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Estimation of an optimal chemotherapy utilisation rate for breast cancer: Setting an evidence-based benchmark for the best-quality cancer care

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ABSTRACT

Background: The proportion of breast cancer patients that received chemotherapy varies widely in high-income countries. An evidence-based estimate of the optimal chemotherapy utilisation rate for a breast cancer population may serve as a useful benchmark for measuring and improving the quality of care.

Methods: An optimal chemotherapy utilisation model was constructed using indications for chemotherapy identified from evidence-based guidelines. Data on the proportion of patient (age, performance status and preference) and tumour (stage, size, grade, nodal status, hormone receptor and HER2 status) attributes were obtained and merged with the treatment indications to calculate an optimal utilisation rate. This model was peer-reviewed by a panel of independent experts.

Results: Chemotherapy was indicated in 17 of the 24 possible clinical scenarios depicted in the optimal utilisation model. The estimated optimal proportion of breast cancer patients who should received chemotherapy at least once was 68%. Sensitivity analyses showed that the range of optimal rate was 60–69%. The optimal rate appears to be substantially higher than the reported actual rates (29–49%).

Conclusion: It is possible to generate an optimal chemotherapy utilisation rate in breast cancer to serve as an evidence-based benchmark. The optimal chemotherapy utilisation rate in breast cancer has remained largely unchanged over the past 15 years. The reported actual utilisation rates of chemotherapy in breast cancer populations appear to have remained below the estimated optimal rate, suggesting that potential opportunities for improvement in the compliance to guideline recommended care exist.

1. Introduction

Chemotherapy plays an integral role in improving the survival and quality of life in many cancer patients. A fundamental requirement for the provision of quality cancer care is to ensure that patients receive appropriate treatment following their diagnosis.[1] Clinical practice guidelines have been published to facilitate the translation of evidence from clinical trials into patient care. Despite these efforts, variation in the utilisation rates of chemotherapy in the breast cancer popula-

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Table 1 – Breast cancer: Indications for chemotherapy – levels and sources of evidence.

Outcome no.	Clinical scenario	Treatment indicated	Level of evidence[a]	References	Proportion of all breast cancer patients
1	Stages 1 and 2, Node Positive, Age <70 years, Good PS	Adjuvant CT	I	NHMRC[7] NCCN[11] NCI PDQ[12] BCCA[13] COIN[17] SIGN[18] St Gallen[19]	0.16
2	Stages 1 and 2, Node Positive, Age 70 years and older, Hormone Receptor Positive, Recurrence, Hormone Treatment Resistant, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	0.03
4	Stages 1 and 2, Node Positive, Age 70 years and older, Hormone Receptor Negative, Good PS	Adjuvant CT	III	NHMRC[7] NCCN[11] NCI PDQ[12] BCCA[13]	0.01
5	Stages 1 and 2, node negative, age <35 years, Good PS	Adjuvant CT	I	NHMRC[8] NCI PDQ[12] St Gallen[19]	0.01
6	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size >2 cm, Good PS	Adjuvant CT	I	NHMRC[7] NCCN[11] NCI PDQ[12] BCCA[13] SIGN[18] St Gallen[19]	0.18
7	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 0–1.0 cm, grade 1 and Hormone Receptor Positive, Recurrence, Hormone Treatment Resistant, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	<0.01
9	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 0–1.0 cm, grade 2/3 or Hormone Receptor Negative, Patient Preference, Good PS	Adjuvant CT	III	NHMRC[7] NCI PDQ[12]	0.04
10	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 0–1.0 cm, grade 2/3 or Hormone Receptor Negative, Patient Declines Adjuvant CT, Recurrence, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	0.01
12	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 1.1–2.0 cm, HER2 Positive, Good PS	Adjuvant CT	II	NHMRC[10] NCCN[11] NCI PDQ[12] BCCA[13] CCO[14]	0.02
13	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 1.1–2.0 cm, HER2 Negative, Hormone Receptor Negative, Patient Preference, Good PS	Adjuvant CT	I	NHMRC[7] NCCN[11] NCI PDQ[12]	0.02

Table 1 – *continued*

Outcome no.	Clinical scenario	Treatment indicated	Level of evidence[a]	References	Proportion of all breast cancer patients
14	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 1.1–2.0 cm, HER2 Negative, Hormone Receptor Negative, Patient Declines Adjuvant CT, Recurrence, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	<0.01
16	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 1.1–2.0 cm, HER2 Negative, Hormone Receptor Positive, Patient Preference, Good PS	Adjuvant CT	I	NHMRC[7] NCCN[11] NCI PDQ[12]	0.07
17	Stages 1 and 2, Node Negative, Age 35–69 years, Tumour Size 1.1–2.0 cm, HER2 Negative, Hormone Receptor Positive, Patient Declines Adjuvant CT, Recurrence, Hormone Treatment Resistant, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	0.01
19	Stages 1 and 2, Node Negative, Age 70 years and older, Recurrence, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] SIGN[18]	0.02
21	Stage 3, Good PS	Neoadjuvant CT / Adjuvant CT	III	NHMRC[9] NCCN[11] NCI PDQ[12] BCCA[13] COIN[17] SIGN[18]	0.07
22	Stage 4, Hormone Receptor Positive, Hormone Treatment Resistant, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] BCCA[13] COIN[17] SIGN[18]	0.02
23	Stage 4, Hormone Receptor Negative, Good PS	Palliative CT	II	NHMRC[9] NCCN[11] NCI PDQ[12] BCCA[13] COIN[17] SIGN[18]	0.01
Total proportion of patients with breast cancer in whom chemotherapy is recommended					**0.68**

Abbreviations: CT, Chemotherapy; PS, performance status; NHMRC, National Health and Medical Research Council; NCCN, National Comprehensive Cancer Network; NCI PDQ, National Cancer Institute Physicians Data Query; BCCA, British Columbia Cancer Agency; CCO, Cancer Care Ontario; SIGN, Scottish Intercollegiate Guidelines Network and COIN, Clinical Oncology Information Network.

a *Levels of Evidence for Indications for Chemotherapy:* Level I, evidence obtained from a systematic review of all relevant randomised controlled trials; Level II, evidence obtained from at least one properly designed randomised controlled trial; Level III, evidence obtained from well-designed controlled trials without randomisation - these include trials with 'pseudo-randomisation' where a flawed randomisation method was used (e.g. alternate allocation of treatments) or comparative studies with either comparative or historical controls; Level IV, evidence obtained from case series. Taken from the National Health and Medical Research Council (NHMRC) hierarchy of levels of evidence[20].

tion exists.[2] Of concern, the EUROCARE study[3] has postulated that the survival difference seen in certain tumour groups between the European countries may be related to the under-utilisation of cancer treatments (e.g. adjuvant chemotherapy in node-positive breast cancer) as well as the variable application of evidence-based guidelines.[3] Although many studies have addressed the quality of adjuvant chemotherapy in breast cancer care, particularly for the node positive group, little is known about clinicians' adherence to guideline indications for chemotherapy in the breast cancer population.

In 1999 the United States Institute of Medicine's National Cancer Policy Board study, 'Ensuring the Quality of Cancer Care', reported that a substantial number of cancer patients received suboptimal treatment and the Board has recommended the establishment of benchmarks to assess compliance to clinical practice guidelines.[1] Current benchmarks for the evaluation of the quality of cancer care delivered are based on either peer-comparison or non-evidence-based estimates. For example, the Commission on Cancer's National Cancer Data Base generates reports that benchmarks the performance

of their 1430 participating hospitals based on peer-comparison of five quality measures.[4] In a comprehensive review on breast cancer patterns of care studies, the benchmark for compliance with guidelines was set at 100%.[2] More recently, the National Initiative for Cancer Care Quality conducted a survey on breast and colorectal cancers in which quality measures with less than 85% adherence were judged as potential areas for improvement.[5] Therefore, an evidence-based optimal chemotherapy utilisation rate remains undefined.

An estimate of the proportion of new cases of breast cancer that should receive chemotherapy at least once during the course of their illness (the optimal chemotherapy utilisation rate) may therefore be a useful benchmark for improving the quality of care and may also assist in the population-based planning of chemotherapy services. In this study, we developed an evidence-based utilisation model to determine the benchmark for the optimal chemotherapy utilisation rate in a breast cancer population.

2. Materials and methods

2.1. Indications for chemotherapy

We defined an indication for chemotherapy as a clinical situation in which chemotherapy is the treatment of choice on the basis of superior clinical outcomes in comparison to other treatment modalities (including best supportive care or no treatment). The superiority of chemotherapy over other treatment options could be based on survival, quality of life or toxicity profile. Chemotherapy could be recommended either alone or in combination with radiotherapy or surgery. The list of drugs classified as chemotherapeutic agents were as defined in the SEER*RX Antineoplastic Drug Database.[6] The optimal choice of individual drugs, numbers of drugs or specific chemotherapy regimens and their cost-effectiveness were beyond the scope of this study.

We identified the indications for chemotherapy in the management of breast cancer from clinical practice guidelines. The guidelines reviewed were published by the Australian National Health and Medical Research Council (NHMRC)[7–10]; the United States National Comprehensive Cancer Network (NCCN)[11] and National Carcinoma Institute (NCI)[12];the Canadian British Columbia Cancer Agency (BCCA)[13] and Cancer Care Ontario (CCO)[14–16]; the United Kingdom Clinical Oncology Information Network (COIN)[17] and Scottish Intercollegiate Guidelines Network (SIGN)[18]; and the St. Gallen Panel.[19] The hierarchy of levels of evidence used to justify the indications for chemotherapy was adapted from the Australian National Health and Medical Research Council.[20] We last reviewed the guidelines in July 2007. Table 1 shows the list of clinical scenarios for which chemotherapy is recommended in a breast cancer population.

2.2. Source of data on patient and tumour attributes

In order to ensure local relevance, we preferentially used Australian population-based data sources (e.g. Australian Institute of Health and Welfare, New South Wales Cancer Registry registries) wherever possible. If Australian data were not available, data from other large Western population-based sources such as United States Epidemiology and End Results and published data from institutional studies were also used. The highest ranked quality data were used in the model to define the base value of the attributes. Table 2 lists all the data sources and the hierarchy used to define the quality of data.[21] In situations where data on the same attributes were available from multiple sources, the data ranked highest quality were used as the base value in the chemotherapy utilisation tree. In situations where data obtained from multiple sources were ranked of equivalent quality, the larger sample size was chosen.

2.3. Performance status

Patient performance status (PS) is an important prognostic factor which also predicts benefits from treatment and is used in clinical trials and daily practice to select and stratify eligible patients for chemotherapy.[22] Chemotherapy is generally recommended for patients with good performance status (ECOG 0–2).[23] No specific population-based PS data were available for breast cancer despite an extensive literature search. Therefore the proportion of age-adjusted good PS patients was estimated by combining the Australian Institute of Health and Welfare data on the proportion of breast cancer by age groups (<55 years old, 55–64 years old, 64–75 years old and >75 years old) with the New South Wales (NSW) Population Health Survey 2005 data on 'difficulty doing work' by each of the corresponding age groups.[24,25]

Participants in the NSW Population Health Survey were asked about the degree of difficulty that they had experienced in undertaking daily work or activities (no difficulty, little difficulty, some difficulty, much difficulty or unable to carry out daily activities or work) in the past 4 weeks. This scale is similar to the Eastern Cooperative Oncology Group (ECOG)[26] scoring scales used to measure PS. Good performance status (ECOG 0–2) was assumed in those who reported 'no difficulty at all', 'a little bit of difficulty' and 'some difficulty'. In the NSW Population Health Survey[24], the rate of good PS (ECOG 0–2) patients varied from 92% (<55 years old) to 87% (>75 years old). The age-adjusted estimated proportion of good PS patients in the breast cancer population was 90%. As there was some uncertainty whether respondents with 'some difficulty' should be included in the good PS group, sensitivity analysis to assess the variation on the estimated optimal utilisation if they were excluded was performed.

2.4. Patient preferences

The benefit of adjuvant chemotherapy in certain subgroups of patients with node negative early breast cancers is small. In these situations, patient preference in deciding whether the benefits outweigh the potential side effects is an important factor.[27] It is common for patients to have a discussion with their medical oncologist about the toxicities of treatment and the expected survival benefit and for the patient to make their treatment choice based on assessing the pros and cons of treatment. A review of four patient preference studies involving 512 patients found that 50% of women with early breast cancer felt that 1% survival benefit was sufficient to

Table 2 – Breast cancer. The incidence of attributes used to define indications for chemotherapy.

Population or subpopulation of interest	Attribute	Proportion of populations with this attribute	Quality of information	References
All registry cancers	Breast cancer	0.13	α	AIHW[41]
Breast cancer	Good PS	0.91	α	AIHW[41]
			δ	NSW Population Health Survey[24]
Breast cancer	Stages 1 and 2	0.88	α	Hill et al.[32]
Breast cancer	Stage 3	0.08	α	Hill et al.[32]
Breast cancer	Stage 4	0.04	α	Hill et al.[32]
Breast cancer, Stages 1 and 2	Node Positive	0.29	α	AIHW[41]
Breast cancer, Stages 1 and 2, Node positive	Age 70 years and older	0.29	α	AIHW[41]
Breast cancer, Stages 1 and 2, Node Positive, Elderly	Hormone Receptor Positive	0.87	α	Hill et al.[32]
Breast cancer, Stages 1 and 2, Node negative	Age <35 years	0.02	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative	Age 35–69 years	0.81	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative	Age 70 years and older	0.17	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative, age 35–69 years	Size >2 cm	0.29	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative, age 35–69 years	Size 0–1 cm	0.26	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative, age 35–69 years	Size 1.1–2.0 cm	0.45	β	NSW Cancer Registry[42]
Breast cancer, Stages 1 and 2, Node negative, size 0–1 cm	Grade 1 and Hormone Receptor Positive	0.2	γ	US SEER[43]
Breast cancer, Stages 1 and 2, Node negative, size 0–1 cm, Grade 1 and Hormone Receptor Positive	Recurrence	0.12	ε	Chia et al.[44]
Breast cancer, Stages 1 and 2, Node Negative, Size 0–1 cm, Grades 2–3 or Hormone Receptor Negative	Recurrence	0.16–0.26	ε	Chia et al.[44]
Breast cancer, Stages 1 and 2, Node negative, Size 1.1–2.0 cm	HER2 Positive	0.13	γ	Joensuu et al.[45]
Breast cancer, Stages 1 and 2, Node negative, Size 1.1–2.0 cm, HER2 Negative	Hormone Receptor Negative	0.17	θ	Andrulis et al.[46]
Breast cancer, Stages 1 and 2, Node negative, Size 1.1–2.0 cm, HER2 Negative, No Adjuvant Chemotherapy	Recurrence	0.25	ε	Chia et al.[44]
Breast cancer, Stages 1 and 2, Node Negative, Elderly	Recurrence	0.19	ε	Troung et al.[47]
Breast cancer, Stages 1 and 2, Node Positive, Elderly	Recurrence	0.45	ε	Troung et al.[47]
Breast cancer, Stage 4	Hormone Receptor Positive	0.68	α	Hill et al.[33]

Abbreviations: AIHW, Australian Institute of Health and Welfare; NSW, New South Wales; US SEER, United States Surveillance Epidemiology and End Results and PS, Performance status.

Hierarchy for epidemiological data: α, Australian National Epidemiological data; β, Australian State Cancer Registry; γ, epidemiological databases from other large international groups (e.g. SEER); δ, results from reports of a random sample from a population; ε, comprehensive multi-institutional database; ζ, comprehensive single-institutional database; θ, multi-institutional reports on selected groups (e.g. multi-institutional clinical trials; λ, single-institutional reports on selected groups of cases; μ, expert opinion.

make chemotherapy worthwhile.[28] A recent Australian study reported that 68–84% of women with early breast cancer considered 3% survival benefit as adequate justification to have adjuvant chemotherapy.[29] From the available patient preferences data[28,29], our model assumes that 50% of women would choose to undergo adjuvant chemotherapy for a 1% survival benefit, and 68–84% of women would accept this treatment for a 3% survival benefit.

The above-mentioned data were incorporated into three branches of the utilisation tree where the indications of adjuvant chemotherapy were for a small benefit for node negative women with early breast cancer. The survival benefits with adjuvant chemotherapy for these three subgroups of women (35–69 years old) were estimated using the computer-based prognostic tool Adjuvant! for Breast Cancer (Version 8.0) program.[30] The first subgroup has an estimated survival benefit of 1% (0.3–2.3%) and features tumour size 1 cm or less which are grades 2–3 or hormone receptor negative. The second subgroup of tumour size 1.1–2 cm, and hormone receptor positive has a similar average survival benefit of 1% (0.3–3.7%). The third subgroup of tumour size 1.1–2 cm, and hormone receptor negative has an estimated average survival benefit of 3% (2–4.3%).

2.5. *Optimal chemotherapy utilisation rate*

Using the TreeAge Pro software (version 1.0),[31] the indications for chemotherapy in Table 1 and the data on proportions of tumour and patient attributes in Table 2 were merged to construct the optimal utilisation tree. Each patient with an indication for chemotherapy treatment was only counted once (i.e. the tree was terminated at the point of chemotherapy being recommended) even if they may have subsequent indications during the course of their illness. This was to standardise the comparison of the optimal rate with reported actual rates of chemotherapy utilisation (defined as the number of patients treated with chemotherapy for the first time divided by the incidence of each specific cancer type during a period).

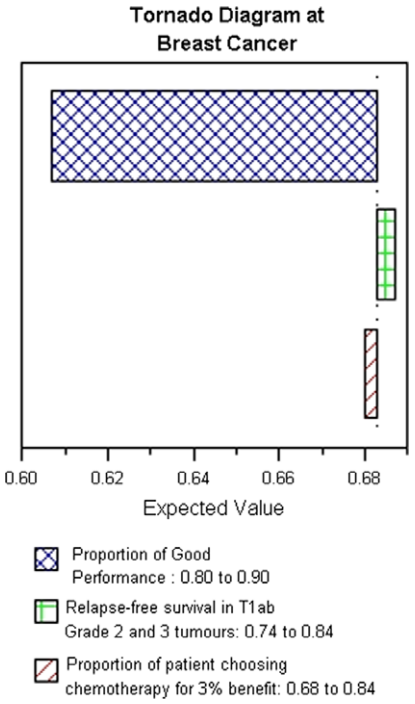

Fig. 2 – Tornado diagram showing sensitivity analyses of optimal chemotherapy utilisation rates for breast cancer. The combined effect of the variables is the range of optimal chemotherapy utilisation rate (61–69%).

Summation of the proportion of patients for each of the clinical scenarios where chemotherapy was indicated generated the optimal chemotherapy utilisation rate. Our model

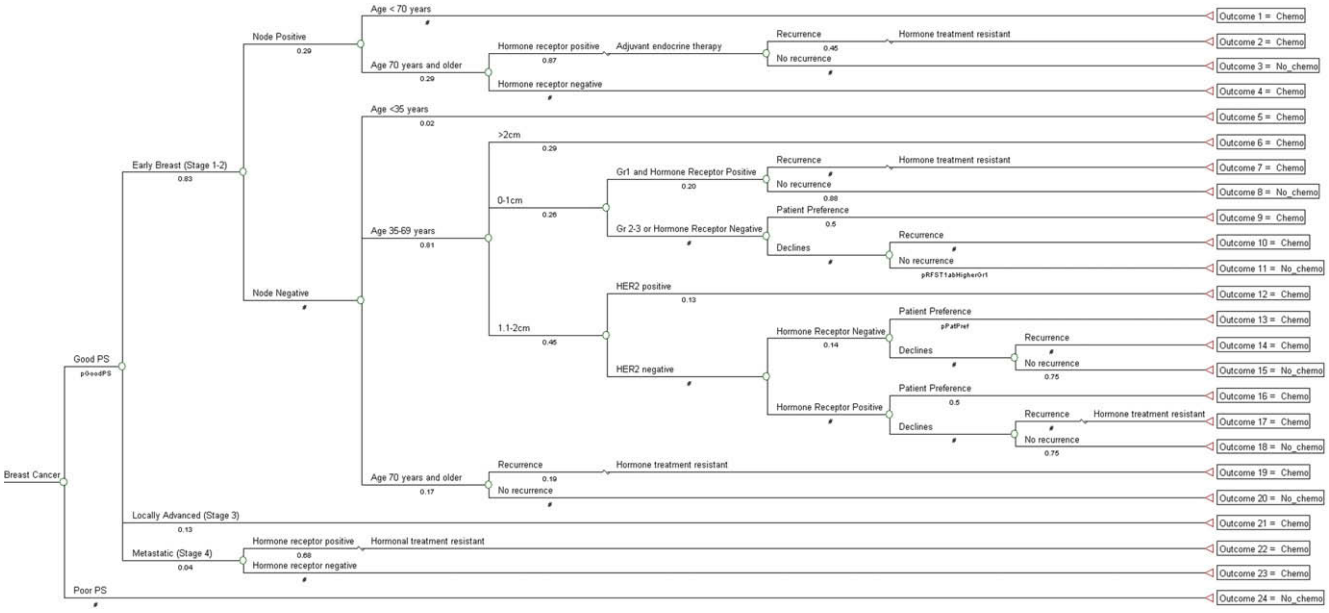

Fig. 1 – Optimal chemotherapy utilisation tree for breast cancer. Each branch of the chemotherapy utilisation trees represents an important tumour or patient-related attribute that affects the chemotherapy decision. Each terminal branch of the trees shows whether or not chemotherapy is indicated for each of the clinical scenarios. The description of the attributes is located above each branch of the utilisation tree with the corresponding data on the proportion of that attribute located below that branch.

was reviewed by independent breast cancer experts to ensure clinical validity. Appropriate changes were made to the models based on the feedback received. The panel of reviewers included members of the Australian New Zealand Breast Cancer Trials Group, New South Wales Oncology Group and Victoria Cooperative Oncology Group.

2.6. Statistical analysis

We tested the robustness of the chemotherapy utilisation model with sensitivity analyses using the TreeAge Pro software.[31] Univariate sensitivity analyses were conducted if the incidence of epidemiological data obtained varied by more than 10% or when there were disagreements between guidelines for a chemotherapy treatment indication. We entered the extreme values (upper and lower limits) of these variables into our model to assess each of their effects on the estimated optimal utilisation rate. A tornado diagram is a set of univariate sensitivity analyses brought together in a single graph.[31] Each bar in the tornado diagram represents a univariate sensitivity analysis and illustrates its effect on the expected range of the optimal chemotherapy utilisation rate. The tornado diagram also enables the calculation of the range of optimal chemotherapy utilisation rate from the combined effect of all the univariate sensitivity analyses.

3. Results

Fig. 1 depicts the optimal chemotherapy utilisation tree for breast cancer. Each branch of the chemotherapy utilisation trees represents an important tumour or patient-related attribute that affects the chemotherapy decision. Each terminal branch of the trees shows whether or not chemotherapy is indicated for each of the clinical scenarios. The description of the attributes is located above each branch of the utilisation tree with the corresponding data on the proportion of that attribute located below that branch.

Chemotherapy was indicated in 17 of the 24 possible outcomes in the utilisation tree (listed in Table 2). The optimal chemotherapy utilisation rate calculated (i.e. the proportion of all patients that should receive chemotherapy at least once during the course of their illness) for breast cancer was 68%. For the first course of treatment (chemotherapy within 6 months after diagnosis), the optimal rate was 59%. When analysed by stage, the optimal rates for the first course of treatment were 56% (Stages I–II), 90% (Stage III) and 29% (Stage IV), respectively. The majority of indications for chemotherapy (14/17) in the utilisation tree was supported by evidence derived from systematic reviews or randomised controlled trials (Levels I and II). The other 3 indications for chemotherapy were based on Level III evidence (well-designed controlled trials without randomisation).

3.1. Sensitivity analysis

There were three instances where the data on patient and tumour attributes varied between sources by more than 10%. Univariate sensitivity analyses were performed to assess the difference on the optimal chemotherapy utilisation rate with the variation of the following proportions: patients with good performance status (0.80–0.90), relapse-free survival of patients with grades 2 and 3 tumours that are 1 cm or smaller in size (0.74–0.84) and patients choosing to have chemotherapy for a 3% survival benefit (0.68–0.84). The tornado diagram (see Fig. 2) illustrates the overall effect of all the variables described above on the optimal utilisation rate. Each bar in the tornado diagram represents a univariate sensitivity analysis and illustrates its effect on the expected range of the optimal chemotherapy utilisation rate. Variations in the proportion of patients with good performance status (80–90%) had the greatest effect on the optimal rate. If patients with ECOG 2 were assumed to be unfit for chemotherapy, the optimal rate will fall from 68% to 61%. The range of optimal chemotherapy utilisation rate for breast cancer was 61–69%.

3.2. Comparison with actual practice

The actual chemotherapy utilisation rates in breast cancer (from 1995 to 2007) reported from large population-based studies in the following countries were: Australia (32–49%)[32,33], Sweden (30–40%)[34], Canada (40–42%)[35], United States of America (40%)[36] and United Kingdom (29%).[37] Although the actual rates were substantially lower than the estimated optimal rate of 68% (see Table 3), the comparison may not reflect current practice as newer evidence and indications for chemotherapy in breast cancer may have increased over the past 15 years. As such, we used the year of publication of the references used to support the guideline recommendations for chemotherapy as a surrogate measure of the progress of recommendations over time. Fig. 3 depicts the cumulative proportion of cases with an indication for chemotherapy over time, which allows for a more accurate and

Table 3 – Comparison of optimal and actual chemotherapy utilisation rates for breast cancer.

Variable	Optimal utilisation (%)		Actual first course of treatment (%)					
	Any time	First course of treatment						
Country	–	–	Australia[28,29]		Ontario (Canada)[35]	NCDB (US)[36]	NYCRIS (UK)[37]	Sweden[34]
Year(s) of survey	–	–	1995	2007	2001–2004	2006	2000–2004	1997
No. of patients	–	–	4237	3961	–	131,965	23,459	512
All stages	68	59	32	49	40–42	40	29	30–40

Abbreviations: NCDB: National Cancer Database, NYCRIS: Northern and Yorkshire Cancer Registry and Information Service, US: United States and UK: United Kingdom.

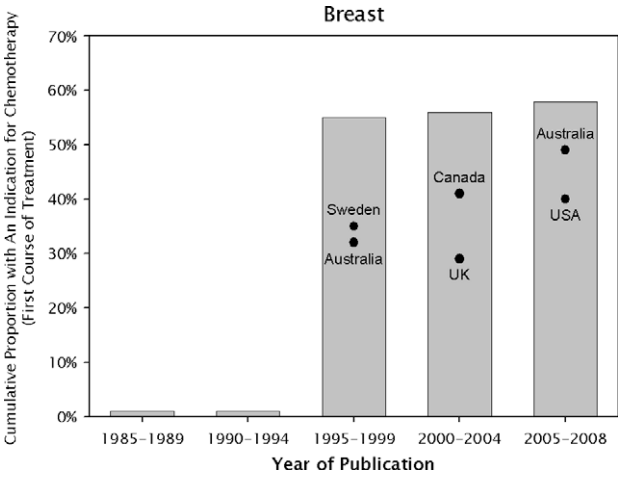

Fig. 3 – Comparison of the proportion with an indication for chemotherapy (first course of treatment) with actual chemotherapy utilisation rates (●) over time.

valid comparison with the historical actual rates. The optimal utilisation rate has risen only slightly from 65% to 68% in the past 15 years. Despite this, the actual rates reported have remained consistently lower for each of the corresponding 5-year time periods. When the optimal and actual utilisation rates were compared by stage using data from the United States National Cancer Database, we also found that the actual rates were lower across all stages: Stages I and II (56% versus 36%), Stage III (90% versus 71%) and Stage IV (29% versus 21%), respectively (30).

4. Discussion

This model depicts the possible clinical scenarios in a breast cancer population where chemotherapy is recommended. Based on the guidelines recommendations, our model estimated that 68% of patients with breast cancer should receive chemotherapy at least once during the course of their illness. This is substantially higher than the rates reported in actual practice, suggesting that chemotherapy may be under-utilised in the treatment of breast cancer in high-income countries.

Current benchmarks are based on peer-comparison (e.g. National Cancer Database reports) or an assumption that the best quality care is 100% adherence to the pre-selected measure.[2,4,38,39] Our model offers an evidence-based approach for benchmarking the optimal chemotherapy delivery to highlight the difference between the ideal and actual care delivered. For instance, in 2006, the United States National Cancer Database[36] reported that the actual chemotherapy utilisation rate in breast cancer was 38%, which was less than our calculated optimal utilisation rate (for the first course of treatment) of 58%, suggesting that a further improvement of up to 20% to guidelines recommended care may be possible. In addition, patients with Stage III breast cancer had the widest gap between the optimal and actual utilisation of chemotherapy rate (90% and 68%, respectively), despite being the cohort with the greatest survival benefit from chemotherapy.

While prior studies of breast cancer care have focused on addressing and improving the quality of chemotherapy delivery in the adjuvant setting,[2,5] little is known about the compliance with other guideline indications for chemotherapy. A review of patterns of care studies in breast cancer care has documented wide variations in the utilisation rates of adjuvant chemotherapy in patients with Stages I–III breast cancer.[2] More recently, several prospective studies have found a high compliance of chemotherapy use in the node positive cohort, in both Australia and the United States.[5,38,39] Although explicit quality measures in the selected cohorts (e.g. receipt of chemotherapy in patients with node positive early breast cancer who are aged 50 years or less) provide an accurate assessment and are useful for quality improvement, they may not necessary reflect the overall quality of chemotherapy delivery in a breast cancer population. Our findings suggest a lower adherence to guideline recommendations for chemotherapy when all potentially eligible patients in a breast cancer population are considered.

The robustness of our model was dependent on two main factors; whether the indications for the use of chemotherapy were uniformly recommended by the guidelines and the quality of the data used to define the proportion of tumour and patient attributes. We found a high concordance for the indications of chemotherapy identified from the guidelines reviewed. In addition, over 80% of these recommendations were supported by Levels I and II evidence (proven benefit from systematic reviews or randomised controlled trials). The majority of the data for the initial ' tree branches' (e.g. stage, node status, age groups and tumour) were from large population-based data sources such as Australian national and state cancer registry databases, therefore reducing the potential effects of sampling bias. To further strengthen its validity and applicability in current clinical practice, independent breast cancer experts reviewed the indications and data used in our model.

There are several limitations in our study. First, our model was constructed from various data sources as no available single population-based database had all the clinical and pathological attributes required to define the indications for chemotherapy. Although we selected the highest quality of data possible, sampling error is likely to occur which could affect the estimated benchmark. Second, the incidence data on patient and tumour attributes used for the terminal ends of the tree were only available from multi-institutional databases. These data sources may be prone to selection and referral bias; patients most fit and mobile are referred and patients least fit or isolated may not be referred. Third, specific performance status data for breast cancer patients were not available. However, this is not likely to be a major issue because the majority of patients present with early disease and are relatively fit. Finally, we were unable to address the issues of competing co-morbidities, which may affect the benchmarks estimated. How co-morbidities affect the overall decision to administer chemotherapy to breast cancer patients is currently unknown. Given that only 4% of breast cancer patients have severe co-morbidities[40], the overall effect on our benchmark is likely to be small.

Despite the limitations, our model offers a clinically relevant and evidence-based approach to estimate a benchmark for improving the utilisation of chemotherapy in breast cancer at a population-based level. This methodology has advan-

tages over other methods for setting benchmarks such as expert opinion or based on current levels of practice because it is evidence based, the assumptions are clearly stated and the model can be tested by sensitivity analysis. This model also has the advantage that it is readily adaptable to any future changes in chemotherapy indications or variations in the frequency data of patient and tumour attributes for any breast cancer population. For instance, any changes in breast cancer screening rates may alter the proportions of early stage breast cancer; this can be easily incorporated into the model to generate an up-to-date benchmark. Gaps in care can be further analysed by stage or specific clinical scenarios to identify the greatest areas for improvement.

It is possible to estimate an evidence-based benchmark for the optimal chemotherapy utilisation rate in a breast cancer population. Our findings suggest that a substantial proportion of eligible breast cancer patients in high-income countries may not be receiving chemotherapy as recommended by clinical practice guidelines. More importantly, the potential benefits from chemotherapy to achieve better outcomes for breast cancer patients are lost when evidence from clinical trials are not translated into clinical practice. Along with other quality improvement initiatives, this evidence-based model may serve as a guide for clinicians and policy makers for assessing and improving the quality of chemotherapy delivery in breast cancer care.

Conflict of interest statement

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