Uncertainty, risk and value of information when allocating resources within and between multiple healthcare programmes

Zaid Chalabi, Department of Public Health and Policy, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E 7HT

David Epstein[*] and Karl Claxton, Centre for Health Economics, University of York, York YO10 5DD

[*] Author for correspondence. Email: dme2@york.ac.uk

Abstract

Aims

Methods have been developed to allocate resources within and between multiple healthcare programmes when there is an exogenous budget and the parameters are known with certainty. Furthermore, methods are also available to calculate the optimal allocation of resources within a single healthcare programme when the parameters are uncertain and there is an exogenous threshold incremental cost-effectiveness ratio (ICER).

The aim of this paper is to determine the optimal resource allocation within and between multiple healthcare programmes when there is an exogenous fixed budget and the parameters are uncertain.

Development

Existing work in this area has been promising but the solutions have required an arbitrary specification of additional variables, and have not incorporated both uncertainty and variability.

We propose a two stage stochastic programming solution. The first stage is to maximise the expectation of the overall benefit (QALYs) whilst ensuring that the expected cost is below the budget constraint. The second stage re-allocates resources such that the budget is now satisfied strictly for every possible permutation of the uncertain parameters in the model and deviation of the expected health benefit from the health benefit from the first stage is minimised.

Conclusions

We demonstrate, using an example, how the method can be used to allocate resources consistently with an objective to maximise health subject to a fixed budget when there is variability and parameter uncertainty. We calculate the expected value of perfect

information for this system and show how the interpretation differs from the case where there is an exogenous ICER.

1. Introduction

The objective of a decision maker is to maximise the health of a population given a fixed budget. If costs and benefits are known precisely, then deterministic mathematical programming methods are available to allocate resources optimally to treatment programmes [1 2]. If parameters are uncertain, then for any allocation decision, there will be a probability that the budget will be exceeded, and decision rules must take account of the opportunity costs arising in these cases.

This paper reviews recent work in this area, and discusses the strengths and weaknesses of the solutions proposed. We propose a novel formulation of a stochastic mathematical programme. We show how it meets the objective, without requiring the decision maker to specify arbitrary additional parameters. It is irrelevant to the allocation problem whether randomness in costs and health benefits arises from variability or uncertainty and we show how the expected value of perfect information can be calculated for the whole system.

2. Decision making under variability and uncertainty

The distinction between *variability* and *uncertainty* in the model parameters should be made clear. This distinction is not made explicit in some of the health economics literature because they often deal directly with costs and benefits rather than with the underpinning model parameters (such as odds ratios or log odds ratios) which generate the costs and benefits. *Variability* in model parameters represents the irreducible heterogeneity in the parameter values whereas the *uncertainty* in model parameters represents the "lack of knowledge" about the distribution of the parameter values which is reducible with additional information [3].

Uncertainty arises because sampling is imperfect, and can be reduced by acquiring further information. Variability arises because patient outcomes in a population will differ, and is irreducible. Consequently, even if the probabilities of the health outcomes are known with certainty, costs and health benefits for the population will be random variables. A standard cost effectiveness analysis (that is, where there is no explicit budget constraint) identifies the strategy which maximises net benefits from a

set of mutually exclusive strategies for a given population. Net benefit is defined with respect to a given threshold willingness to pay for additional health benefits, and the budget is determined implicitly. Because there is no fixed budget, the risk-neutral decision maker need not be concerned with variability, and can define net benefits in terms of mean costs and benefits, where the expectation is taken over first-order uncertainty.

If the budget is fixed, then risk neutral decision makers should aim to allocate resources to maximise expected health benefits subject to expected costs being less than or equal to the budget. Costs and benefits will be random variables arising from both variability and uncertainty. Since costs are random variables, for nearly any *ex ante* decision about the allocation of resources, there will be a probability that the budget will be exceeded. If, *ex post*, the budget is exceeded, then there will be a loss of benefits as less expensive programmes are substituted for more expensive ones (or additional funding diverted from other sectors of the economy). To allocate resources optimally, *ex ante* decision makers must consider all potential realisations of costs and health benefits, and identify which programmes will be adjusted in order to minimise the expected loss of health benefits. It is irrelevant to this allocation problem whether randomness in costs and health benefits arises from variability or uncertainty

The question is then: What decision rules should be employed in order to meet the objective to maximise total health subject to a budget constraint? Work in this field has been promising and alternative formulations of the decision framework have been proposed. How can we decide between these alternatives? The decision framework should satisfy a number of conditions. Firstly, it should not require the decision maker to specify arbitrary parameters, that is, which are not measurable in the "real world". Measurable parameters include unit costs of treatments, probabilities of events, and the budget and other constraints. Secondly, the decision framework must guarantee at least one feasible solution. Thirdly, the framework should consider randomness arising from uncertainty and variability.

Sendi *et al* suggested a stochastic programming solution [4]. Al *et al* have suggested a similar stochastic programming solution which allows the decision maker to specify other utility functions than risk neutrality [5]. Sendi *et al* assumed costs and benefits

were random variables with bivariate parametric distributions. They maximise the expected health benefits subject to the probability of exceeding the budget being less than an arbitrary set value, say 0.05. To take account of the opportunity costs of the additional resource requirements if the budget is exceeded, they include a penalty in the objective function. When the budget is exceeded, the health outcomes lost by deriving resources from other sectors is modelled by multiplying expenditure in excess of the budget by a parameter representing the shadow price.

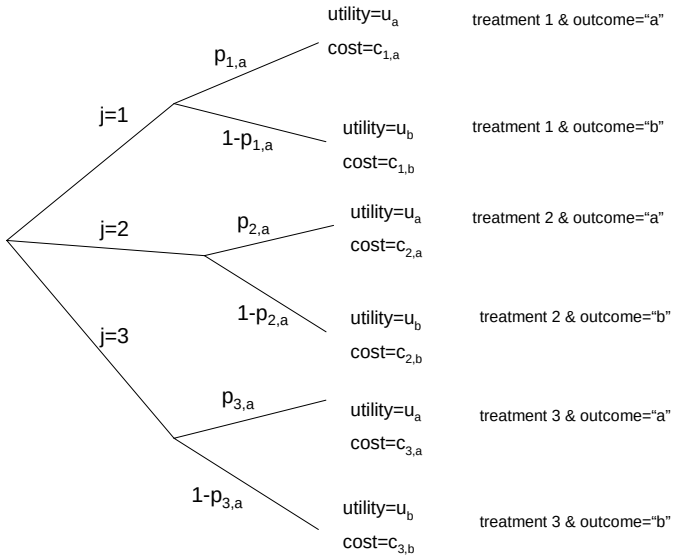
The frameworks of Sendi *et al* and Al *et al* do account for the opportunity costs in terms of lost benefits if the budget is exceeded. However, they require the decision maker to specify two arbitrary parameters. The maximum probability that the budget should be exceeded is arbitrary because it does not correspond with any measurable quantity in the real world. The marginal shadow price of additional budget is arbitrary because it should be endogenous to the problem, that is, once the budget has been specified the shadow price of additional expenditure should be determined within the model.

They also do not distinguish between variability and uncertainty. This is because they consider uncertainty to be a property of costs and benefits however costs and benefits can instead be considered functions of more fundamental parameters. Furthermore they do not incorporate value of information analysis within their frameworks.

3. Illustrative model

To present the new framework we propose an illustrative model. Consider first a basic decision tree model for one healthcare programme ($k = 1$) and one population group ($i = 1$). The structure of the model with three treatments ($j = 1 \ldots 3$) is represented by the following decision tree:

Basic Model



The three treatments are $j=1$ (current treatment), $j=2$ and $j=3$ (new treatments). A patient can be allocated only one of the three treatments. We assume two health outcomes: "*a*" and "*b*": "*a*" could represent a disease state and "*b*" good health.

The above model has the following parameters:

- $p_{1,a}$, $p_{2,a}$ and $p_{3,a}$ are respectively the probabilities of outcome "*a*" conditional on treatments 1, 2 and 3.
- $p_{1,b}$, $p_{2,b}$ and $p_{3,b}$ are respectively the probabilities of outcome "*b*" conditional on treatments 1, 2 and 3.
- u_a and u_b are respectively the utilities of health states "*a*" and "*b*". We assume for simplicity that utilities are independent of treatments
- $c_{1,a}, c_{2,a}$ and $c_{3,a}$ are respectively the unit costs associated with state "*a*" under treatments 1, 2 and 3.
- $c_{1,b}, c_{2,b}$ and $c_{3,b}$ are respectively the unit costs associated with state "*b*" under treatments 1, 2 and 3.

We now extend the above model structure to three healthcare programmes and three population groups per healthcare programme. We maintain three treatments per

healthcare programme. We also assume that there are two health states (binary outcomes) per healthcare programme which we label for convenience as "*a*" and "*b*". The actual health outcomes could differ between healthcare programmes.

There are several sets of model parameters:

- $\left(u_{ik,a}, i=1\ldots3, k=1\ldots3\right)$ are the utilities associated with the outcome "*a*". $u_{ik,a}$ is the utility of outcome *a* for population group *i* in healthcare programme *k*
- $\left(u_{ik,b}, i=1\ldots3, k=1\ldots3\right)$ are the utilities associated with outcome "*b*". $u_{ik,b}$ is the utility of outcome *b* for population group *i* in healthcare programme *k*
- $\left(c_{ijk,a}, i=1\ldots3,\ j=1\ldots3, k=1\ldots3\right)$ are the unit costs associated with outcome "*a*". $c_{ijk,a}$ is the cost associated with treatment *j* and outcome "*a*" for population group *i* in healthcare programme *k*.
- $\left(c_{ijk,b}, i=1\ldots3,\ j=1\ldots3, k=1\ldots3\right)$ are the unit costs associated with outcome "*b*". $c_{ijk,b}$ is the cost associated with treatment *j* and outcome *b* for population group *i* in healthcare programme *k*.
- $\left(p_{ijk,a}, i=1\ldots3,\ j=1\ldots3, k=1\ldots3\right)$ are the probabilities of health outcome "*a*". $p_{ijk,a}$ is the probability of occurrence of health outcome "*a*" in population group *i* in healthcare programme *k* conditional on treatment *j*.
- $\left(p_{ijk,b}, i=1\ldots3,\ j=1\ldots3, k=1\ldots3\right)$ are the probabilities of health outcome "*b*". $p_{ijk,b}$ is the probability of occurrence of health outcome "*b*" in population group *i* in healthcare programme *k* conditional on treatment *j*.

Assuming without loss of generality that there are no uncertainties in the utilities and unit costs, the set of uncertain parameters (denoted by Φ) are

$$\Phi = \left(\left(p_{ijk,a}, p_{ijk,b}\right), i=1\ldots3,\ j=1\ldots3, k=1\ldots3\right) \quad (1)$$

3.1 Model outputs and decision variables

The model outputs are the total benefit and cost. The total benefit is:

$$B(X,\Phi)=\sum_{k=1}^{3}\sum_{j=1}^{3}\sum_{i=1}^{3}\left(n_{ijk,a}\times u_a+n_{ijk,b}\times u_b\right)\times x_{ijk} \quad (2)$$

where

- $n_{ijk,a}$ is the number of patients in population group *i* and healthcare programme *k* that end up in health state "*a*" when treated with treatment *j*
- $n_{ijk,b}$ is the number of patients in population group *i* and healthcare programme *k* that end up in health state "*b*" when treated with treatment *j*
- x_{ijk} is the proportion of population group *i* in healthcare programme *k* that are allocated treatment *j* .

In Equation (2), x_{ijk} is a decision variable. The set of all the decision variables is given by:

$$X=\left(x_{ijk};i=1\ldots3,\ j=1\ldots3,k=1\ldots3\right) \quad (3)$$

$n_{ijk,a}$ and $n_{ijk,b}$ are random variables. Each is described by a Binomial distribution (Γ):

$$n_{ijk,a}\sim\Gamma\left(n_{ik},\ p_{ijk,a}\right) \quad (4)$$

$$n_{ijk,b}\sim\Gamma\left(n_{ik},1-p_{ijk,a}\right) \quad (5)$$

where

- n_{ik} (a fixed quantity) is the index of the Binomial distribution Γ. It is the total number of patients in population group *i* and healthcare programme *k*, $n_{ik}=n_{ik,a}+n_{ik,b}$.

- $p_{ijk,a}$ is the "success probability" of the Binomial distribution and is (as defined above) the probability of health outcome "*a*" conditional on treatment *j*.

Denote the set of health outcomes by

$$\Delta = \left(n_{ijk,a}, i = 1 \cdots 3,\ j = 1 \cdots 3, k = 1 \ldots 3\right) \tag{6}$$

B (total health benefit) in Equation (2) is a random variable. It a weighted sum of random variables generated by Binomial distributions. Its expected value with respect to *variability* (denoted by E_{Δ}) is

$$E_{\Delta}(X, B) = \sum_{k=1}^{3}\sum_{j=1}^{3}\sum_{i=1}^{3} n_{ik} \times x_{ijk} \times \left(p_{ijk,a} \times u_{ik,a} + \left(1 - p_{ijk,a}\right) \times u_{ik,b}\right) \tag{7}$$

Similarly the total cost is given by

$$C(X, \Phi) = \sum_{k=1}^{3}\sum_{j=1}^{3}\sum_{i=1}^{3} \left(n_{ijk,a} \times c_{ijk,a} + n_{ijk,b} \times c_{ijk,b}\right) \times x_{ijk} \tag{8}$$

Its expected value (with respect to variability) is

$$E_{\Delta}(X, C) = \sum_{k=1}^{3}\sum_{j=1}^{3}\sum_{i=1}^{3} n_{ik} \times x_{ijk} \times \left(p_{ijk,a} \times c_{ijk,a} + \left(1 - p_{ijk,a}\right) \times c_{ijk,b}\right) \tag{9}$$

The total set of random parameters (Z) comprises the set of uncertain parameters and the set of health outcomes, i.e.

$$Z = \Phi \cup \Delta = \left(p_{ijk,a},\ p_{ujk,b}, n_{ijk,a}, n_{ijk,b}; i = 1 \ldots 3,\ j = 1 \ldots 3, k = 1 \cdots 3\right) \tag{10}$$

Of course, the distributions of Δ depend on those of Φ.

3.2 Model constraints

Because each patient in population group *i* and healthcare programme *k* can be allocated only one of the three treatments available, then

$$\sum_{j=1}^{3} x_{ijk} = 1 \qquad \forall i = 1\ldots 3, k = 1\ldots 3 \tag{11}$$

Assume initially that there is a simple budget constraint which is that the total budget should not exceed Ψ (a fixed quantity, defined *a priori*).

4. Expected Value of Perfect Information

EVPI is defined usually in terms of a single healthcare programme [6]. It sets an upper bound on the return on doing further research to resolve *uncertainties* in model parameters as investment in further research makes sense if EVPI exceeds the cost of doing the research. In the classical EVPI setting with no explicit budget constraint, decisions refer to mutually exclusive treatments and the expression for EVPI requires the value of the societal willingness to pay per Quality Adjusted Life Years (QALY).

In addition to health economics, the literature on EVPI spans also the disciplines of risk analysis and operations research (OR). The stimulation for this work came from the review of the OR papers of Artstein and Wets in relation to stochastic programming and value of information. They formulated value of information analysis within a stochastic programming framework.

The authors use measure and set theory to develop their framework however their framework can also be interpreted using probability theory. Although Artstein [7] introduces chance-constrained stochastic programming problems within the context of value of information, their focus has been on unconstrained stochastic optimization problem formulation [8-11].

Their examples consisted of mainly one-parameter models and they derived analytical expressions for the value of perfect information obtained on the parameter. They

noted that information is being sought on the probability distribution of the parameter and not on the parameter value *per se*. In other words, information is being obtained to reduce 2nd order uncertainty (uncertainty in probability distribution function of the parameter).

They defined the set of all possible probability density functions assigned to the parameter and asserted that perfect information will specify one of them as the true distribution. This set is known as an "information sensor", or the "probability on probabilities". The concept of an information sensor is a generic mathematical descriptor of uncertainty which includes Bayesian and hierarchical models.

Motivated by their approach, we formulated the EVPI for our decision tree model as follows. Recall that EVPI (Ω) is the difference between the expected value (with respect to Φ) of a decision made with perfect information about all parameters ($\Omega_{perfect}$) and a decision made now based on current knowledge (Ω_{now}):

$$\Omega = \Omega_{perfect} - \Omega_{now} \tag{12}$$

Consider first Ω_{now}. We propose a two-stage stochastic programming solution to meet the conditions described above. The first stage is to maximise the expectation of the overall health benefit whilst ensuring that the expected cost is below the budget constraint. This identifies a "target health benefit" the system should aim to achieve. The second stage re-allocates resources such that the budget is now satisfied strictly for every possible permutation of the uncertain parameters in the model and deviation of the expected health benefit from the health benefit from the first stage is minimised. The second stage considers the set of feasible solutions, wherein the budget is satisfied for all possible "states of the world" (permutations of the uncertain parameters), and chooses the optimal solution as the one which minimises the loss in overall expected benefits, compared to the "target health benefit" identified in the first stage.

Mathematically Ω_{now} is obtained from the solution of the following two-stage optimisation problem:

$$\max_X\left(E_\Phi\left(B(\Phi, X)\right)\right)$$
$$E_\Phi\left(C(\Phi, X)\right) \le \Psi$$
$$\sum_{j=1}^{3} x_{ijk} = 1 \quad \forall i = 1\cdots 3; k = 1\ldots 3$$

$$\min_Y\left(E_\Phi\left(B\left(\Phi, \hat{X}\right)\right) - E_\Phi\left(B(\Phi, Y)\right)\right) \tag{13}$$
$$C(Z, Y) \le \Psi \quad \forall Z$$
$$\sum_{j=1}^{3} y_{ijk} = 1 \quad \forall i = 1\cdots 3; k = 1\ldots 3$$

$$\Omega_{now} = E_\Phi\left(B\left(Z, \hat{Y}\right)\right)$$

where

- X is the decision vector of the 1st stage problem
- $\hat{X}$ is the optimal decision vector of the 1st stage problem
- Φ is the set of uncertain parameters (Equation 1)
- Z is the total set of random parameters (Equation 10)
- E_Φ is expectation with respect to the uncertain parameter space Φ
- E_Z is expectation with respect to Z (see immediate paragraph below)
- $\hat{B} = E_\Phi\left(B\left(Z, \hat{X}\right)\right)$ is the optimal benefit of the 1st stage problem
- Y is the decision vector of the 2nd stage problem
- $\hat{Y}$ is the optimal decision vector of the 2nd stage problem
- Ω_{now} is the expected (with respect to Φ) benefit of the 2nd stage problem

In the general nonlinear case, the expectation in (13) should be with respect to the total parameter set Z. However because *B* and *C* are linear functions of the health outcome variables, then $E_Z(B) = E_\Phi(B)$ and $E_Z(C) = E_\Phi(C)$. For the same reasons, $E_\Phi\left(B(\Phi, X)\right) = E_\Phi\left(B(Z, X)\right)$ and $E_\Phi\left(C(\Phi, X)\right) = E_\Phi\left(C(Z, X)\right)$.

Note that in the 1st stage problem, expectation is carried out with respect to the uncertain parameters before solving the constrained optimisation problem. In other

words, one constrained optimisation problem is solved. The problem has two constraints: the first ensures that the expected budget is satisfied and the second ensures that all individuals get one and only one treatment.

A problem of any mathematical programming formulation is that it may not be able to generate any feasible solutions. A sufficient condition to guarantee that at least one solution is feasible for any budget and any realisation of costs is that each healthcare programme must include an option of a *no cost* treatment. This is a strong assumption, because even if it were possible to provide a treatment option with no acquisition cost, there might still be costs conditional on treating subsequent events.

The 2nd stage problem requires the budget to be satisfied for all possible states of the world, i.e. $C(Z,Y) \leq \Psi \quad \forall Z$. In practice, a finite limit needs to be placed on the number of possible states considered. The solution of the 2nd stage problem re-allocates resources ensuring that the budget constraint is satisfied for every random parameter permutation whilst minimising deviation of the expected benefit from the optimal incremental benefit of the 1st stage problem. It is assumed that if no feasible solution to the 2nd stage problem, then $\hat{Y} = \hat{X}$ and $\Omega_{now} = E_{\Phi}\left(B(\hat{X},\Phi)\right)$.

To solve the 2nd stage problem, the inequality constraint is discretized into M constraints $C(Z_m,Y) \leq \Psi$ where $m = 1 \ldots M$ is the set of M inequalities corresponding to M permutations of the total set of random parameters which consists of M_1 permutations of parameter set Φ and, conditional on Φ, M_2 permutations of Δ, i.e. $M = M_1 \times M_2$. The M_1 samples are drawn using Latin Hypercube Sampling (stratified Monte Carlo sampling [12]) and M_2 are drawn using Binomial distributions.

Consider next $\Omega_{perfect}$. A stochastic programming solution is also required to calculate the expected value of a decision made with perfect information. For each realisation of the uncertain parameters, a two stage decision is made. The first stage is to maximise the expectation (with respect to variability) of the overall health benefit whilst ensuring that the expected cost, taken over the variability in cost, is below the budget constraint. The second stage re-allocates resources such that the budget is now

satisfied strictly for every possible realisation of the randomness in costs and deviation of the expected health benefit from the health benefit from the first stage is minimised. $\Omega_{perfect}$ is then obtained by taking the expectation of maximum health benefit over all the realisations of uncertain parameters:

$$
\begin{aligned}
&\max_{X}\left(E_{\Delta}B(\Phi, X)\right)\\
&E_{\Delta}\left(C(\Phi, X)\right) \le \Psi \quad \forall\Phi\\
&\sum_{j=1}^{3} x_{ijk} = 1 \quad \forall i = 1\cdots 3; k = 1\ldots 3
\end{aligned}
$$

$$
\begin{aligned}
&\min_{Y}\left(E_{\Delta}\left(B\left(\Phi, X^{*}\right)\right) - E_{\Delta}\left(B(\Phi, Y)\right)\right)\\
&C(Z, Y) \le \Psi \quad \forall\Phi\\
&\sum_{j=1}^{3} y_{ijk} = 1 \quad \forall i = 1\cdots 3; k = 1\ldots 3
\end{aligned}
\qquad (14)
$$

$$
\Omega_{perfect} = E_{\Phi}\left(B\left(\Phi, Y^{*}\right)\right)
$$

where $X^{*}(\Phi)$ and $Y^{*}(\Phi)$ are respectively the optimal decision vectors of the 1st and 2nd stage problems. As in (13) it is assumed that of no feasible solution exists to the 2nd stage problem in (14), then $Y^{*} = X^{*}$.

Stochastic programming problem (14) is the counterpart of (13) except in two aspects:

- In (14), the expectation in the 1st and 2nd stage problems is with respect to the set of health outcome parameters Δ.
- The 1st stage problem is solved for every permutation of the uncertain parameter vector Φ. If as above M_1 values of vector Φ are sampled, then M_1 constrained optimisation problems are solved. Each of the optimisation problems has two constraints: one is associated with ensuring that each individual gets only one treatment and the second is associated with the budget limit.

5. Discussion

In this paper we have proposed a method to allocate resources to multiple healthcare programmes when costs and benefits are stochastic. Our method takes account of opportunity cost if budgets are exceeded either from uncertainty or variability, avoids the use of arbitrary parameters, and takes into account both of costs and benefits. We calculate EVPI for the whole system under a single budget constraint. The method accounts for the fact that perfect information eliminates uncertainty but cannot reduce variability, therefore decisions made even with perfect information must consider costs and benefits to be random variables.

If all parameters in the model were deterministic, a mathematical programme can calculate the shadow price of the budget constraint, interpreted as the reciprocal of the willingness to pay for health benefits. Where parameters are stochastic, there is no shadow price because there is no unique budget constraint function in the second stage. Rather, we solve the mathematical programme for all potential realisations of costs and benefits. Further work will focus on solving the mathematical programme using illustrative data and constraints.

Clearly, if there is no unique shadow price for the budget constraint then it is not possible to define a threshold ICER to decide whether or not a new technology is cost-effective at the margin and should be adopted by the system, or, conversely, to decide whether an existing technology should be displaced. This is because there is uncertainty about the costs and benefits of all the other interventions adopted as well as the particular intervention under consideration. If expenditure on other patient groups were greater than expected, then the programme under consideration might have to be cut back. This implies that all allocation decisions have to be made simultaneously.

When the budget is fixed for the whole system EVPI represents the gain in the expected total health of the population from eliminating the uncertainty surrounding fundamental parameters. Since no unique shadow price exists to convert health outcome to a money value, can we compare benefits of further research with the costs?

One way of doing this would be to calculate the additional budget needed to obtain the same expected total health under current information as that expected under perfect information with a smaller budget constraint. The difference in budget is the additional expenditure we would be willing to pay for the additional information.

The mathematical programme we have proposed here may well be infeasible for some cases. We have proposed the use of corner solutions (treatment options with zero cost) to ensure that at least one feasible solution is always achievable. In some patient populations this may not be possible or ethical. In the absence of corner solutions we may need to relax the requirement that the first stage of the mathematical programme maximises expected benefits subject to expected cost being less than the budget constraint. One way is to introduce a parameter that represents the maximum probability that the budget should be exceeded. However, unlike Sendi *et al*, we suggest that this can be found empirically by relaxing the constraints until a solution is found rather than (arbitrarily) defined a-priori.

In the formulation presented here, costs and benefit functions are linear with respect to uncertain parameters, and also linear with respect to the decision variables (constant returns to scale). In principle, the formulation is genereralisable to non-linear cost and benefit functions but the mathematics would need to be re-worked and the issue of feasibility would need to be revisited.

This work raises many questions for the academic and policy making communities. We have assumed throughout that the health system is managed with a single global budget constraint. How well does this match reality? What are the incentives and penalties for decision makers to keep within budget? What are the implications if budgets are devolved and binding at lower tiers of management (such as local purchasing bodies) or are binding over set periods of time (annually or every three years)? What macroeconomic externalities can and should be taken into consideration, such as the effect of health policies on prices, taxation and productivity? The authors welcome the comments of HESG members on this work.

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