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Health economics of targeted intraoperative radiotherapy (TARGIT-IORT) for early breast cancer: a cost-effectiveness analysis in the United Kingdom

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ABSTRACT

Objective The clinical effectiveness of targeted intraoperative radiotherapy (TARGIT-IORT) has been confirmed in the randomised TARGIT-A (targeted intraoperative radiotherapy-alone) trial to be similar to a several weeks' course of whole-breast external-beam radiation therapy (EBRT) in patients with early breast cancer. This study aims to determine the cost-effectiveness of TARGIT-IORT to inform policy decisions about its wider implementation.

Setting TARGIT-A randomised clinical trial (ISRCTN34086741) which compared TARGIT with traditional EBRT and found similar breast cancer control, particularly when TARGIT was given simultaneously with lumpectomy.

Methods Cost-utility analysis using decision analytic modelling by a Markov model. A cost-effectiveness Markov model was developed using TreeAge Pro V.2015. The decision analytic model compared two strategies of radiotherapy for breast cancer in a hypothetical cohort of patients with early breast cancer based on the published health state transition probability data from the TARGIT-A trial. Analysis was performed for UK setting and National Health Service (NHS) healthcare payer's perspective using NHS cost data and treatment outcomes were simulated for both strategies for a time horizon of 10 years. Model health state utilities were drawn from the published literature. Future costs and effects were discounted at the rate of 3.5%. To address uncertainty, one-way and probabilistic sensitivity analyses were performed.

Main outcome measures Quality-adjusted life-years (QALYs).

Results In the base case analysis, TARGIT-IORT was a highly cost-effective strategy yielding health gain at a lower cost than its comparator EBRT. Discounted TARGIT-IORT and EBRT costs for the time horizon of 10 years were £12 455 and £13 280, respectively. TARGIT-IORT gained 0.18 incremental QALY as the discounted QALYs gained by TARGIT-IORT were 8.15 and by EBRT were 7.97 showing TARGIT-IORT as a dominant strategy over EBRT. Model outputs were robust to one-way and probabilistic sensitivity analyses.

Conclusions TARGIT-IORT is a dominant strategy over EBRT, being less costly and producing higher QALY gain.

Strengths and limitations of this study

- This economic analysis extrapolated TARGIT-A (targeted intraoperative radiotherapy-alone) randomised trial data over a 10-year time horizon.
- It is the first cost-effectiveness analysis of TARGIT-IORT using the Markov model and 5-year published data.
- Cost associated with radiation treatment toxicity and the higher environmental and social costs of taking a several weeks' course of radiotherapy were not included in this study; inclusion of such costs would further improve the cost-effectiveness of TARGIT-IORT.

Trial registration number ISRCTN34086741; post results

INTRODUCTION

Breast cancer is the most common form of cancer among women in industrialised countries, accounting for about 30% of all female cancers and remains the leading cause of death among women aged 35–55 years.[1 2] The recommended treatment for a large proportion of women with early localised breast cancer consists of a wide excision of the primary tumour. To be effective in controlling the disease, this preferred form of breast-conserving surgery needs to be followed by postoperative radiotherapy, traditionally delivered in the form of whole-breast external-beam radiation therapy (EBRT).[3] EBRT after lumpectomy for breast cancer reduces the risk of local recurrence in the conserved breast. When the reduction in local recurrence is more than 10% at 5 years, there is a demonstrable reduction in mortality at 15 years.[4] However, the disadvantage is that EBRT is traditionally given over 3–6 weeks

as a course of small daily doses of fractionated radiation. Such a prolonged course is inconvenient for the patients and also contributes substantially to a long waiting list. For many women, the journey to the radiotherapy centre is very arduous[5] and many others find it prohibitive and choose a mastectomy instead. Furthermore, if there is a significant delay in treatment, the outcome from breast cancer can be worse.[6] Over the past 20 years, diagnostic and therapeutic medical interventions have evolved into more patient-focused, less invasive techniques. The large international multicentre randomised controlled trial (RCT) of targeted intraoperative radiotherapy-alone (TARGIT-A) that included 3451 patients from 11 countries has confirmed that, in women with early breast cancer, the technique of targeted intraoperative radiotherapy (TARGIT-IORT) is safe and as effective.[7] TARGIT-IORT and EBRT resulted in similar local recurrence-free survival.[8] Furthermore, recent meta-analysis of various partial breast irradiation versus whole-breast irradiation studies demonstrates a better overall survival due to a reduction in non-breast cancer mortality.[9 10]

Provisional recommendations for the use of TARGIT-IORT with INTRABEAM in the UK National Health Service (NHS) were issued by the UK National Institute for Health and Care Excellence (NICE) on 25 July 2014.[11]

TARGIT-IORT during lumpectomy was included as a recommended option for suitable women with early breast cancer in the 2016 Association of Gynecological Oncology (AGO) guidelines; AGO is an autonomous community of the German Society of Gynecology and Obstetrics (DGGG) and the German Cancer Society.[12] The Australian Government Medical Services Advisory Committee recommended TARGIT-IORT for public funding (Medicare Benefits Schedule) after considering the available evidence in relation to safety, clinical effectiveness and cost-effectiveness (CE) in May 2015; it received budgetary approval and eligible patients from Australia could avail of this treatment from 1 September 2015.[13]

TARGIT-IORT is being used worldwide in over 300 centres for the treatment of breast cancer. With over 60 centres each in the USA and Germany, centres in the Middle Eastern countries, Australasia, Far East, South America, all offering TARGIT-IORT, more than 20 000 patients have been treated. Over 1000 patients treated in centres from the USA found excellent results with the use of TARGIT-IORT.[14]

Unlike regular radiotherapy, TARGIT-IORT is a single-dose internal radiation therapy performed during surgery after removal of the tumour. TARGIT-IORT delivers radiotherapy directly into the tumour bed. It is administered at the time of lumpectomy, immediately following cancer removal, during the same anaesthetic, using a radiation device INTRABEAM, which was developed by University College London clinical scientists in collaboration with the industry. The radiation is switched on for 25–30 min and is accurately targeted to the tissues that are at highest risk of local recurrence. The TARGIT-A trial showed how such a single dose of TARGIT-IORT given at the time of surgery could eliminate the need for whole-breast EBRT in over 80% of suitable patients. This would avoid numerous hospital visits and minimise radiation exposure to healthy tissue and organs.

Although it is obvious that the cost of a treatment consisting of a single dose of radiation is likely to be less than a 3–6 weeks' course of radiation, it is only a formal CE analysis that can objectively determine the exact difference in cost.

Therefore, this work aims to determine the CE of TARGIT-IORT in patients with early breast cancer. This is necessary as such health economic evaluation of the TARGIT-IORT using INTRABEAM could inform reimbursement policy decisions and its implementation in usual practice. We assessed the CE of TARGIT-IORT compared with EBRT for the treatment of early breast cancer in the UK.

MATERIALS AND METHODS

Model approach

Modelling is a valuable tool in the systematic and transparent synthesis of evidence to support policy decisions. With a series of numbers and mathematical and statistical relationships, modelling creates a representation of real-world events.[15] To assess the clinical, social and economic benefits of TARGIT-IORT over the current practice of whole-breast irradiation, we constructed a decision analytic model based on outcome probabilities from the published TARGIT-A trial data (prepathology cohort) and costs from the INTRABEAM manufacturer and UK NHS tariffs.[7] Utility values for the model health states were drawn from the published literature.[16] A CE Markov model was developed using TreeAge Pro V.2015 (TreeAge Software, Williamstown, Massachusetts, USA) to capture the costs and outcomes of the two breast cancer radiation therapy options, namely: conventional whole-breast radiation as reference strategy and TARGIT-IORT using INTRABEAM as new innovative strategy. Model outputs were represented in terms of life-years, quality-adjusted life-years (QALYs), cost and CE ratio. The analysis was conducted from the NHS healthcare payer's perspective and to address uncertainty, one-way and probabilistic sensitivity analyses were performed. A discount rate of 3.5% was applied to the future costs and effects as per the NICE pharmacoeconomic guidelines.[17]

Model description

The decision analytic model compared two competing breast cancer radiation strategies in a hypothetical cohort of patients with early breast cancer. Treatment outcomes were simulated for both strategies for a time horizon of 10 years. We used the TARGIT-A trial as an evidence to inform the model structure and incorporated disease progression as various model health states.[7] Currently, these clinical effectiveness data published in the Lancet are the only level 1 randomised evidence available for the

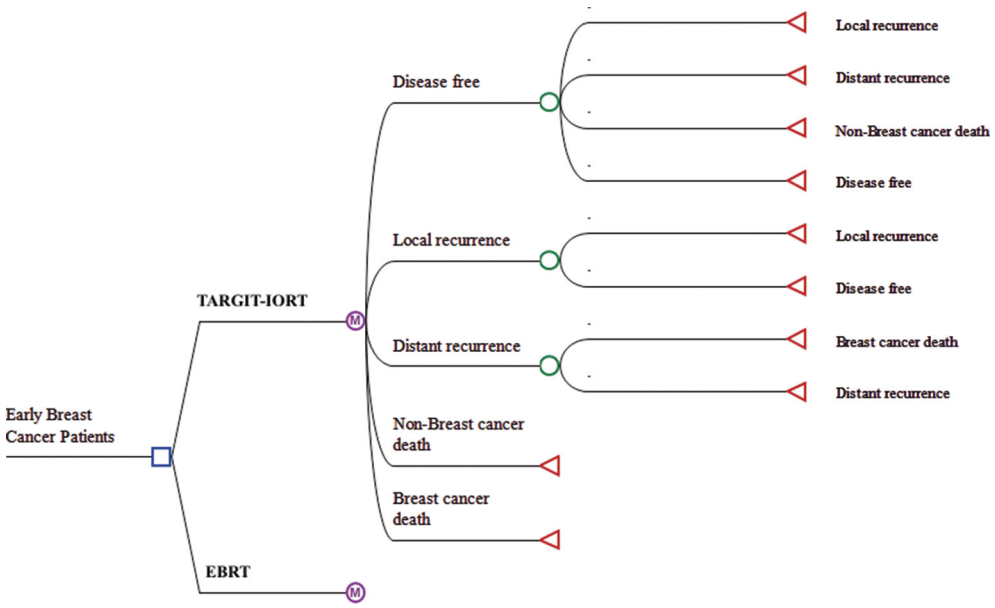

Figure 1 Markov model structure. EBRT, external-beam radiation therapy; TARGIT-IORT, targeted intraoperative radiation therapy.

TARGIT-IORT. The TARGIT-A trial was conducted as a pragmatic risk-adapted design reflecting a real-world situation.[7]

Our model uses five distinct health states: disease free; local recurrence; distant recurrence; death from breast cancer; and non-breast cancer death (figure 1). The TARGIT-A trial defines 'local recurrence' as recurrence in the conserved breast. All patients start the model in the disease-free state and may then either: stay in the disease-free state; have a distant recurrence; have a local recurrence; or die from non-breast-cancer(BC) causes. Patients moving to the distant recurrence health states may remain there or die of breast cancer death. Model cycle length was 1 year.

Model parameters

Transition probabilities

The baseline disease progression parameters used in the model were obtained from the TARGIT-A trial. Since TARGIT-A is the only available trial for TARGIT-IORT effectiveness, all the transition probabilities were calculated using these data. Five-year events rates published in the study were converted to annual rates using MS Excel natural logarithm (ln) function and then to annual probabilities using exponential function.[7]

Costs

The costs included in the model are those for initial radiation treatment by EBRT and TARGIT-IORT along with the costs of being disease free, cost of local and distant recurrences. The cost of TARGIT-IORT was supplied by the manufacturer of INTRABEAM device and was confirmed with experts. Cost of EBRT includes cost to deliver 15 fractions of radiotherapy on a megavoltage machine and the cost of preparation for simple radiotherapy. NICE clinical guideline 80 recommends delivery of 15 fractions of radiotherapy to complete a course of treatment.[18] As per the experts, these costs are £157 per fraction of radiotherapy and £737 for the preparation. Costs of EBRT and cost of disease-free health states were taken from the NHS Reference Costs 2012–2013 using a Health Resource Group (HRG) code. HRG coding is an activity-based payment system of the NHS England and HRG grouping consists of patient events that have been judged to consume a similar level of resource. Costs of recurrences were taken from published literature[19] and were converted to year 2014 costs using Bank of England cost conversion tool.[20] Total costs of recurrences included diagnostic and treatment costs of recurrences (local/distant).

Utility

Utility values for various health states in the model were assigned from the published literature.[19] Authors have reported that a cross-sectional study of 26 representative UK patients with early breast cancer was used to derive utilities for various health states in the model. Utilities for different health states were elicited using standard gamble method that compared the health states to perfect and worse health and then worse health against perfect health and death. The patients in the various health states in the model were assigned these utility weights to estimate the number of QALYs gained. The details of model parameter value point estimates, ranges and their sources are given in table 1.

Model assumptions

a. All patients enter the model in the disease-free state after initial breast cancer surgery and radiation therapy. In this state, patients can die of non-breast cancer causes.

Table 1 Model parameters

Name	Deterministic value	Range		Distribution	Source
		Minimum	Maximum		
Discount rates					
Cost discount rate	0.035			Fixed	Pharmacoeconomic guidelines (NICE)[17]
Outcome discount rate	0.035			Fixed	Pharmacoeconomic guidelines (NICE)[17]
Costs*					
Costs of TARGIT-IORT	2069	1552	2586	Triangular	Carl Zeiss, UK
Costs of EBRT	3092	2319	3865	Triangular	HRG code SC29Z, NHS reference costs 2012–2013[33]
Annual cost of being disease free	1200	900	1200	Triangular	HRG code JA09H, NHS reference costs 2012–2013[33]
Annual cost of local recurrence	4231	3173	5289	Triangular	Mansel *et al*[19]
Annual cost of distant recurrence	5417	4063	6771	Triangular	Mansel *et al*[19]
Probabilities					
Probability of disease free to local recurrence in TARGIT-IORT patients	0.00424	0.00318	0.0053	Triangular	Vaidya *et al*[7]
Probability of disease free to local recurrence in EBRT patients	0.00221	0.00166	0.00276	Triangular	
Probability of disease free to distant recurrence in TARGIT-IORT patients	0.00984	0.00738	0.0123	Triangular	Vaidya *et al*[7]
Probability of disease free to distant recurrence in EBRT patients	0.0096	0.0072	0.012	Triangular	Vaidya *et al*[7]
Probability of disease free to non-breast cancer death in TARGIT-IORT patients	0.003	0.0025	0.00375	Triangular	Vaidya *et al*[7]
Probability of disease free to non-breast cancer death in EBRT patients	0.009	0.00675	0.01125	Triangular	Vaidya *et al*[7]
Probability of breast cancer death in TARGIT-IORT patients	0.00671	0.00503	0.00838	Triangular	Vaidya *et al*[7]
Probability of breast cancer death in EBRT patients	0.0055	0.00412	0.00687	Triangular	Vaidya *et al*[7]
Probability of distant recurrence to breast cancer death in TARGIT-IORT patients	0.682	0.511	0.853	Triangular	Calculated
Probability of distant recurrence to breast cancer death in EBRT patients	0.569	0.426	0.710	Triangular	Calculated
Probability of local recurrence to disease free	1			Fixed	Expert opinion/model assumption
Utilities					
Utility value in disease-free patients	0.989	0.742	1	Triangular	Mansel *et al*[19]
Utility value in local recurrence	0.911	0.683	1	Triangular	Mansel *et al*[19]
Utility value in distant recurrence	0.882	0.661	1	Triangular	Mansel *et al*[19]

*All costs are in 2014 British pound sterling.
EBRT, external-beam radiation therapy; HRG, Health Resource Group; NHS, National Health Service; NICE, National Institute for Health and Care Excellence; TARGIT-IORT, targeted intraoperative radio therapy.

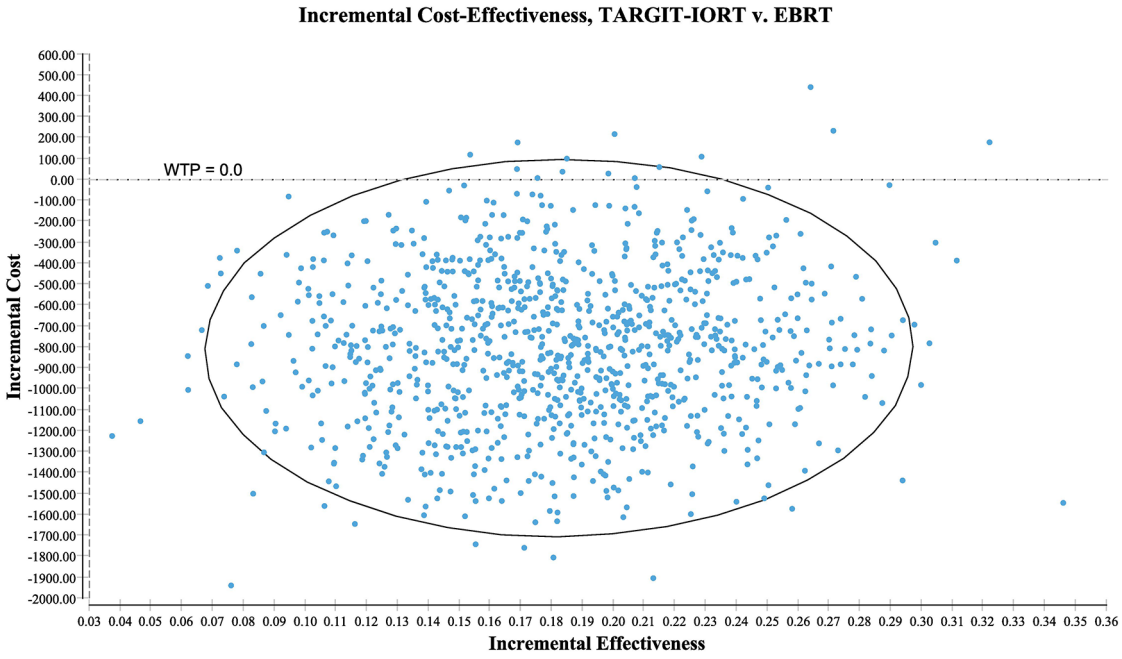

Figure 2 Incremental cost-effectiveness scatterplot. Each of the 1000 dots represents the result of the Monte Carlo simulation of cost-effectiveness of TARGIT-IORT over EBRT. So, if the dot is above the WTP threshold, it means that additional cost is involved in adopting TARGIT-IORT. If it is below the WPT threshold, then there is health gain at lower cost. In this plot, 97.8% of the dots are below the WTP threshold of zero. EBRT, external-beam radiation therapy; TARGIT-IORT, targeted intraoperative radiation therapy; WTP, willingness to pay.

b. It is only possible to die from breast cancer while in the distant recurrence state.
c. All patients from the local recurrence state are back to the disease-free state after treatment of local recurrence.

Model analysis

The model assumes that the patient is always in one of a finite number of states of health referred to as Markov states. The time horizon of the analysis is divided into equal increments of time, referred to as Markov cycles, in this case 1 year. During each cycle, the cohort of patients is redistributed over the Markov states, thus theoretically patients may make a transition from one state to another. Each state is assigned a utility and a cost. Total costs and utility for TARGIT-IORT versus EBRT for the model time horizon were calculated depending upon the distribution of the cohort over the Markov states and the length of time spent in each state. Discounted and undiscounted expected life-years and costs (discount rate 3.5%) for both strategies were calculated. Based on the discounted expected values, the incremental cost-effectiveness ratio (ICER) for TARGIT-IORT was calculated over EBRT.

Model uncertainty

Sensitivity analysis is intended to allow for the examination of the effects of uncertainties on the results of an economic evaluation. In any economic model, various inputs, including outcome probabilities and costs, are required. These typically come from different sources and may be associated with uncertainty. In sensitivity analysis, the values of these inputs are changed (usually between a reasonable maximum and minimum value), and the model is rerun. The extent to which the conclusions that the economic evaluation lead to (eg, one option is more cost-effective than the other) are consistent across a range of sensitivity analyses reflects the robustness of the findings. To address the uncertainty about the clinical effects of treatment, one-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were performed.

In a one-way sensitivity analysis, a single input is varied between a maximum and minimum value (±25%). In PSA, each input parameter into the model is assumed to arise from a probabilistic distribution of values for that input. For the one-way (deterministic) sensitivity analysis, the highest and lowest values of each input parameter were assumed to be 25% above and below the original estimate for that parameter.

For PSA, second-order Monte Carlo simulation was performed to test parameter uncertainty (variability between different samples coming from one population). PSA allows systematic propagation of uncertainty in all model parameters by assigning distributions to parameters and using a Monte Carlo simulation technique. All model parameters derived from the literature or other sources were considered for accuracy, credibility and plausibility at meetings of the expert panel. In some cases, identifying a suitable distribution for estimates and describing the uncertainty around these

Table 2 Cost-effectiveness results

Strategy	Cost	Incremental cost	Effectiveness	Incremental effect	ICER
EBRT	13 280	Reference strategy	7.97	Reference strategy	
TARGIT-IORT	12 455	−825	8.15	0.18	Dominant

EBRT, external-beam radiation therapy; ICER, incremental cost effectiveness ratio; TARGIT-IORT, targeted intraoperative radiation therapy.

values was problematic. Therefore, in such circumstances, uncertainty was calculated as a potential range of plausible values of ±25% of the estimate. It was assumed that the point estimate was the most likely 'real' value and therefore, by using the triangular distribution it was ensured that the upper and lower bounds of variability did not exceed clinical plausibility. This distribution emphasises the 'most likely' value over the minimum and maximum estimates. A triangular distribution is a continuous probability distribution with a probability density function shaped like a triangle. It is defined by three values: the minimum value, the maximum value and the real (peak) value. The triangular distribution has a definite upper and lower limit to avoid extreme values.

Results of 1000 Monte Carlo simulations were graphically displayed in the form of CE planes showing the uncertainty surrounding the CE of TARGIT-IORT and its subsequent probability of being cost-effective at different values of willingness to pay (WTP) thresholds was shown as Monte Carlo CE acceptability chart.

RESULTS

Base case results

In the base case analysis, TARGIT-IORT was a highly cost-effective strategy yielding health gain at a lower cost than its comparator EBRT. The difference in the cost of delivery of TARGIT-IORT versus EBRT was £1023, favouring TARGIT-IORT. Discounted TARGIT-IORT and EBRT costs for the time horizon of 10 years were £12 455 and £13 280, respectively. TARGIT-IORT gained 0.18 incremental QALY as the discounted QALYs gained by TARGIT-IORT were 8.15 and by EBRT were 7.97. TARGIT-IORT dominated EBRT as it provides an additional QALY at a lower cost than EBRT (table 2).

Results of sensitivity analyses

One-way sensitivity analyses revealed that the model was robust to all one-way sensitivity analyses and TARGIT-IORT remains a dominant strategy over EBRT in all parameter variations. Probabilistic sensitivity analyses were conducted to estimate the effect of overall uncertainty in the economic evaluation through repeated

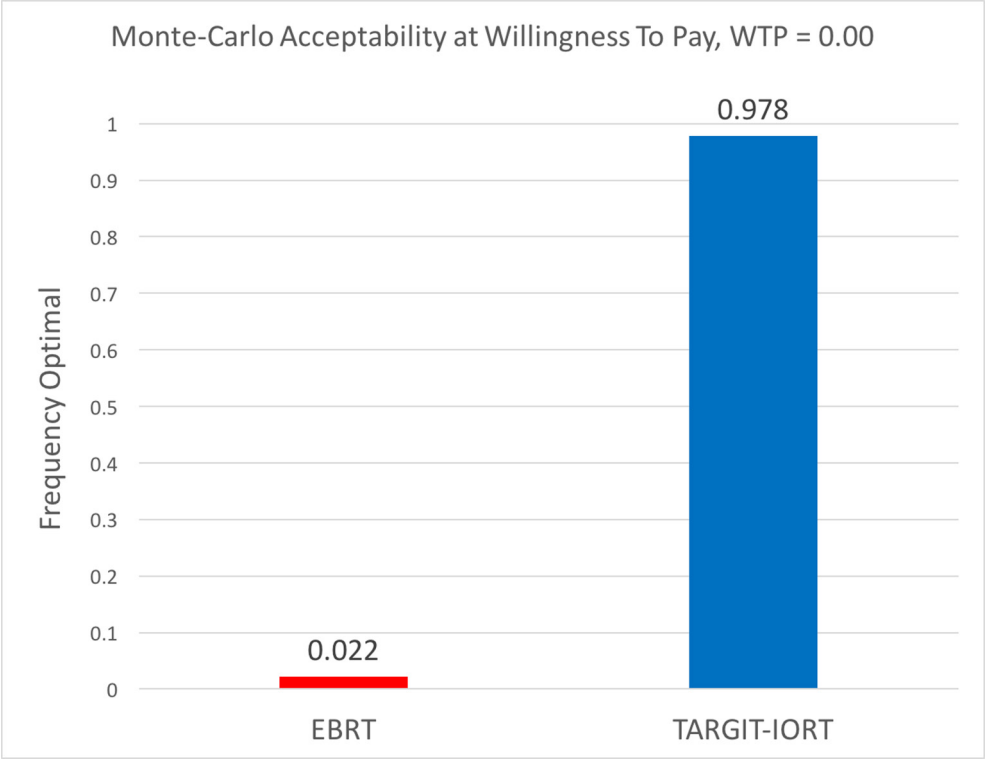

Figure 3 Monte Carlo acceptability. These bar charts show the number of ICER simulation results as seen in figure 2, above and below the WTP threshold of zero. It shows that there is a 97.8% probability of TARGIT-IORT being cost effective at the WTP threshold of zero; the corresponding probability for EBRT being cost-effective is 2.2%. EBRT, external-beam radiation therapy; TARGIT-IORT, targeted intraoperative radiation therapy; WTP, willingness to pay.

sampling of mean parameter values from a series of assigned distribution. In the PSA, the results were robust over a range of plausible estimates of model parameters. PSA results are presented as means of 1000 probabilistic model outputs and were found to be similar to the deterministic results. Based on probabilistic model runs, net monetary benefit framework was applied to draw the 'incremental cost-effectiveness' plane (figure 2) which shows that TARGIT-IORT is cost saving in 97.8% iterations (figure 3). The CE acceptability chart shows that TARGIT-IORT is cost-effective at zero thresholds of WTP.

DISCUSSION

We used published data from the TARGIT-A trial to investigate the CE of TARGIT-IORT in patients with early breast cancer. The findings suggest that in comparison to the EBRT which involves delivering whole-breast radiations in multiple sessions, individuals treated with TARGIT-IORT, during the surgery performed to remove the breast cancer, had higher mean health gain (QALYs) at a lower mean cost. The model outputs indicate definite cost savings by the use of TARGIT-IORT within a risk-adapted strategy rather than using EBRT in call cases. The model runs for 10 years which is very conservative as most events related to breast cancer occur in the first 5 years.[21] These findings, based on extrapolation of the relevant outcomes obtained from the analysis of complete trial data, were generally found to be robust to uncertainty surrounding various model parameter inputs and assumptions. Based on probabilistic analysis, TARGIT-IORT had a 98% chance of being cost-effective at zero WTP. The one-way sensitivity analysis demonstrates that our estimates of the ICERs were reasonably robust to a 25% change in the base case input values.

The finding that TARGIT-IORT has the highest chance of being the most cost-effective option is driven by a number of factors: (1) its greater estimated QALY and utility gains due to fewer non-breast-cancer deaths in the TARGIT-IORT cohort; (2) its lower cost compared with EBRT; (3) its non-inferiority to EBRT in terms of cancer recurrence; and (4) the high likelihood of its being superior to EBRT in terms of non-breast-cancer mortality. The latter is supported by a recently published meta-analysis of partial breast irradiation versus whole-breast irradiation[10] and a published correspondence[9] which include the data from the earliest cohort in the TARGIT-A trial, which have a median follow-up of 5 years.

This study provides evidence that TARGIT-IORT is an economically attractive intervention in the carefully selected eligible patients of early breast cancer. Our research has been conducted using recognised economic modelling techniques and followed comprehensive International Society for Pharmacoeconomics and Outcomes Research - Society for Medical Decision Making (ISPOR-SMDM) task force guidelines on modelling good research practices.[22] We undertook a wide range of sensitivity analyses and confirmed the robustness of our findings.

In our model, costs associated with management of acute and long-term radiotoxicity were not included because of similar overall toxicity rates in the two treatments (seroma needing aspiration was more common with TARGIT-IORT 2.1% vs 0.8%, while grade 3 or grade 4 radiation toxicity was more common with EBRT 0.5% vs 2%). The low level of radiotoxicity (<3%) is unlikely to make a significant cost difference.

The environmental and social costs[5] as well as travel costs have not been included into the model. These are usually borne by the patient, but in many health systems they are borne by the health system. In any case, these costs including management of toxicity costs will further add to the CE of TARGIT-IORT.

We would like to believe that the results of this CE analysis may be generalisable in many statutory healthcare systems. Our belief regarding the generalisability of results to other similar healthcare systems is based on the fact that EBRT has relatively high costs than TARGIT-IORT across the healthcare jurisdictions. TARGIT-IORT costs will remain lower than EBRT in most healthcare settings because of many factors even if tariffs are different; EBRT has a high and recurring investment for the linear accelerators and bunkers, associated with need of maintenance and personnel attendance; it is labour intensive, which is deemed to translate into high personnel costs. Moreover, EBRT is delivered in multiple fractions and patient transportation and accommodation costs can be additionally taken into account. Higher EBRT tariffs from other healthcare settings and inclusion of cost of EBRT bunker in this analysis will make ICER more favourable to TARGIT-IORT.

Complex medical practice is difficult to transform into a decision model. This study shares the general limitations of economic modelling along with several other limitations. Due to data limitations, this analysis used a cohort-based model ignoring heterogeneity. The time horizon of the CE analysis was not lifetime but 10 years. Extrapolation beyond 10 years was not undertaken because of the relatively shorter follow-up period of effectiveness trial. The analysis was done from payer's perspective. A societal perspective could measure costs, including impacts on the rest of society, patients and families. One weakness of the study is that the clinical effectiveness data used to inform disease progression in the model are drawn from a single albeit large randomised study . Another important limitation was regarding the health state utility weights used in the economic model. Although these utilities were taken from UK studies using the EQ-5D and valued using the UK general population tariff, a small sample size challenges the validity of these utility weights.

Our CE model results are in line with the previously published studies from Esserman *et al*,[23] Alvarado *et al*,[24] Picot *et al*,[25] Shah *et al*[26] and Vaidya *et al*,[27] which came to the same conclusion that TARGIT-IORT is more cost-effective than standard EBRT. Newer EBRT techniques such as Intensity Modulated Radiotherapy (IMRT) with higher equipment and human resource costs the difference

between TARGIT-IORT tariffs and EBRT tariffs, even if used for partial breast irradiation, would have been even higher.

In our CE model, TARGIT-IORT dominates EBRT. Flipping it on its head, if TARGIT-IORT were the standard strategy, there would be no health-economic justification for adopting whole breast-EBRT. If no radiation at all is implemented for very low-risk patients then no radiation dominates TARGIT-IORT, at the cost of higher local recurrence rate that may not be acceptable to clinicians and patients. The recurrence rate with no radiotherapy even in the best prognosis and older patients is up to 1 in 17. With TARGIT-IORT with just one selection criterion (oestrogen receptor positive) this is very low (1 in 71).

Preferences elicited from health professionals working with patients with breast cancer accepted TARGIT-IORT as an alternative treatment option to EBRT for early breast cancer.[28] In this era where decisions are shared by doctors and patients, informed by the best evidence available, reflect patients' own values and preferences and involve them more directly, TARGIT-IORT has been shown to be the preferred choice compared with EBRT by the patients as well as the doctors.[29-32]

Contributors AV and PV were involved in conception and design, analysis and interpretation of the data, drafting and revision of the manuscript and its final approval. CBG, BB and MB were involved with the concept, health economic input into the analysis, interpretation of results, writing of the manuscript and approving the final version. JSV was involved with the concept, clinical input into the analysis, interpretation of results, writing of the manuscript and approving the final version. JSV is not related to AV or PV and did not know them before this particular project.

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Competing interests None declared.

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Data sharing statement No additional data available.

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