Priority-setting decisions for new cancer drugs: a qualitative case study

Douglas K Martin, Joseph L Pater, Peter A Singer

Summary

Background Frameworks for legitimate and fair priority setting emphasise the importance of the rationales for priority setting decisions. However, priority setting rationales, in particular for new cancer drugs, are not well described. We describe the rationales used by a committee making funding decisions for new cancer drugs.

Methods We did a qualitative case study of a priority setting committee (Cancer Care Ontario Policy Advisory Committee for the New Drug Funding Program) by analysing documents, interviewing committee members, and observing committee meetings.

Findings We identified and described decisions and rationales related to 14 drugs in eight disease conditions over 3 years. Our main findings were that: priority setting existed in relation to resource mobilisation; clinical benefit was the primary factor in decisions; in the context of an expanding budget, rationales changed; rationales could change as costs for individual treatments increased; when all options were reasonable, groups funded a range of options and let patients decide; and priority setting rationales involve clusters of factors, not simple trade-offs.

Interpretation Observing priority-setting decisions and their rationales in actual practice reveals lessons not contained in theoretical accounts.

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See Commentary page 1660

Introduction

A goal of priority setting is justice, which involves legitimate authorities using fair processes. Frameworks for legitimate and fair priority setting emphasise the importance of rationales for particular priority setting decisions. However, priority-setting rationales are not well described.

Priority-setting rationales are important in both primarily private (eg, USA) and public (eg, UK, Canada) health-care systems. In primarily public systems, rationales are more often open to public deliberation, whereas in primarily private systems, in which there is no democratic political mechanism for health-care priority setting, rationales are often implicit.

Surveys of the public have explored rationales as hypothetical “trade-offs” such as lifesaving technologies versus community services, withholding of life-prolonging medical care from critically ill elderly people, equity versus cost-effectiveness or good outcomes, “do-no-harm” principle versus maximising outcomes, helping the worst-off versus maximising outcomes, and personal treatment preferences versus abstract measures of utility.

Observing priority-setting decisions as a trade-off between equity and efficiency oversimplifies a very nuanced decision. Moreover, public opinion regarding hypothetical scenarios does not permit generalisations to actual decision making. Only a few empirical studies have examined actual priority setting, and these studies tend to focus narrowly on discrete technologies.

Cancer is the leading cause of death in Canada (27·2% of all deaths). Because the cost of new cancer drugs is rising dramatically, priority setting for new cancer drugs is critical. The National Institute of Clinical Excellence (NICE), on behalf of the UK’s National Health Service, conducts appraisals of new technologies, including new cancer drugs, and recommends which should be made available to patients. However, NICE’s priority-setting rationales (eg, docetaxel and paclitaxel for breast cancer) are limited to factors related to evidence of clinical outcomes. To our knowledge, only one study has explored rationales in priority setting for cancer. Foy and colleagues described a collaboration between a specialist cancer hospital and six regional health authorities in the UK with respect to funding new cancer drugs. They reported that funding decisions were based on evidence thresholds determined from information on effectiveness; the evidence thresholds were affected by political pressures, financial constraints, and the value placed on some clinical outcomes. The limitation of this study is that only four selected cases were examined in detail and, though the factors affecting decision making were described, the specific rationales for each decision were not.

In a previous paper, we described a model of priority setting for new cancer drugs as a diamond having six inter-related facets, one being the rationales used in priority-setting decisions. To our knowledge, there is no
in-depth description or analysis of rationales for priority setting decisions regarding new cancer drugs.

The purpose of this paper is to examine priority setting for new cancer drugs; specifically, we aim to provide an overview of decisions and rationales used, and describe how the rationales are assembled.

Methods

Design and setting

We have done a qualitative study of priority-setting decisions and rationales for new cancer drugs made by Cancer Care Ontario, a provincial disease management organisation responsible for cancer care in the province of Ontario, Canada. The analysis presented here was part of a larger qualitative case study of priority setting for new technologies in cancer and cardiac care.23

In this paper, we have focused on the Cancer Care Ontario Policy Advisory Committee for the New Drug Funding Program, which began in May, 1997, to "manage the selection and introduction of all new drugs within the funds provided and ensure that utilisation of new drugs will be accompanied by appropriate clinical practice guidelines."22 The Cancer Care Ontario Policy Advisory Committee consisted of administrators, oncologists, oncology researchers, a pharmacist, an ethicist, patients, and members of the public. Cancer Care Ontario negotiates its budget with the Ministry of Health annually, and the initial funding provided by the Ministry of Health for the New Drug Funding Program was Can$11 million per year. In Ontario, chemotherapy drugs like those under consideration by the Cancer Care Ontario Policy Advisory Committee are available only through public funding via either the New Drug Funding Program or hospital budgets, and are delivered in Regional Cancer Centres administered by Cancer Care Ontario and hospitals.

This study was approved by the Committee on Use of Human Subjects of the University of Toronto. Both the parent organisation, Cancer Care Ontario, and the Cancer Care Ontario Policy Advisory Committee consented to participate in this study. Individual participants gave their consent to be interviewed.

Data collection and analysis

The data for this study consisted of all documents produced by the committee (eg, minutes, correspondence), which were obtained in original form; interviews with 11 of 15 committee members, which were audiotaped and transcribed; and observations of all 12 meetings from inception (May, 1997) to May, 2000—we audiotaped and transcribed all meetings and transcribed and documented the researchers' observations in field notes.

We identified all the funding decisions during the study period and the rationales for each decision as discussed in meetings and articulated in documents. Original documents were used directly where appropriate (table). Participant interviews provided some insight into the thoughts of individual members regarding particular decisions.

Results

During the study period, the Cancer Care Ontario Policy Advisory Committee considered 14 drugs for eight diseases. These decisions and their rationales are summarised in the appendix (available from the Lancet offices and the authors at www.utoronto.ca/jcb/Research/prioritysetting/lancetaddendum2001.htm). Panel 1 summarises what we have identified from our study of these decisions regarding rationales for priority setting of new cancer drugs.

In the first few meetings, the committee members discussed whether to develop a list of possible funding recommendations ranked according to some priority measure, compare the potential costs of the recommendations against a known fixed budget, and then try to draw a line at the end of the resources. However, the ensuing discussion about potential priority measures failed to generate agreement. Therefore, they decided to attempt to make judicious decisions based on available evidence for each drug they encountered. They agreed that if they found themselves in a position where they did not have sufficient resources to fund the drugs they approved, they would advocate for more resources from the Ministry of Health on behalf of patients. Over the study period, the committee twice appealed to the ministry for budget increases and both were granted. Thus priority setting existed in relation to resource mobilisation.

The table (the actual table used by the Policy Advisory Committee) provides an overview of drugs, diseases, and factors considered. The table was continually updated as new drugs and information emerged. The version of the table presented here was the last version used. The table was a "work in progress", the numbers initial estimates, and the missing data indicative of the actual information available to the committee at the time of each decision. The hierarchy of benefit and evidence was developed by the committee chair at the request of the public members of the committee (panel 2).

The committee used all the factors described in the table to develop rationales for each decision. In some cases, evidence evolved over time—before, during, and after decision making. In all decisions, benefit to patients was the primary factor in decisions. Other factors, including some not found in the table, were also considered including presence or absence of alternative treatments, total population of patients affected, total cost to the system, quality of evidence, access to treatment, pressure from physician and patient groups, and historical precedent. Formal cost-effectiveness analysis, often proposed as a means of resolving difficult priority setting questions, was rarely available and not used (note its absence from the table). However, the concept was used informally, for example one member discussed ways of achieving "the biggest bang for the buck". Benefit to patients was the primary factor in decisions.

Over the study period, Cancer Care Ontario twice appealed to the Ministry of Health for budget increases and both were granted. As the budget expanded, the members' primary justification for funding decisions expanded from, initially, only prolongation of survival and relief of symptoms to include tumour shrinkage or reduction in toxicity. Also, the committee initially vacillated about funding drugs that had only non-

Panel 1: Lessons from priority setting for new cancer drugs

- Priority setting existed in relation to resource mobilisation
- Clinical benefit was the primary factor in decisions
- In the context of an expanding budget, rationales change
- Rationales can change as costs for individual treatments increase
- When all options were reasonable, groups funded a range of options and let patients decide
- Priority-setting rationales involve clusters of factors, not simple trade-offs

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<table>
<thead>
<tr>
<th>Drug/disease</th>
<th>Benefits</th>
<th>Magnitude of benefits</th>
<th>Quality of evidence</th>
<th>Alternatives</th>
<th>Cost/ month ($Can)</th>
<th>Average duration of treatment</th>
<th>Patients treated</th>
<th>Yearly system cost ($Can)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vinorelbine in non-small cell lung cancer (NSCLC)</td>
<td>Prolongation of survival; reduction in symptomatic toxicity compared to standard therapy</td>
<td>6–8 weeks</td>
<td>Single randomised trial of reasonable size; multiple randomised trials of meta-analysis</td>
<td>Standard Rx, other new agents</td>
<td>$700</td>
<td>2 months</td>
<td>900</td>
<td>$1 200 000</td>
</tr>
<tr>
<td>Gemcitabine in NSCLC</td>
<td>Reduction in symptomatic toxicity compared to standard therapy</td>
<td>48% vs 22%</td>
<td>Small randomised trial of reasonable size</td>
<td>Standard Rx, other new agents</td>
<td>$1200</td>
<td>2 months</td>
<td>900</td>
<td>$2 100 000</td>
</tr>
<tr>
<td>Paclitaxel in NSCLC</td>
<td>Prolongation of survival</td>
<td>37% vs 32% 1-year survival</td>
<td>Single randomised trial of reasonable size</td>
<td>Standard Rx, other new agents</td>
<td>$1500</td>
<td>2 months</td>
<td>900</td>
<td>$2 700 000</td>
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<tr>
<td>Irinotecan in metastatic colorectal cancer</td>
<td>Tumour shrinkage</td>
<td>20% vs 0%</td>
<td>Phase II data</td>
<td>No Rx</td>
<td>$3000</td>
<td>2 months</td>
<td>650</td>
<td>$7 800 000</td>
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<tr>
<td>Bisphosphonates in myeloma</td>
<td>Prolongation of survival; relief/prevention of symptoms/complications of disease</td>
<td>6 months 10–20% lower fractures</td>
<td>Single randomised trial of reasonable size; multiple randomised trials of meta-analysis</td>
<td>None</td>
<td>$475</td>
<td>12 months</td>
<td>350</td>
<td>$1 995 000</td>
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<tr>
<td>Bisphosphonates in metastatic breast cancer (MBC)</td>
<td>Relief/prevention of symptoms/complications of disease</td>
<td>30–40% reduction in fractures or need for radiotherapy</td>
<td>Multiple randomised trials of meta-analysis</td>
<td>None</td>
<td>$240</td>
<td>12 months</td>
<td>1440</td>
<td>$4 147 200</td>
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<td>Paclitaxel in ovarian cancer</td>
<td>Prolongation of survival</td>
<td>10–12 month increase in median survival</td>
<td>Multiple randomised trials of meta-analysis</td>
<td>None</td>
<td>$1900</td>
<td>per 3 weeks</td>
<td>440</td>
<td>$2 050 000</td>
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<tr>
<td>Topotecan in taxane failures</td>
<td>Tumour shrinkage</td>
<td>20% vs %</td>
<td>Phase II data</td>
<td>Anthracylines-cyclophosphamide HMM, supportive care</td>
<td>$2500</td>
<td>4 months</td>
<td>200</td>
<td>$800 000</td>
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<td>Dextrazoxane</td>
<td>Reduction in symptomatic toxicity compared to standard therapy</td>
<td>13% vs 3% CHF</td>
<td>Multiple randomised trials of meta-analysis</td>
<td>Stop anthracyclines</td>
<td>$425</td>
<td>4 months</td>
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<td>Amifostine</td>
<td>Reduction in symptomatic toxicity compared to standard therapy</td>
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<td>Dose reduction</td>
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<td>$774</td>
<td>6 months</td>
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<td>Gemcitabine in pancreatic cancer</td>
<td>Prolongation of survival; relief/prevention of symptoms/complications of disease</td>
<td>5 weeks; 18% vs 2% survival at one year</td>
<td>Single randomised trial of reasonable size</td>
<td>5FU</td>
<td>$1200</td>
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<tr>
<td>Raltitrexed in colorectal cancer</td>
<td>Reduction in symptomatic toxicity compared to standard therapy</td>
<td>Less mucositis</td>
<td>Multiple randomised trials of meta-analysis</td>
<td>FUF</td>
<td>$650</td>
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<tr>
<td>Vinorelbine in MBC</td>
<td>Tumour shrinkage</td>
<td>20–25% response vs 7%</td>
<td>Phase II data</td>
<td>Taxanes, mitoxantrone/vinblastine</td>
<td>$700</td>
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<tr>
<td>Paclitaxel in MBC</td>
<td>Tumour shrinkage</td>
<td>20–25% response vs 7%</td>
<td>Phase II data</td>
<td>Docetaxel, vinorelbine/mitoxantrone/vinblastine</td>
<td>$1900</td>
<td></td>
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<tr>
<td>Docetaxel in MBC</td>
<td>Prolongation of survival</td>
<td>Increased median survival from 10–12 months</td>
<td>Single randomised trial of reasonable size</td>
<td>Mitoxantrone/vinblastine (paclitaxel, vinorelbine)</td>
<td>$1940</td>
<td></td>
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<tr>
<td>Liposomal anthracyclines for Kaposi sarcoma in HIV-positive patients</td>
<td>Prolongation of survival; reduction in symptomatic toxicity compared to standard therapy; tumour shrinkage</td>
<td></td>
<td>Multiple randomised trials of meta-analysis</td>
<td>Doxorubicin, bleomycin, vincristine.</td>
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<td>Rituxan in follicular lymphoma</td>
<td>Tumour shrinkage</td>
<td>60% response rate</td>
<td>Phase II data</td>
<td>Other chemotherapy</td>
<td></td>
<td></td>
<td>230</td>
<td>$3 500 000</td>
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<tr>
<td>Trastuzumab in combination with paclitaxel in MBC</td>
<td>Prolongation of survival</td>
<td>12% increase in 1-year survival</td>
<td>Small randomised trial</td>
<td>Docetaxel</td>
<td>180</td>
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<td>$460 000</td>
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<tr>
<td>Trastuzumab alone in previously treated patients with MBC</td>
<td>Tumour shrinkage</td>
<td>12–15% response rate</td>
<td>Phase II data</td>
<td>Mitomycin/vinblastine capcitabine</td>
<td>180</td>
<td></td>
<td></td>
<td>$2 500 000</td>
</tr>
</tbody>
</table>

CAN=Canada; Rx=treatment; %=not known; HMM=hexamethylmelamine; CHF=congestive heart failure; FU=fluorouracil; FA=folinic acid.

**Overview of drugs, diseases, and factors**
randomised evidence of benefit (ie, phase II data), but eventually came to accept non-randomised evidence.

Panels 3 and 4 show two actual examples of decisions and their rationales. Priority-setting rationales involve clusters of factors, not simple trade-offs. Initially, the committee members considered whether to develop substantive criteria that they would then apply to each decision. However, finding that they were uncertain about the criteria, they decided to start making decisions and subsequently “discover” the criteria. This strategic decision revealed that priority-setting rationales involve clusters of factors, not simple trade-offs (eg, benefit, harm, evidence, need, cost, availability of alternatives, precedent, convenience, budget constraints, &c). These factor-clusters were compared with previous factor-clusters in a type of casuistry of priority setting that helps to ensure consistency. For example, when considering trastuzumab for patients with previously treated metastatic breast cancer, where the potential benefit was tumour shrinkage and only phase II data were available, the committee assessed previous decisions and rationales for other drugs where the potential benefit was tumour shrinkage and only phase II data were available (eg, irinotecan and rituxan). Clusters of factors took different, more or less complex shapes with each decision. Some decisions involved one drug for one disease and its attendant cluster of factors (eg, irinotecan for the treatment of colorectal cancer). Some decisions involved clusters of drugs, each with their own cluster of factors, for one disease (eg, gemcitabine, paclitaxel, and vinorelbine for the treatment of non-small cell lung cancer). Other decisions involved clusters of drugs, clusters of diseases, and, as a result, a complex cluster of factors (eg, pamidronate and clodronate for the treatment of myeloma and breast cancer).

Panel 4: Vinorelbine, docetaxel, and paclitaxel in metastatic breast cancer

In phase II trials, all three drugs showed response rates that were higher than expected from standard therapy. There was no quality of life data available. In addition, one randomised study, reported in abstract form, suggested that docetaxel increased survival compared with standard therapy. Significant toxicity was associated with all three drugs; the toxicity of paclitaxel was felt to be most problematic: docetaxel had less toxicity and vinorelbine, the least. It was noted that vinorelbine is more convenient to administer, requiring 1 h infusions. Regarding costs, paclitaxel is the most expensive, followed by docetaxel and vinorelbine, respectively. It was generally felt that vinorelbine would provide the “biggest bang for the buck”. However, since paclitaxel and docetaxel were already funded and in common use, a decision not to fund them in favour of vinorelbine could have met with strong opposition from physicians and patients. The panel felt that, in the absence of evidence that made one of the three drugs clearly preferable, physicians and patients would tend to choose vinorelbine, a choice that would result in overall cost savings.
priority-setting activities—ie, the pies are seldom fixed. In the case we studied, the committee successfully negotiated with the Ministry of Health for more resources. Groups that adhere to a rigorous and fair process that involves multiple stakeholders directly and who make their rationales publicly known are often in a strong position to negotiate for more resources—ie, a bigger pie.

Cost-effectiveness analysis was not a primary consideration of this committee. Although the concept of value-for-money was considered, formal cost-effectiveness analysis was not used. This finding does not prove that cost-effectiveness analysis is flawed, but it accords with other studies which have also concluded that “simple solutions”, such as cost-effectiveness analysis, are theoretically flawed and impossible to implement in practice.26 27

Priority-setting decisions can be assembled in a comparative or non-comparative manner.27 Comparative decision making, for example, might be a situation in which the committee had tried to decide whether they should fund a breast cancer drug or a prostate cancer drug from a fixed pot of money. Comparative decision making gives rise to the perception of “winners and losers”, thus increasing moral tension. The decision making reported here was non-comparative—each factor-cluster was examined independently. Non-comparative decision making eliminates having to make comparisons across categories of patients receiving very different treatments. However, a potential problem with non-comparative decision making is that budget restrictions influence priority setting only as an after-thought, which is essentially the experience reported here. The committee approved the drugs they felt justified in funding, and then addressed budget restrictions by advocating for sufficient funds to implement those decisions.

Even when treatment costs are fixed and cost-effectiveness analysis is available, changes in overall costs to the health-care system (eg, when populations of patients increase) may cause a change in rationales. Although the importance of patient’s choice is a prevalent feature of published reports, we have shown that it is a substantial part of the decision making process. We also analysed the way in which rationales are assembled.28 The previous conception of priority setting as trade-off (eg, equity vs efficiency) was too simplistic and abstract to describe actual priority setting reasoning. Priority-setting decisions involve clusters of factors that vary according to the decision. Rationales are assembled by combining these factor-clusters in support of a particular decision. Finally, each decision and rationale is compared with previous decisions and rationales in a casuistry or “case law” that helps to ensure consistency.

Are the rationales right? Do they have moral force? This study examined the priority-setting rationales used by a committee consisting of members drawn from different backgrounds (eg, researchers, providers, administrators, patients, and public) who engaged in what they believed to be a fair process to make priority-setting decisions with the goal of making the best treatments available to people with cancer. A justifiable starting assumption is that the rationales formulated by such a committee of fair-minded people have some inherent moral force.1,29

But are there legitimate limits on rationales? For example, what if a group of decision makers is inherently sexist (eg, in the public) who engaged in what they believed to be a fair process to make priority-setting decisions with the goal of making the best treatments available to people with breast cancer? One response may be that the same ethical frameworks for priority setting that emphasise rationales also emphasise transparency and publicity,1,2 which helps ensure that potentially unethical decisions are exposed for examination and challenge. Thus giving reasons may be seen as a mechanism for improving the quality of the funding decisions. Moreover, discriminatory decisions on the part of priority-setting decision makers could be readdressed through the legal system, which provides protection against discrimination.

A related problem is how to align rationales with normative policy goals and information about these goals. For example, the mandate of the Cancer Care Ontario Policy Advisory Committee was “to provide equal access to new effective agents for eligible patients throughout the province”—note the focus on availability and effectiveness.28 The rationales developed by the committee were primarily focused on the benefit of each drug to patients. The primary information used by the committee was published evidence of benefit, whereas cost-effectiveness information played only a limited part. Thus, the goals, rationales, and information seem aligned. However, a systematic method for aligning organisational goals with priority-setting decisions has yet to be developed.

Contributors

Douglas K Martin collaborated in study conception and design, collected and analysed the data, and was primary author. Joseph L Pater contributed to the data analysis and writing. Peter A Singer contributed to conception, design, data analysis, and writing.

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References

Clinical picture: An unwanted tattoo

Lorenzo Alonso Vega, José Antonio Sáliz de Quevedo García, Carlos Tej Santamaria, Miguel Carrascosa Porras

A 20-year-old man was injured by a lightning strike during a thunderstorm. The lightening hit a lorry, splashed onto some nearby people, and finally hit and knocked down the patient. He was initially paralysed from the waist downwards but conscious; paraesthesias, upper-extremity weakness, or aphasia were not present. The keraunoparalysis (lightning paralysis), resolved spontaneously in 30 min. On admission to hospital, physical examination revealed superficial thoracic burns and a painless, arborescent erythema on his left shoulder (figure). An electrocardiogram was normal and the serum concentration of creatine kinase was within normal limits. The branching pattern of cutaneous marks vanished in approximately 16 h. Feathering skin injuries are pathognomonic of lightning and are known as Lichtenberg’s figures or flowers, filigree burns, keraunographic markings, arborescent burns, and ferning. While these have not been characterised histologically, they do not appear to be true burns and usually fade within a few hours, as occurred in our patient.

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