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**Title:** Social value and individual choice: the value of a choice-based decision making process in a collectively funded health system

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## 1. INTRODUCTION

Many countries around the world use cost-effectiveness analysis (CEA) to inform centralised decisions about the funding of healthcare technologies as a part of health technology assessment (HTA). CEA informs the health system, providing an empirical estimate of the additional health gained from a new intervention net of any health forgone resulting from opportunity costs consequent on other activities being displaced to fund the new intervention. This process involves the selection of a limited number of interventions that are cost-effective and deemed appropriate for funding from a limited pool of resources. A corollary of these decisions is restriction of access to some technologies, which are not considered cost-effective. This may lead to a potential conflict with the selections that patients or doctors on their behalf would make, something that we refer as *choices at individual level*, if they were permitted to exercise their preferred choice.

The implementation of decisions based on the average cost-effectiveness across the target population carries the risk of restricting technologies in some patients for whom those technologies are cost-effective, and *vice versa*. For this reason, there has been an interest in reflecting heterogeneity in cost-effectiveness (Espinoza et al., 2014a, Basu, 2011, Basu, 2009, Sculpher et al., 2002, Basu et al., 2015), which can be operationalized in practice by restricting interventions to specific sub-groups defined in terms of the characteristics observed at treatment selection (Coyle et al., 2003). However, it has been argued that heterogeneity is most fully understood at the patient-doctor dyad level, which is where most information is available to forecast the expected (net) benefits for a particular patient (Basu, 2011). Thus, decisions based on cost-effectiveness at the individual level would, in principle, produce the maximum population health. Therefore, if patients (or doctors on their behalf)

choose according to the same principles adopted by a centralized decision maker, choices made at individual level would provide an optimal policy.

Relying on a policy where interventions are selected at individual level consistent with maximizing net health benefits might be plausible for some groups of patients. However, it is unlikely that all individuals (or their doctors) will make such choices. Rather, many patients will choose different alternatives; some of them will seek to maximize their own health prospects, while others will make decisions based on a broader set of considerations, only a proportion of which can be observed. Therefore, permitting free choice of interventions at the patient-doctor dyad level can lead to negative effects in terms of net population health.

Despite this, centralised health care decision makers may support patient choice for as an end in itself; because it has value for its own sake (Sen, 1988). Even in collectively funded health systems, therefore, there have been policy objectives defined in terms of “patient centred care” or “shared decision-making” where allocation of resources might be, at least to some extent, determined by decisions made at individual level.

On the other hand, the implementation of centralised decisions is associated to additional costs to ensure adherence to those guidelines. Even when heterogeneity has been taken into account as subgroup recommendations, guidelines might be difficult to implement. In fact, more transactions costs related to implementation might be expected from more complex guidelines, such as the ones including heterogeneity (Espinoza et al., 2014b). In this context, when the potential transaction costs are high, a decision process that relies largely on choices made at individual level might be attractive for the health care system.

This paper aims to explain this apparent policy contradiction. We focus on the choice between mutually exclusive treatments, not included in a coverage scheme yet. It offers a framework for how and when choices at individual level can be used by health systems in the

context of the adoption and reimbursement of new health technologies. It addresses the question of whether the implementation of choice-based policies in collectively funded health systems can represent an efficient use of limited resources, or alternatively, how much health improvement the system should be willing to forgo in order to permit the patient-doctor dyad to select their treatments.

The paper is structured as follows. First, it reviews the concept of the value of reflecting heterogeneity in the context of CEA. Second, it examines the comparison between centralized decisions to restrict the funding of interventions based on average cost-effectiveness against decisions based on maximising individual expected health. Third, it compares centralized decisions according to subgroup-based cost-effectiveness against decisions based on maximising individual expected health. Then it compares the central decision maker's objective of maximizing population health through decisions informed by CEA and an alternative system where patients (and doctors) choose according to different criteria. The manuscript ends with an application of the framework in a case study, followed by a consideration of the strengths, weaknesses and the applicability of a choice-based approach in health care decision-making.

## **2. THE VALUE OF HETEROGENEITY IN COST-EFFECTIVENESS ANALYSIS**

CEA is a comparative analysis between two main elements: (i) the additional health gains of a new technology respect to one or more existing interventions; and (ii) the health forgone for other patients as a result of opportunity costs due activities being displaced within the health system to fund the new technology. When comparing two interventions, the analysis usually expresses the difference between the expected costs of the new versus the standard alternative (incremental costs) divided by the difference of benefits measured, for example, as quality-adjusted life years (incremental QALYs). This incremental cost-effectiveness ratio (ICER),

which represents the additional cost that must be paid in order to gain an extra unit of benefit, is compared with an estimate of the opportunity cost of the alternative use of the resources in the health system, a concept that is operationalized as the cost-effectiveness threshold ( $\lambda$ ). If the ICER is greater than the  $\lambda$ , then the new strategy should be rejected (Figure 1).

The same decision rule can be presented as incremental net health benefits (INHB), which corresponds to the difference between the incremental benefits and incremental costs, with the latter being expressed in health terms (dividing the incremental costs by  $\lambda$ ) (Stinnett and Mullahy, 1998). When the INHB is greater than zero, the same decision rule applies indicating that the new strategy is cost-effective.

Used to support centralized decision-making by a health care system, the ICER indicates the 'average' cost-effectiveness, even though ICERs were estimated for subgroups, which is another average for a more restricted set of patients. In reality there are individuals with different incremental expected costs and effects, and hence, with different individual ICERs. This heterogeneity is explained by several elements, including clinical sources such as baseline risk and treatment effect variations, but also in other factors such as costs, and patient preferences.

In particular, the heterogeneity in preferences refers, on one hand; to the different outcomes people pursue regards to a particular health problem given their own context. On the other hand, it refers to preferences revealed when valuating health states, i.e. some people value more one hypothetical health state than others, for example in the context of time trade-off or standard gamble exercises (Espinoza et al., 2014a). It is important to highlight

This concept is illustrated in Figure 1, adapted from a previous presentation by Basu and Meltzer (2007). Whilst the average cost-effectiveness indicates that the new strategy should not be adopted because its ICER is higher than  $\lambda$ , individual estimates suggest that the new

strategy is not cost-effective for the subject 1, it is cost-effective for subject 3 and it is dominated for the individual 2. The set of points representing individuals is the joint distribution of potential outcomes since each point corresponds to the difference between the observed outcome and its estimated counterfactual or potential outcome<sup>1</sup>. The estimation of the joint distribution is an empirical challenge given the lack of information to reveal total heterogeneity (Espinoza et al., 2014a). Nevertheless, in principle, it supports an optimal allocation of the limited resources. The potential improvement in population health due to decisions based on an estimate of this joint distribution has been referred in the literature as the expected value of individualized care (Basu and Meltzer, 2007) or value of heterogeneity (Espinoza et al., 2014b).

<<Figure 1 about here>>

Alternatively, individual cost-effectiveness can be expressed in terms of INHB for each patient ( $INHB_i$ ). Positive estimates will be obtained in individuals located below the  $\lambda$  line and negative estimates will relate to individuals above the  $\lambda$  line. The sum of positive and negative  $INHB_i$  should produce the average incremental NHB (INHB) as follows:

$$INHB = 1/n \sum_i^n INHB_i \quad (1)$$

where  $n$  is the number of individuals of the joint distribution of potential outcomes and the subindex  $i$  is the  $i$ -th individual.

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<sup>1</sup> The joint distribution of potential outcomes refers to the Rubin's causality model. The potential outcomes are defined as the observed consequences ( $Y$ ) of alternative treatments ( $t=0,1$ ) in one particular individual ( $i$ ), i.e. the outcome observed *de facto* and the counterfactual (unobservable). Thus, the joint distribution is defined by  $G(Y_{0i}, Y_{1i})$  (HOLLAND, P. 1986. Statistics and causal inference. *Journal of the American Statistical Association*, 81, 945-960.)

The central decision maker may, then, seek to exploit the theoretical advantages in allocating resources according to individual cost-effectiveness as, in principle, it can lead to an increase in population health. There are, however, some constraints related to its implementation. For example, there may be additional costs associated with implementing more complex central decisions and with monitoring and enforcing them. These transaction costs also fall on the limited budget and hence impose additional opportunity costs in terms of population health. The central decision maker may, therefore, gain efficiency through simplification by making treatment decisions at the level of broad sub-groups rather than the individual (Espinoza et al., 2014b).

### **3. THE POTENTIAL VALUE OF ALLOWING PATIENT CHOICE**

An alternative approach to imposing central decisions regarding which treatments will be funded from the health budget – whether these are based on average, individualised or sub-group cost-effectiveness – is to permit choices made at individual level. Hereafter, we use the term individual choices equally as decision made at individual level, i.e. including doctors or health professionals on behalf of patients or their relatives. It has long been recognised that, because patients (supported by their doctors) will generally select treatments on the basis of expected outcomes without regarding to any opportunity cost imposed on others due to limited collective funding, this may lead to inefficiencies in a system focused on maximising population health (Eddy, 1991). Therefore, to compensate for the risk of such inefficiencies, one or more of the following needs to apply for a choice-based approach to treatment allocation to be worth considering.

Firstly, following Basu's (2011) analysis, across a population, the many patient-doctor dyads that make treatment choices provide an opportunity to learn more about which individual



characteristics explain successful treatment than can be estimated from clinical trials and implemented by a central decision maker. Although analysts will face limitations trying to understand heterogeneity, for example, through subgroup analysis (Sleight, 2000, Sun et al., 2010, Wang et al., 2007), using large routinely available datasets where patients have revealed their choices, some estimates at individual level can be produced to inform future choices (Basu, 2011).

The second factor, which may support the use of choices emanating from patient-doctor dyads, to allocate finite collective resources relates to transaction costs. For treatment decisions which exhibit marked heterogeneity in cost-effectiveness and would require complex centralised guidelines in terms of which treatment is cost-effective for which types of individuals, high transaction costs are expected in terms of communicating, monitoring and imposing the decisions, and these can be avoided with a choice-based approach. In contrast, a decision process that encourage decisions at individual level might produce significant savings to the system (Veroff et al., 2013).

A third factor having the potential to support the use of choices at individual level relates to what factors are considered important to policy makers. Although seeking to achieve the greatest impact on population health from available resources is likely to be important to decision makers, many systems will consider the opportunity to offer treatment choices to patients as valuable in its own right. This manifests itself through policies which promote patient autonomy (Oshana, 2003, Redley et al., 2011) in determining their care and which seek to encourage decision processes where patients play an active role such as shared decision-making (Sculpher et al., 1999, Charles et al., 1997). Although interest in these policies may partly be explained by their anticipated impact on patients' health outcomes, it seems policy makers value patient choice independent of any health effect. As such, patient

choice is seen to offer something akin to a ‘process benefit’: something patients (and hence policy makers) inherently value. For example, the UK National Health Service (NHS), which is characterised by a widespread use of CEA to support decisions about central funding of many new technologies, has recently published the 2014/15 Choice framework. This is the result of the effort of the British NHS in providing more opportunities to patients for making their own choices. The document presents a set of activities where patients can make choices about their care indicating the limits due to the available resources as well as the process to complain when choices have not been offered.

Another factor relates with the value of choice when evidence is weak or highly uncertain, where decisions are most likely to be driven by patient preferences. These preference-sensitive decisions are difficult to be introduced in routine HTA processes, at least in the short run (Brooker et al., 2013, Utens et al., 2014). However, it is totally consistent giving formal consideration in decisions at individual level. In this context, some important research is being undertaken to introduce aids tools for patients and clinicians (van der Weijden et al., 2010, Van der Haterd et al., 2016).

Given this range of considerations regarding the circumstances under which patient choice may be considered appropriate for treatment choices given limited collective resources, a framework is needed to address the question as to when a choice-based decision-making process can be considered a good use of limited resources, or alternatively, how much health the society should be willing to forgo in order to implement a choice-based decision-making process. Although this description of the health system is a very good representation of a public national health system (e.g. the NHS in the UK), the analysis applies to any collectively funded system (public or private).

Let us consider the problem faced by the centralised decision maker when the decision based on average cost-effectiveness is to reject the new intervention. Figure 2 shows a hypothetical cloud of points (oval on the cost-effectiveness plane) that represents the joint distribution of potential outcomes. Six areas are defined based on incremental costs, incremental benefits and the cost-effectiveness threshold (represented by the  $\lambda$  line). Each represents the sum of expected individual net health benefits of individuals that share similar incremental benefits and costs; and therefore, they are placed in the same area.. For example, all subjects in area A expect lower benefits from the new treatment and higher costs; and all individuals in area D have positive incremental costs and benefits but their ICER is higher than the threshold,  $\lambda$ . Thus, all individuals in areas A, B and D have negative  $INHB_i$  from the new treatment since they are located above the  $\lambda$  line, whereas all subjects in areas C, E and F have positive  $INHB_i$ .

If the  $INHB$  estimated based on average costs and benefits indicates that the new strategy should be rejected (as the central dot is above the  $\lambda$  line), the net gains of a centralized decision-making process can be characterized as the difference between the gains and the losses of individuals. Graphically, the gains can be represented as the density of the distribution that lies above  $\lambda$ , i.e. the area (A+B+D), whereas the loss corresponds to the area below  $\lambda$ , i.e. (E+F+C) (Figure 2). Thus, the net societal gain of a centralized guideline is:

$$(A+B+D) - (E+F+C) \quad (2)$$

As an alternative to centralized recommendations, the decision maker can implement a policy where patients and doctors jointly select the treatment without restrictions imposed by the central authority. This choice based approach might be predicated on a series of assumptions:

(i) patients (and doctors) will use as much individual information as possible so that they can make a good prediction of the position of the patient in the joint distribution; and (ii) they will choose in a way that maximizes the individual patient's expected health benefits, where health is measured with the same metric used by the central decision maker (e.g. QALYs). If this is the case, the gains for the society under a choice-based process are  $(A+B+E+F)$ . Individuals in A and B will choose the standard treatment, which is also the correct decision based on their  $INHB_i$ . On the other hand, patients in E and F will choose the new strategy, which is also the correct decision from the perspective of the cost-effectiveness. In contrast, subjects in C and D would make choices in the opposite direction of what should be chosen based on  $INHB_i$  and, therefore, they represent a loss to population health. Finally, the net social gain under a choice-based process, where benefits are solely in terms of effects on population health, is:

$$(A+B+E+F) - (C+D) \tag{3}$$

<<Figure 2 about here>>

The net social gain, in terms of population health of a centralised process is equivalent to the net social gain under a choice-based process under the following condition:

$$[(A+B+D) - (E+F+C)] = [(A+B+E+F) - (C+D)] \tag{4}$$

Which simplifies to:

$$D = E + F \quad (5)$$

This expression reveals the relevant areas when comparing the two approaches. When  $D$  is greater than  $(E+F)$ , a centralised process provides more benefits in terms of population health. In contrast, when  $(E+F)$  is greater  $D$ , a choice-based process is preferable. The difference  $(E+F)-D$  can be expressed as the additional health benefits of choice-based decisions.

There are two additional elements to the framework. First, as discussed above, the implementation of a centralised decision based on cost-effectiveness may entail some additional transaction costs ( $C_r$ ).  $C_r$  includes the additional effort to disseminate a guideline that might not have the approval of the whole clinical community, as well as the cost of monitoring adherence to the guideline and correcting any inappropriate treatment use. Second, a choice-based decision-making process aims at taking into account as much patient information as possible, which is the result of the exchange of information between patients and health professionals and other relevant actors. This process might be thought as, for example, the implementation of the shared decision-making model (Charles et al., 1997, Sculpher et al., 1999, Gulland, 2011), which is not exempt of additional costs. These costs ( $C_{ch}$ ) include the extra time of health professionals and extra costs to reveal the specific clinical characteristics and patient preferences to identify the more appropriate treatment. Because in most situations  $C_r \geq 0$  and  $C_{ch} \geq 0$ , they should be subtracted from the net social gain in Equation 4.

$$[(A+B+D) - (E+F+C)] - C_r = [(A+B+E+F) - (C+D)] - C_{Ch} \quad (6)$$

This is equivalent to:

$$2[D - (E + F)] = (C_r - C_{Ch}) \quad (7)$$

Which simplifies to:

$$D - (E + F) - (C_r - C_{Ch})/2 = 0 \quad (8)$$

If Equation 8 is true, centralised and choice-based decisions are equivalent. If the magnitude is greater than zero, it represents the additional health that the health system would get if a centralised process were implemented instead of a choice-based process.

So far in this section the assumption is that the health system (and society) only value changes in population health. However, as discussed above, there may be value to policy makers of offering treatment choice to patients independent of its impact on health outcomes. If the health system is willing to implement a choice-based process in spite of the expected gains in population health resulting from centralised decisions (i.e. if the magnitude in Equation 8 is greater than 0), the magnitude of that positive value can be seen as representing the value of a choice-based process in the health care system.

#### **4. SUBGROUP RECOMMENDATIONS VERSUS CHOICE BASED DECISION- MAKING**

The methods presented in the previous section can be extended to the case where the central decision maker generates different recommendations for different subgroups, i.e. a

centralised-stratified decision-making process. Let us assume the simplest case with two strategies (new versus standard) and two subgroups where rejection is recommended for one subgroup and adoption is recommended for the second subgroup. Because there is no guarantee that the specification used to define subgroups will be able to separate out individuals among areas defined in Figure 2, we illustrate two subgroups as two clouds on the cost-effectiveness plane, each containing points in all possible areas (Figure 3). Following the same approach used above, the net social gain in the  $j$ -th subgroup where the recommendation is to reject the new strategy can be estimated as:

$$(A_j+B_j+ D_j) - (E_j+F_j+ C_j) \quad (9)$$

Likewise, the net social gain in the  $k$ -th subgroup where the recommendation is to adopt the new strategy can be calculated as:

$$(E_k+F_k+ C_k) - (A_k+B_k+ D_k) \quad (10)$$

The net social gain of the whole population is the sum of Equations 9 and 10:

$$[(A_j+B_j+D_j) - (E_j+F_j+C_j)] + [(E_k+F_k+C_k) - (A_k+B_k+D_k)] \quad (11)$$

This expression can also be generalized to estimate the net social gain when more subgroups have been considered. In this case, there might be more than one subgroup where rejection has been recommended ( $j=1, 2, \dots, J$ ). Likewise, there might have more than one subgroup

where the adoption of the new strategy has been recommended ( $k=1, 2, \dots, K$ ). Thus, the net social gain can be expressed as:

$$\sum_{j=1}^J [(A_j + B_j + D_j) - (E_j + F_j + C_j)] + \sum_{k=1}^K [(E_k + F_k + C_k) - (A_k + B_k + D_k)] \quad (12)$$

This expression is equivalent to Equation 2 in Section 3. Therefore, a centralised-stratified decision process is equivalent to a choice-based process if Equation 12 is equal to Equation 3.

$$\begin{aligned} \sum_{j=1}^J [(A_j + B_j + D_j) - (E_j + F_j + C_j)] + \sum_{k=1}^K [(E_k + F_k + C_k) - (A_k + B_k + D_k)] & \quad (13) \\ = [(A + B + E + F) - (C + D)] & \end{aligned}$$

<<Figure 3 about here>>

## 5 AVERAGE RECOMMENDATIONS VERSUS CHOICE BASED ON AN ALTERNATIVE MAXIMAND

The assumption that patients and society focus on the same health outcome can be relaxed by considering individuals (or their doctors) who change their decisions when they seek to maximise another outcome, which is personally important to them. This outcome might be, for example, the likelihood of returning to paid employment over the subsequent year. Thus, in those subjects who rejected the new strategy (based on the rule of maximising QALYs), which implied societal gains (areas A and B in Figure 2), a change in their decisions will impose societal losses. As a consequence, they should be subtracted from the (A+B) density.



Likewise, in those individuals whose adoption of the new treatment represented a societal gain (E+F) a change in their treatment choice (based on a different decision rule) will represent a societal loss. Analogously, for areas C and D, where rejection and adoption, respectively, were understood as societal losses, a change in the decision implies a societal gain. These changes that affect only the net gains of a choice-based decision process can be expressed as:

$$[(A_y+B_y+E_y+F_y) - (A_z+B_z+E_z+F_z)] - [(C_y+D_y)- (C_z+D_z)] \quad (14)$$

where  $y$  represents the density of individuals whose decision is the same under both types of outcome, and  $z$  represents the density of individuals whose decision changed when they apply an alternative decision rule. As mentioned above, in the case of a centralized decision the areas are the same as in Equation 2. However, for the purpose of comparability with the choice-based case, they must be expressed as a sum of individuals'  $y$  and  $z$ , even though under a centralized process both individuals will receive the same treatment:

$$(A_y+ A_z +B_y+ B_z +D_y + D_z) - (E_y+ E_z +F_y + F_z + C_y + C_z) \quad (15)$$

Following the same logic explained in Section 3, a centralised decision process is equivalent to a choice-based process if Equation 15 is equal to Equation 14:

$$(A_y+ A_z +B_y+ B_z +D_y + D_z) - (E_y+ E_z +F_y + F_z + C_y + C_z) =$$

$$[(A_y+B_y+E_y+F_y) - (A_z+B_z+E_z+F_z)] - [(C_y+D_y)- (C_z+D_z)]$$

which simplifies to:

$$A_z + B_z + D_y = E_y + F_y + C_z \quad (16)$$

(17)

In this case, the net social gains are not only affected by the individuals in area D, E and F. Since subjects might change their decisions individuals in areas A, B and C also matter, in particular those who effectively change their decisions ( $A_z$ ,  $B_z$  and  $C_z$ ).

This analysis needs the identification of the outcome based on which individuals will make decisions, i.e. the new maximand. Then, expected costs and benefits must be estimated for both outcomes simultaneously in order to identify which individuals keep or change their decisions.

From this point onwards, the area of the northeast quadrant between  $\lambda$  and the Y axis will be called NNE quadrant (north-northeast) and the area below the  $\lambda$  line and the Y axis will be called NSE quadrant (north-southeast).

## **6 CASE STUDY**

In this section, the methods proposed in this paper are applied to a case study. The analysis is based on the study RITA-3, a multicentre clinical trial (n=1,810) that compared the efficacy of an intensive versus a conservative treatment strategy for the early management of patients with non-ST-elevation acute coronary syndrome (Fox et al., 2005, Fox et al., 2002). The average results of the trial showed that an invasive strategy is efficacious but is not cost-effective at a threshold of £20,000 per additional QALY, which sets a potential conflict between a centralised decision based on cost-effectiveness and choices made at individual

level (Henriksson et al., 2008). In this example, given the condition of the patients, we assume doctors will make the choices on their behalf.

The incremental costs and QALYs were estimated for each patient using the trial data. A set of regression equations was used to estimate the parameters needed to populate the decision model. Because the equations were conditional to a set of individual level covariates, parameters could be estimated for each patient. Figure 4a shows the cloud that represents the joint distribution of potential outcomes, which corresponds to 1,810 patients in the trial.

<<Figure 4 about here>>

An alternative way of conducting the calculations is to estimate the average  $INHBi$  of one particular area weighted by the proportion of the density of the area. Thus, the average  $INHBi$  of the NNE quadrant is 0.099 net QALYs and its density represents 58% of the whole joint distribution (weighted average 0.0578 net QALYs). Likewise, the average  $NHBi$  of the NSE area is 0.146 net QALYs and its density is 33.7% of the joint distribution (weighted average 0.0493 net QALYs). As a consequence, the difference between NNE and NSE, estimated for a relevant population of 556,723 patients in the UK for the next ten years (assuming a discount rate 3.5% and an annual incidence rate of 59,756 patients), is 4,732 net QALYs or £94,640,000 in monetary terms (assuming a threshold value of £20,000 per QALY gained). The calculation used absolute values because the sign reveals whether the decision (accept or reject), and the magnitude represent the expected health the system gains (or avoid losing), which is what it has been modelled conceptually in sections 3, 4 and 5.

If we assume that the transaction costs of implementing either of the decision-making processes is similar, which can be considered reasonable in this health problem,  $(C_r - C_{ch})$  tends to zero. Therefore, if policy makers' focus is in gains in population health, then a centralised guideline based on cost effective is the more appropriate policy. If there is an

interest of implementing choices at individual level as an end in itself and as an additional source of social value, independent of population health, then policy makers would need to be willing to forgo 4,732 QALYs (an opportunity loss) over the next ten years to implement such a policy .

The second situation is the comparison between guidelines based on subgroups versus a choice based decision-making process. This analysis requires the definition of an optimal guideline based on subgroups. It has previously been shown that the optimal guideline for the trial RITA-3 considers alternative paths on the basis of the combination of six covariates (Espinoza et al., 2014b). In this study, we will use those results to estimate the opportunity loss of a choice based decision-making process.

The joint distribution of potential outcomes presented in Figure 4a occupies the NNE, NSE and NW quadrants only. In this case the challenge is to identify those patients who either should or should not receive the new strategy according to the subgroup guideline, which is illustrated in Figures 4b and 4c respectively. The expected net social gain in the subgroups where the decision is to reject the new strategy was 0.0448 net QALYs (estimated according to Equation 9). The expected net social gain in the subgroups where the standard strategy was recommended was -0.0265 net QALYs (estimated according to Equation 10). The expected net social gain due to a choice based decision-making process for this case is  $(A+E+F-D)$  because other areas are zero (according to Equation 3), or similarly  $(NW + NSE - NNE = -0.029)$ . Finally, the value of choice, i.e. the expected health that the system should be willing to forgo in order to implement a choice based decision-making process for a relevant population of 556,723 patients is  $((0.0448 - 0.0265 + 0.029)*556,723)$ , which corresponds to 26,333 net QALYs over the next ten years.

The third situation can be addressed when we are able to identify the outcome that patients use instead of QALYs. The RITA-3 trial offers an opportunity to explore this situation since the health problem, as many other emergency conditions, describes a clinical setting where conducting informed or shared decision-making is difficult. Instead, it is very likely that the doctor will make the decision on behalf of the patient following the evidence published in the clinical report. Consistent with that idea and for illustrative purposes, it is assumed that doctors will make their prescriptions maximising patient's survival (life years). It also assumes that doctors have knowledge about the effect of individual characteristics on health outcomes, which is equivalent to the maximization of life years at individual level.

The RITA-3 cost-effectiveness model, as many other decision models, allows us to estimate the expected individual life years' increment as well as QALYs. The analysis identifies individuals who would receive a different strategy if the rule of maximising life years was applied. According to Equation 11 the densities of interest are  $A_z$ ,  $B_z$ ,  $C_z$ ,  $D_y$ ,  $E_y$ , and  $F_y$ . The study showed that the incremental life years are positive in all (1,810) patients. Thus, every patient in the NW quadrant (area A) would receive invasive treatment, which means that  $A_z$  is equal to A. Further, individuals in the remaining areas do not change their decisions, i.e.  $E_y$  plus  $F_y$  is equal to E plus F and  $D_y$  is equal to D.  $B_z$  and  $C_z$  are equal to zero.

The average  $IiNHB$  of the NW quadrant is 0.25 QALYs and its density is 8.23% (weighted average of 0.02 QALYs). Applying equation 11 to the actual data, the calculation can be reduced to  $(2 [NNE+NW-NSE]) = 2 [32,225 + 11,626 - 27,454]$  which results in 16,397 QALYs or £327,940,000 in monetary terms (assuming a threshold value of £20,000 per QALY gained). Under this scenario, therefore, decision makers would need to be willing to forgo an opportunity loss of this magnitude if it were to select a choice-based policy.

## **7. Discussion**

Many countries have adopted a process for decisions about the funding of health care interventions where the selection of alternatives is informed by cost-effectiveness evidence. These decisions are usually implemented as centralised decisions, which are expected to be followed by all health professionals of the healthcare system. Furthermore, offering the opportunity of making choices at individual level is an important objective of many health systems, which is not limited to the access to healthcare providers but also to the selection of diagnostic pathways and treatments. However, there is a potential conflict between central decision makers whose objective is to maximise population health subject to limited resources and individuals who pursue the maximization of their own individual health (or other outcomes) without necessarily taking into account the consequences of their decisions upon other individuals' health. This happens with expensive technologies that are considered not to be cost-effective at (sub-) population level. In this paper we argue that the magnitude of this conflict depends on how potential outcomes of each individual are distributed on the cost-effectiveness plane and can be expressed as the amount of health that would be forgone if decisions regarding treatments were devolved to the patient level. We present a framework to estimate the value of a choice-based decision-making process in a health system that seeks to maximise population health with the limited resources.

The paper describes three different analyses: a comparison between a guideline based on the average cost-effectiveness and choice based decisions; a guideline based on subgroups and choice based decisions; and the comparison between a guideline based on the average and the choice based process based on the maximization of a different outcome. A fourth possible situation is the comparison between a guideline based on subgroups and choice based decisions with a different outcome. This scenario is not examined in detail because is a simple extension of the methods presented here.

Choice based decisions are assumed to be an informed selection made by the patient-doctor dyad. Although we have presented the arguments why decisions at individual level might be valuable, our framework restricts the choice model to a more simple approach. It assumes that patients will make choices based on what evidence has proved to be better for them. Then it expands the framework to the case where they introduce additional (unobserved) variables modifying the maximand, accepting that its identification is matter of further research. In addition, we are also aware that making decisions at individual level generate additional costs, including additional tests or time, which might also introduce inefficiencies. This is why the estimate of  $C_{ch}$  is important, and further research might be focused on revealing a good estimate of it. The increasing literature on tools for shared decision-making might be useful for this task.

A predictable but nonetheless interesting finding is that the value a health care system will have to associate with offering choice to patients for its own sake (independent of its impact on population health) will have to be greater when it is compared with centralised decision-making based on subgroup recommendations. This result is to be expected because when different decisions for different subgroups have been made, the expected health loss due to lack of understanding of the heterogeneity is lower and the expected population health gains are greater than the average case.

The method introduced in this article relies completely on the estimation of the joint distribution of potential outcomes. This distribution can be estimated through decision modelling using individual level data with specific information about patient level characteristics (Basu and Meltzer, 2007, van Gestel et al., 2012). This is the approach used for the case study presented in Section 6. One of the strengths of this example is that all relevant parameters (transition probabilities, costs and outcomes) have been estimated

conditional to six individual characteristics. One limitation, however, is that the estimation was made using observed covariates only. In many cases there is significant unobserved heterogeneity that might determine important differences in the distribution, part of which may be successfully exploited by patients and/or doctors in the shared decision-making process. This is not a limitation of the methods presented here itself but a broader limitation to our current capacity to predict the counterfactual for each individual. Basu (2011) has shown how the joint distribution can be estimated considering patient choices as a source of unobserved heterogeneity. The application of those methods to this framework is an opportunity for future research.

In this paper we used the ex post information about efficacy produced in a clinical trial to estimate an ex ante information about cost-effectiveness and the value of decisions at individual level. Moreover, the analysis has been restricted to those interventions that are not yet covered; hence, it has excluded some existing and alternatives that are already covered among which patients and might make choices. Of course the possibility of selection among a greater number of alternatives with a range of characteristics will have an impact on health. For example, if there are two drugs available for a chronic condition, patients might choose one that is less effective because it need one daily intake instead of two. Health consequences derived from those choices have not been studied in this research because they do not generate any conflict between centralized decisions and choices at individual level in terms of coverage. However, we agree this is an important issue that might be matter of future research.

The method introduced in this paper is a comparison based on current information and it does not consider the uncertainty around the estimates. Decision uncertainty is regularly characterized and reported in cost-effectiveness analysis to address the question of whether



further research represents a good use of the limited budget. In this paper, the main question is framed in the context of decision-making with current evidence and the methods are consistent with it. However, we acknowledge that, if future patients can benefit from further research, so is the future decision about implementing a choice based decision process. This is an issue that require further research.

The estimates produced here are not intended to solve a set of other normative questions but only to produce empirical information that might be helpful. These questions include (a) the magnitude of health that the society *should* be willing to forgo in order to satisfy the autonomy of patients; and (b) the types of patients where this analysis should be considered. We argue that the answers to those questions still rely on the deliberative decision process, which can benefit from the estimates produced in this analysis.

Finally, we argue that the estimates generated using these methods might become a valuable part of the health technology assessment process. If the objective of the health system is to implement some degree of patient's choice in treatment selection, the judgment as to whether a choice based process can be implemented can be facilitated by the information generated from the analysis presented here. When the magnitude of the expected health forgone is small, the health system might want to implement a choice based policy, for example, as shared decision-making. Although this process does not replace the production of evidence-based guidelines, the effort of the system would be to emphasise the role of shared decision-making instead of the fulfilment of the guideline.



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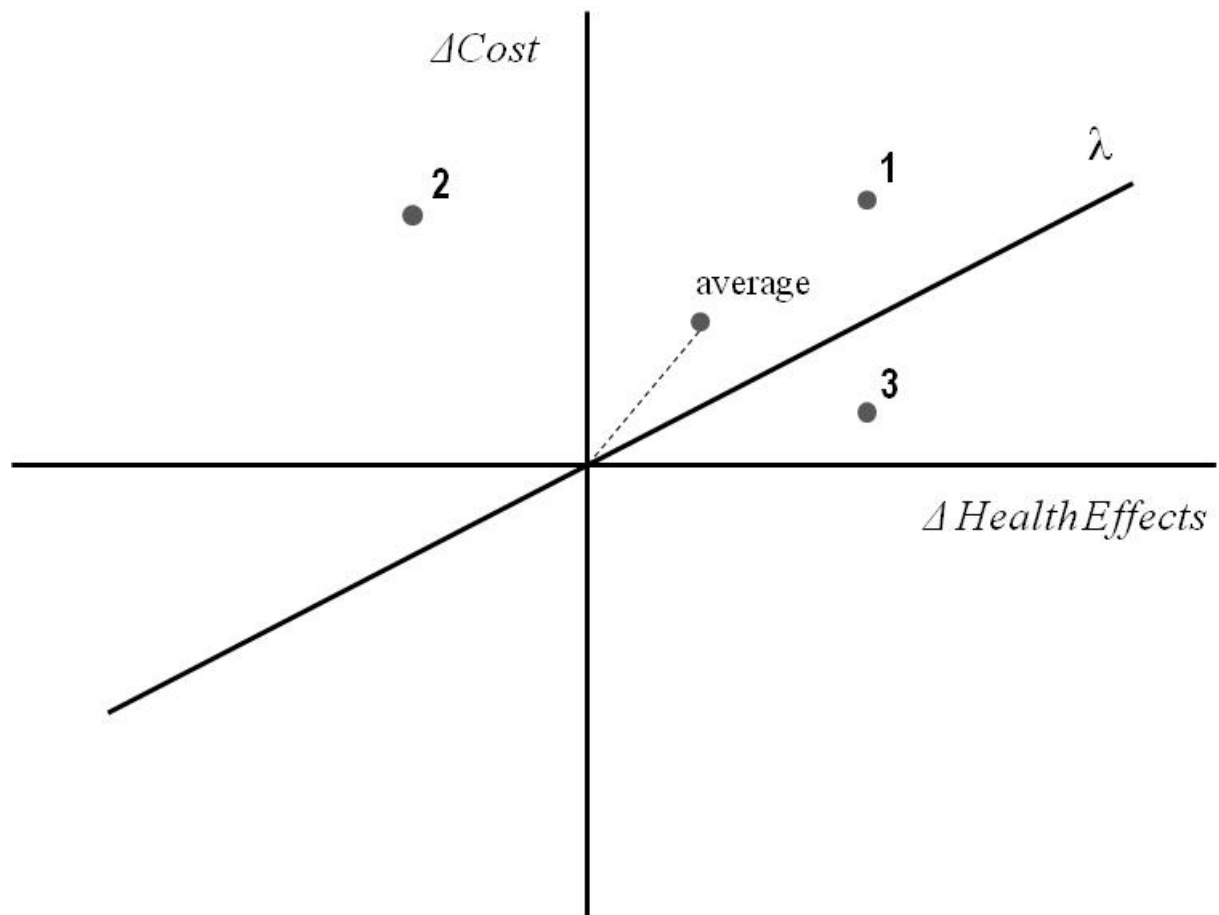
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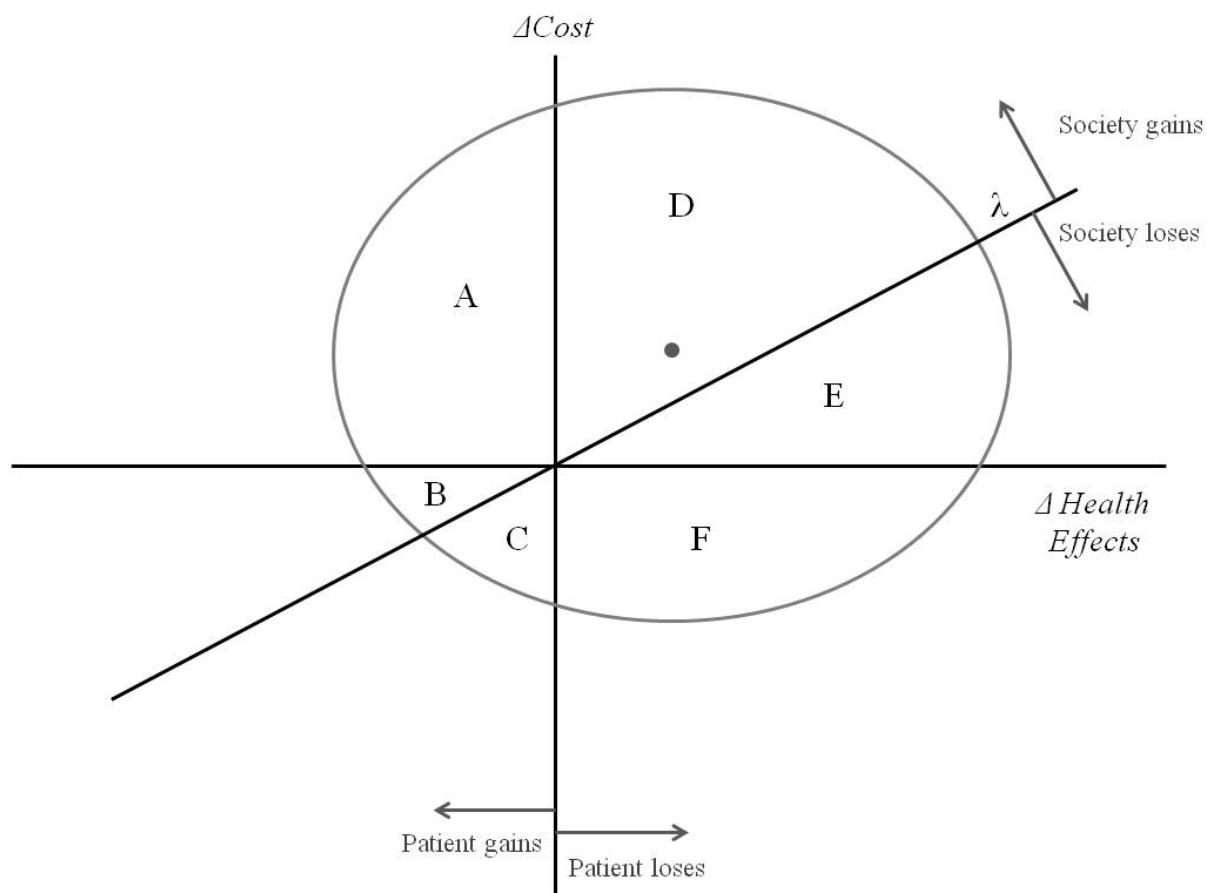
## FIGURES

Figure 1. Representation of average and individual expected incremental costs and effects in the cost-effectiveness plane.



Note: The graph has been adapted from Basu and Meltzer (2007). The line  $\lambda$  represents the cost-effectiveness threshold reflecting opportunity costs. The average point represents the mean incremental costs and effects compared to standard care at the origin. This indicates in this case that the alternative is not cost-effective (as it is located above the threshold line – its ICER is greater than  $\lambda$ ). Point 1 represents a subject for which the new strategy is not cost-effective, just as the average estimate. In contrast, point 3 shows an individual for which the new strategy is cost-effective (as they are located below the threshold line – their ICERs are less than  $\lambda$ ). Finally, point 2 shows the case of an individual where the new strategy is dominated by the standard (less effective and more costly).

**Figure 2. Trading off the centralised treatment decisions based on cost effectiveness and patient choice.**

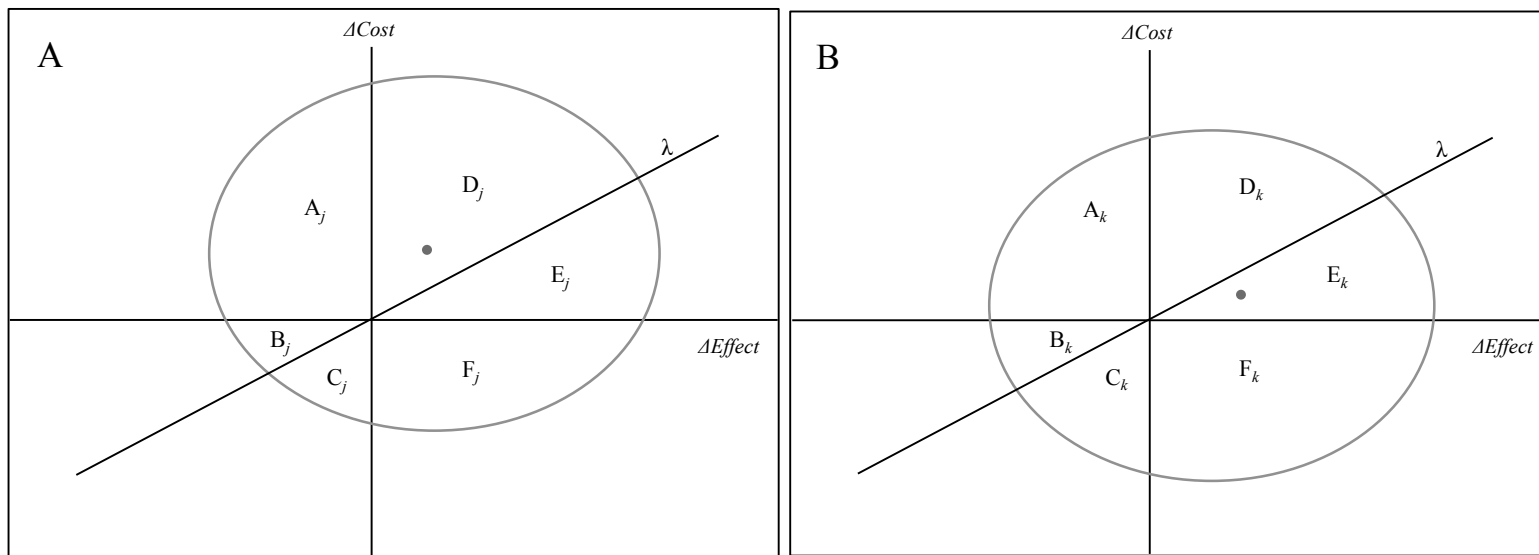


Note: The line  $\lambda$  represents the cost-effectiveness threshold. The central dot represents the average incremental costs and health effects of a new strategy compared with the standard. The oval represents the joint distribution of potential outcomes of individuals in terms of incremental costs and health effects. When making a centralised decision to reject the treatment on the basis of average cost-effectiveness (as the average ICER is above  $\lambda$ ), When benefits are considered only in terms of changes in population health, individuals located in areas below the threshold line (for whom treatment would be cost-effective) are considered social losses (who cannot benefit from treatment due to its rejection), whereas those located above the line are gains (society gains by restricting access to them).

- Patients can be situated in one of the following areas according to their individual incremental costs and effects
- A new treatment is more expensive and less effective
  - B new treatment is cheaper and less effective
  - C new treatment is cheaper and less effective and the incremental net health benefits are greater than zero
  - D new treatment is more expensive and more effective and the incremental net health benefits are smaller than zero
  - E new treatment is more expensive and more effective
  - F new treatment is cheaper and more effective



**Figure 3. Centralised-stratified based recommendations versus choice based decisions**



Note: The areas in Figure A represent the different location of individuals (j) for whom a rejection decision applies. Areas in Figure B illustrate individuals (k) for whom an adoption decision applies.

**Figure 4. Estimated joint distribution of potential outcomes of RITA-3 case study for (a) the all sample; (b) patients who should receive the new strategy according to the subgroup based guideline and; (c) patients for whom the new strategy should be rejected according to the subgroup based guideline**

