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Title:

Use of economic evidence in clinical decision making: a discrete choice analysis

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1. Introduction

The debate on the use of research results in public policy has evolved over time and the principles underpinning evidence-based medicine have recently been discussed in the context of health care management and policy making [1, 2]. Particular attention has been given to the use of economic evidence, i.e. formal cost-effectiveness analysis of healthcare technologies and services. The increasing amount of empirical research is performed to inform the allocation of scarce healthcare resources at various levels [3, 4]. Consequently, the incentives and barriers to actual use of cost effectiveness research in healthcare have been investigated in several studies [5].

Most of the available studies have analysed the influence of cost-effectiveness analysis at policy (macro) and healthcare facility (meso) level, while a limited number have investigated the perceptions' and decision criteria of professionals [3, 6-12]. The available evidence suggests that cost effectiveness analysis is not the dominant criterion used by clinicians in their decisions. In fact, there is limited evidence of the "enlightenment use" where economic evidence provides a background information that affects the way clinicians make decisions rather then being directly used when deciding on particular treatment strategy [5].

All available studies investigating the impact of cost effectiveness information on clinicians' decision making limited their findings to a description of clinicians' views and perceptions, with very few providing a measure of relative importance of cost-effectiveness criteria [11, 12]. Given the essential role of professionals in evaluating novel treatment strategies in healthcare, it is of great interest to assess to what extent the results of formal economic evaluation analyses influence their decision making process.

It has been acknowledged that decision making is a complex intellectual process and several models of decision behaviour have been proposed in economics [13]. Decision makers rely on different type of information from various sources in making their judgements. The issue of uncertainty as an unavoidable ingredient of any decision making process was first discussed by Simon in his early contributions [14-16].

With specific regards to healthcare, clinicians make their decisions within limits posed by incompleteness and uncertainty of information available to them. This implies that their choices involve trade-offs between different types of information, since the final judgement about innovative treatment will rarely rely on evidence base that would satisfy all decision making criteria. In other words, given that it is impossible to have perfect and complete information the evidence-base will always have weakness and limitations, thus the clinicians have to weight different criteria. To

understand how the decisions are taken under conditions of uncertainty and limitations in available evidence is of great interest. This raises the question of whether and how do clinicians perform the trade-offs between different criteria, what is the relative importance of economic evidence in their decision making framework and how it can be measured?

The purpose of this study is to evaluate the impact of cost effectiveness information on clinicians' decisions by exploring the potential of discrete choice experiments (DCE) to assess the relative importance of different types of evidence in clinical decision making. DCE is an approach to eliciting values originally developed by mathematical psychologists for applications in market research [17]. The technique has been used to investigate a variety of issues in health economics literature including patients' and clinicians' preferences for health outcomes [18-22], patients' preferences for characteristics of health care services, [23, Caldow, 2007 #4, 24-30], provider preferences for job characteristics, [31-33] and priority setting [34-37].

The use of DCE methods to investigate the relative importance of cost effectiveness information in clinical decision making is a novel application. The advantage of these methods over an approach where clinicians directly assign weights themselves to the different aspects of evidence base is that DCE asks the respondents to make choices between different scenarios involving different levels of the dimensions deemed as important. Thus, DCE forces the respondents to trade off some type of evidence for others and incorporates opportunity costs in the elicitation process [21].

We are aware of only two studies that used a DCE framework for a similar purpose, however with a different target population [34, 37]. In an explorative study conducted by Baltussen and colleagues, DCE was used to determine the importance of different priority setting criteria in Ghana. Thirty policy makers were asked to choose between 12 pairs of scenarios describing interventions in terms of medical and non-medical criteria. The economic impact (cost-effectiveness) was considered an important criterion together with poverty reduction, targeting severe diseases or younger patients [34]. Johnson and colleagues investigated the preferences for technology adoption criteria, including threshold values for cost-effectiveness ratios and compared the criteria weights between a sample of industry stakeholders with the with the results of a study of National Institute for Health and Clinical Excellence (NICE) recommendations. The target sample included the industry stakeholders with presumably high level of knowledge of health economics and the main decision criteria were incremental cost-effectiveness ratio (ICER), uncertainty regarding ICER, disease burden and budget impact of the technology [37].

Although these two studies shed light on the validity of the DCE methods to elicit the importance of economic evidence, none specifically addressed clinicians in their sample and none have attempted to

estimate whether clinicians trade-off between different types of evidence when deciding upon a new treatment (for example, how information on cost effectiveness of a new drug compares to the quality of clinical evidence associated with it). One may hypothesise that, faced with structural and inevitable weaknesses of the evidence base clinicians may be forced to trade-off between different criteria, for example, between relatively lower quality of clinical evidence and more favourable economic profile of the new drug.

The purpose of this study is to elicit clinicians' preferences in evaluating and adopting new treatments in cardiology. More specifically, the aim is to estimate the relative importance cost effectiveness information plays in cardiologists' decision making.

From a policy point of view it is important to determine whether clinicians consider cost effectiveness information relevant in order to understand the clinical decision making process and to help set an agenda for further research. To investigate the importance of economic evidence among cardiologists is of particular interest considering that, since the early 1980s, the field of cardiology interventions has been systematically investigated according to economic principles [38, 39]. A plethora of empirical studies investigating cost and effectiveness of treatments in cardiology is available. Although the results of these analyses received considerable attention among decision makers, to date no systematic analysis that we know of has addressed how clinical cardiologists respond to this information.
From a methodological point of view it is of interest to explore the validity of discrete choice methods and to test if the clinicians are willing to trade between different types of evidence when deciding upon the new treatment.

The remainder of this paper is organized as follows. The theoretical framework underpinning DCE in health economics is described in Section 2. The distinct phases of discrete choice analysis and methods applied in this study are presented in Section 3. The survey results are given, followed by a discussion of theory, methods and policy implications in Section 5. Finally, conclusions are outlined in Section 6.

2. Theoretical framework

The theoretical underpinnings for the DCE are rooted in the Random Utility theory (RUT) [40] and Lancaster's economic theory of value [41]. According to Lancaster's approach, each good or service is a bundle of potential characteristics (attributes) and each individual has a set of unique relative utility weights for attribute levels that compose a good or service. In other words, the individual derives utility from the combination of good's attributes, not a good in itself. Combining the utilities

of different attributes provides an individual's overall utility. When faced with alternative choices, the rational individual will always chose the alternative that maximizes their utility.
In the DCE, individuals are faced with a series of alternatives and asked to make choices on the basis of their preferences. The indirect utility yielded by the specific option is assumed to be a function of choice-specific dimensions. Thus, the individual would choose option B over A if:

$$U(X_B, Z) > U(X_A, Z) \quad \text{(Equation 1)}$$

Where U represents the individual's indirect utility function from defined scenario A or B, X_A and X_B are utility bearing attributes of options A and B respectively, and Z socioeconomic characteristics of the individuals that may influence his/her preferences (utility).
In choosing between options, individuals are assumed to know the nature of his/her utility function while the researcher is not. In other words, U is a latent variable which is not directly observed. All we observe is whether an option was chosen or not. This leads to the introduction of a random component of utility that accounts for the analyst's inability to accurately observe individual's behaviour. The error term reflects the unobservable factors influencing individual's preferences. Thus, within the random utility framework indirect utility U is:

$$U(X_A, Z) = V(X_A, Z) + \varepsilon_A \quad \text{(Equation 2)}$$
$$U(X_B, Z) = V(X_B, Z) + \varepsilon_B$$

Where V is the observable component of utility estimated empirically, X_A , X_B and Z as defined above and ε_i (i=A,B) represents the unobservable factors in the individual utility function and errors in measurement and observation by respondents (error term)[40].

Consequently, Equation 1 becomes:

$$V(X_B, Z) + \varepsilon_B > V(X_A, Z) + \varepsilon_A \quad \text{(Equation 3)}$$

Using a DCE in which the respondent is forced to choose between options A and B, the probability that the respondent will choose B over A is given by:

$$\text{Prob}[U(X_B, Z) > U(X_A, Z)] = \text{Prob}[(\varepsilon_A - \varepsilon_B) < (V(X_B, Z) - V(X_A, Z)] \quad \text{(Equation 4)}$$

The chosen form (for example normal or logistic) for the distribution of $(\varepsilon_A - \varepsilon_B)$ determines the appropriate estimation technique for the specification of utility difference (probit or logit). Because

each respondent is asked to make multiple choices, the error term cannot be assumed to be independent and panel data estimation techniques are necessary (i.e. random effects probit) .
Finally, when analysing the data, assumptions must be made about the functional form of the indirect utility function. Assuming the linear additive function, the regression model is specified in terms of differences in attributes between the two choices:

$$\Delta U = \beta_0 + \beta_1 (X_{1B} - X_{1A}) + \beta_2(X_{2B} - X_{2A}) + \ldots\ldots\beta_n (X_{nB} - X_{nA}) + (\varepsilon_B - \varepsilon_A) \qquad \text{(Equation 5)}$$

Where U represents the difference in indirect utilities from the defined scenario, β_0, β_1, $\beta_2 \ldots \beta_n$ are the parameters of the model to be estimated, Xn's represents the levels of the *n* attributes of the commodity being valued ($n-1, 2, \ldots, k$), and $(\varepsilon_B - \varepsilon_A)$ is unobservable error term of the model. β_0 reflects the subject's preferences for one commodity over another when all attributes in the model are the same (alternative specific constant).
The estimated parameters can be interpreted as the marginal utility from a change in the level of the attribute as one moves from option A to option B. The ratio of any two parameters is the marginal rate of substitution between them.

In a random utility framework the choice is modelled by comparing the two indirect utility functions so that the terms common to both of them are dropped out, as happens with individual characteristics in Equation 5. In other words, in this homogenous model the decision to choose A over B or B over A is independent of the individual's observable characteristics. In this case the model leads to restrictive assumptions about the parameters to be estimated and thus doesn't allow not for non random variations in coefficients. However, it may be assumed that some of the respondents' characteristics (for example age or prior knowledge) will lead to different preferences for the attributes. To allow for such non-random variations (heterogeneity) in preferences, interaction terms between respondents' characteristics and attributes can be included in the model [27, 29].

Based on this theoretical framework the underlying assumption in this study is that clinical decision making can be described by its distinct dimensions, i.e different decision criteria. The clinicians derive their preferences from the levels attributed to decision criteria available in different options. The clinicians make a series of choices between alternative options by choosing the option that maximizes their level of utility. In other words, the clinicians' choices are a result of the difference between the two indirect utility functions where each utility function is associated with a different option. Response data are modelled within a benefit (or satisfaction) function which provides information on whether or not the given dimensions are important; the relative importance of dimension and the rate at which individuals are willing to trade between dimensions [42].

3. Methods

In this study DCE was conducted on a sample of Italian cardiologists, who were asked to evaluate the innovative treatment in a specifically designed clinical scenario. Estimation of preferences using the DCE framework is undertaken in 6 distinguished stages [43]:

1) Hypothetical scenario design
2) Identifying the relevant dimensions (attributes)
3) Assigning levels to the dimensions
4) Generating the questionnaire
5) Establishing preferences
6) Model estimation to value total and marginal utilities

1. Hypothetical scenario design

A crucial element in the design of a DCE instruments relates to definition of a hypothetical scenario, to be followed by the construction of efficient choice sets.

Due to the hypothetical nature of stated preference techniques, the respondents are often unfamiliar with the choices they will be faced with in the questionnaire. Thus, setting up the context in which the respondents should imagine themselves when choosing between the options offered is of paramount importance in DCE design. This includes providing sufficient information to the respondents about the commodity being valued and context of choice. In most of the cases the scenario is set by the policy question posed by the research. In the present study, policy objective was to elicit clinicians' preferences for different decision criteria applied when adopting the new treatment in cardiology. Thus, we wanted to design a scenario which would be perceived sufficiently appealing to get clinicians' attention and sufficiently realistic to encourage them to take the questionnaire seriously. The scenario was designed after consultations with 3 senior cardiologists. The respondents were asked to imagine themselves in a situation in which they had to decide whether to adopt an innovative treatment for reducing the risk of cardiovascular mortality in a patient with specific characteristics (Figure 1).

2. Identifying key dimensions in clinical decision making context

The attributes selected for the DCE were initially identified on the basis of theoretical arguments in the literature and subsequently validated in two focus group interviews with clinicians. More specifically, the first list of dimensions identified from the literature was discussed with 8 clinicians attending a major national conference of cardiologists in March 2007 in Florence, Italy (the first focus

group). It was accepted that identifying the full list of decision criteria used by clinicians is a very complex task since many aspects of a new treatment contribute to the final adoption decision. It is argued in the DCE literature that number of attributes should not exceed 4-6 dimensions in order not to impose significant cognitive burden on respondents [42]. In this exploratory study we decide to limit the number of dimensions to 3 and concentrate on the most important criteria as identified in the focus groups.

One of the three dimensions sought to evaluate the importance of cost effectiveness information vs. other types of evidence. Six out of 8 interviewed clinicians mentioned that economic impact would be "something they would look into, as well". That dimension was identified as "economic impact" and it was included in terms of the treatment's incremental cost-effectiveness ratio.

All interviewed clinicians agreed that the *quality/solidity of clinical* evidence and *size of health gain* were key dimensions in evaluating the new treatments in cardiology. This was expected, as evidence based effectiveness are dominant decision making criteria in medicine. We believed that it was important to include dimensions reflecting not only the clinical effectiveness (expressed as the size of health gain) but also the source of evidence (quality of clinical evidence) since both of them are deemed to contribute to clinicians' utility.

3. *Assigning levels to key dimensions*

The key dimensions identified in the previous phase were then assigned levels. In general, levels may be cardinal, ordinal or categorical. Pragmatically, the levels must be plausible and actionable, thus encouraging respondents to take the exercise seriously. Furthermore, the levels must be capable of being traded-off [44]. Although the choices to be presented to the clinicians were hypothetical, they had to be as realistic as possible to encourage valid responses. In the present study attributes were assigned ordinal levels following the discussion with 3 cardiologist and 2 focus group interviews. Levels reflected the format in which evidence about the new treatments is usually conveyed to physicians. As regards dimension 1 (quality of clinical evidence) the levels were first defined on the basis of commonly accepted guidelines in evidence based cardiology [45-47]. In the interviews, however, cardiologists stated that the minimum level of evidence that they would require is "one reasonable size randomized controlled trial" and that anything below that (i.e. observational studies or national registries) would not be considered and thus couldn't be trade-off. A similar reasoning applied to "size of health gain" dimension. The interviewed clinicians stated that in a context scenario described above relative risk reduction (RRR) of 20% would be considered "clinically relevant" while RRR of 5% would not. In addition, it was suggested that the information on both relative and absolute risk redictions should be provide din the survey. Finally, three levels were attributed to economic dimension to distinguish between different cost-effectiveness profiles: very, moderately and not cost effective.

The levels chosen are presented in Table 1.

4. Generating the questionnaire

The number of scenarios increases with the number of characteristics and levels. Rarely can all the scenarios generated be included in the questionnaire (full factorial), and experimental designs are used to reduce the number to a manageable level (fractional factorial). A full factorial design is considered to be more robust since it allows investigation of all interaction effects. The hypothetical scenarios combining all different levels of dimensions were identified and the dimensions and levels chosen gave rise to 18 possible scenarios (3^2 x 2). Due to the low number of dimensions and levels in our study, full factorial design was considered feasible and all 18 scenarios were included in the questionnaire.

Once the scenarios are defined, they must be placed in the choice sets. In doing so, it is important that statistical design properties of orthogonality, minimum overlap, level and utility balance are maintained [48]. Orthogonality means that levels of attributes appear in choice sets with equal frequency with each level of each other attribute and it ensures that the levels of each attribute vary independently of one another. Minimum overlap means that there are as few overlaps as possible of levels for each attribute in each choice set. Level balance means that the levels of each attribute appear with equal frequency. Utility balance means that the options in each set should have similar probabilities of being chosen.

The choice sets were defined using the *cyclical foldover* approach [49]. According to this method, each of the alternatives in the full factorial design is allocated in different choice sets. Dimensions of the pairing alternatives are then constructed by cyclically adding alternatives into the choice set based on their dimension level. The dimension level in the new alternative is the next higher (or lower) dimension level and if the highest level is attained, the attribute level is set to its lowest level. In our study we have two dimensions with 3 levels (1-3) and one with 2 levels (1-2). So, for example, alternative with level 1 in the first dimension (lowest quality of clinical evidence) , level 1 in the second (small size of health gain) and level 2 in the third (moderately cost-effective) would be labelled 112. To generate comparison levels are "folded over". Thus, in this choice set the alternative 112 is paired with alternative 223 (medium quality of clinical evidence, large size of health gain and very cost effective). This creates one choice set. By construction, this design ensures for orthogonality, minimum overlap and level balance hence it satisfies the principles of optimal design for choice experiment [17]. Utility balance requires prior knowledge of parameters to be estimated. Because the focus group did not directly investigate the relative importance of different attributes, it is not possible to make any statements regarding this design criterion.

The fold-over procedure is repeated for all the scenarios in full factorial design so the total of 18 pair wise choices was created. Each choice included the clear trade-offs between different dimensions. To reduce the cognitive burden on respondents and increase the response rate, the 18 choices were randomly split between two questionnaires (Q1 and Q2), each containing 9 choices from full factorial design. This is an acceptable and valid way of identifying overall preferences, providing that each sub sample is large enough and that there are no significant differences in preferences between them [21].

To examine the effects of respondents' characteristics on the relative importance of the attributes, additional questions were asked for socio-demographic details (age, sex and Region), self assessed extent of knowledge of economic evaluation techniques on a scale from 1 (poor) to 5 (very good knowledge) and the number of studies read in the last year (none, 1 to 3, more than 3). This information provided us with potential covariates in the model estimation and help set the background for the analysis. In order to further test the results of discrete choice experiment clinicians were asked to give their level of agreement on a scale from 1 (completely disagree) to 5 (fully agree) on the following statements:
Statement n. 1: *Economic evaluation analysis is currently used by Italian cardiologists.*
Statement n. 2: *Economic evaluation analysis should exercise more impact on decisions in cardiology*
Statement n. 3: *The only economic variable considered by Italian cardiologists is the cost of a drug.*
Finally, the time needed to complete the questionnaire and the perceived level of difficulty was recorded for better interpretation of results. .

5. Establishing preferences for clinicians

The next stage obtained preferences for scenarios included in the questionnaire. The questionnaire was pre-tested on 25 respondents. Following pre-testing, minor modifications were made which included small changes in the scenarios and revisions to the number of patients indicated in the "quality of clinical evidence" attribute to make it more consistent with actual size of secondary prevention RCTs in cardiology. The first version included the final question that asked the respondents to make a simple ranking of the three dimensions included in DCE. It was observed that in a few cases respondents used their ranking answers to adjust the choice previously made in the choice sets. Because the survey was designed to be self-completed, we had no means of preventing this from happening in the main study, so we decided to take out the ranking question from the final version.

Combinations of the different key dimensions and associated levels describe different situations in which clinicians can find themselves when deciding upon treatment. Respondents are supposed to choose the situation in which they would prefer adopting a treatment based on their preferences for

different dimension levels specific to each situation. The choice between the pair wise situation is assumed to be determined by the clinicians' trade-offs of the dimensions and the respondent is expected to choose the situation which will give the respondent the highest utility.

The sample frame of our survey included the attendees of the 2007 National Congress of Cardiologist in Florence, Italy (ANMCO). We distributed questionnaires on the chairs during two major plenary sessions and the respondents were asked to return the questionnaire in the boxes available at the exit of the conference rooms any time during the congress. In both sessions, the chairman mentioned the study and invited the attendees to fill out the questionnaires. Two researchers were available to respond to any required information from the attendees.

6. Estimating marginal utilities

The clinicians' response to each question was included in the model as the binary dependent variable, equal to 1 if option B was chosen and 0 if option A was chosen. The independent variables were the difference in the levels of key dimensions. The independent variables were dummy coded to allow for non linear effects and the "worst" level of each dimension was the omitted category. "Worst" in this case refers to a priori expectations that higher quality of clinical evidence, larger health gain and more favourable cost-effectiveness profile would be preferred by clinicians. Consequently, the results show the increments in utility associated with the movements from the level one (worst level) of each dimension to the levels two and three.
Assuming a normal distribution of error term, a probit model was used to estimate clinicians trade-offs between the dimensions and relative importance of each dimension in the first instance, as exploratory analysis (Model 1). In order to account for multiple observations from a single respondent a random effect extension of the probit model was used in the main analysis (Model 2).
Under the assumption that the marginal utilities for each dimension are not linear, the baseline empirical model was specified as:

$$\Delta U = (\beta_{0B} - \beta_{0A}) + \beta_1 * \Delta \text{Quality\_high} + \beta_2 * \Delta \text{Quality\_mod} + \beta_3 * \Delta \text{Gain\_high} + \beta_4 * \Delta \text{ICER\_very} + \beta_5 * \Delta \text{ICER\_mod} + \varepsilon + \mu$$

Where:
Δ Quality_high, Δ Quality_mod = difference in dummy variables for levels 3 and 2 of quality of clinical evidence dimension, respectively
Δ Gain_high = difference in dummy variable for larger health gain
ΔICER_very, Δ ICER_mod = difference in dummy variables for levels 3 and 2 of economic impact, respectively

The coefficients β_1 to β_5 are to be estimated from the model. The inclusion of constant terms is a violation of the theoretical basis of the model since the questionnaire stated that all dimensions of decision making, other than those specified, should be considered to be equivalent between the options. Thus, in theory, the clinician should have no a priori preference for one option over another regardless of the level of attributes associated. However, the constant term was included to test and control for any model misspecifications due to unobserved dimensions or unobserved interactions between clinicians' socio-economic characteristics and dimensions. The constant term can be interpreted as the difference in average utility of scenario A and B caused by an omitted dummy variable that is a function of other included dimensions or the existence of 'left'/'right' bias [31].

There are two error terms in random probit estimation. One error terms represents the individual specific error μ and the other error term represents a common random error ε. The correlation between the two corr (ε, μ)= ρ takes account of any correlation between observations from any one respondent. The basic random effects probit model assumes homogeneity in preferences across different groups of clinicians. Different methods are proposed in the literature to account for heterogeneity in preferences across respondents. The most common approach is to extend the basic model with a series of interaction terms between respondent's characteristics and difference in dimension levels. Because the main objective of the study was to estimate the relative importance of the cost effectiveness information and due to limited degrees of freedom, only this dimension was interacted with clinicians' socio demographic variables (age, sex, region) and his/her self assessed level of knowledge of economic evaluation techniques (Models 3 and 4). A likelihood ratio test was used to exclude insignificant interaction terms from the reduced model and to test the final reduced model against the restricted (no interactions) model. All models were estimated using software package Stata 9.2.

Theoretical expectations regarding coefficients

Theoretical validity of the valuations was assessed by determining whether the estimated parameters were of anticipated sign in the basic model. Given the model specification and dummy coding, all parameters were expected to have a positive sign since they represent the increment in utility in moving from lower levels of dimensions to higher levels. Only one theoretical expectation was set for the model with interactions: the clinicians with good knowledge of economic evaluation techniques are assumed to have higher preference for this attribute (positive coefficient is expected for this interaction term). For the rest, our null hypothesis was that there are no differences amongst different age groups, regions and genders in the influence of economic evidence on choices.
To further test the validity of the model, the results from the random effects probit model were compared with clinicians' responses to the three statements described above. The correlation between rank variables was analysed using Spearman's rank correlation coefficients, while the differences in

level of agreement between different groups were assessed with non parametric tests (Mann Whitney test). It was hypothesised that if the dimension concerning the economic impact were important to specific groups of clinicians, it would be possible to confirm this result by analysing the level of agreement for the statement n.2.

Consistency in responses and dominant preferences

Dominance tests were used to appraise the consistency of responses. In this, within the choice set one option was better on all levels and should have been chosen by respondents. Questionnaires Q1 and Q2 each included two dominated choices. Since there is evidence that individuals make random errors when completing DCEs [50], it was assumed that those who failed only one test had made a random error and were therefore included in the analysis. Respondents who failed two tests were defined as inconsistent and dropped.

The methodological aim of this study is to explore whether clinicians make trade-offs in line with expectations in the compensatory decision making framework underpinning DCE. Compensatory decision making assumes that respondents can be compensated for a decrease in one dimension with an increase in the other dimension implying that the respondents are willing to trade-off dimensions. It has been argued, however, that, individuals may have dominant preferences that they are not willing to trade off, i.e. only one attribute matters (so called lexographic ordering) [51]. In the case of a lexicographic ordering of goods or characteristics, an individual is not prepared to trade-off and so goods or characteristics cannot be substituted for one another (non-compensatory decision making). Evidently, existence of dominant preference undermines the theoretical assumptions of DCE and at present, there is little consensus about whether and how to account for dominant preferences in DCE, even though their existence has implications for how results are interpreted. It is worth noting that somewhere in between a strict lexicographic ordering and perfect compensatory decision making is target setting behaviour. This form of hierarchical choice allows for some substitution. It operates by an individual setting a target (or threshold) for the first attribute and that this must be reached before the second most important attribute is considered [51].

In order to investigate these issues in our study we identified the respondents with dominant preferences using the method already suggested in the literature [51]. Respondents with dominant preferences are defined as individuals who always chose the scenario with the "best" level of a particular dimension. The random effects probit model was expanded with interaction terms to account for any implication of "dominance" in parameter estimation. A dummy variable indicating whether the individual had a dominant preference (or not) was multiplied by each main effects dimension to create five interaction terms, thereby testing the null hypothesis that there was no

difference between coefficients. Finally, the model was estimated without the individuals that appeared to have dominant preferences (Model 5).

4. Results

Sample characteristics

We distributed the questionnaires at the ANMCO conference and one hundred and twenty nine clinicians completed the questionnaire and provided us with usable data for the analysis by the end of the event. Table 2 displays main sample characteristics. The majority of respondents were males (82%), from the northern regions (55%) and in 45 to 65 age bracket (77%). The average time to complete the questionnaire was 8.39 minutes (range 2 to 30 minutes) while 72.4% of respondents considered the questionnaire to be easy or moderately easy to answer.

The strength of agreement for the three statements provided in the questionnaire varied greatly. None of the respondents strongly agreed (rated 5) with the statement that economic evaluation techniques are currently used by Italian cardiologists, while more than 70% of them agreed (rated 4 and 5) that these analyses should be more used in the field (Table 3). The overall perceived level of knowledge was 2.87 (SD 0.93, range 1 to 5), with 55% of clinicians claiming to have read 1 to 3 studies in the previous year.

Results of discrete choice experiment

Out of 129 completed questionnaires, only 2 respondents (1.6%) failed the two consistency tests and were excluded from the subsequent analysis. A total of 1143 observations were included in the regression models 1 and 2. The results and model characteristics are presented in Table 4. In both models, all attributes had coefficients that were significantly different from zero and of the expected (positive) sign. In other words all three dimensions have a significant impact on the clinicians' choice of innovative drug adoption scenario. The coefficients can be interpreted as the effect of difference between option 2 and option 1 on the likelihood of choosing option 2 over option 1, with the sign reflecting whether the level of the dimension was higher or lower in option 1. A positive coefficient implies that an increase in the dimension level will make it more likely that the clinician would adopt the new treatment. Compared with the lowest level of quality of clinical evidence, both medium and higher levels increase the likelihood of the option being chosen although to different extent. Increase in marginal utility for higher quality is larger than for medium quality. The similar applies for the economic impact: very cost effective and cost-effective treatments increase the likelihood of being chosen when compared to non cost-effective option. Marginal utility gain increases with more

favourable economic impact. Finally, larger health gain significantly increases the likelihood of a drug being adopted.

In terms of relative importance, very favourable cost-effectiveness profile was considered to be the most important dimension closely followed by high quality clinical evidence and large health gain.
The random effects probit estimates were very similar to the probit in all cases, and the both models appear to fit the data very well with 82.9% of observations correctly predicted. The only difference relates to the constant term that proved significant in a simple probit estimation, while it lost its significance in the random extension of the models (Model 2). The value of ρ, measuring the correlation between responses for the same clinician, is statistically significant suggesting that a random effects specification was appropriate and that there were unobserved interactions between clinicians characteristics and attributes.

Heterogeneity of preferences for dimension among different clinicians' groups was tested in a random effects probit model with interaction terms. The effects of interacting all three dimensions with dummy variables for age group, geographical area and perceived level of knowledge are presented in Table 5 (Model 3). Model 4 is a reduced model derived from performing a backward stepwise elimination of insignificant variables of Model 3. The economic dimension was found to be significantly more important for clinicians below 45 years of age and those with good knowledge of economic evaluation techniques. More specifically, younger clinicians valued significantly more the scenarios in which the new treatment was cost-effective and highly cost-effective profile. The good extent of knowledge significantly interacted only with cost-effective level while the interaction term was not significant for highly cost effective profile. This result implies that this group of clinicians had some kind of "threshold" for their decision making criteria: it was deemed important that the drug reached the cost-effectiveness threshold more than having a very favourable cost-effectiveness profile.
The reduced model with significant interactions improved model fit in comparison to model with non interaction terms (using a likelihood ratio test), but adding further interaction terms did not improve the model fit.

These results were further investigated by analysing the clinicians' level of agreement with the three statements provided in the questionnaire. The correlation between level of knowledge of economic evaluation techniques and level of agreement with the statements n. 2 and n.3 resulted significant (but of low magnitude ($p<0.05$, Spearman coefficient 0.07 and 0.15 for the statement n.2 and 3. respectively). The clinicians who claimed good knowledge of economic evaluation analysis agreed significantly more with the statements that economic evaluation analysis should be used more in cardiology and that the only economic criterion cardiologists currently use is the cost of a drug.

Similarly, younger clinicians (age <45) expressed stronger agreement with the wider use of economic evaluation in cardiology than their older colleagues.

Testing for dominant preferences

Overall 30 clinicians out of 127 valid responses (23.6%) exhibited dominant preferences for one of the three attributes. The level of dominant preferences was similar to other studies [35]. The majority of clinicians with dominant preferences have dominating preferences for the size of health gain dimension (n= 14, 47%). Only 7 clinicians always choose the scenario with the best level of quality of clinical evidence while 9 of them always chose the scenario with the most favourable economic profile.

We estimated a model including interaction terms for whether the individual demonstrated dominant preferences for one of the attribute (results not shown). The coefficients for the interaction terms between the dummy variable (dominant=1 when the respondent had dominant preferences) and relative dimension describe how the respondents with dominant preferences differ from the respondents that do not appear to have dominant preferences. None of the interaction terms was significantly different from zero.

Furthermore, in order to reduce any concern about the effects of dominant preferences, the baseline model was estimated without data from these individuals (Model 5). The results did not differ significantly between the two models (with and without individuals appearing to have dominant preferences): the sign, order and significance levels of the coefficients remained the same, with some slight changes in their magnitude.

5. Discussion

To our knowledge, this is the first empirical study that investigates the use of cost effectiveness information by clinicians in discrete choice experiment framework. The majority of available studies have relied on traditional survey methods to investigate clinicians' attitudes and perceptions of economic information in their decisions. We argue that discrete choice experiment provides a feasible and preferable methodological framework to elicit clinicians' decision making criteria. In our study more than 70% of clinicians found the questionnaires to be easy to complete. While acknowledging that clinical decision making is a complex process, it forces the respondents to trade off between different criteria and thus incorporates opportunity cost of decisions taken. This approach is preferred because it mimics the real-life decisions clinicians are faced with regularly when deciding upon new treatments.

There are a number of limitations to our study that could be addressed in future research. First, and perhaps the most important limitation, concerns the choice of a sample. The sample was drawn from the population of national conference attendees and was based on voluntary participation. Given the exploratory nature of our study and limited sources available, it was not feasible to invest in a fully representative sampling procedure, and we cannot state that our respondents represent an unbiased sample of Italian cardiologists. However, limited socio-demographic data available about our respondents (age, sex and region) show that the sample was distributed in line with expectations across national territory and different age groups.

Second, we used a very limited form of test for dominant preferences, which may not be sufficiently powerful to detect this violation of the standard axioms. In addition to using the criterion of whether an individual always chose the scenarios with the best level of one of the three dimensions, it would have been useful to incorporate additional information about the relative importance of the different dimensions [51]. We rejected a question asking respondents to rank the dimensions in the present study, as some respondents in the pilot used this question to "adjust" choices previously made in the discrete choice questionnaire. We did, however, included three statements to indirectly investigate clinicians' preferences for the economic dimension to test the validity of responses in discrete choice survey. Our results are in line with the available evidence suggesting that measurement of attitudes using simple ranking is consistent with measurement of preferences in discrete choice framework [52].

While acknowledging the limitations, our study provides new evidence on the use of economic evaluation at clinical level decision making.

The results obtained are comparable to those already reported in the literature using traditional surveys, to a certain extent. We find that the cost effectiveness information resulted to be an important ingredient of clinicians' decision strategies. This result is consistent with those obtained in a recent review of empirical studies investigating the impact of economic evaluation at different level of decision making in healthcare. The authors of the review concluded that there is moderate influence of economic arguments at the micro level (clinical). [5].

In our study, achieving a favourable cost-effectiveness ratio ("moderately cost effective") appears to be more important in determining choices than increasing the quality of clinical evidence by conducting larger clinical trials. It appears even more important than the increase in the size of health gain associated with drugs under evaluation. At first glance, this result may be somewhat surprising and is in contrast to another study recently conducted in Italy [3], in which only a small proportion of surveyed clinicians stated that economic evaluation analysis was beneficial at the clinical level. It should be noted, however, that this result was obtained when asking clinicians to choose one among three levels of decision making for which they thought the economic evaluation can contribute the

most. Given the responsibilities for the consequences of decisions taken at macro (policy) and meso (organizational) level, majority of clinicians chose these two levels over the clinical one. In our study, clinicians were not asked to give their general opinion about the value of economic evaluation analysis but to imagine themselves in a hypothetical clinical scenario. Thus, they were "forced" to evaluate the importance of economic evidence at this specific level of decision making.
Our results further show that age and knowledge play important role in clinicians' preferences. Younger cardiologists value cost-effectiveness information more than their older colleagues in Italy. This implies an existence of some sort of generational difference in this respect. We are not aware of any other study investigating the impact of age on clinicians' attitudes towards the economic evidence, so we can not compare our results with other settings.

In regards to knowledge, several studies reported that that more training in the field as one of the main incentives to the wider use of cost effectiveness information [3, 5]. In this study we have been able to show that clinicians with higher perceived level of knowledge value significantly more the economic information for their decisions. It is interesting to note that this conclusion applies only for the intermediate level of cost-effectiveness dimension ("moderately cost-effective"), while the significance couldn't be found for the most favourable "very cost effective" term. This suggests that clinicians with good knowledge of economic evaluation may in fact apply some sort of "threshold" when evaluating the cost effectiveness information. In other words, it is important that the drug reaches this threshold, whilst further improvement of its economic profile doesn't affect clinicians' choices.

As expected, size of health gain has important impact on the choice of therapies. Judging from the estimated coefficients, the improvement in the size of health gain was more important than the incremental improvement of quality of clinical evidence. We believe that this is an interesting finding since it implies that, in our study, clinicians are more interested in the outcome of clinical trails rather then the number or size of those trials. Obviously this conclusion is limited to the levels presented to clinicians in our survey. All three levels of quality of clinical evidence referred to one or more randomized clinical trials (RCTs), i.e. the gold standard source of evidence in medicine. In other words, as long as there is at least one published RCT of relatively acceptable size, clinicians will "trust" it as appropriate evidence base for their choices.

From the methodological point of view, this study illustrates the application of discrete choice experiments to evaluate the importance of cost-effectiveness information for clinicians' choices. Thus, it provides some valuable insights in discrete choice methods in this novel application. .

The focus group interviews and pilot study revealed that clinicians had some idea bout the trade offs involved when deciding between alternative treatments. However, they were clearly not familiar in discussing the trade offs explicitly and hence the choice exercise may have seemed somewhat abstract to those who filled the questionnaire. The clear definition of a context in which the discrete choice is applied was crucial in this respect. We argue, therefore, that the qualitative research methods prior to design discrete choice questions should be used not only to define attributes and levels for the survey but to identify the scenario to which the survey will be applied. In other words, even though the abstractness of the context is unavoidable due to the hypothetical nature of the discrete choice experiments, researchers should put a significant effort to increase the realism of the context to elicit valid and reliable responses. The use of appropriate language and wording is fundamental, as few studies have shown that the choice of words for dimensions in the questionnaire, may significantly influence their interpretation by respondents, and hence the study results [27, 35].

The internal validity of DCE addresses typically the extent to which the respondents' answers accord with theoretical assumptions. The results demonstrate that the expected sign of the coefficient matches the theoretical predictions, for all three dimensions and associated levels.

One of the greatest challenges of discrete choice experiments is to establish their external validity. Would the clinicians make the same choices if found in a same situation in real life? This question will probably remain unanswered until economic evaluation studies become more accessible to clinicians to guide their therapeutic decisions on regular basis. If that happens, it may become possible to compare our results with clinicians' revealed preferences.

Conclusions

Overall, a DCE framework appears to be a feasible methodology for eliciting clinicians' decision making criteria. This explorative study revealed that clinicians are in general able to understand the trade offs and are able to answer the discrete choice questions. We propose that similar study design can be used to investigate clinicians' preferences in other clinical areas beyond cardiology. By investigating the relative importance clinicians attach to different types of evidence, the results of these studies, together with the current one, may eventually be used to inform allocation of resources for conducting research.

References

1. Black, N., Evidence based policy: proceed with care. *Bmj,* 2001. 323(7307):275-9.

2. Klein, R., From evidence-based medicine to evidence-based policy? *J Health Serv Res Policy,* 2000. 5(2):65-6.

3. Fattore, G. and A. Torbica, Economic evaluation in health care: the point of view of informed physicians. *Value in Health,* 2006. 9(3):157-67.

4. Williams, I. and S. Bryan, Understanding the limited impact of economic evaluation in health care resource allocation: a conceptual framework. *Health Policy,* 2007. 80(1):135-43.

5. van Velden, M.E., J.L. Severens, and A. Novak, Economic evaluations of healthcare programmes and decision making: the influence of economic evaluations on different healthcare decision-making levels. *Pharmacoeconomics,* 2005. 23(11):1075-82.

6. Kapiriri, L., O.F. Norheim, and D.K. Martin, Priority setting at the micro-, meso- and macro-levels in Canada, Norway and Uganda. *Health Policy,* 2007. 82(1):78-94.

7. Wu, O., et al., The impact of economic information on medical decision making in primary care. *J Eval Clin Pract,* 2004. 10(3):407-11.

8. Ubel, P.A., et al., The influence of cost-effectiveness information on physicians' cancer screening recommendations. *Soc Sci Med,* 2003. 56(8):1727-36.

9. Kangis, P. and L. van der Geer, Pharmaco-economic information and its effect on prescriptions. *J Manag Med,* 1996. 10(5):66-74.

10. Brody, B., et al., The impact of economic considerations on clinical decisionmaking: the case of thrombolytic therapy. *Med Care,* 1991. 29(9):899-910.

11. Kapiriri, L., T. Arnesen, and O.F. Norheim, Is cost-effectiveness analysis preferred to severity of disease as the main guiding principle in priority setting in resource poor settings? The case of Uganda. *Cost Eff Resour Alloc,* 2004. 2(1):1.

12. Kapiriri, L. and O.F. Norheim, Criteria for priority-setting in health care in Uganda: exploration of stakeholders' values. *Bull World Health Organ,* 2004. 82(3):172-9.

13. Grandori, A., A Prescriptive Contingency View of Organizational Decision Making. *Administrative Science Quarterly,* 1984. 29(2):192-209.

14. Simon, H.A., Decision-Making and Administrative Organization. *Public Administration Review,* 1944. 4(1):16-30.

15. Simon, H.A., Administrative Decision Making. *Public Administration Review,* 1965. 25(1):31-37.

16. Simon, H.A., The Logic of Rational Decision. *The British Journal for the Philosophy of Science,* 1965. 16(63):169-186.

17. Louviere, J.J., D.A. Hensher, and J.D. Swat, *Stated Choice Methods. Analysis and Application*. 2000, Cambridge: Cambridge University Press.

18. Ashcroft, D.M., E. Seston, and C.E. Griffiths, Trade-offs between the benefits and risks of drug treatment for psoriasis: a discrete choice experiment with U.K. dermatologists. *British Journal of Dermatology,* 2006. 155(6):1236-41.

19. Lancsar, E.J., et al., Using discrete choice experiments to investigate subject preferences for preventive asthma medication. *Respirology,* 2007. 12(1):127-36.

20. Ryan, M., K. Major, and D. Skatun, Using discrete choice experiments to go beyond clinical outcomes when evaluating clinical practice. *Journal of Evaluation in Clinical Practice,* 2005. 11(4):328-38.

21. Ryan, M., et al., Using discrete choice experiments to estimate a preference-based measure of outcome--an application to social care for older people. *Journal of Health Economics,* 2006. 25(5):927-44.

22. Sculpher, M., et al., Patients' preferences for the management of non-metastatic prostate cancer: discrete choice experiment.[see comment]. *BMJ,* 2004. 328(7436):382.

23. Ryan, M., et al., Rapid prenatal diagnostic testing for Down syndrome only or longer wait for full karyotype: the views of pregnant women. *Prenatal Diagnosis,* 2005. 25(13):1206-11.

24. Coast, J., et al., Preferences for aspects of a dermatology consultation. *British Journal of Dermatology,* 2006. 155(2):387-92.

25. Gerard, K. and V. Lattimer, Preferences of patients for emergency services available during usual GP surgery hours: a discrete choice experiment. *Family Practice,* 2005. 22(1):28-36.

26. Gerard, K., et al., The introduction of integrated out-of-hours arrangements in England: a discrete choice experiment of public preferences for alternative models of care. *Health Expectations,* 2006. 9(1):60-9.

27. Hanson, K., et al., Preferences for hospital quality in Zambia: results from a discrete choice experiment. *Health Economics,* 2005. 14(7):687-701.

28. Longo, M.F., et al., Involving patients in primary care consultations: assessing preferences using discrete choice experiments.[see comment]. *British Journal of General Practice,* 2006. 56(522):35-42.

29. Scott, A., M.S. Watson, and S. Ross, Eliciting preferences of the community for out of hours care provided by general practitioners: a stated preference discrete choice experiment. *Social Science & Medicine,* 2003. 56(4):803-14.

30. Ryan, M., et al., Trade-offs between location and waiting times in the provision of health care: the case of elective surgery on the Isle of Wight. *Journal of Public Health Medicine,* 2000. 22(2):202-10.

31. Scott, A., Eliciting GPs' preferences for pecuniary and non-pecuniary job characteristics. *Journal of Health Economics,* 2001. 20(3):329-47.

32. Ubach, C., et al., What do hospital consultants value about their jobs? A discrete choice experiment. *BMJ,* 2003. 326(7404):1432.

33. Wordsworth, S., et al., Preferences for general practice jobs: a survey of principals and sessional GPs. *British Journal of General Practice,* 2004. 54(507):740-6.

34. Baltussen, R., et al., Towards a multi-criteria approach for priority setting: an application to Ghana. *Health Economics,* 2006. 15(7):689-96.

35. Bech, M., Politicians' and hospital managers' trade-offs in the choice of reimbursement scheme: a discrete choice experiment. *Health Policy,* 2003. 66(3):261-75.

36. Farrar, S., et al., Using discrete choice modelling in priority setting: an application to clinical service developments. *Social Science & Medicine,* 2000. 50(1):63-75.

37. Johnson, F.R. and M. Backhouse, Eliciting stated preferences for health-technology adoption criteria using paired comparisons and recommendation judgments. *Value in Health,* 2006. 9(5):303-11.

38. Bogden, P.E. and I.J. Schatz, Cost-effective cardiology: the new challenge. *JAMA,* 1985. 253(3):400.

39. van Hout, B.A., et al., Economic evaluation in the field of cardiology: theory and practice. *Progress in Cardiovascular Diseases,* 1999. 42(2):167-73.

40. McFadden, D., *Conditional logit analysis of qualitative choice behaviour*, in *Frontiers in Econometrics*, P. Zarembka, Editor. 1973, Academic Press: New York. p. 105-142.

41. Lancaster, K., A new approach to consumer theory. *Journal of Political Economy,* 1966. 74:134-157.

42. Ryan, M. and K. Gerard, Using discrete choice experiments to value health care programmes: current practice and future research reflections. *Applied Health Economics & Health Policy,* 2003. 2(1):55-64.

43. Ryan, M., K. Gerard, and G. Currie, *Using discrete choice experiments in health economics*, in *The Elgar Companion to Health Economics*, J. A, Editor. 2006, Edward Elgar Publishing, Inc: Nothampton. p. 405-415.

44. Ryan, M., et al., Use of discrete choice experiments to elicit preferences. *Quality in Health Care,* 2001. 10 Suppl 1:i55-60.

45. Cook, D.J., et al., Clinical recommendations using levels of evidence for antithrombotic agents. *Chest,* 1995. 108(4 Suppl):227S-230S.

46. Sackett, D.L., Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest,* 1989. 95(2 Suppl):2S-4S.

47. Guyatt, G.H., et al., Users' guides to the medical literature. IX. A method for grading health care recommendations. Evidence-Based Medicine Working Group. *Jama,* 1995. 274(22):1800-4.

48. Viney, R., E. Savage, and J. Louviere, Empirical investigation of experimental design properties of discrete choice experiments in health care. *Health Economics,* 2005. 14(4):349-62.

49. Carlsson, F. and P. Martinsson, Design techniques for stated preference methods in health economics. *Health Econ,* 2003. 12(4):281-94.

50. Miguel, F.S., M. Ryan, and M. Amaya-Amaya, 'Irrational' stated preferences: a quantitative and qualitative investigation. *Health Econ,* 2005. 14(3):307-22.

51. Scott, A., Identifying and analysing dominant preferences in discrete choice experiments: An application in health care. *Journal of Economic Psychology,* 2002. 23:383-98.

52. Phillips, K.A., F.R. Johnson, and T. Maddala, Measuring what people value: a comparison of "attitude" and "preference" surveys. *Health Services Research,* 2002. 37(6):1659-79.

Figure 1. Example of a choice presented to clinicians

The context

Imagine the following situation: a female patient, 65 years old, with family history of cardiovascular diseases, one mild acute myocardial infarction experienced at the age of 60, comes to see you for a specialist visit in the hospital. The blood exams show total cholesterol 230mg/dl and blood pressure is 150/95 mm Hg. The baseline risk of cardiac mortality is 10%.
You must decide whether to prescribe an innovative treatment in order to reduce the cardiac mortality risk. Your decision must be based exclusively on the basis of evidence presented to you in different scenarios. The scenarios differ according to the quality of clinical evidence available, size of health gain estimated in target population and cost-effectiveness profile of the new drug.
For each question below you are asked to choose in which situation you would be more favourable of adopting the new treatment (Situation A or Situation B).

1. Which scenario you would prefer? (please tick box below)

Scenario A □ Scenario B □

Scenario A	*Scenario B*
Evidence obtained from 3 RCTs, all three favourable for the treatment (n=30,000) Relative Risk Reduction 5% (Absolute Risk Reduction 0.5%) Not cost effective (ICER= 200,000 € per life years gained)	Evidence obtained from one small RCT (n=3,000) Relative Risk Reduction 20% (Absolute Risk Reduction 2%) Very cost-effective (ICER= 5,000 € per life years gained)

Table 1. Attributes and levels used in DCE

Attributes	*Variable**	*Levels definition*
Quality of clinical evidence	Quality_high	Evidence obtained from 3 RCTs, all three favourable for the treatment (n=30,000)
	Quality_mod	Evidence obtained from one big RCT (n=10,000)
		Evidence obtained from one small RCT (n=3,000)
Size of health gain	Gain_high	Relative Risk Reduction 20% (Absolute Risk Reduction 2%)
		Relative Risk Reduction 5% (Absolute Risk Reduction 0.5%)
Economic impact	ICER_very	Very cost-effective (ICER= 5,000 € per life years gained)
	ICER_mod	Cost-effective (ICER=50,000 € per life years gained)
		Not cost effective (ICER= 200,000 € per life years gained)

* Attribute levels are dummy coded with the "worst" level being the reference (omitted) category

Table 2. Sample characteristics

	N.	*%*
Sex		
Female	23	18.1
Male	104	81.2
Region		
North	69	54.8
Centre	31	24.6
South	27	20.6
Age		
<45 years	23	18.4
45 - 65 years	96	76.8
>65 years	26	4.8
Self assessed extent of knowledge of economic evaluation techniques		
1 (poor)	12	9.5
2	27	21.3
3	53	42.1
4	33	26.2
5 (very good)	1	0.8
Number of economic evaluation studies read in the last year		
none	20	15.9
1 to 3	70	55.1
more than 3	37	29.0

Table 3. Level of agreement of respondents with the proposed statements

Statement	*Mean*	*Median*	*1 (strongly disagree)*	*2*	*3*	*4*	*5 (strongly agree)*
Economic evaluation analysis is currently used generally by Italian cardiologists	2.5	3	11.8%	36.2%	41.7%	10.2%	0.0%
Economic evaluation analysis should be used more by Italian cardiologists	3.9	4	3.9%	3.9%	19.7%	41.7%	30.7%
Italian cardiologist use the cost of a drug as the only economic criteria in treatment decisions	2.5	2	2.4%	30.7%	18.1%	22.8%	3.9%

Table 4. Probit and random effects probit baseline models

Dimensions	*Model 1*	*Model 2*
	Coefficients (se)	Coefficients (se)
Quality_high	0.865 (0.071)***	0.949 (0.079)***
Quality_mod	0.535 (0.066)***	0.585 (0.071)***
Gain_high	0.792 (0.051)***	0.874 (0.060)***
ICER_very	1.074 (0.073)***	1.133 (0.084)***
ICER_mod	0.757 (0.069)***	0.811 (0.074)***
Constant	0.102 (0.046)*	0.111 (0.0620)
N of observations	1143	1143
N of respodents	127	127
Log likelihood	-487.02	-479.31
Prob (Chi2)	< 0.0001	< 0.0001
Rho	0.384	0.394
ρ (95% confidence interval)		0.161 (0.086-0.282)
Proportion 1s correctly predicted	82.9%	82.9%
Proportion 0s correctly predicted	79.4%	79.4%

***p<0.0001 *p<0.05

Table 5. Random effects probit, including interactions terms (full and reduced model)

Dimensions	*Model 3*	*Model 4*
	Coefficients (se)	Coefficients (se)
Quality_high	0.974 (0.082)***	0.965 (0.081)***
Quality_mod	0.603 (0.073)***	0.596 (0.072)***
Gain_high	0.894 (0.062)***	0.887 (0.061)***
ICER_very	1.033 (0.098)***	1.077 (0.089)***
ICER_mod	0.610 (0.093)***	0.631 (0.091)***
Good_knowledge* ICER_very	0.178 (0.175)	
Good_knowledge* ICER_mod	0.357 (0.152)*	0.272 (0.126)*
Age_45*ICER_very	0.445 (0.221)*	0.449 (0.223)*
Age_45*ICER_mod	0.516 (0.183)**	0.517 (0.184)**
Age 45_65* ICER_very	0.620 (0.347)	
Age 45_65* ICER_mod	0.276 (0.317)	
North * ICER_very	0.058 (0.156)	
North * ICER_mod	0.062 (0.142)	
Constant	0.089 (0.063)	0.0935 (0.139)
N	1143	1143
Log likelihood	-470.817	-473.107
Prob (Chi2)	<0.0001	<0.0001
Rho	0.404	0.401
LR test with no interactions - Chi2 (p -value)	16.99 (0.030)	12.41 (0.006)
LR test with full set of interactions - Chi2 (p value)	-	4.58 (0.4693)

***p<0.0001 **p<0.01 *p<0.05

Table 6. Random effects probit baseline estimates with and without dominant individuals

Dimensions	*Model 2 – full set of respondents*	*Model 5 No dominant preferences*
	Coefficients (se)	Coefficients (se)
Quality_high	0.949 (0.079)***	1.116 (0.099)***
Quality_mod	0.585 (0.071)***	0.723 (0.087)***
Gain_high	0.874 (0.060)***	0.887 (0.071)***
ICER_very	1.133 (0.084)***	1.345 (0.109)***
ICER_mod	0.811 (0.074)***	1.029 (0.096)***
Constant	0.111 (0.0620)	0.146 (0.071)
N of observations	1143	873
N of respodents	127	97
Log likelihood	-479.31	-339.02
Prob (Chi2)	< 0.0001	<0.001
Rho	0.394	0.437
ρ (95% confidence interval)	0.161 (0.086-0.282)	0.145 (0.063-0.299)
Proportion 1s correctly predicted	82.9%	82.9%
Proportion 0s correctly predicted	79.4%	79.4%

***p<0.001