P_1)]/t_1$ and $P = 1-e^{-rt_2}$, the transition probability was calculated (Table 2). For example, the follow-up time from modified disease-free survival to local recurrence in this study was 94 months, with a cumulative recurrence-free probability P_1 of 0.994. A Markov cycle was 12 months in a year, and the unit of follow-up time was converted from month to year to obtain the parameter t_1.

Table 2
One-way sensitivity analysis parameter change range and probability sensitivity analysis probability distribution setting

		Range		Distribution
Parameters	Baseline	Upper boundary	Lower boundary	
Cost				
Cost of local recurrence hospitalization(first year)	10147.18	2971.96	17322.39	Lognormal
Cost of local recurrence outpatient(first year)	3728.43	2305.50	5151.35	Lognormal
Cost of distant metastasis hospitalization per year	10652.42	9233.85	12070.99	Lognormal
Cost of distant metastasis outpatient per year	2984.55	2649.14	3319.96	Lognormal
Cost of hospitalization for 3 months before death	3585.82	2533.61	4638.03	Lognormal
Cost of outpatient for 3 months before death	874.56	713.96	1035.15	Lognormal
Cost of MAST + RECON hospitalization(first year)	10221.30	9192.74	11249.86	Lognormal
Cost of MAST + RECON outpatient (first year)	6070.98	5233.55	6908.42	Lognormal
Cost of BCT hospitalization(first year)	7475.54	4659.50	10291.58	Lognormal
Cost of BCT outpatient (first year)	6905.61	6051.87	7759.35	Lognormal
Cost of MAST hospitalization(first year)	6630.24	6114.63	7145.85	Lognormal
Cost of MAST outpatient (first year)	4210.88	3608.80	4812.97	Lognormal
Annual cost of follow-up for MAST + RECON	1448.12	1166.11	1730.13	Lognormal
Annual cost of follow-up for BCT	1198.82	961.66	1435.99	Lognormal
Annual cost of follow-up for MAST	770.22	770.22	1090.77	Lognormal
Transportation cost of MAST + RECON	253.97	203.17	304.76	Lognormal
Cost of losing work of MAST + RECON	1202.54	962.03	1443.04	Lognormal
Transportation cost of BCT	219.34	175.47	263.20	Lognormal
Cost of losing work of BCT	997.85	798.28	1197.42	Lognormal
Transportation cost of MAST	230.88	184.70	277.06	Lognormal
Cost of losing work of MAST	1125.78	900.62	1350.93	Lognormal

		Range		Distribution
Utilities				
Local recurrence (first year)	0.779	0.641	0.917	Beta
Distant metastasis	0.737	0.657	0.817	Beta
Disease-free for MSAT + RECON(first year)	0.868	0.694	1	Beta
Disease-free for MSAT + RECON(subsequent year)	0.933	0.746	1	Beta
Disease-free for BCT(first year)	0.872	0.823	0.921	Beta
Disease-free for BCT(subsequent year)	0.923	0.903	0.943	Beta
Disease-free for MSAT (first year)	0.785	0.729	0.842	Beta
Disease-free for MSAT (subsequent year)	0.900	0.883	0.918	Beta
Transition probability				
Local recurrence of MAST + RECON	0.002299	0.001839	0.002759	Beta
Distant metastasis of MAST + RECON	0.016980	0.013584	0.020376	Beta
Distant metastasis after local recurrence of MAST + RECON	0.000000	0.000000	0.100000	Beta
Death after distant metastasis of MAST + RECON	0.112083	0.089666	0.134500	Beta
Local recurrence of BCT	0.002666	0.002133	0.003199	Beta
Distant metastasis of BCT	0.006892	0.005514	0.008270	Beta
Distant metastasis after local recurrence of BCT	0.201328	0.161062	0.241594	Beta
Death after distant metastasis of BCT	0.016473	0.013178	0.019768	Beta
Local recurrence of MAST	0.000768	0.000614	0.000922	Beta
Distant metastasis of MAST	0.010451	0.008361	0.012541	Beta
Distant metastasis after local recurrence of MAST	1.000000	0.800000	1.000000	Beta
Death after distant metastasis of MAST	0.334939	0.267951	0.401927	Beta
Discount rate	3%	0	5%	Constant

Because the annual local recurrence probability was calculated, $t_2 = 1$ was taken. The local recurrence probability of MAST was calculated by the formula as 0.000768. Table 2 summarizes the transition probability parameters used for model input.

Cost

This research considered the direct and indirect costs from the perspective of the whole society. All costs were expressed in US dollars ($), and the exchange rate was US $1 = 6.93 yuan (January 13, 2020). Table 3 summarizes the cost data used for model inputs. The direct cost was calculatedas the direct medical costs and the patient's transportation expenses, and the indirect cost included the patient's lost time. Direct medical costs were derived from all inpatient and outpatient records of patients in the electronic medical record system and were collected according to the state Markov model.

This study also considered the first year of transportation costs for patients in different surgical treatment groups. The calculation of transportation costs was considered as the sum of the number of inpatient and outpatient visits × the average transportation cost per visit. The average transportation cost of each visit referred to the related literature published by Chengdu, China, on health economics evaluation[21]. Based on taxi fares, the transportation cost was set at 80 yuan/time.

The calculation of the cost of lost work in this study was based on the sum of the average number of days of hospitalization and the number of outpatient visits in the first year of treatment for patients in different surgical treatment groups × average daily lost time. By calculation, the loss time in the MAST + RECON group was 47 days, the loss time in the BCT group was 39 days, and the loss time in the MAST group was 44 days. According to the announcement issued by the Statistics Bureau of Sichuan Province of China, the average daily wage of employees in all units of Sichuan Province in 2018 was $9338.67/year, calculated as $25.59/day. Therefore, the lost labor cost of the MAST + RECON group was calculated to be $1202.54, the lost labor cost of the BCT group was $940.71, and the lost labor cost of the MAST group was $1125.78.

Health Utility

It was necessary to determine the health utility value of the patients of the three surgical treatment plans within one year of treatment, after the second year or more, the cases of relapsed breast cancer within one year (state R) and those of metastatic cancer (state M). The EQ-5D-5L scale was used to investigate the health utility value of 446 Chinese breast cancer patients. The health utility value of recurrent breast cancer within one year (state R) was 0.779, and the health utility value of metastatic cancer (state M) was 0.737. The health utility values of patients undergoing BCT and MAST were also obtained from the survey. Since only 3 of the 446 patients surveyed underwent MAST + RECON, the health utilities of this surgical treatment group could not be calculated. Therefore, we used the health utility mapping model established earlier in this research group to map the value of FACT-B to EQ-5D-5L to obtain the health utility of this type of patient[22]. The value of FACT-B in breast cancer patients undergoing breast reconstruction surgery was taken from the literature[23, 24], and we calculated the average value of FACT-B reported in these studies. The final health utility data used for model input are shown in Table 2.

Sensitivity Analysis

A one-way sensitivity analysis was performed to test the robustness of the economic model and the impact of the key input parameters on the results. The upper and lower 95% CI limits were used as the upper and lower limits of the parameter change, and the remaining parameters adopted ± 20% of the baseline value as the upper and lower limits of the parameter change. The discount rate used 0% and 5% as the upper and lower limits, respectively. The parameter settings are listed in Table 2.To evaluate the results of the basic cost utility, a Monte Carlo simulation was performed on the Markov model, and 1,000 samples were simulated to resolve the uncertainty strategy.

Results

Base-case analysis

The results of the base-case analysis in this study are shown in Table 3. After running for 60 cycles, the total cost of the MAST group is $35,282.24, and the discounted quality-adjusted life year is 17.94 years. The total cost of the MAST + RECON group is $69,428.82, and the discounted quality-adjusted life year is 18.71 years. The total cost of the BCT group is $73,661.08, and the discounted quality-adjusted life year is 20.49 years. Compared with the MAST group, the MAST + RECON group and BCT group have an incremental effect cost ratio of $106708.06/QALY and $15050.53/QALY, respectively. Among them, the incremental cost-effectiveness ratio of the BCT group is less than the WTP threshold of $27,931.04. Within this threshold, we consider that BCT is more cost-effective than the other surgical treatments and is the preferred solution.

Table 3

Base-case estimates of cost and health benefits for different surgical treatment approaches

Surgical treatment approaches	Cost($)	Incremental cost($)	QALYs	Incrementa QALYs	Incremental cost per QALY
MAST	35282.24	-	17.94	-	-
MAST + RECON	69428.82	34146.58	18.26	0.32	106708.06
BCT	73661.08	38378.84	20.49	2.55	15050.53

Sensitivity analysis

Fig. 3 show the tornado diagrams of the one-way sensitivity analysis. It can be seen from the figures that different factors have different effects on the results. A one-way sensitivity analysis comparing BCT with MAST shows that the three factors that had the greatest impact on ICER are the probability of disease-free survival to distant metastasis in the MAST group and the probability of both distant metastasis and health utility value for the second year and above in the BCT group. When all the parameters are changed within the specified range, the ICER is still lower than the WTP value.

This study also conducted a probability sensitivity analysis to explore the effect of parameter distribution changes on the results. The cost parameters were lognormal distributions, and the health utility and transition probability parameters were beta distributions[25]. Fig. 4 shows the acceptable curve of the probability sensitivity analysis. The results show that the probability of the cost-effectiveness of MAST decreases with an increasing WTP threshold, while that of both MAST+RECON and BCT increase with an increasing WTP threshold. When the WTP is greater than the crossing WTP value of the two acceptance curves of MAST and BCT, which is $15050.53/QALY, the probability of the cost-effectivenessof BCT is greater than that of MAST. When the WTP is $27,931.04/QALY, the probability of choosing BCT is 67.6%, the probability of choosing a MAST is 27.5%, and the probability of choosing a MAST+RECON is 4.9% (Fig. 5).

Discussion

Surgery is the main treatment for early breast cancer. There are many surgical options for breast cancer, including MAST, BCT, andMAST + RECON[26]. The choice of BCT and MAST + RECON is affected by the patient's economic conditions and type of medical insurance[16], so the use ratios for these alternatives in China are low. However, compared with MAST, BCT has no significant difference in overall survivaland evidences a better quality of life[27]. Similar conclusions were obtained after modified radical mastectomy plus breast reconstruction[28]. Therefore, this study explores the cost-effectiveness of the three surgical treatment paths from the perspective of health economics to evaluate whether the increased cost-effectiveness ratio of BCT and MAST + RECON compared with MAST is cost-effective. To our knowledge, this is the first study (a) to assess the cost-utility of different surgical approaches to early breast cancer from a Chinese perspective, (b) to use real-world costs and transition probabilities, and (c) to use local cost and health utility data to build a Markov model; in addition, the health utility mapping model established in this study was used in the health utility acquisition channels. This study simulated a 60-year cohort using Markov modeling to assess the cost of obtaining each QALY. The surgical decision-making of early breast cancer patients addressed in this study can provide decision-making references for patients and medical staff and provide the basis for the formulation of relevant policies of medical insurance departments.

In the 60-year time frame, compared with MAST, the QALYs of BCT and MAST + RECON increased by 2.55 years and 0.32 years, respectively, and the cost increased by $38,378.84 and $34,146.58, respectively. Compared with the MAST group, the two groups of BCT and MAST + RECON had incremental cost-effectiveness ratios of $15050.53/QALY and $106708.06/QALY, respectively, of which the ICER of BCT was less than the threshold. According to this threshold, we think that the breast-conserving surgical path is more cost-effective than the other surgical treatments. When analyzing the increased QALYs of BCT compared with those of MAST, it is mainly seen that patients who undergo BCT have better a quality of life during the first year and during follow-up. In addition, the probability from distant metastasis to death in patients undergoing BCT is lower than that for the other treatment alternatives. Previous studies have found that compared with modified radical mastectomy, the difference between the local recurrence rate and distant metastasis rate is not statistically significant[5−7]. The survival analysis in this study also obtained similar conclusions. However, this study also found that patients with BCT had a lower probability of metastasis from distant metastasis to death. Studies by Fisher S et al. [29] have also showed that compared with patients receiving BCT, all-cause and breast cancer-specific death risks of patients receiving MAST are significantly higher. This outcome may cause patients with BCT to metastasize for a longer time, which will bring more costs and increase the QALYs. In a health economics evaluation study of breast cancer after breast-conserving radiotherapy conducted by Yongrui Bai et al. [30], the QALYs of patients after BCT were found to be between 8.44 and 13.79 years. The QALYs of BCT obtained in this study equal 20.49 years, which is slightly higher than the results of the previous study. The reason for the differences between thefindings is that the initial age of the current study's cohort was 39 years; thus, the cohort in the current study was younger.

Since most breast cancer patients are long-term survivors with high social costs, we need to accurately evaluate the cost of breast cancer compared to other malignancies[31]. Therefore, from the perspective of society as a whole, this study considers the indirect costs of breast cancer treatment in addition to the direct costs. From the perspective of indirect costs, the transportation costs and lost-time costs of breast-conserving surgery are the lowest, which may be related to less trauma regarding the operation and shorter hospital stays.

This study used one-way sensitivity analysis and probability sensitivity analysis, and the results showed that the study had stability. Below the WTP threshold, none of the parameter changes could make the MAST cost-effective.

This study has certain limitations. First, the study was based on clinical and follow-up data from confirmed patients from 2011 to 2017, with a maximum follow-up time of 9 years. Survival analysis calculates the transition probability of each state; thus, extrapolating the survival situation may not reflect the disease outcome process of patients with early breast cancer very accurately. However, a sensitivity analysis was performed in this study, which indicated that the results of this study are stable and reliable. As the patient follow-up time of the research group is extended, we will also regularly update the results of this study to make this study more accurate.

Second, the health utility value of breast reconstruction surgery did not come from our direct investigation. We found that the proportion of breast reconstruction surgery in this study was only 2%. Due to the convenience sampling used in the previous health utility survey, only 3 of 446 patients had breast reconstruction surgery, which could not meet the needs of the Markov model established in this study. Therefore, we established a mapping model of FACT-B to EQ-5D-5L[22],and we mapped the quality of life score of FACT-B published in China to the EQ-5D-5L score. Although the health utility value obtained by this method is not first-hand information, when direct health utility data cannot be obtained, this method is currently the only solution for cost-utility analysis[32]. We believe that this method is more accurate than directly using a health utility value of breast cancer from abroad or using a health utility value from other cancers. Generally, the quality of life of MAST + RECON is better than that of BCT and MAST. The health utility value of BCT obtained after mapping in this study is 0.933, which is higher than that of both MAST-RECON and MAST. The health utility value also further illustrates the effectiveness of the mapping algorithm.

Overall, this study is the first to compare the different surgical treatment approaches for early breast cancer from a cost-utility perspective. The results show that, from the perspective of Chinese society, BCT is more cost-effective than both MAST and MAST + RECON. Our analysis will help clinicians make the best decisions when treating patients with early breast cancer who need surgery.

Abbreviations

BCT: Breast-conserving therapy; ICER: Incremental cost-effectiveness ratio; MAST: Mastectomy; MAST+RECON: Mastectomy with reconstruction ; QALYs : Quality-adjusted life years

Declarations

Ethics approval and consent to participate

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was provided by all the patients. The study obtained the approval by the the Ethics Committee, West China School of Medicine/West China Hospital, Sichuan University(approval number 2017-255).

Consent for publication

Not applicable.

Availability of data and materials

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

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Conception and design: QY, XRZ ,WZ. Analysis and interpretation: QY, XRZ. Data collection: TL, PH, HZ. Writing the article:QY. Critical revision of the article: XRZ ,WZ. Final approval of the article: QY, WZ. Overall responsibility: QY, WZ. All authors have read and approved the final version of the article. Financial acquisition: WZ.

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Figures

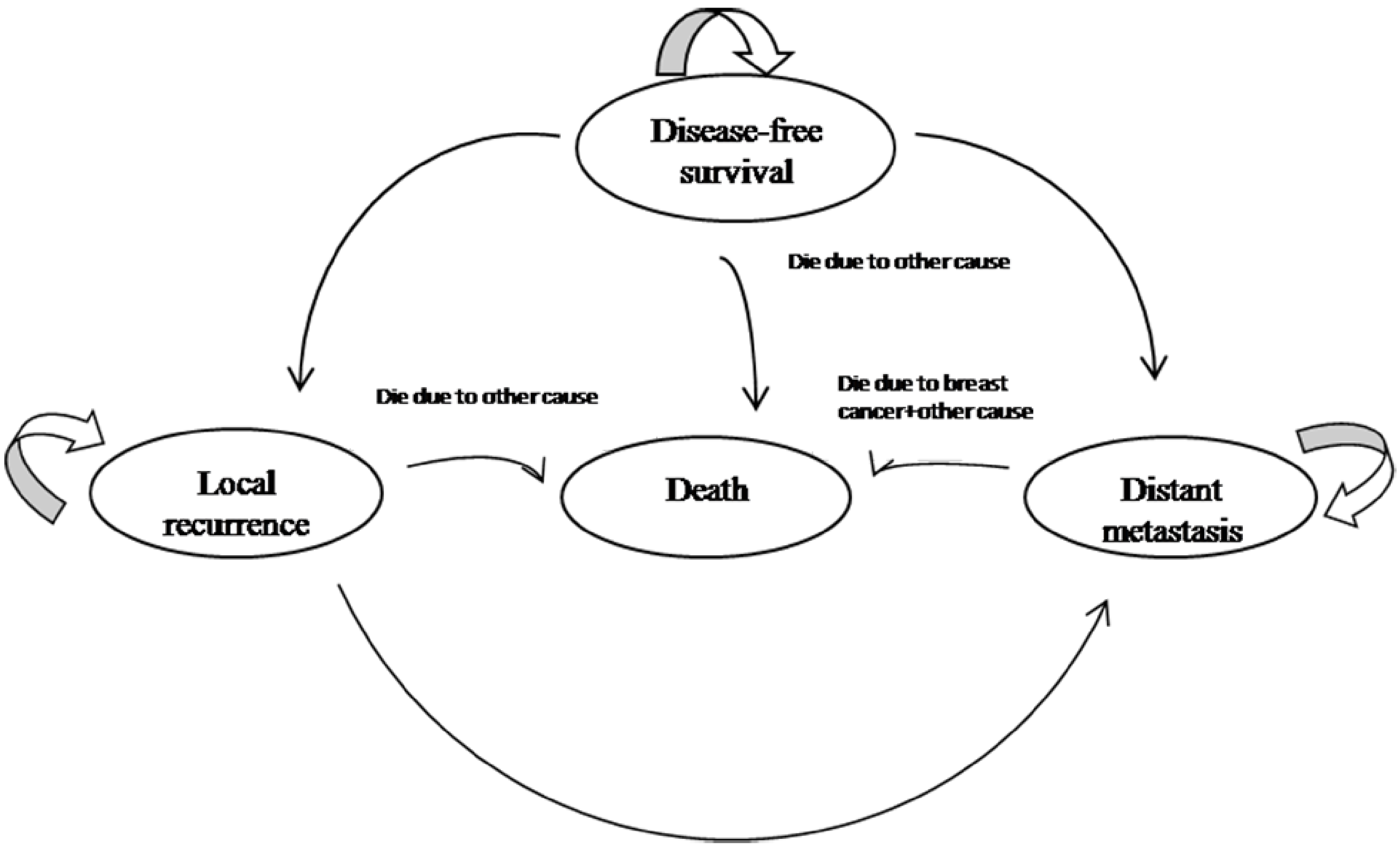

Figure 1

Markov basic model structure

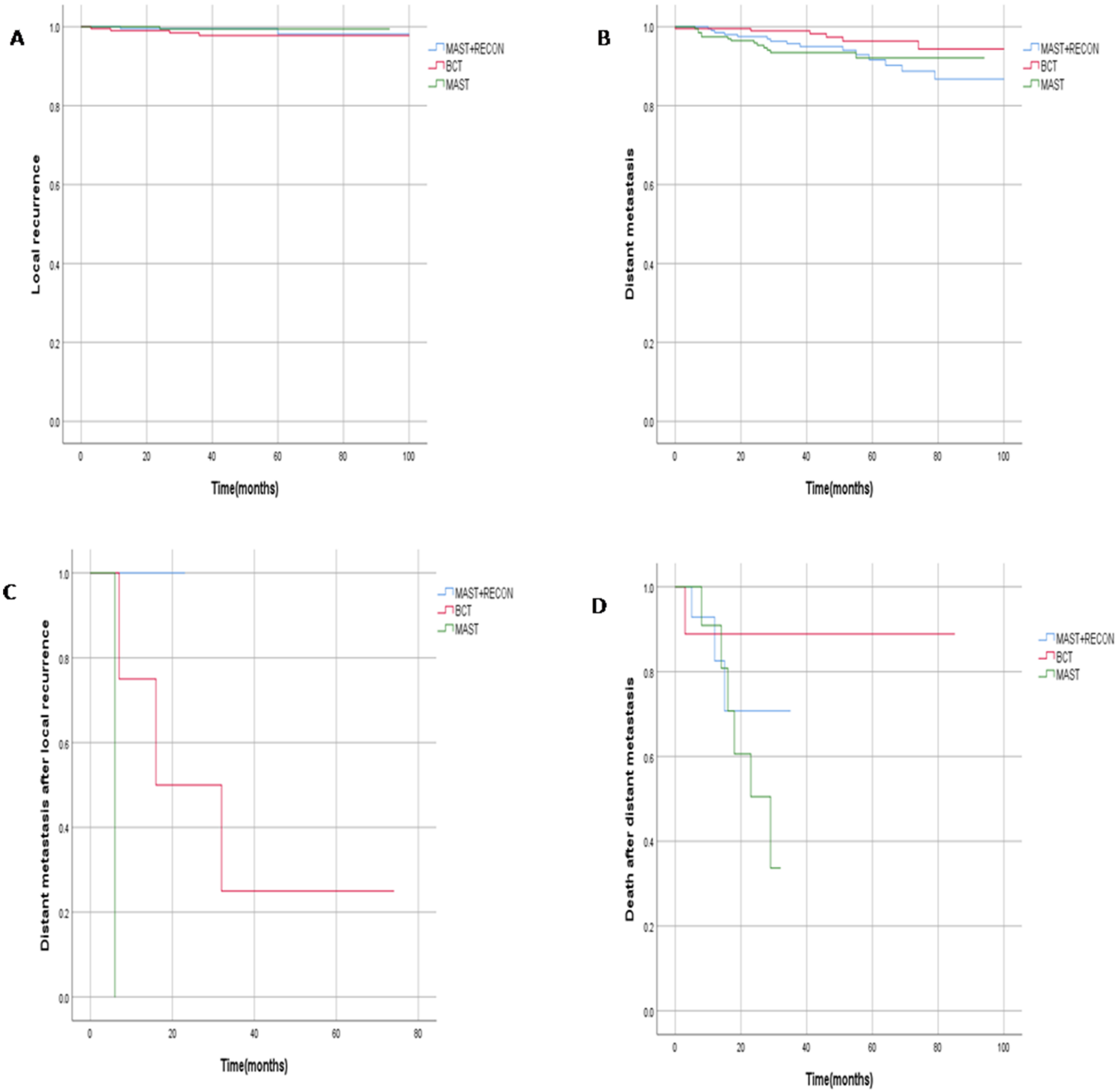

Figure 2

Kaplan-Meier curves. (A) Kaplan-Meier estimates of the local recurrence. (B) Kaplan-Meier estimates of the distant metastasis. (C) Kaplan-Meier estimates of distant metastasis after local recurrence. (D) Kaplan-Meier estimates of death after distant metastasis.

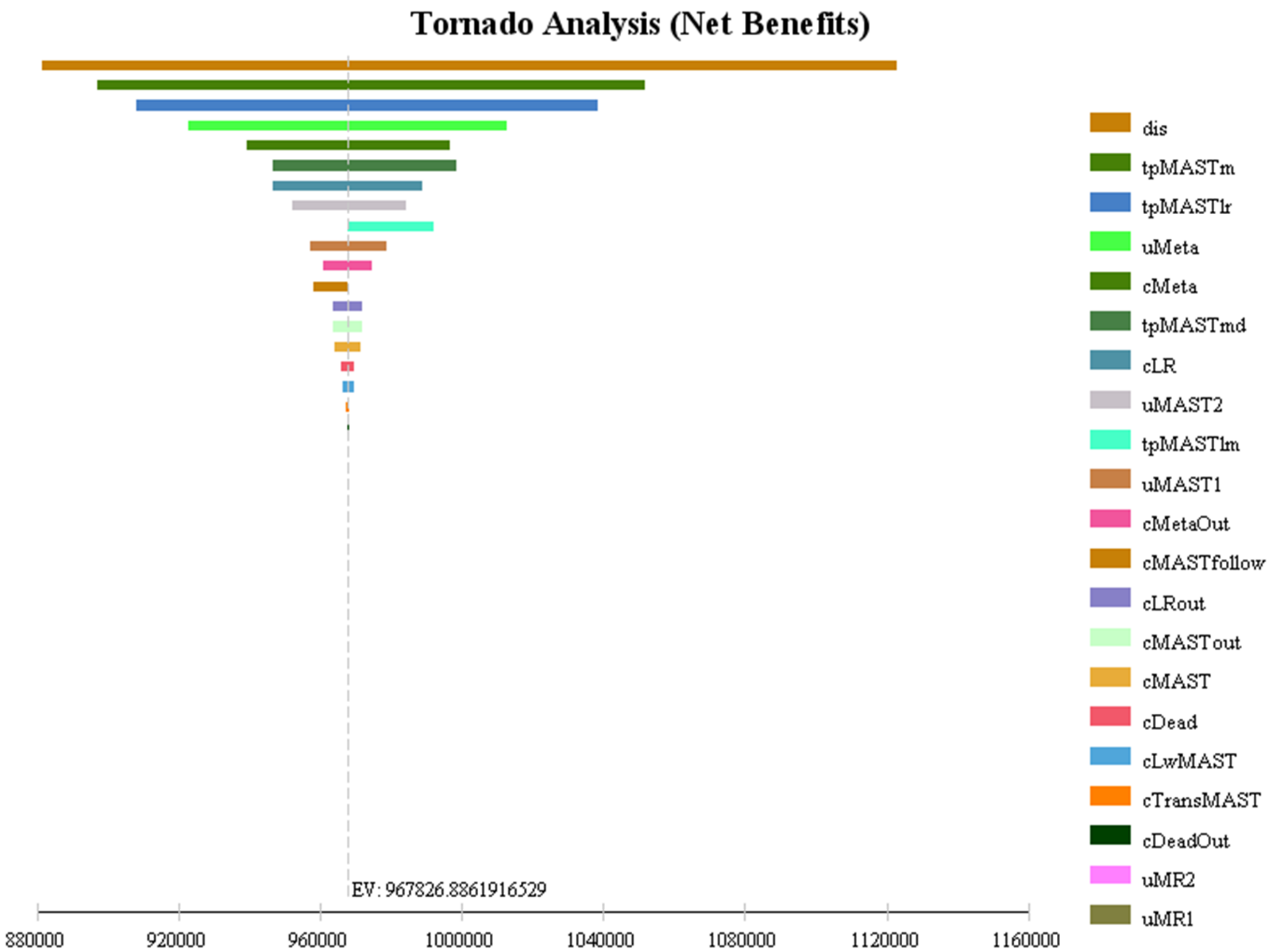

Figure 3

Tornado diagram presenting a one-way sensitivity analysis for BCT compared to MAST. The most influential factors are at the top of the diagram: going from the most influential to the least: tpMASTm, transition probability of distant metastasis of MAST; tpBCm, transition probability of distant metastasis of BCT;uBC2, utility of disease-free for BCT(subsequent year) ; uMAST2, utility of disease-free for MSAT (subsequent year); cBCfollow, annual cost of follow-up for BCT ; cMASTfollow, annual cost of follow-up for MAST ; cBC, cost of BCT hospitalization(first year) ; cMeta, cost of distant metastasis hospitalization per year ; uMeta, utility of distant metastasis ; tpBClr, transition probability of local recurrence of BCT ;dis, discount rate ; uBC1, utility of disease-free for BCT(first year) ; cMetaOut, cost of distant metastasis outpatient per year ;tpMASTlr, transition probability of local recurrence of MAST ; tpBClm, transition probability of distant metastasis after local recurrence of BCT; cMAST,cost of MAST hospitalization(first year) ; tpMASTmd, transition probability of death after distant metastasis of MAST ; cLR, cost of local recurrence hospitalization(first year) ; cLwMAST,cost of losting work of MAST

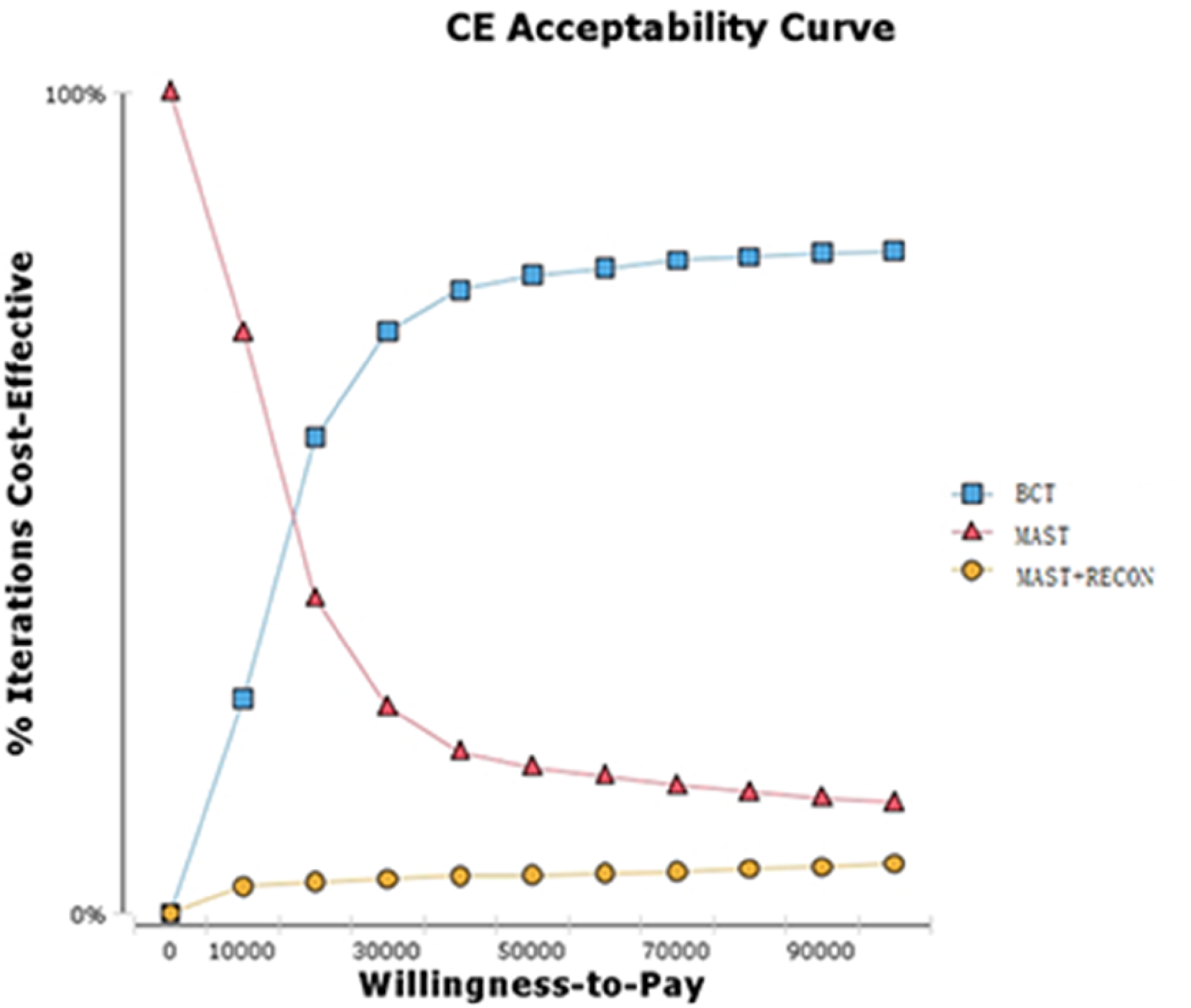

Figure 4

Probability sensitivity analysis acceptance curve

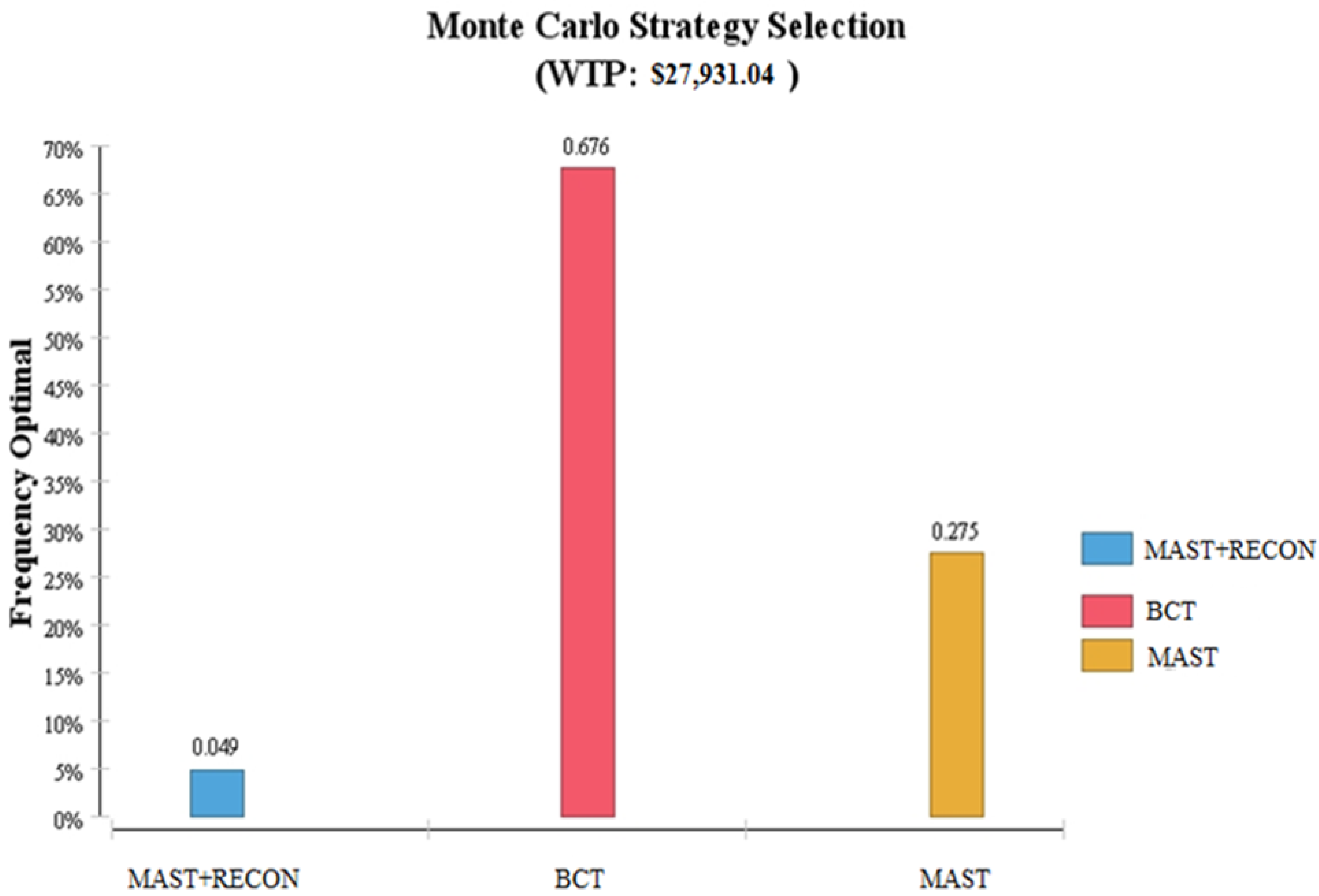

Figure 5

Histogram of probability sensitivity analysis