Cost-effectiveness Analysis of the Oncotype DX® Test to Reduce Under-Treatment in Patients with HR+/HER2- Node Negative Early-Stage Breast Cancer and Grade 2 T1c Tumours

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Background

- The Oncotype DX Breast Recurrence Score® test is used in addition to risk classification tools, such as the Nottingham Prognostic Index (NPI) and PREDICT, to guide adjuvant treatment decisions in hormone positive (HR+) and human epidermal growth factor receptor 2 negative (HER2-) early-stage breast cancer.
- The TAILORx trial (1) has shown that the Oncotype DX test can identify patients with node-negative early-stage breast cancer Recurrence Score® (RS) results 0-25 who can safely be spared chemotherapy, whereas patients with RS result >25 experience a meaningful reduction in distant recurrence when treated with adjuvant chemotherapy (2,3).
- The Oncotype DX test has been shown to be cost-effective compared to using clinicopathologic risk alone to guide adjuvant chemotherapy treatment for patients with node-negative tumours and intermediate risk of recurrence (defined as NPI>3.4) (4,5).
- Recent audit data suggests that 17% of patients with grade 2 T1c (G2 T1c) node negative tumours, categorised as low-risk using NPI and PREDICT and thus allocated endocrine therapy alone in current practice, are likely to benefit from adjuvant chemotherapy.
- An existing cost-effectiveness model was adapted to estimate the cost-effectiveness of the Oncotype DX test in comparison to using clinicopathologic factors alone to guide chemotherapy decisions in this subgroup.

Study Objectives

- Adapt an existing cost-effectiveness model for the Oncotype DX test using clinical inputs for chemotherapy allocation and probability of distant recurrence for the G2 T1c subgroup.
- Estimate the cost-effectiveness of the Oncotype DX test compared to using clinicopathologic risk alone in the G2 T1c subgroup with respect to the NICE threshold for cost-effectiveness of £20,000 per quality-adjusted life-year (QALY) over a lifetime horizon.

Methods

- A previously developed Markov model (Figure 1) with four health states (distant recurrence-free, distant recurrence, AML (acute myeloid leukemia), and death) was adapted with distant recurrence-free interval data obtained from the RSClin tool, which integrates data from TAILORx, NSABP-14 and NSABP-20 studies (6).
- Chemotherapy allocation conditional on RS result category was obtained from the Clalit registry (7) and the UK National Registration and Analysis Service (NCRAS) for decisions based on clinicopathologic risk alone as reported in the NICE appraisal for tumour profiling in early-stage breast cancer (4).
  It was assumed that all patients with RS>25 would be allocated to chemotherapy, which was tested in scenario analyses.
- Total costs were estimated in 2020 GBP from an NHS and personal social services perspective in the UK in line with the reference case set by NICE (8).
- The results of the analysis were presented in terms of incremental cost-effectiveness ratio (ICER) per QALY gained.
- Univariate sensitivity analyses were presented using a Tornado diagram and a probabilistic sensitivity analysis (PSA) was presented using a scatter diagram and a cost-effectiveness acceptability curve (CEAC). Scenario analyses were conducted to test key assumptions for chemotherapy allocation and chemotherapy benefit.
- The full methods for the model and inputs have been described elsewhere (5).

Figure 1. *Structure of the Markov model*

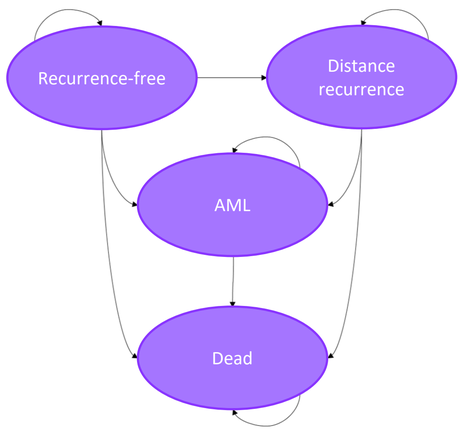
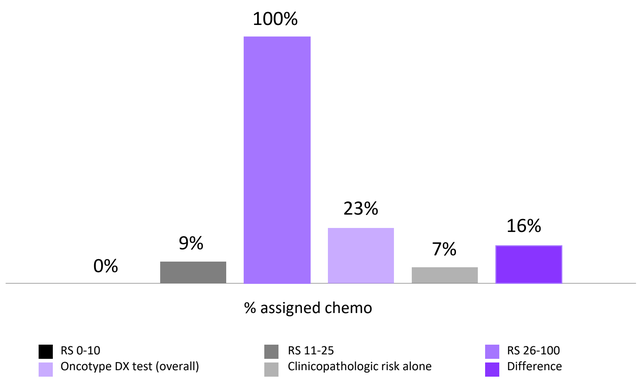


Figure 2. *Chemotherapy allocation with and without the Oncotype DX test*



Results

- Compared to using clinicopathologic risk factors alone, the Oncotype DX test was more effective (0.09 additional QALYs) and more costly (£1,894), with an ICER of £20,767.
- The cost of the Oncotype DX test and the additional cost of chemotherapy was partly offset by the reduced lifetime cost of local and distant recurrence.
- The univariate sensitivity analysis demonstrated that the model results were most sensitive to distant recurrence probabilities for the RS>25 group, followed by discount rates applied to costs and outcomes (Figure 3).
- A probabilistic analysis with 5,000 runs demonstrated substantial parametric uncertainty in the model. The probability of cost-effectiveness of the Oncotype DX test at the NICE ceiling threshold of £20k/QALY was 47.3% and 68.5% at a willingness-to-pay (WTP) thresholds of £20,000 and £30,000, respectively (Figures 4 and 5).
- The model results did not change substantially with more conservative inputs for the proportion of high-risk patients in the subgroup, and chemotherapy allocation with and without the Oncotype DX test. Varying the chemotherapy benefit in RS>25 according to the confidence intervals from RSClin had a large impact on the results (Table 2).

Disclosure statement

This study was funded by Exact Sciences. Vladislav Berdunov (first and presenting author) has no further conflicts of interest to declare

Table 1. *Summary cost-effectiveness analysis results*

Endpoint	Oncotype DX test	Clinicopathologic risk alone	Difference
Total cost	£16,015	£14,122	£1,894
The Oncotype DX test	£2,580	£0	£2,580
Chemotherapy & endocrine therapy	£1,618	£702	£916
Short-term adverse events	£241	£75	£166
Disease management w/o recurrence	£1,340	£1,337	£3
Local recurrence	£159	£194	-£35
Distant recurrence	£8,049	£9,840	-£1,791
AML	£109	£34	£75
Terminal care	£1,918	£1,939	-£21
Total QALYs	13.11	13.02	0.09
Total life-years	16.92	16.81	0.12
ICER per QALY			£20,767
Probability of cost-effectiveness (£20k/QALY)			47.3%
Probability of cost-effectiveness (£30k/QALY)			68.5%

Figure 3. *Tornado diagram representing the top 10 parameters which contributed to model uncertainty*

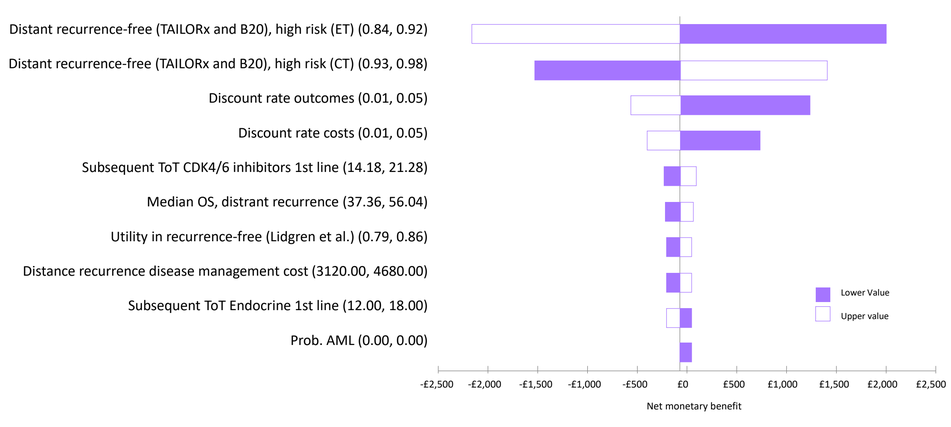


Figure 4. *Scatter diagram for the PSA*

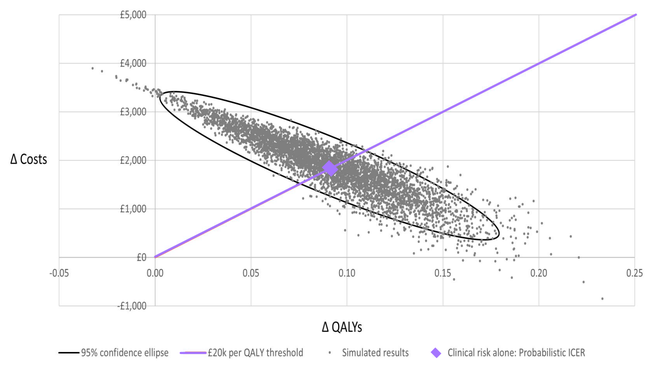


Figure 5. *CEAC for the PSA*

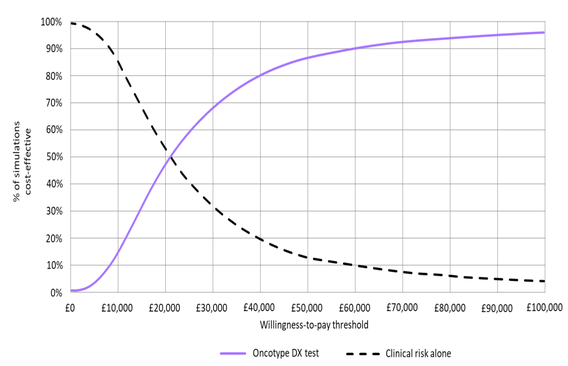


Table 2. *Scenario analysis results*

Scenario	Δ Cost	Δ QALYs	ICER per QALY
Base case	£1,894	0.09	£20,767
High RS % 14% (TAILORx overall population)	£2,011	0.08	£26,679
Chemotherapy allocation with RS>25 set to 89% (NHS England data)	£1,973	0.08	£24,498
Chemotherapy allocation w/o Oncotype DX set to equal to NPI>3.4 (40%, NCRAS)	£353	0.08	£4,325
Absolute chemotherapy benefit in RS>25 reduced from 7.4% to 4.7% (RSClin)	£2,559	0.05	£49,773
Absolute chemotherapy benefit in RS>25 increased from 7.4% to 10.1% (RSClin)	£1,216	0.13	£9,263

Conclusions

- The Oncotype DX test has a potential to be a cost-effective addition to current practice to inform adjuvant treatment decisions for patients with HR+/HER2- early-stage breast cancer and node negative G2 T1c tumours.
- Reducing under-treatment for 17% of patients with high RS increases quality and length of life and reduces the need for costly treatments for metastatic breast cancer.
- The model results were robust to conservative assumptions for chemotherapy allocation, but the estimate of chemotherapy benefit in the RS>25 group remains a significant source of uncertainty and should be the subject of future research.
- Future studies should examine the impact of the RxPONDER findings on chemotherapy treatment decision-making in this subgroup.

References

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CEAC = cost-effectiveness acceptability curve; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; ICER = incremental cost-effectiveness ratio; NICE = National Institute of Health and Care Excellence; NCRAS = National Cancer Registration and Analysis Service; NPI = Nottingham Prognostic Index; PSA = probabilistic sensitivity analysis; QALY = quality-adjusted life-year; RS = Recurrence Score.

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