Preferences for cancer treatments: an overview of methods and applications in oncology

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This review provides cancer clinicians and researchers with an overview of methods for assessing preferences, with examples and recommendations for their application in oncology. Decisions about cancer treatments involve trade-offs between their relative benefits and harms. An individual’s preference for a cancer treatment reflects their evaluation of the relative benefits and harms in comparison with a given alternative or alternatives. Methods of preference assessment include the ranking or rating scale, standard gamble (SG), time trade-off (TTO), visual analogue scale, discrete choice experiment (DCE), and multi-attribute utility instrument (MAUI). The choice of method depends on the purpose of preference assessment; the ranking or rating scale, SG, TTO, and DCEs are best suited to clinical decisions, whereas MAUIs are best suited to health policy decisions. Knowledge of patients’ preferences for cancer treatments can better inform clinical decisions about patient management by enabling the tailoring of decisions to individual patients’ values, attitudes, and priorities and health policy decisions through economic evaluations of cancer treatments and their suitability for coverage by health payers.

Key words: decision-making methods, neoplasms, preferences

introduction

The aim of cancer treatment is to improve length of life and quality of life (QOL). Improvements in length of life are generally modest. Effects on QOL can be harmful, by adding symptoms of treatment-related toxicity, but it can also be beneficial, by reducing or delaying cancer-related symptoms. Decisions about cancer treatments involve trade-offs between these possible benefits and harms. Such trade-offs are a personal judgement that may differ between individuals—some may judge the survival benefits of a cancer treatment to outweigh its potential toxicity, but those who place a greater value on QOL may not.

An individual’s preference for a treatment reflects their evaluation of its relative benefits, harms, costs, and inconveniences in comparison with a given alternative or alternatives. An individual’s preference may also be assessed by determining their preference for a given health state in comparison with an ideal health state (usually ‘perfect health’). Health states can apply to cancer treatments by describing, e.g. particular combinations of toxic effects and outcomes of a treatment, such as health state A (mild nausea, moderate fatigue, disease free) and health state B (severe nausea, severe fatigue, disease recurrence) referring to adjuvant chemotherapy for early breast cancer.

The strength of an individual’s preference for a treatment is a measure of their willingness to accept it. Preferences can be expressed in terms of either the minimum benefit needed to make worthwhile the given harms, inconveniences, and/or costs or in terms of the maximum harms, inconveniences, and/or costs willing to be borne in return for a given benefit.

The concept of preferences for treatments is related to, but different from, those of health-related quality of life (HRQL) and utility. HRQL is a subjective evaluation of the effects of disease and treatment on how an individual is feeling or doing. Utility is a way of valuing HRQL and represents an individual’s relative satisfaction with a health state, on a scale from 0 (representing death) to 1 (representing perfect health). Preferences are a subjective evaluation of how an individual weighs up the potential effects of a treatment on their HRQL and length of life. Decisions about cancer treatments are often ‘preference sensitive’. This means that there is no single alternative among the available options, i.e. best for every individual, but instead the optimal decision depends on each individual’s values, attitudes, and priorities [1]. For example, in choosing between doses of radiation therapy for localised prostate cancer, a higher dose might increase both cure rates and toxicity; the optimal choice depends on how an individual weighs these benefits and harms [2, 3].

Knowledge of individuals’ preferences for cancer treatments can better inform decisions in clinical practice and health policy. The purpose of preference assessment for clinical decisions is to tailor decisions about cancer treatments to...
specific subgroups of patients or to individual patients. For health policy decisions, preference assessment is a component of economic evaluation, which is used to inform decisions about resource use such as whether and for whom new and expensive cancer treatments should be funded by a government. Cancer clinicians increasingly need to understand the basis for health policy decisions because they determine the availability of cancer treatments and thereby influence patient care.

Published studies of patients' preferences for cancer treatments have used many different definitions of the term 'preferences' and a variety of methods to elicit these preferences. The aim of this paper was to provide cancer clinicians and researchers with an overview of methods for assessing preferences for cancer treatments, with examples and recommendations for their application.

methods of preference assessment

Preferences may be assessed by general methods, such as ranking or rating, or by more specific methods including the standard gamble (SG), time trade-off (TTO), visual analogue scale (VAS), discrete choice experiment (DCE), and multi-attribute utility instrument (MAUI). Most methods elicit 'stated' preferences (what someone reports they would do in a hypothetical situation) rather than 'revealed' preferences (what someone has actually done). The main methods are summarised in Table 1 and discussed below.

ranking or rating

Preferences are most simply assessed by asking individuals to rank or rate a given set of alternative cancer treatments on a Likert scale or other scales. Such studies are relatively straightforward to design and are quick and easy for patients to complete. They generally provide ordinal data about patients' preferences.

For example, a rating study was used by Koedoot et al. [4] to determine preferences for palliative chemotherapy in 140 patients with metastatic cancer. Patients were interviewed before seeing an oncologist and were asked to rate their preference for having chemotherapy on a seven-point Likert scale ranging from 'strong aversion to chemotherapy' to 'strong preference for chemotherapy'. Most patients (68%) preferred having chemotherapy at baseline, one quarter had no preference, and few (7%) had an aversion to chemotherapy. These preferences were related to the patients' actual treatment choice: most patients (78%) who preferred chemotherapy chose to have it and almost all patients with an aversion to chemotherapy chose to have best supportive care without chemotherapy.

standard gamble

The SG is based on a model of decision making under uncertainty called expected utility theory [5, 6]. The expected utility of an option is the sum of the utility of each of its possible outcomes multiplied by its probability. According to expected utility theory, individuals behaving rationally under uncertainty will make decisions that maximise their expected utility. This means that patients should choose cancer treatments that maximise their quantity of life and QOL.

The SG asks individuals to choose either a gamble between perfect health (for a given time) and immediate death or a certain but intermediate health state (for the same given time) (Figure 1). In the gamble, perfect health has a probability of \( P \) and death has a probability of \( 1 - P \). The value of \( P \) is varied until the individual is indifferent to the choice between the gamble and the certain intermediate health state, at which point \( P \) is the utility for the certain intermediate health state [7, 8].
Uncertainty is a fundamental feature of both the expected utility theory and the SG. The expected utility theory and SG therefore reflect real-life medical decisions, which are also made under conditions of uncertainty due to probabilistic outcomes [9]. Uncertainty adds to the complexity of medical decisions and may arise from the diagnosis, the natural history of the disease, and the effects of treatment [10]. For example, a patient deciding whether to have adjuvant chemotherapy for early breast cancer may know the probability of the benefit of the treatment (e.g., 10% improvement in survival at 10 years) but not the actual benefit they will obtain from the treatment (cure, delayed recurrence, or no benefit). The decision to have chemotherapy depends on the probability of each of the possible outcomes, their desirability, and the individual's attitudes.

The main advantage of the SG is that it is the only method of preference assessment where choices are necessarily made under uncertainty, and so it is consistent with expected utility theory and provides a sound theoretical basis for health economic analyses. As such, the SG is often considered to be the gold standard method of preference assessment, although this view has been challenged [11]. The main limitations of the SG include that it is cognitively demanding because it requires the consideration of complex probabilities, although these may be partially ameliorated with visual aids [12]. The SG also relies on expected utility theory being a good model of decision making under uncertainty, but this may not always be true. For example, individuals are generally risk averse and only accept gambles with very small probabilities of immediate death. This creates a ceiling effect in the SG and reduces its sensitivity to detect small differences between different health states [13].

The SG was used by Kilbridge et al. [14] to determine patients’ preferences for health states associated with adjuvant interferon (IFN) for high-risk melanoma. Ninety-five patients were interviewed to determine their utilities for four health states representing different levels of IFN toxicity (nil, mild–moderate, or severe clinical side-effects; severe laboratory side-effects) and three outcomes (recurrence and cancer death with or without IFN, disease free). Mean utilities for being disease free (0.96) and with all levels of IFN toxicity (0.81–0.92) were significantly higher than utilities for recurrence and cancer death with IFN (0.62) or without IFN (0.61). In other words, patients rated the toxic effects of IFN as being relatively minor in comparison with melanoma recurrence or death and were therefore willing to accept the possible toxic effects of IFN in order to reduce the probability of melanoma recurrence and death.

**time trade-off**

The TTO was developed by Torrance et al. [15] as an alternative to the SG. The TTO offers a choice between two alternative health states under certainty: health state i for time t followed by death or perfect health for time x < t followed by immediate death. The duration of x is varied until the respondent is indifferent between the two alternatives: the preference for health state i is x/t (Figure 2). This method can be modified to accommodate health states considered worse than death [7].

The advantages of the TTO over the SG are that it is less cognitively demanding because it does not involve probabilities. Limitations of the TTO include that it reflects decisions made under certainty, not uncertainty, and so it is not consistent with expected utility theory. This lack of uncertainty also detracts from the clinical realism of the TTO. For example, having effective chemotherapy increases the probability of living longer, but it does not guarantee it. The TTO is also affected by ‘discounting’ where the time being traded is undervalued by individuals if it assumed that this time comes at the end of their life [16].

The TTO was used by Simes and Coates [17] to determine patients’ preferences for adjuvant chemotherapy in early breast cancer. Patients who had adjuvant chemotherapy for early breast cancer were interviewed to determine the survival benefits that made the harms and inconveniences of chemotherapy worthwhile. They chose between a given survival time without chemotherapy versus a longer survival time with chemotherapy. Most patients needed only modest survival gains to make chemotherapy worthwhile (an extra 6–12 months with baselines of 5 or 15 years without chemotherapy). A recent update showed many judged even smaller benefits sufficient to make chemotherapy worthwhile (an extra 1 day) [18]. Similar methods have been used to determine patients’ preferences for adjuvant endocrine therapy for early breast cancer [19, 20], adjuvant chemotherapy for early colon cancer [21], and clinicians’ preferences for adjuvant chemotherapy in non-small-cell lung cancer [22].

**visual analogue scale**

A VAS is an anchored linear rating scale on which individuals assign their preference for a health state. It is a quick and easy method of preference assessment but has several key limitations. These include (i) the use of ill-defined anchors (e.g., ‘best imaginable’ rather than ‘perfect health’ and ‘worst possible’ rather than ‘death’) that limit comparisons between individuals or groups, (ii) measurement biases (such as the reluctance for respondents to choose the extreme ends of a continuous scale), (iii) the values elicited are consistently lower than those elicited by SG or TTO, (iv) the ratings are made under conditions of certainty not uncertainty, and (v) there is no ‘trade-off’ and so a VAS gives ‘values’ rather than ‘utilities’ [12, 23, 24]. The VAS is thus considered inadequate as a sole method of assessment in a preference study and is best used in conjunction with other methods like the SG or TTO [25].

A VAS was used by Sun et al. [26] to determine patients’ preferences for health states associated with chemotherapy for advanced ovarian cancer. Seventy women who were having chemotherapy for newly diagnosed or recurrent ovarian cancer rated 27 health states on a scale from 0 to 100. The health states included 4 anchor health states (perfect health, current health, clinical remission), 6 health states for chemotherapy-induced nausea and vomiting (CINV) of varying severity, and health states for 17 other
side-effects of chemotherapy (e.g. alopecia, fatigue). Patients most preferred perfect health, clinical remission, and complete control of CINV and least preferred more severe states of CINV and death. Health states were generally rated higher by patients having chemotherapy for newly diagnosed ovarian cancer than patients having chemotherapy for recurrent ovarian cancer.

discrete choice experiment
DCEs are a type of choice-based conjoint analysis originating in mathematical psychology, which are widely used in marketing and applied economics (such as transport) and have been recently adapted to health care. The principle underlying the DCE is that the value of an option is determined by the values of its attributes [27]. With regard to cancer treatments, this means that the outcomes of a treatment can be described by its attributes and the extent to which an individual values the treatment depends on how they value these attributes [28].

A DCE is carried out by identifying the most important attributes of a cancer treatment (e.g. improvement in survival, temporary nausea) and assigning different levels to each attribute (e.g. life expectancy of 4, 8, or 12 years; urinary function that is unimpaired, somewhat, or severely impaired). Scenarios that involve combinations of the different levels of the attributes are developed (e.g. life expectancy of 12 years with severe problems with leaking urine). Patients’ preferences for the scenarios are elicited by asking them to choose between selected pairs of scenarios (e.g. life expectancy of 12 years with severe problems with leaking urine versus life expectancy of 8 years with occasional problems with leaking urine; Figure 3). The results are analysed with regression models [28, 29].

The main advantage of DCEs over the SG and TTO is that they allow the simultaneous assessment of multiple attributes rather than a dichotomous choice between one attribute and survival [30]. Hence, DCEs recognise that individuals may value many more attributes of treatment than just QOL and survival or that several aspects of QOL are relevant (such as urinary, bowel, and sexual function in treatment of localised prostate cancer). DCEs are relatively simple because preferences are inferred from a series of stated choices between options rather than explicitly identified by respondents (as in the SG and TTO), and respondents are not required to quantify their strength of preference for any treatment [31]. Despite this, DCEs may be cognitively demanding because respondents need to make simultaneous comparisons of multiple attributes and levels of attributes, before they make their choice. Hence, the number of choices, attributes, and levels must be weighed against the cognitive burden they place on respondents [32].

DCEs were used by King et al. [33] to determine patients’ preferences for treatments of localised prostate cancer. Patients chose between paired hypothetical scenarios to determine the tolerability of side-effects and the survival gains needed to make these treatments and their side-effects worthwhile. Each scenario included life expectancy and one of the three levels of seven different side-effects (impotence, libido, urinary leakage, urinary blockage, bowel symptoms, fatigue, and hormonal symptoms). The findings indicated that the least tolerable side-effects were urinary dysfunction and bowel symptoms followed by hormonal symptoms and fatigue. Severe sexual dysfunction was less troublesome than expected, with similar tolerability to mild urinary and bowel symptoms. The average survival gains needed to make treatment worthwhile varied over a wide range from an extra 4 months (for chronic severe erectile dysfunction, a common side-effect of androgen deprivation therapy) to an extra 28 months (for chronic severe urinary leakage, experienced by about one in five men following radical prostatectomy).

multi-attribute utility instrument
MAUIs may be used to assess preferences for health economic evaluations. Economic evaluations that compare the incremental costs of a treatment to its incremental effects (by dividing the costs by the effects to produce a cost per effect) are called cost-effectiveness analyses. Preferences are required for a specific kind of cost-effectiveness analyses called cost–utility analyses, where the effects of a treatment are measured in terms of quality-adjusted life years (QALY). QALYs are a measure of quantity and QOL that are calculated by summing the number of years in each health state multiplied by its utility. One year of perfect health is equivalent to 1 QALY, immediate

<table>
<thead>
<tr>
<th>Option A</th>
<th>With this treatment option you will experience the following:</th>
</tr>
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<tbody>
<tr>
<td>Never able to achieve an erection when you want one</td>
<td></td>
</tr>
<tr>
<td>Less sexual desire</td>
<td></td>
</tr>
<tr>
<td>Severe problems with leaking urine (no urinary control whatsoever)</td>
<td></td>
</tr>
<tr>
<td>Some problems with urine blockage (have a weak urine stream but get some relief or comfort afterwards)</td>
<td></td>
</tr>
<tr>
<td>No bowel problems</td>
<td></td>
</tr>
<tr>
<td>Severe tiredness and loss of energy</td>
<td></td>
</tr>
<tr>
<td>Severe hot flushes and moodiness</td>
<td></td>
</tr>
<tr>
<td>Most people who have this option live between 3 and 21 years, but on average for 12 years</td>
<td></td>
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<table>
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<tr>
<th>Option B</th>
<th>With this treatment option you will experience the following:</th>
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<tbody>
<tr>
<td>No problems achieving an erection when you want one</td>
<td></td>
</tr>
<tr>
<td>Less sexual desire</td>
<td></td>
</tr>
<tr>
<td>Occasional problems with leaking urine</td>
<td></td>
</tr>
<tr>
<td>Some problems with urine blockage (have a weak urine stream but get some relief or comfort afterwards)</td>
<td></td>
</tr>
<tr>
<td>Occasional loose bowel movements with discomfort/pain</td>
<td></td>
</tr>
<tr>
<td>Some tiredness and loss of energy</td>
<td></td>
</tr>
<tr>
<td>No hot flushes or moodiness</td>
<td></td>
</tr>
<tr>
<td>Most people who have this option live between 3 and 8 years, but on average for 4 years</td>
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</tbody>
</table>

Would you choose option A or B?

Option A........ ✔ ............... OR Option B.................

Figure 3. Example of a pair of hypothetical scenarios in a discrete choice experiment [33].
Patients completed the HUI3 at baseline and throughout the study to rate eight attributes of their HRQL. Using these responses, an overall utility score was determined for each patient using values previously obtained from the general Canadian population, and an average utility score was then determined for each arm of the trial. These utility scores were combined with survival data from the trial to calculate the number of QALYs gained by using cetuximab, and this was then combined with the estimated increment in direct medical costs to determine the cost-effectiveness of cetuximab. The cost-effectiveness of cetuximab was high (~$300 000 per QALY gained) but lower for patients with wild-type K-ras type tumours (~$200 000 per QALY gained). From a health policy perspective, these ratios indicated that funding cetuximab for patients with wild-type K-ras mutations was at the upper bounds of what might be considered to be cost effective.

**discussion**

whose perspective for preference assessment?

An important methodological issue for preference assessment is whose preferences should be assessed: those of patients, health professionals, or lay people. Patients with cancer will generally assign the highest utilities for a given health state, followed by health professionals, and then lay people [43–46]. The optimal perspective is dependent on the intended purpose of the preference assessment and the viewpoint from which the results will be interpreted and applied.

For clinical decisions, the perspective of patients is paramount. Patients who have experienced a cancer treatment will generally have higher utilities (for the health states) and stronger preferences (for the treatments) than patients who are treatment naive [47, 48]. The perspective of health professionals is relevant to better understand how any differences in preferences between patients and health professionals may influence advice, discussions, and decisions about cancer treatments. The perspective of lay people provides insight into how these treatments and benefits are viewed by

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**Figure 4.** Use of a MAUI to determine patients’ preferences for a cost–utility analysis of a cancer treatment. HRQL, health-related quality of life; HUI3, Health Utility Index Mark 3; MAUI, multi-attribute utility instrument; RCT, randomised controlled trial; QALY, quality-adjusted life years.
the wider community and how preferences can change when a person becomes a patient.

For health policy decisions, there is ongoing debate as to whether the perspective of patients or lay people (those of the community, also called ‘societal preferences’) should be used. Societal preferences are recommended for health economic analyses [49–51] because the goal of economic evaluation is to determine the optimal allocation of a society’s health resources to maximise its health [23, 52]. However, the use of societal preferences can lead to claims of discrimination because health states associated with cancer and other diseases are typically valued lower by lay people than by those affected.

**recommendations for methods for preference assessment**

The optimal method of preference assessment depends on its intended purpose. Simple ranking or rating, SG, TTO, and DCE are best suited to clinical decisions about patient management, whereas the MAUI is best suited to health policy decisions about the allocation of resources.

For clinical decisions, if the problem concerns a treatment that has a risk of immediate death versus prolonged survival in perfect health as its most likely outcomes, then the SG is probably the most appropriate method (e.g. surgery for a ruptured aortic aneurysm). If the problem concerns a trade-off between improving length of life and temporarily impairing QOL, then the TTO may be more suitable (e.g. adjuvant chemotherapy for early breast cancer). If the cancer treatment has multiple attributes, particularly disparate long-term toxic effects, then a DCE may be the most appropriate method (e.g. surgery for rectal cancer).

**recommendations for future preferences research**

Studies of preference for cancer treatments are most useful where the trade-offs between the benefits and harms are finely balanced, and this is where future research should focus. For example, intraperitoneal chemotherapy for advanced ovarian cancer improves overall survival, but adds the inconvenience of an intraperitoneal access device, the toxic effects of intraperitoneal treatment, and has had variable uptake in clinical practice [53, 54]. Preference studies that determine the survival benefits patients judge necessary to make intraperitoneal chemotherapy worthwhile should help guide decisions about its use and role.

Targeted therapies also provide a focus for future preferences studies due to their unique profile of benefits, harms, inconveniences, and high costs. For example, adjuvant sorafenib in renal cell cancer (as currently being investigated in the SORCE trial) [55] may prove to be an effective adjuvant treatment where there currently is none. A preference study nested within this trial will determine the survival benefits patients judge necessary to make worthwhile the extended duration of treatment (1 or 3 years), toxicity (rash and diarrhoea), and cost (≈$80 000/patient/year).

For health policy decisions, there will be an ever-increasing need for preference assessment in cost–utility analyses of new cancer treatments to better inform the optimal allocation of scarce health resources in the setting of rising health care costs. Such research is relevant worldwide, particularly in jurisdictions where cost–utility analyses are used to determine decisions about coverage and reimbursement for cancer treatments such as in Australia, UK, Canada, and parts of Europe [56–59]. As noted above, randomised clinical trials provide the ideal opportunity for prospectively assessing the cost–utility of new cancer treatments.

In conclusion, preferences for cancer treatments may be determined by various methods, the choice of which depends on whether the primary purpose is to better inform clinical decisions or health policy decisions. Knowledge of patients’ preferences helps patients, clinicians, and policymakers to better tailor decisions about cancer treatments to individuals, subgroups, and populations.

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**references**
