Cancer Care Coordinators to Improve Persistence with Tamoxifen in Breast Cancer

evaluating its cost-effectiveness in early breast cancer

SUMMARY

For women with estrogen receptor positive (ER+) breast cancer, five years of oral hormone therapy such as tamoxifen is recommended. Highly effective hormone therapy is partly responsible for the marked reduction in breast cancer mortality seen over the last decade. However, the long treatment duration and the potential for side-effects mean early discontinuation is common: in one large UK study, up to 30% of women discontinued tamoxifen before 5 years. We evaluated the cost-effectiveness of a cancer care coordinator (CCC) directed at helping premenopausal women with ER+ early breast cancer persist with tamoxifen for 5 years, compared with no CCC. We specifically investigated the cost-effectiveness of a CCC across eight different breast cancer subtypes, representing relatively good to relatively poor prognoses.

We evaluated CCCs in improving tamoxifen persistence in breast cancer

The CCC here is a clinical nurse specialist who provides information on tamoxifen, checks in with the women regularly by phone, and addresses any barriers to persistence. The target population is premenopausal women with ER+ breast cancer, who are prescribed oral tamoxifen for five years. They are further divided into eight different breast cancer subtypes, defined by progesterone receptor (PR) status, human epidermal growth factor receptor 2 (HER2) status, and local/regional tumor spread. Local ER+/PR+/HER2- subtype has the best prognosis, regional ER+/PR-/HER2+ has the worst prognosis, and the other six subtypes fall in between these two extremes.

We used a macrosimulation model to estimate cost-effectiveness using NZ data

For each subtype, the model estimates how much health benefit is gained (in quality-adjusted life years or QALYs) from the CCC, and how much it costs or saves the health system. These are combined into an Incremental Cost-Effectiveness Ratio or ICER.

Is it cost-effective?

The cost-effectiveness of a CCC for regional ER+/PR-/HER2+ breast cancer (worst prognosis) was NZ$ 23,400 per QALY gained, compared to NZ$ 368,500 for local ER+/PR+/HER2- breast cancer (best prognosis). If we used a cost-effectiveness threshold of NZ$ 45,000 per QALY (i.e. we assume the government is happy to pay NZ$ 45,000 for 1 QALY), then a CCC would only be cost-effective in the four subtypes with the worst prognosis.

Our bottom line

In this evaluation of a CCC to improve tamoxifen persistence in early breast cancer, the poorer the prognosis, the greater the health gains from a CCC and the better the cost-effectiveness. This analysis demonstrates the value of investigating cost-effectiveness by different subtypes within a disease, potentially allowing more targeted allocation of limited health resources.

IN MORE DETAIL

A Cancer Care Coordinator (CCC) to Improve Tamoxifen Persistence in Breast Cancer

In women with estrogen receptor positive (ER+) breast cancer, at least five years of hormonal therapy (such as tamoxifen for premenopausal women) is strongly recommended. However, the long duration of treatment, the potential for side-effects, and the fact that tamoxifen is taken orally and as an outpatient mean that early discontinuation is common. In one large UK-based study, about 30% of women on tamoxifen had discontinued their treatment within the first five years. The need for interventions to improve persistence with hormonal therapy is well-described. In our model, this intervention is a cancer care coordinator (CCC), a hospital-based clinical nurse specialist who helps women persist with tamoxifen.

The CCC:

- provides a 30-minute face-to-face information session at the first specialist appointment when tamoxifen is prescribed
- checks in with the woman by phone regularly (a 15-minute phone call every three months in the first year, then every six months for the remaining four years), asking about tamoxifen persistence and identifying/addressing any barriers
- is also available for women to contact as needed

We compared the CCC to no CCC.

Model

We began with a NZ population of women under 50 years (assumed to be premenopausal) with ER+ invasive early breast cancer, assuming they were all prescribed tamoxifen for five years and did not switch to other hormonal therapies. We used a Markov model to follow this population through to death or 110 years. The model 'allowed' for women to persist with tamoxifen, discontinue tamoxifen, die of breast cancer, die of other causes, and develop two rare side-effects of tamoxifen: venous thromboembolism (clots in the legs or lungs), and endometrial cancer. The model estimated:

- Health gain in quality-adjusted life years or QALYs
- Health system costs in NZ$
- Cost-effectiveness in Incremental Cost-Effective Ratios (compared to no CCC)

This was done for each of the eight subtypes:

- Local ER+/PR+/HER2- (best prognosis, 5-year relative survival of 99%)
- Local ER+/PR-/HER2-
- Local ER+/PR+/HER2+
- Local ER+/PR-/HER2+
- Regional ER+/PR+/HER2-
- Regional ER+/PR-/HER2-
- Regional ER+/PR+/HER2+
- Regional ER+/PR-/HER2+ (worst prognosis, 5-year relative survival of 79%)

Prognosis here refers to *baseline* prognosis (i.e. prognosis before any tamoxifen has been taken).

QALY or Quality-Adjusted Life Year:

The remaining life expectancy, adjusted for quality of life. Think of one QALY as one year of life in perfect health.

ICER or Incremental Cost-Effectiveness Ratio:

The difference in costs between one intervention and its comparator, divided by the difference in health gain. An ICER tells you how much more (or less) cost-effective an intervention is compared to something else.

Assumptions in the Model

Our model contains multiple assumptions. Some of these assumptions apply across all BODE^3 evaluations, and are described in a range of protocols at the BODE^3 website here. Some assumptions are specific to this topic: please email tony.blakely@otago.ac.nz for more information.

Some of our key assumptions include the following:

- We used a health system perspective and so did not include costs and consequences beyond the health system (such as productivity costs).
- We allowed for expected or background disease and limited the maximum amount of QALYs that could be gained with increasing age.
- We applied a 3% discount rate to costs and QALYs gained.
- There was no direct published evidence for how much a CCC could potentially reduce tamoxifen discontinuation. We estimated that a CCC would reduce the annual tamoxifen discontinuation rate by a third (based on a meta-analysis of nurse-led interventions to improve adherence to chronic medications). Given the lack of direct evidence, we allowed for generous uncertainty in the model, allowing this amount to be as low as 8% and as high as 65%.
- We assumed the benefit of tamoxifen on breast cancer mortality lasted for 10-15 years after it was stopped.

QALYs, Costs & Cost-Effectiveness

QALYs

The QALYs each patient gains ranges from 0.0002 QALYs for the best-prognosis subtype (local ER+/PR+/HER2-), rising to 0.06 QALYs for the worst-prognosis subtype (regional ER+/PR-/HER2+). This can be thought of as 0.07 to 21 extra days of life in perfect health.

Costs

The mean incremental health system costs also rise from NZ$ 365 for the best-prognosis subtype to NZ$ 1,370 for the worst-prognosis subtype.

Cost-Effectiveness

The cost-effectiveness is poorest for the best-prognosis subtype (ICER of NZ$ 368, 521 per QALY), and best for the worst-prognosis subtype (ICER of NZ$ 23,442 per QALY). The other subtypes lie predictably between these two extremes.

A Note on Cost-Effectiveness Thresholds and Willingness-To-Pay

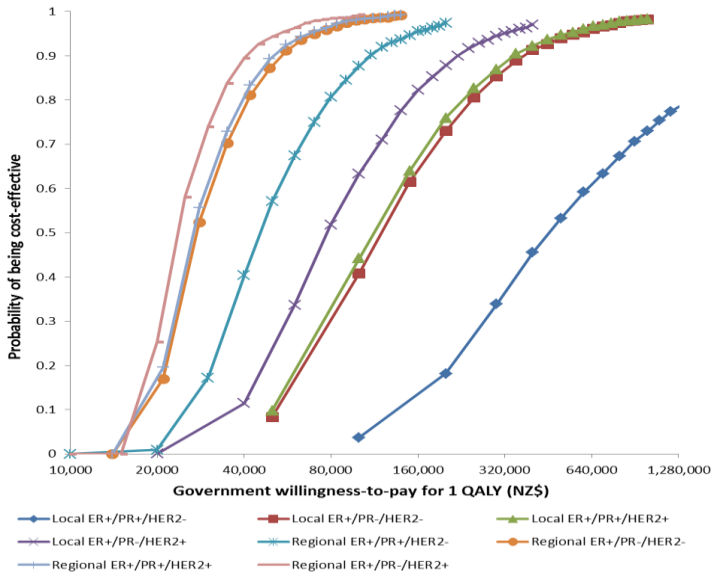
There is no consensus on a cost-effectiveness threshold in NZ. Our statements on cost-effectiveness stem from World Health Organization guidance, which is based on Gross Domestic Product (GDP) per capita. In NZ, GDP per capita is approximately NZ$ 45,000. If the ICER for an intervention is less than NZ$ 45,000 per QALY, we deem it cost-effective. However, you can use your own threshold or other yardsticks of cost-effectiveness. It should also be noted that policy decisions are made on multiple considerations, and cost-effectiveness is only one of these.

Cost-effectiveness Threshold or Willingness-To-Pay:

Society's willingness to pay for an extra unit of health gain e.g. a QALY. If the ICER for an intervention is less than the threshold, the government can view it as cost-effective and may fund it. If ICER is greater than the threshold, it is not deemed to be cost-effective and the government may not fund it.

Cost-Effectiveness Acceptability Curve

There is always uncertainty around the estimates of cost-effectiveness. There is also variation in how much the Government is willing to pay to gain 1 QALY. The graph below is a cost-effectiveness acceptability curve which takes both these factors into account. The x axis shows different levels of willingness-to-pay for 1 QALY. The y axis shows the probability of a CCC to improve tamoxifen persistence in early breast cancer being cost-effective compared to no CCC. Each coloured curve is a different subtype, from the worst prognosis subtype to best prognosis subtype as you move from left to right.



We assume here that at least a 70% probability of being cost-effective is acceptable to policy-makers. If the Government is willing to pay only NZ$ 20,000 per QALY, a CCC would not be cost-effective for any subtype of breast cancer. If the Government is willing to pay NZ$ 80,000 per QALY, a CCC would be cost-effective (≥ 70% probability) for the four subtypes with the worst prognosis. Only at NZ$ 160,000 per QALY would a CCC be cost-effective (≥ 70% probability) for most breast cancer subtypes (seven out of eight).

Costs, QALYs & Cost-Effectiveness in Different Populations

Ethnicity	A CCC was more cost-effective for Māori than for non-Māori for the four breast cancer subtypes with the best prognosis, and similarly cost-effective for the other subtypes.
Deprivation	Similar cost-effectiveness for most deprived patients as compared to least deprived.

Equity Analysis

Māori have higher background disease and death compared to non-Māori. Māori are thus automatically disadvantaged in economic evaluations because Māori have a limited envelope of QALYs that can be gained. We conducted an 'equity analysis' to adjust for this, applying non-Māori rates of background disease and death to Māori instead of using Māori rates. Cost-effectiveness for Māori improved even further, becoming more cost-effective than for non-Māori across essentially all subtypes.

Uncertainty in our Results

There is unavoidable uncertainty present in the values we put into our models, and thus uncertainty in estimates of costs, health gains, and cost-effectiveness. The most uncertainty came from the effect of the CCC in reducing annual tamoxifen discontinuation rates, the cost of the CCC per year, and the effect of tamoxifen in reducing breast cancer mortality.

Changing Some Assumptions

The results of the evaluation are sensitive to different assumptions. For example:

What if we exclude future health system costs unrelated to breast cancer?	The cost-effectiveness improves for all subtypes by 12 to 23%.
What if we reduced health system costs by 20%?	Cost-effectiveness improves for almost all subtypes by 2 to 12%.
What if we included the impact of tamoxifen on breast cancer recurrence, not just breast cancer mortality?	Cost-effectiveness improves markedly across all subtypes by 10 to 60%.

Our Bottom Line

1. In this evaluation of a CCC to improve tamoxifen persistence in early breast cancer, the poorer the baseline prognosis, the greater the health gains from a CCC and the better the cost-effectiveness. If we used a cost-effectiveness threshold of NZ$ 45,000 per QALY then a CCC would only be cost-effective in the four subtypes with the worst prognosis.
2. This analysis demonstrates the value of investigating cost-effectiveness by different subtypes within a disease, potentially allowing more targeted allocation of limited health resources.