Recognizing Preference Diversity: The Use of Preference Sub-Groups in Cost-Effectiveness Analysis

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ABSTRACT

Societal preferences are typically incorporated into cost-effectiveness analyses (CEA) on the basis of the average health state utilities of a sample of public raters. The cost-effectiveness of a program is then assessed on an ‘all-or-nothing’ basis: the program is declared either cost-effective or not for all patients in clinically homogenous sub-groups. However, this approach fails to recognize variability between individuals in their preferences. In this conceptual paper, we consider how the preferences of the individual can be handled within a societal CEA. The concept of preference sub-group analysis is described and its implications assessed.

Consider, for example, the choice between lumpectomy and mastectomy for a group of women with breast cancer who are homogeneous clinically but heterogeneous in preferences, and assume that lumpectomy is the more costly procedure. If the incremental cost-effectiveness ratio (ICER) for lumpectomy on the basis of the public’s average preferences is considered acceptable, it would seem unreasonable to refuse mastectomy to those patients who would prefer mastectomy, the cheaper treatment. If the ICER of lumpectomy is not considered acceptable, should it be refused to all patients regardless of the strength of preference of those wanting the procedure? We argue that, in this situation, it is important to explore if sub-groups of individuals, from amongst the sample of public raters, exist (characterized by age, marital status etc.) whose preferences are sufficiently different to the average to generate an acceptable ICER.

We address some important practical and conceptual issues of this framework including the implications of the search for sub-groups for the design of valuation studies. The framework has important implications for the practice of CEA and, in particular, for the use of health state valuation systems.
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1. Introduction

Given the multi-dimensional nature of the consequences of health care programs, the principles and practice of preference measurement have been an important theme in the methods literature of economic evaluation [Pliskin et al., 1980; Llewellyn-Thomas et al., 1982; Torrance, 1986; Mehrez and Gafni, 1989; Nord, 1992; Gafni, 1994; O'Brien and Viramontes, 1994; Deverill et al., 1998]. The most frequently used form of economic evaluation in health care is cost-effectiveness analysis (CEA), where preferences typically take the form of health state values or utilities. Typically, these are factored into analyses on the basis of the average preferences of a sample of raters, with little consideration for systematic variation in preferences between individuals. This gives rise to the 'all-or-nothing' approach to economic evaluation which predominates in applied CEA [Sculpher, 1998]; that is, a focus solely on average preferences in deciding whether a program is cost-effective or not.

The all-or-nothing approach to handling preferences in CEA is in contrast to the way that variation in clinical parameters is usually dealt with. In the face of clinical heterogeneity, clinical sub-group analysis seeks to identify clinical and socio-demographic variables which predict clinical outcomes. The purpose of this is to sub-divide patients into those for whom treatment is cost-effective and those for whom it is not. The rationale for clinical sub-group analysis in CEA is that identifying patients for whom a given treatment is most likely to be effective will increase overall efficiency, given the objective of maximizing the health benefits delivered by publicly-funded health care.

This paper argues that a similar efficiency case can be made for formally recognizing in CEA the existence of variation in preferences between individuals. Possible alternatives to the focus on average preferences in CEA have recently been suggested [Nease and Owens, 1994; Sculpher, 1998; Dowie, 1998]. However, these approaches have been developed in a context where preference data are provided by a sample of patients. There are strong arguments for CEA to reflect community preferences when it is being used to help allocate collective resources [Gafni, 1991; Gold et al., 1996].

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1 The term cost-utility analysis is often used when utilities are used within a study's benefit measure. In this paper, cost-effectiveness is used in a generic sense to include this form of analysis.
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In addition to an efficiency argument, a more formal recognition of preference variation in CEA may, in some contexts, avoid conflicts in health care decision making. For example, the trend towards evidence-based medicine and the generation of evidence-based practice guidelines, focusing only on the effectiveness of interventions [Sackett et al, 1996], may show that a treatment is effective for a particular condition. However, the health care system, informed by the results of CEA, may not consider that the treatment’s incremental costs are justified by its additional benefits, and refuse to fund the treatment from collective resources. Despite this, at the level of the doctor-patient encounter, an individual patient may have a strong preference for the more costly and more effective intervention. The absence of cost-effectiveness is not synonymous with a lack of effectiveness, and there is no clinical reason why the patient should be precluded from having the more costly treatment. This causes the doctor’s dilemma of whether to reveal all effective management options to the patient, or only those that the system deems cost-effective. However, not revealing effective management options is likely to be at odds with the clinician’s professional and ethical principles; it is also likely to be in conflict with the stated principles of evidence-based medicine [Sackett et al, 1996].

The argument in this paper is that these tensions are accentuated by the all-or-nothing approach to CEA and its focus on average preferences. For this reason, and to increase overall efficiency, we argue that variation in preferences between individuals should be recognized in CEA, and we further explore the methodological and practical questions that are likely to arise when attempting to do so in the context of the recommended methods of CEA and their underlying assumptions.
2. Preferences in CEA

There is a strong argument that using the values of a representative sample of the community is the most appropriate way of factoring preferences into CEA when the results are used to inform allocation of collective health care resources [Gafni, 1991; Gold et al, 1996]. At a policy level, this is reflected in the recommendations of the US Panel on Cost-Effectiveness of Health and Medicine [Gold et al, 1996], and in guidelines for the economic evaluation of pharmaceuticals in support of applications for public reimbursement [Canadian Coordinating Centre for Health Technology Assessment, 1997]. At the level of applied studies, a greater focus on community preferences in CEA is shown with the increasing use of health state valuation systems such as the Health Utilities Index [Feeny et al, 1995] and the EuroQol (EQ-5D) [Kind, 1996].

The use of community values introduces two challenges to CEA as a tool for decision making, neither of which has yet been fully considered: to aggregate preferences while still reflecting preference variation; and to minimize, when possible, the risk of conflict between the community and patient preferences.

2.1 The current process of aggregation

Whether CEA incorporates the preferences of the community or of some other group, some form of aggregation is necessary to summarize disparate preferences within a given evaluation. Although there are arguments both for the use of the median and the mean to provide the 'representative' preference [Dolan, 1997], inter-personal comparison of preferences is inherently value-laden. Typically, however, aggregation has been through the use of mean values, and this has been the basis of calculating the community tariffs or 'weights' for the health state valuation systems. Considerable variation typically exists in community preferences, however. For example, in a survey of 3395 community raters, the mean value of a health state characterized by severe pain but good levels of health on other domains (the EQ-5D health state 11131) was 0.20; but the standard deviation was 0.60 and the inter-quartile range was -0.33 to 0.72 [Dolan et al, 1996b].

In practice, however, once an average preference has been calculated, there is no consideration of any systematic variation in preferences between raters. This gives rise to the 'all-or-nothing' approach to economic evaluation which predominates in applied CEA [Sculpher, 1998]. The all-or-nothing approach to CEA, where the decision rule is that a program is deemed cost-effective if it dominates its comparator(s) or has an ICER lower than a pre-determined threshold, focuses solely on the average health state values from its sample of raters. The combination
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of the decision rule and the use of average preferences results in a program either being considered 'cost-effective' or 'not cost-effective' for all individuals regardless of the variation between individuals which underlies the average preferences. Sensitivity analysis is sometimes used to assess how robust a study's conclusions are to variation in average health state values, but this is still undertaken within an all-or-nothing framework as it remains the case that average preferences are assumed to apply to everyone.

2.2 The importance of variation in preferences between individuals

To what extent is the all-or-nothing approach to CEA likely to be consistent with the expectations of the community and with the current decision rules guiding a CEA? In the face of the clinical variation which makes treatments effective for some patients and not for others, it would be unlikely that all patients with, for example, stable angina would be expected to have the same treatment. This is reflected in the use of clinical sub-group analysis in CEA, where sub-groups of patients are defined in terms of clinical and socio-demographic characteristics that appear to predict clinical outcomes. Hence, due to clinical variation, a treatment that is considered cost-effective for some patients may not be so for others. For example, in a CEA of alternative interventions for ischaemic heart disease, ICERs were calculated separately according to severity of symptoms, ventricular function and number of diseased vessels [Wong et al., 1990]. Whilst coronary angioplasty was considered the most cost-effective option in patients with severe angina, depressed ventricular function and 2-vessel disease, conservative therapy was considered more cost-effective in patients with mild angina, normal ventricular function and single-vessel disease.

Therefore, assuming the acceptability of a decision rule which compares estimated ICERs with a maximum that the decision maker is willing to pay, the ICER for a treatment may come below the threshold for some individuals but rise above it for others, for reasons of systematic variability in effectiveness between individuals. In this context, decision making is not bound by the average clinical outcome, because it is possible to increase the overall benefits achieved by finite collective resources by recognizing that treatments are more effective for some sub-groups of patients than others.

Just as there exists variation between individuals in risk characteristics predictive of clinical outcome, there is inter-personal variation in preferences regarding the outcomes and process characteristics of interventions. Would not the community expect this preference variation also to be taken into account in health service decision making? The same efficiency argument that can be used to support the recognition of clinical variation in CEA can be used to
justify the reflection of preference variation. The overall benefit an individual derives from health care is a function both of its process and outcome attributes, and the individual’s preferences regarding those characteristics. In principle, therefore, reflecting preference variation in CEA, and the policy decisions emanating from such studies, offers a way of increasing the overall benefit achieved from collective health care resources. The practical problem is how to segment the community according to individual preferences, to incorporate this into applied CEAs and to operationalize the results in clinical decision making.

The current process of aggregating community preferences involves the search for the figurative ‘representative individual’ whose preferences should count in CEA. However, the large variation in preferences between individuals means that such an individual could never exist. In principle, if the preferences of each and every individual in the community could be elicited, the optimal segmentation of the community could be achieved. Applying the existing decision rule, the ICER of a given intervention could be calculated for each individual according to their specific preferences and, depending on how it compared with the threshold ICER, that treatment could be defined as cost-effective or not for each person prior to their becoming a patient. However, this process is not feasible and some form of sampling is necessary to elicit community preferences.

The need to sample does not, however, mean that preference variation should be ignored. As for variation in predictors of clinical outcome, heterogeneity in preferences can, in principle, be translated into sub-group analysis. For example, in the choice between lumpectomy and mastectomy for the treatment of breast cancer, individuals might attach different levels of importance to avoiding the course of radiation therapy that accompanies lumpectomy, compared to the cosmetic advantages of retaining the breast. In the context of a CEA of lumpectomy versus mastectomy, the use of the average preferences of all raters might result in mastectomy generating similar benefits to lumpectomy and, given an additional cost for lumpectomy, in mastectomy being deemed the more cost-effective option. However, there may exist a sub-group of raters whose preferences are sufficiently different to the whole-group average to generate greater benefits for lumpectomy and to produce an ICER for lumpectomy which is below the decision maker’s maximum. Is the use of average community values the best way of representing the heterogeneity of individuals’ preferences? There would seem to be a strong case to adopt preference sub-group analysis in CEA as a way of further refining the results and policy implications of studies.
3. Preference conflicts between community raters and the individual patient

The use of sub-group analysis in CEA may also help to avoid, in some situations, conflict between the preferences of community raters and those of the individual patient. Recent trends in health care decision making have generated a paradox: on one hand there is a recognized need for CEA to help the system achieve greatest benefits from limited resources based on community preferences; but on the other hand, there is an increasing emphasis on empowering the patient to take part in the decision making process with their doctor at the clinical level [Coulter, 1997; Charles et al, 1997; Gafni et al, 1998; Entwistle et al, 1998]. For example, by providing improved information about treatment options, offering decision aids to patients and a greater role for the patient in the decision making process, it is hoped that treatment decisions more clearly reflect the preferences of the individual patient [Gafni et al, 1998].

If it is considered appropriate for the clinician to inform the patient about all interventions which are deemed to be effective, how can a potential conflict be averted when an individual patient expresses a strong preference for an effective but non-cost-effective (based on the use of average preferences) treatment? This conflict can arise in two different ways that are discussed below. The case of mastectomy versus lumpectomy offers a useful practical example.

3.1 Strong patient preference for less costly intervention

Assume lumpectomy is the more costly procedure but also that the treatment generates greater benefit on the basis of the average preferences of a representative sample of community raters. Further assume that the ICER of lumpectomy relative to mastectomy is less than a maximum threshold and is thus considered good value for money by a given decision maker, and local clinicians are informed that they can provide lumpectomies to clinically appropriate women. In this context, should the clinician only offer lumpectomies? How should a woman be managed whose own treatment-related preferences are markedly different to the community average and strongly in favor of mastectomy?

Given that the results of the CEA do not imply that mastectomy is not effective, it would surely be unreasonable (even from a pure resource allocation perspective) to withhold the cheaper therapy from someone who strongly prefers it. In this situation, it would seem acceptable to recognize the preferences of the individual patient in the clinical decision making process.
3.2 Strong patient preference for the more costly intervention

Let the differential cost and benefit of lumpectomy and mastectomy remain as before, but now assume that the decision maker considers the ICER of lumpectomy relative to mastectomy to be too high. In this context, clinicians would typically be instructed that, for all women with the clinical characteristics considered in the CEA, mastectomy is more cost-effective. However, assuming the doctor feels compelled to explain both procedures to the patient, given that both are clinically effective, how should the system react to a woman whose preferences are markedly different to the average of the community raters, and who would prefer lumpectomy, the more costly intervention?

This conflict can be addressed in different ways. In some health care systems, it will be acceptable to allow the patient to pay for their preferred treatment themselves; in others this would be considered inappropriate. This decision is a political one, depending on the ethical and equity objectives that underlie the health care system.

An alternative approach, that may help avoid this conflict in some situations, is to explore whether preference sub-groups from amongst community raters exist and to use this in the CEA. In the example introduced above, the use of average community preferences generated greater benefits for lumpectomy, but not sufficient to produce an ICER which is acceptable to the decision maker (i.e. it falls above the maximum ICER). However, there may exist a sub-group (or sub-groups) of community raters whose average preferences, when incorporated into the CEA instead of the whole-group average, would increase the gain in benefits from lumpectomy sufficiently to generate an ICER that is acceptable to decision makers. For example, there may be a large proportion of community raters below the age of 40 years who, in imagining experiencing health states related to breast cancer and its treatment, feel very strongly that their health-related quality of life would suffer if they were to lose their breast, and this perception could be reflected in significantly different values for health states compared to the average of all community raters.

The existence of a preference sub-group in the community whose health state values could alter the results of a study from those based on average values, suggests that it may be inappropriate to adopt an all-or nothing approach and to focus only on average preferences in determining the policy implications of the CEA results. Rather, there would seem to be a case for recognizing that the community is willing to offer funding for either alternative for those patients who have similar characteristics to individuals in the preference sub-group in the community. In the breast cancer example above, if the preference sub-group in the community were
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characterized by their age (e.g. younger than 40 years), then patients in that age group who prefer lumpectomy could receive that treatment with collective funding despite mastectomy being more cost-effective on the basis of average community preferences.

It should be emphasized that the logic of preference sub-group analysis does not imply that some sub-groups should not be offered a choice of therapy when it is available to everyone on the basis of average preferences. Consider the situation where the ICER of lumpectomy, on the basis of average community preferences, falls below a decision maker’s maximum and this form of management is, therefore, deemed more cost-effective and is offered to all women with appropriate clinical characteristics. There may be a sub-group of raters, however, whose preferences are sufficiently different to the average to take their sub-group-specific ICER for lumpectomy above the threshold. However, to offer a choice of mastectomy and lumpectomy to all women except those sharing similar characteristics to the preference sub-group would be inappropriate. This is because preference heterogeneity remains in sub-groups, so averaging is still required. Removing choice from a sub-group would ignore the fact that a proportion of its members may have preferences for lumpectomy at least as strong as the whole-sample average. Those members of the sub-group who would prefer mastectomy - and whose preferences are largely responsible for driving the sub-group-specific ICER for lumpectomy below the maximum threshold - are not forced to undergo lumpectomy: they could reasonably be given their preferred intervention because it is the cheaper alternative.
4. The practical implications of preference sub-groups

A range of practical issues is raised by the concept of preference sub-groups amongst community raters and their implications for CEA.

4.1 When does a sub-group become a formal preference sub-group?

An important practical issue relates to when a group of individuals within the community sample would be formally defined as a preference sub-group that could trigger preference-based treatment allocation amongst patients. Two factors are important here. The first is that the preferences of this group of individuals would have to make a difference. That is, when these preferences are incorporated into a CEA, they need to alter the ICER sufficiently to make a difference to the policy decision: to take the ICER below the decision maker’s maximum when it was above that threshold on the basis of whole-group average preferences.

The second important practical factor in defining a group of community raters as a formal preference sub-group is whether they can be identified. In other words, does the group share characteristics other than the strength and direction of their preferences? As mentioned above, if the preferences of all members of the community could be elicited, it would not be necessary to sample the community or to seek out preference sub-groups. However, given that it is not feasible to elicit everyone’s preferences, there needs to be a practical way of characterizing which types of individual are likely to have preferences which differ from the average so that this can be operationalized in routine practice with patients (e.g. use of socio-demographic characteristics).

4.2 Identifying preference sub-groups

In the same way as clinical sub-group analysis, the process of identifying preference sub-groups from amongst community raters can be undertaken prospectively or retrospectively. If a new survey of community raters is being undertaken, it would be possible formally to stratify the sample to reflect the characteristics of individuals that might be expected to affect their preferences. For example, there may be an a priori case to suggest that, in terms of preferences, younger people would differ from older people and females would differ from males. The use of stratification would represent a major shift in the methods of community valuation surveys and would probably increase the necessary sample sizes.

The other way of identifying preference sub-groups is retrospectively, using data from earlier surveys of community preferences. Given the potential statistical dangers of finding
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spurious associations between the characteristics of raters and their preferences, it would be necessary to generate plausible hypotheses for sub-group characteristics prior to data analysis. Although this sort of analysis has been undertaken on existing survey data [Dolan et al, 1996a], the range of socio-demographic data collected in these studies has been limited and would probably confine preference-sub group analysis to age and gender. Furthermore, as with the retrospective analysis of clinical data, it is often not statistically possible to identify patient characteristics predictive of preference sub-groups because of a small sample size within a study which was not designed for that task.

4.3 Preference measurement

A further important practical issue, regarding the movement away from all-or-nothing economic evaluation towards the recognition of variation in preferences amongst individuals, is how preferences are measured in CEA. So far in this paper it has been assumed that the measurement of community preferences for use in CEA provides an accurate reflection of the preferences of community raters as they imagine the health states and attributes described to them.

Although several benefit measures have been suggested for use in CEA including, the risk-neutral and risk-adjusted quality-adjusted life-year (QALY) [Pliskin et al, 1980], healthy-years equivalent [Mehrez and Gafni, 1989] and saved young life [Nord, 1992], in practice CEAs typically use standard QALYs (i.e. risk-neutral QALYs) as their measure of benefit. However, the assumptions necessary to link the QALY to individual preferences are probably unrealistic [Pliskin et al, 1980; Loomes and McKenzie, 1989; Gafni and Birch, 1995]. This limitation may be less critical in the context of an all-or-nothing approach to CEA if the QALY is considered a reasonable normative basis for decision making. However, the premise of preference-sub group analysis is that an outcome may be valued differently by different people and that, where possible, this should be recognized within a CEA and the decisions emanating from it. Therefore, the normative basis for the choice of benefit measure in CEA is not sufficient if preference-based sub-group analysis is to be adopted.
5. Discussion

In the face of clinical variation, it is recognized that CEA needs to reflect the existence of clinical sub-groups. Hence it may not be deemed cost-effective to allocate patients who share the same primary diagnosis to the same treatment: to do so would be inefficient and probably considered unethical. The same case can be made for recognizing preference variation between individuals. This argument is strengthened if community preferences reflect caring externalities. In particular, instead of using individuals' rating of health attributes when imagining they were experiencing them, preference studies could also take account of individuals' valuation of other people being given their preferred treatment. For example, this information could be used to conclude that, although a particular person would prefer mastectomy for themselves, they also value the opportunity for others to have lumpectomy if they prefer it. In some contexts, this caring externality may be sufficient to justify the additional cost of treatments that are deemed not to be cost-effective on the basis of individualistic ('selfish') preferences, even with preference sub-group analysis. However, as yet, no methods have been developed to reflect caring externalities in CEA [Gafni and Birch, 1995].

Are any specific equity issues raised by the concept of preference sub-group analysis? It may be the case, for example, that lumpectomy is considered to have too high an ICER on the basis of average preferences, but a sub-group of public raters is identified whose preferences are such that their sub-group-specific ICER is acceptable. If the preference sub-group was characterized as receiving higher than average income, would it be acceptable to operationalise this preference sub-group at the clinical level? In considering this issue, the first point to note is that the preferences of wealthy individuals could, in principle, be dominant in determining the more cost-effective management on the basis of an all-or-nothing approach. If all wealthy individuals in the sample of public raters and, say, 10% of the poor had strong preferences for lumpectomy, it may be sufficient for lumpectomy to have an acceptable ICER on the basis of average preferences, despite the fact that most poor individuals had a preference, albeit perhaps a weak one, for mastectomy. If variation in preferences can lead to equity concerns, these may apply regardless of whether preference-based sub-group analysis is undertaken.

A second point is that, if individuals in a preference sub-group are identified on the basis of characteristics which would raise equity concerns should they be operationalised as a means of offering additional choice in health care, it is always open to the decision maker to ignore the existence of that particular sub-group. In the case of the breast cancer example above, the decision maker who is worried about the equity implications of preference sub-group analysis
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could decide that wealth is not a valid basis for distinguishing between individuals. However, any process which overrides the preferences of particular groups of individuals - whether within an all-or-nothing CEA or in the use of preference sub-groups - needs to set down clear principles in advance and not react in an ad hoc fashion to the results of specific studies.

In principle, there is close symmetry in the methods of clinical and preference sub-group analysis. If it were ever possible to test each new intervention in all individuals prior to their becoming sick, perfect segmentation of the population into those for whom a treatment is effective and those for whom it is not would be possible, and the most effective treatment on an individual-patient basis would always be known in advance. Similarly, if the preferences of all individuals could be elicited prior to their becoming patients, it would be possible to maximize overall benefits from limited collective resources by reflecting preferences in treatment allocation.

Neither is realistic, and the aim of both clinical and preference sub-group analysis is to make the best possible use of data generated by research - controlled trials and observational studies in the case of clinical outcomes; surveys of the community for preferences. In both cases, the task is to identify sub-groups of individuals which differ in terms of the effectiveness of interventions, for clinical sub-group analysis, and of preferences for preference sub-group analysis. However, in order for this research activity to provide useful and practical information for routine health care decision making, it must be possible to identify individuals within sub-groups at an operational level. That is, there needs to be some way of characterizing members of sub-groups in research in a way that can be used to assist actual policy decisions.

In terms of both clinical characteristics and preferences, the process of identifying sub-groups is not perfect, and often it will not be possible to explain variation in a way that can be operationalized. Moreover, unless there is a perfect correlation between individuals’ clinical outcome (or preferences) and their characteristics, some form of averaging will inevitably be required within sub-groups. Other practical issues with both forms of sub-group analysis need to be considered. For example, an implication of recognizing either clinical or preference variation in CEA may be that a specific centre may have to make available two different interventions, whereas if CEA was undertaken only on the basis of average clinical outcomes or community preferences, only one would be needed. This may have cost implications for the centre in terms, for example, of staff training and the lower utilization of fixed assets.
It should be recognized that incorporating preference sub-group analysis into CEA will not be easy practically. Given the strength of the argument for the use of preference sub-groups at a conceptual level, however, it is important to move in the right direction in applied CEA. Some practical changes in CEA present themselves that could be put into effect relatively easily. Firstly, the practice of using preferences from groups such as clinicians and nurses as ‘surrogates’ for community raters runs contrary to the logic of preference sub-group analysis because, although their preferences might be similar on average, the sub-group variation is unlikely to be the same in a community sample and a surrogate sample. Secondly, in CEAs where study-specific preferences are elicited from a new sample of individuals rather than using existing data from valuation systems, thought should be given to how preferences might plausibly differ by rater characteristic, and this should be reflected in sampling methods. Thirdly, the same logic applies to the design of future valuation studies to elicit preferences for valuation systems (e.g. HUI and EQ-5D): samples should be stratified by characteristics that are thought likely to influence preferences and additional socio-demographic data collected on raters.

Just as the practical implications of sub-group analysis do not preclude its use in CEA to reflect some clinical variation, so too they should not be used as an argument to ignore heterogeneity in preferences. If applied CEA is able to move further towards reflecting all the factors that lead to variation between individuals in the benefit they derive from health care interventions, there is likely to be an increase in the overall efficiency of the resource allocation process informed by those studies, as well as greater acceptance of the methods of CEA on the part of clinical decision makers and patients.
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CHEPA conferences are held annually in the third week of May. The two-day conferences are designed to bring
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