Universidade do Minho
Escola de Economia e Gestão

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Public Stated Preferences for Pharmaceutical Funding Decisions

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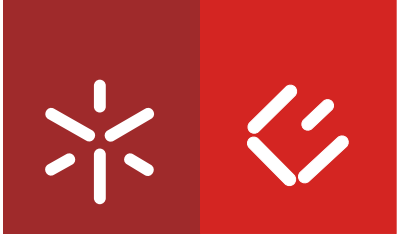

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Public Stated Preferences for Pharmaceutical Funding Decisions

Masters Dissertation
Masters in Health Economics and Policy

Supervised by:
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DECLARAÇÃO

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Abstract

Introduction: In Portugal, the pharmaceutical consumption is subsidized by public funds. The rising NHS expenditures and the recent need of cost containment policies emphasize the discussion on priority setting in health care and raise questions of which criteria are appropriate to support funding decisions. Decision-makers base the pharmaceutical funding grant on clinical and economical evidence. Vulnerable sub groups, such as chronically ill and elderly with low income, benefit of higher financing rates than the general population. Little is known about the preferences of the public for pharmaceutical funding criteria in Portugal. Discrete Choice Experiments (DCEs) are suitable for the estimation of stated preferences as they measure of benefit that describes the good through a bundle of attributes and levels and it is based on the assumption that an individual's valuation depends upon the levels of these attributes. DCE have the potential to contribute to outcome measurement for use in economic evaluation, uniquely allowing the investigation of diverse questions, such as clinical, economic and ethical. **Aim:** This work seeks to investigate criteria considered important by the Portuguese public for allocating resources for pharmaceuticals. In particular, we estimate the importance of the severity of the disease for which the treatment is indicated, the prevalence of the disease in Portugal, the efficacy of the pharmaceutical and the government costs per person treated. **Method:** A self-completion DCE survey, with 18 binary choice sets, was administered to two samples of the general population. Choice data are used to consider the relative importance of changes across attribute levels, and to model utility scores and relative probabilities. **Results:** A total of 90 individual completed the DCE. For the levels and units presented in the DCE, all attributes were statistically significant, in both samples. The attributes "severity of the disease for which the pharmaceutical is indicated" and "efficacy of the new pharmaceutical" had the higher utility values. The coefficient for the cost attribute was negative. **Conclusions:** This is the first DCE in Portugal that extends the discussion of prioritization in the health care sector, namely on the pharmaceutical funding decision, to the general population. This study sets foundation for future research and supports the acceptability of the public for DCEs.

Key-words: Pharmaceuticals Funding, Pharmaceuticals Reimbursement, Stated Preferences, Discrete Choice Experiment.

Resumo

Introdução: O consumo de medicamentos em Portugal, é em parte, financiado pelo Estado, através de um sistema de comparticipação de medicamentos. O aumento da despesa do SNS e a recente necessidade de implementação de políticas para a contenção da despesa pública enfatizam a discussão sobre os critérios apropriados para fundamentar as decisões de priorização e financiamento dos cuidados de saúde. Atualmente, a decisão para atribuição de comparticipação de medicamentos baseiam-se na evidência de benefício clinico e económico. No entanto, nenhum estudo investigou as preferências sociais para o financiamento de medicamentos em Portugal. A metodologia selecionada, escolha discreta, tem o potencial de contribuir de forma única para a avaliação económica na saúde, englobando critérios clínicos, económicos e éticos. **Objetivo:** O presente trabalho tem como objetivo investigar critérios considerados importantes pela população portuguesa para o financiamento de medicamentos. Em particular, estimou-se a importância dos atributos: severidade da doença para o qual o medicamento está indicado, prevalência da doença em Portugal, eficácia do medicamento e custo para o estado por pessoa tratada. Método: Foi administrado um questionário, DCE, com 18 pares de alternativas, a duas amostras da população de Braga.

Resultados: No total, 90 indivíduos responderam ao questionário. Os atributos severidade da doença para o qual o medicamento está indicado e eficácia do medicamento obtiveram os valores de utilidade mais elevados. Para os níveis apresentados, todos os atributos fora estatisticamente significativos, em ambas as amostras. O coeficiente para o atributo "custo para o estado por pessoa tratada" foi negativo.

Conclusão: Este é o primeiro estudo português a estender a discussão do financiamento de medicamentos à população geral. Este estudo contribui para o desenvolver de investigações futuras e evidencia a aceitabilidade dos DCE junto da população.

Palavras-chave: Financiamento, Medicamentos, Preferências Socias, Escolha Discreta.

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Chapter 1. Introduction

1. Background

There is a general agreement that the market mechanism fails to allocate resources efficiently and equitable in the health care sector (Amaya-Amaya, Gerard & Ryan, 2008) . Hence, this task often falls to the government through public policies (Ryan, Scott, Reeves, Bate and Russell, 2001). In the absence of market forces as the definition of the allocation of resources, policy makers seek alternative means of choosing between competing demands on the health care budget. In other words, they set priorities. This priority setting has always been a feature of publicly financed health care systems (Hauck, Smith & Goddard, 2004), but some call for a more explicit approach.

The design of health policies raises an important question: how should public funds be allocated balancing the available scarce resources, the unlimited demand for health care services and the continuing rising health care expenditures? (Ryan et al. 2001)
The European countries trust these issues to their National Health System (NHS) that has as a main objective the provision of medical services in line with cost-effectiveness, quality and equitable principles (Mossialos, Mrazek & Walley, 2004). The appropriate criteria that should be used in setting priorities in a publicly funded health care, remains open to debate (Bryan et al., 2002) although cost-effectiveness methods have become popular.

The eventual goal of economic evaluation, in the context of health services is to make decisions about resources that fulfil the interests of society. It seems therefore pertinent that the social values that fundament the decision process should be informed by the preferences of a representative sample of members of the society, who pay for and are eligible to benefit from the resource(s). (Farrar, Ryan, Ross and Ludbrook, 2000; Whitty, Rundle-Thiele and Scuffham, 2008; Koonal and Shah, 2010)

In Portugal, the health expenditure represents 10.4% of the GDP while the pharmaceutical expenditure represent over 15.5% on of NHS budget (INFARMED 2011). These

numbers, allied with the economic difficulties Portugal faces, result in a great pressure on the health care budget, particularly on pharmaceutical cost containment. The entry and financing of new pharmaceuticals is regulated by the National Authority of Medicines and Health Products (INFARMED, I.P.). The allocation criterion used is the potential health gain produced by an intervention, often measured in terms of Quality Adjusted Life Years (QALYs).
Although the exact amount is not officially defined, INFARMED is generally willing to pay € 30.000/QALY for reimbursement. For orphan pharmaceuticals the price raises to between €50.000 and €80.000 per QALY (Veiga, Correia, Meireles, Dias, 2011). INFARMED states that the decision rule followed under this approach is the maximization of health gain under budget constraints (Veiga et al. 2011). However, the definition of the exact amount INFARMED is willing to pay has been not subject to public scrutiny.

Little is known in Portugal about the preferences of the public, namely about the subsidy of pharmaceuticals. As the public is increasingly interested and engaged into public policies, its values should be used to inform better and more efficient policy. Moreover, public involvement may help to strengthen the relationship between citizens and decision makers, ultimately resulting in clinical, licensing, reimbursement, and policy decisions that better reflect the preferences of stakeholders, especially patients (Whitty, Rundle-Thiele & Scuffham PA, 2008). Aligning clinical practice, drug development, and health policy with patient preferences may also improve the effectiveness of health interventions, possibly improving the adoption of, satisfaction with, and adherence to clinical treatments or public health program (Koonal & Shah 2009).

2. Aim

The study seeks to investigate criteria considered important by the Portuguese public for allocating resources for pharmaceuticals. In particular, the importance of the severity of the disease for which the treatment is indicated, the prevalence of the disease in Portugal, the efficacy of the new pharmaceutical and the government costs per person treated.

There is good amount of research on the Portuguese pharmaceutical policy and fi-

nancing. However, little is known about the preferences of the Portuguese public, namely about the financing of pharmaceuticals. Hence, the present study brings a fresh approach to the Portuguese pharmaceutical policy discussion.

3. Methods

We use a preference elicitation method, namely the discrete choice experiment (DCE), to elicit societal preferences. Individuals are presented with choice sets comprising different hypothetical combination of new pharmaceutical attributes: severity of the disease for which the treatment is indicated; prevalence of the disease; efficacy of the new pharmaceutical and government cost per person treated. The questionnaire was divided in three sections: a first part with some warm-up questions, a second section for the choice questions and a third one which aimed to gather information about demographics, health status and insurance coverage. Data were analysed with STATA 10® and are discussed from a policy design point of view.

4. Organization And Contents

A DCE requires a multidimensional approach of theoretical and practical stages. After the preceding introduction and reasoning of this work, chapter two intends to describe the Portuguese pharmaceutical sector, at a glance. Although the discussion of the pharmaceutical market is out of the scope of this work, it is important for the reader to acknowledge the Portuguese pharmaceutical context, for a better understanding of the framework and the results.

Chapter three summarizes the literature and seeks to describe the process through which the method was chosen. It focus on the use of DCE in health care, namely on pharmaceutical funding research.

Chapter four explains the method with emphasis on the main steps of the DCE. This includes the definition of the attributes and levels, the experimental design, the qualitative work that tested the questionnaire, the sample design and the survey administration process. The presentation and discussion of the DCE are presented in chapter five and the conclusion that arises from them, take place on chapter six.

Chapter 2. Pharmaceutical Policy

Recent economic events had large influence on the managing of the state budget and the design of pharmaceutical policies. Namely, in May 2011, the Portuguese government agreed a reform program with an obligation to enforce healthcare budget cuts as part of austerity measures (Carone et al., 2012). The present chapter intends to summarize the main features of the Portuguese pharmaceutical funding context in order to contextualize the research and its results.

1. Pharmaceutical Expenditures

The Portuguese health system is based in three funding systems: the National Health Service (NHS), special social health insurance schemes for certain professions (health subsystems) and voluntary private health insurance. Health is pubicly financed with general taxes. Nonetheless, in general, the use of health care services and health products, including pharmaceutical consumption, is dependent on a co-payment (Vogler and Leopold, 2009)

The Portuguese pharmaceutical sector has been characterized by a substantial increase in expenditure since the beginning of the 1990s (Barros et al. 2011). This increase may be explained by demographic factors (e.g. the ageing population, development of chronicle diseases) and medical progress factors (e.g. introduction of new biological pharmaceuticals, which are more expensive) (Carone et al. 2012).

Rising health care costs as well as the global economic downturn has led healthcare payers to opt for austerity measures such as a reduction of healthcare budgets, price and reimbursement cuts, and the enhancement of generic uptake (Toumi, 2012). Recently, cost containment is a crucial target of policy makers and the expenditures are starting to slightly decrease. Table 1 represents the evolution of the pharmaceutical expenditures between 2007 and 2011. In 2011, the pharmaceutical expenditures represented approximately 15,5% of the NHS budget (INFARMED, 2011), which contrast with the data from 2007, when the pharmaceutical expenditure was higher (17.9%).

More updated data is yet to be published, but, regarding the new pharmaceutical policy, it is expected a maintenance on tendency to decrease expenditures.

TABLE 1 – PHARMACEUTICAL EXPENDITURE (INFARMED 2011)

	2007	2008	2009	2010	2011
NHS Expenditure with pharmaceuticals in NHS Budget	17.9%	18.3%	18.5%	17.7%	15.5%
NHS Expenditure in Medicines as a % of GDP	0.83%	0.85%	0.93%	0.95%	0.78%

2. Pharmaceutical Policy

Several changes have been introduced to the NHS in order to reduce the public pharmaceutical expenditure. In the past decade Portugal implemented a wave of reforms. To design policy towards the demand of pharmaceuticals involves sensible decisions. Prescribed pharmaceuticals are generally considered as a cost-effective method of providing health care in the majority of patients. Rather than an exhaustive presentation and debate, in this section we summarize the more relevant aspects of the pharmaceutical policy for the present study mainly the reimbursement policy. Details of pharmaceutical policy can be found in (Veiga et al 2011). INFARMED is the entity responsible for the most relevant aspects of the pharmaceutical policy, mainly approving the market entry and all pharmaceuticals to be reimbursed by the NHS , as well as setting their co-payment levels.

2.1. Reimbursement System

Pharmaceutical funding is provided through a reimbursement system for pharmaceuticals listed in a positive list, currently defined in the Decree law n° 106-A of the 1st October. The World Health Organization (WHO), 2001, presents an interesting document, containing guidelines on “how to develop and implement a national drug

policy". These guidelines refer that a national reimbursement system is an important part of a drug policy and a fundamental tool to apply the principles of equitable access to medicines and rationalization of pharmaceutical expenditures, objectified by health policies. WHO (2001), points health as a human right and states that the access to health must include the access to pharmaceuticals, as they play a crucial role in health care, providing a cost-effective answer to many health problems. Furthermore, barriers on the access to pharmaceuticals have socioeconomic consequences, increasing the human capital costs and the future health costs (Veiga et al. 2011). The health care market failures, namely uncertainty, dictate the presence of a national reimbursement system. Uncertainty lays on the impossibility to predict illness, its severity or its duration. Besides, the costs related to the disease may be unaffordable, even to those with high incomes (Veiga et al. 2011).

Based upon equity and social fairness grounds, it is expected that a national reimbursement system contemplates a positive discrimination of vulnerable social groups such as elderly, children, chronic patients and individuals with low income. This results in higher reimbursement levels to individuals considered vulnerable, reducing their coinsurance rates (Veiga et al. 2011). While there are solid arguments to support existence of a public reimbursement system for the funding of the pharmaceutical consumption, its prioritization criterion remains debatable.

2.2. Economic Evaluation Criteria

Economic evaluation methods to support decisions regarding pricing and reimbursement are gaining relevance in developed countries (Tele and Groot 2009). In Portugal, since 1998, economic evaluation has become more important for reimbursement decisions, guided by official guidelines for carrying cost-effectiveness studies. Firms that seek financing for a pharmaceutical product are required to submit the economic evaluation according to the Methodological Guidelines for Economic Evaluation Studies, published by INFARMED in 1998. Companies must provide pharmacotherapeutic and pharmacoeconomic information demonstrating the therapeutic added value (ATV) related with the alternatives already reimbursed. The report has to follow the methodological document. Only after that, the pharmaceutical companies can apply for reimbursement to INFARMED Since then, the utilization of efficiency criteria in reimbursement decisions decisively increased.

Based on the pharmacological information in these documents, INFARMED makes prior appraisal of the new pharmaceuticals, placing it into one of six categories that make it eligible for reimbursement (INFARMED, 2013):

- Medicines that contain new therapeutic entities, with innovate mechanisms of action and higher efficacy and tolerability than the existing treatments;
- New medicines with a similar qualitative composition to others already marketed and reimbursed, with the same dosage form, and at a 5% lower price than the lowest priced, reimbursed, non-generic drug;
- New dosage form, new doses, or new packaging of already reimbursed drugs with the same qualitative composition, provided that there is a therapeutic and economic advantage;
- New medicines which do not possess a significant therapeutic innovation nor qualitative composition to similar, already reimbursed medicines, but have an economic advantage compared to them;
- Combination products containing already reimbursed active substances, and the price does not exceed the sum of the prices of the same medicines when given alone in identical dosages;
- Combinations of active substances that don't exist in the market alone and have shown advantage in clinical trials over drugs in the same therapeutic group.

The result of this evaluation is a pharmacotherapeutic report with information on: size of the package and strength needed; therapeutic alternatives; grade of additional therapeutic value (ATV), measure units of the product and alternatives ("Decree-Law No. 118/92, 25th June" 1992).

The application is then analysed to evaluate the economic advantage, based on the information provided by the applicant. If the product does not demonstrate an ATV compared to the alternative the economic evaluation is only based on the comparison of prices (considering the differences in daily posologies) (WHO 2007). In this case, the new pharmaceutical must have a lower price than the comparators in order to be approved to enter the reimbursement list.

Although the exact amount is not officially defined, INFARMED is generally willing to pay €30.000/QALY for reimbursement. To orphan pharmaceuticals the price raises to between €50.000 and €80.000 per QALY (Veiga et al. 2011)

Considering that the per capita income is low, and the companies do not risk placing most of the pharmaceuticals on the market without getting reimbursement, the reim-

bursement rules have come to be used as an instrument of price negotiation (Teixeira and Vieira 2008; WHO 2007).

2.3. Positive List

National reimbursement regulations are framed in an inclusive or exclusive criteria. The aim of the positive list is to limit the number of reimbursed pharmaceuticals. A positive list contains the drugs that will receive different levels of reimbursement. Overall, the positive list can have a cost-containment effect due to the pharmaceuticals companies' behaviour, which are likely to set lower prices in order to secure their revenues by an increase in volume (Tele and Groot, 2009).

After the approval of the reimbursement status, each pharmaceutical is subjected to a reassessment, made by INFARMED, every three years. Criteria to delist pharmaceuticals include, among others, excessive prices, lower therapeutic efficacy proven by a pharmacoepidemiologic study and the reclassification for OTC status without reasons of public health that justify its reimbursement (Decree-Law No. 205/2000 1st September).

2.4. Reimbursement Categories

Co-payments are the most used cost-control measures on the demand side in the European countries. . Cost-sharing mechanisms have been introduced mainly for two reasons: a) to ease the public expenditure burden on health, and b) to address the problem of moral hazard, namely unnecessary or frivolous use. From an economic point of view, co-payments are effective when price elasticity is higher, as in the pharmaceutical field (Tele and Groot, 2009).

After the inclusion in the positive list, the drug is classified in one reimbursement group .The Portuguese pharmaceuticals reimbursement scheme is divided into 4 categories, as described in table 2. The legal basis of the reimbursement categories is settled by the Ordinance No. 924-A/2010 in which the reimbursement rates for pharmaceuticals are defined according to its pharmacotherapeutic group.

TABLE 2 - **REIMBURSEMENT CATEGORIES (INFARMED 2012)**

Reimbursement category	Reimbursement rate	Criteria
Category A	90%	Essential pharmaceuticals to treat chronic diseases or life-saving pharmaceuticals (100%), such as cancer and diabetes
Category B	67%	Medicines essential for the treatment of severe illness. Essential pharmaceuticals of therapeutic value for the treatment of serious chronic diseases (such as anti-asthmatic, cardiovascular pharmaceuticals)
Category C	35%	Non priority pharmaceuticals, with proven therapeutic value (such as anti-infective, vaccines not included in the National Vaccination Plan, immunoglobins, anti-parasitic)
Category D	15%	New pharmaceuticals whose therapeutic value is not yet proven. It is a transitional category created in 2000.

The reimbursement of pharmaceuticals indicated in specific pathologies or special groups of patients is subject to a special scheme (Table 3). Examples are the reimbursed pharmaceuticals for haemopilia or for Alzheimer disease ("Decree-Law No. 205/2000 1st September" 2000; WHO 2007). It is clear that, at least at this stage of pharmaceutical financing, INFARMED does apply equity principles, favouring pharmaceuticals for chronic disease.

Additionally, pensioners with low incomes have an extra co-insurance rate by the NHS. The rank in category A is increased by 5% and, in categories B, C and D, by 15%. This applies only for pensioners whose total annual income does not exceed 14 times the guaranteed minimum income (WHO 2007).

TABLE 3 – SPECIAL REIMBURSE SCHEMES

Disease	Pharmaceuticals covered	Co- payment (%)
Paramyloidosis	All pharmaceuticals	100%
Lupus	Phrmaceuticals included on the positive list	100%
Hemophilia	Phrmaceuticals included on the positive list	100%
Hemoglobin disorders	Phrmaceuticals included on the positive list	100%
Alzheimer's disease	nº 13020/2011 (2ª série), de 20 de Setembro	37%
Manic depressive disorders	Lithium carbonate	100%
Inflamatory bowel disease	Pharmaceuticals defined on Order nº 1234/2007 (2ª série), de 29 de Dezembro de 2006	90%
Rheumatoid arthritis and Ankylosing spondylitis	Pharmaceuticals defined on Order n.º 14123/2009 (2ª série), de 12 de Junho	69%
Oncologic pain	Pharmaceuticals defined on Order nº 10279/2008, de 11 de Março de 2008	90%
Non oncologic pain	Pharmaceuticals defined on Order nº 10280/2008 (2ª série), de 11 de Março de 2008	90%
Medically assisted procreation	Pharmaceuticals defined on Order n.º 10910/2009, de 22nd April	69%
Psoriasis	Pharmaceuticals indicated for psoriasis treatment	90%

Chapter 3: Literature Review

1. The Use Of Stated Preferences In Health Care

There are several methods to elicit public preferences and the decision of which method to use depends mostly on the goods in question (Ryan et al., 2001). The preference-based outcome is generally divided into two approaches: revealed preference (RP) and stated preference methods (SP). The first one, RP method, collects behavioral data by the exploration of people's preferences as indirectly revealed through their choices in markets, specifically related to the value of interest. RP are difficult to use in the health care market for several reasons. First, willingness-to-pay (WTP) values for health care interventions or treatment alternatives are rarely available (Özdemir, 2009) as health care services have public good chracteristics (Gerard et al. 2008). There is an agency relationship between the supplier and the patient, as the former will generally be better informed than the latter (Gerard et al. 2008), which contributes to bias in the RP outcome. This specific nature of health care market requires a different approach, which relies on stated-preference (SP) data. SP involves asking the same individuals to state their preferences in hypothetical markets (Gerard et al. 2008; Louviere, Hensher and Swait 2000) and are also useful to elicit preferences for goods that are not yet in the market (Ryan & Skåtun 2004), allowing decision makers to make well documented decisions in advance. Another reason for favoring SP techniques is that they are based on hypothetical choices that can be precisely specified in advance using a design that allows straightforward identification of all effects of interest (Gerard et al. 2008). This is in contrast to RP data, which cannot be controlled a priori so that model identification cannot be guaranteed (Amaya-amaya et al. 2008) as attributes are collinear in market data, making it impossible to predict the effect of independent variation in an attribute with RP (Kjær, 2005).

2. Theoretical Foundations Of The Discrete Choice Experiments

DCEs are an attribute-based approach that enables collecting SP data (Gerard et al. 2008). They are designed to allow individuals to express their preferences for non-marketed goods or goods which do not exist yet (Telser & Zweifel 2007). In a DCE, respondents are presented a sequence of hypothetical scenarios composed by two or more competing alternatives that vary along several attributes, one of which may be a cost attribute, as the out of pocket price of each alternative or its government cost. In each case, respondents are asked to indicate which of the presented scenarios they prefer. In this way an indifference hyper plane in attribute space is approximated (Telser & Zweifel 2007).

DCE characterize a consumer's underlying utility function, and thus may improve policy makers' ability to perform benefit transfers (Gerard et al., 2008). Furthermore, WTP is to be inferred indirectly rather than explicitly pricing the good. This is highly desirable in a health care context where, as mentioned, some individuals may refuse to place a monetary value on human health in the CVM format, increasing the incidence of protest zero bids (Gerard et al., 2008)

The theoretical foundation of the DCE is far from being linear as it comprises research on axiomatic conjoint measurements, information integration theory of psychology, random utility theory models in economics, discrete multivariate statistical models for contingency (crosstab) tables, and the optimal design of statistical experiments (Kjær 2005; Lancsar and Louviere 2008).

The discrete choice experiment is founded in random utility theory (RUT) and is consistent with Lancaster's theory (1966) of characteristics and neoclassic economics. RUT plays a key role in the understanding and interpretation of the behavioural processes examined in the DCE and assumes that utility (U) for individual i conditional on choice j can be decomposed into an explainable component, Vij and a non-explainable random component Ɛij, as in equation 1 (Lancsar and Louviere, 2008) :

$$U_{ij} = V_{ij} + \varepsilon_{ij} \quad , \quad j = 1, \ldots, J$$

(Eq.1)

This random variation may be due to unobserved attributes affecting choice, inter-individual differences in utilities depending upon the heterogeneity in tastes, measurement errors and/or functional specification (Manski, 1977). The explainable component, is

a function of (at least) attributes of the good and the characteristics (covariates) of individual choosers, often modeled as shown in equation 2 (Lancsar and Louviere, 2008):

$$U_{in} = V\, X_{ij,}\, \beta + \varepsilon_{ij}$$

(Eq.2)

Utility is a latent, unobserved quantity; it is assumed that the choices observed are indicators of utility. Respondent chooses option 1 if, and if only, its utility is higher than the utility of any other option in the set of J alternatives. Assuming a joint probability distribution for, the probability P that utility is maximized by choosing option 1 (Lancsar and Louviere, 2008):

$$\begin{aligned} P\left(Y_i = 1\right) &= Prob\left(U_{i1} > U_{ij}\right) \\ &= Prob\left(V_{i1} + \varepsilon_{i1} > V_{ij} + \varepsilon_{ij}\right) \\ &= Prob\left(V_{i1} - V_{ij} > \varepsilon_{ij} - \varepsilon_{i1}\right) \forall \;\; j \neq 1 \end{aligned}$$

(Eq.3)

Where Y is a random variable denoting the choice outcome. DCE models are derived by assuming a distribution for the random component. For example, if the errors are independently and identically distribute (iid) as extreme value type 1 random variates, this results in a conditional logit specification for the choice probabilities (Lancsar and Louviere, 2008):

$$P\left(Y_i = 1\right) = \frac{e^{\mu V_{i1}}}{\sum_{j=1}^{J} e^{\mu V ij}} \;\;,\;\; j = 1,\; \ldots,\; J$$

(Eq.4)

3. Methodology

The DCE methods allow different approaches but there are some mandatory stages researchers need to go through in order to obtain the appropriate outcomes. It is crucial to carefully define the method, with acknowledge of the available time and how much will it cost. Ultimately, these choices have impact on the quality of the results (Champ & Welsh 2006, Kjaer 2005). Although there is no gold standard on the

way to carry out a DCE, the approach taken here is the same suggested by Ryan, 1996 and described on table 4, for its reliability, simplicity and large use on health care field. In our study, stage one and two are presented together (Kjaer 2005).

TABLE 4 – THE DESIGN STAGES OF A DCE

Stage 1	Identification of attributes
Stage2	Identification of levels
Stage 3	Experimental design
Stage 4	Data collection: development and administration of the survey
Stage 5	Analysis of data

3.1. Identification Of Attributes And Levels

While conducting a DCE, the researcher must focus carefully on the selection of attributes and levels that will describe the good. The DCE potential of eliciting preferences based on the individuals' valuation of the diferent levels of attributes that describe a good is the more attractive feature on the health care market (Amaya-amaya et al. 2008). While a DCE can not incorporte all relevant attributes, it is important to include the most relevant ones, that are meaningful for respondents and policy makers. If an important attribut is ommited, respondents can make assuptions about it, affecting the validity of the model estimated. This is an important issue to be assessed using qualitative work, such as pilot studies (Kløjgaard et al. 2012; Lancsar & Louviere 2006). The combination of the set of attributes must be able to describe what the choice is about, and the attributes must be chosen so that respondents will be willing to make trade-offs between them, following the latent economic theretical framework with compensatory decision-making. Further, and although it may sound appelaing to include a lot of attributes, researcher may guarantee that a limited number of attributes is included, in order to keep a simple and understandable task and to keep respondents commited to it. When defining the levels of each attribute, it is important to remain focus that, as the attributes' levels must be relevant and easy to comprehend. Besides, the range selected for the levels must allow for the trade-offs between them, while still being plausible for respondetns. In other words, a good experiment is one that balances a sufficiently rich set of attributes and choice sets, with enough variation in the attribute levels therefore being able to produce meaningful trade offs

(Amaya-amaya, Gerard, and Ryan 2008).
The best way to enhance all the desirable features of attributes and levels is to perform a good amount of qualitative work (Kløjgaard et al.2012). Qualitative work includes gathering information from various sources such as focus groups, interviews, expert opinions and literature review. (Kløjgaard et al. 2012).

3.1.1. The Cost Attribute

The cost attribute is a quantitative constrained and negatively valued attribute with a distinct role in DCE. Its inclusion provides the DCE an elicitation procedure for willingness-to-pay (WTP) or willingness to accept compensation (WTAC) for an improvement (or deterioration) of one of those attributes. This implies that benefits are estimated in monetary terms and causes the DCE to be consistent with welfare economics (i.e. the potential Pareto improvement condition) (Kjær 2005).
Inclusion of a cost attribute makes it possible to indirectly obtain the respondent's WTP for either the good in its entirety (an alternative) or the respondent's WTP for the attribute respectively, i.e. marginal WTP (also termed part worth or implicit price) (Kjær 2005). Results from different studies can then be compared and - on the grounds of economic efficiency - used in priority-setting. Rather than showing the price of the good, WTP is estimated indirectly. This is highly desirable in a health care context where, as mentioned, some individuals may refuse to place a monetary value on human health in the CVM format, increasing the incidence of protest zero bids (Gerard et al., 2008)
The use of cost to estimate WTP raises questions about the definition of the cost attribute in a collectively funded health care system, where the inclusion of cost might result in the scenarios being considered unrealistic and immoral (Ryan, 1999). Most health care services in Portugal, are paid at the point of consumption as a co-payment, that is, part of the costs are supported by public funds, while the remaining is financed through user payment (Barros, 2011). Marginal WTP is simply the marginal rate of substitution in which the numeraire is the cost attribute. The estimation of welfare is based on using the coefficient of the cost attribute to assess the marginal utility of income (Kjær, 2005). Costs can take many different forms in a DCE, including options such as consumer price, transportation cost, salary, donation, tax payment, tax payment in a referendum context, etc. (Kjær 2005).

3.2. Experimental Design

The experimental design consists in framing the selected attributes and levels into choice sets (Kjær 2005). This stage focus on the design of the hypothetical choice sets, including the formation and pairing of alternatives within choice sets. One of the crucial objectives of the experimental design is to create the DCE in such a way that the number of alternatives is minimized while being able to infer utilities for all possible alternatives – which implies keeping the choice task simple to the respondents and at the same time being able to extract all the necessary information from the choices (Kjær 2005). A designed experiment is therefore a way of manipulating attributes and their levels to permit rigorous testing of certain hypotheses of interest (Louviere et al. 2000).

The total number of possible choice sets, the full factorial, depends directly of the number of attributes and levels, with an exponential relationship - the number of possible alternatives increases exponentially when the number of attributes and levels increases (number(#) of alternatives = #levels^#attributes). For example, if there are five attributes, three with four levels and two with two levels, the full factorial produces 256 combinations. Commonly, it is not possible to present respondents with all possible alternatives and a reduction of the number of choice sets must be done. First of all, it is important to reduce the number of attributes and level to a minimum. Next, methods exist that can reduce the number of alternatives included in the questionnaire, while keeping the statistical properties of the design. One such method is the use of orthogonal arrays. Orthogonal designs are based on orthogonal arrays from design catalogues (e.g. Hahn and Shapiro,1966), statistical programs (e.g. SPEED, (Bradley, 1991); SPSS, (SPSS Inc., Chicago, IL, USA)) or web-sites (Sloane, 2009). These arrays have the properties of orthogonality (attributes are statistically independent of one another) and level balance (levels of attributes appear an equal number of times). The profiles obtained from the orthogonal design are the choices for a binary DCE (de Bekker-Grob, Ryan & Gerard 2012). However, it is important to be aware that all fractional designs involve some loss of statistical information. This loss of information can sometimes be significant, as fractional factorial designs limit the ability to take higher order effects into account, i.e. interactions between two or more attributes (Louviere et al. 2000).

3.2.1. Ensuring Design Efficiency

As mentioned, the use of a fractional design compromises the amount of information collected and the quality of such information. In order to minimise biases, it is important to test the design for its efficiency. What appears to be important is the pairing of the alternatives into choice sets. The pairing of alternatives needs to be made in such a way that the differences in attribute levels for each choice set are not multi-correlated. In addition, as only a fraction of the total possible alternatives is to be presented to the respondents in fractional factorial design, the selection of alternatives also needs to considered in the light of design efficiency. Theory supports the satisfaction of some properties to ensure the maximum statistical efficiency in choice design (i.e. the extraction of maximum information from the choice task). Together, these principles are called design efficiency, also termed D-efficiency. D-efficiency relates to the design matrix in such a way that efficiency is maximized when the size of the covariance matrix of the estimated parameters is minimized. To optimize D-efficiency, four principles need to be considered simultaneously. Improving any principle, holding the others constant, improves efficiency. In many cases it is impossible to create a design that satisfies all four principles, as some of the principles might conflict with each other (Huber & Zwerina 1996).

Level balance simply means that the levels of an attribute occur with equal frequency in the design, e.g. each level of a four-level attribute should occur in precisely one-fourth of the included alternatives. This ensures that all levels are weighted equally in the trade-off options that the respondent faces (Huber & Zwerina 1996. The use of a block design or a fractional factorial design, level balance needs to be taken into consideration in order to optimize efficiency.

Orthogonality is an important part of D-efficiency. Orthogonality is respected when the joint occurrence of any two levels of different attributes appears in profiles with frequencies equal to the product of their marginal frequencies (Huber & Zwerina 1996). Orthogonality is thus satisfied when the difference in the levels of each attribute varies independently over choice sets, meaning that the levels of the attributes vary in a criss-cross manner. As ‘pure’ optimal orthogonal designs are only available for a very small number of very specific problems, the primary purpose is to optimize the design as best one can by minimising multicollinearity (Kuhfeld et al. 1994). A high degree of multicollinearity will result in a design in which unique estimates of the parameters cannot be obtained, making it impossible to draw any statistical inferences, i.e. hy-

pothesis testing, from the sample

Minimal overlap relates to the statistical properties when pairing the alternatives. A design has minimal overlap when a level does not repeat itself in a choice set. In order to optimize orthogonality of the level differences, the scenarios are matched to ensure minimal overlap (i.e. optimal orthogonality ensures minimal overlap). Minimal overlap is important in choice designs, because the contrast between attribute levels is only meaningful as differences within a choice set. Minimal overlap ensures that the probability of an attribute level repeating itself in each choice set is as small as possible, and thus maximizes the information obtainable from the choice sets (Huber & Zwerina 1996).

Utility balanced is present when the utilities of alternatives within each choice set are approximately equal. To achieve this, the researcher needs to take the utility weights of the attributes into account when designing the DCE. The rationale for this principle is to ensure that respondents are actually trading. The efficiency gain arises because choices between alternatives that have similar utility provide better information about the coefficients. This means that two alternatives that differ in their levels but have approximately the same utility are more likely to ensure that the respondents are placed in a situation in which they are forced to trade. Application of the utility balance concept thus implies that the impact on choices of small differences in utility is registered resulting in more precise parameter estimates. What makes this principle troublesome, however, is that it requires prior estimates of the coefficients. There are several ways to generate useful sets of prior estimates. The most used method is to conduct a small pilot study to generate tentative estimates. Huber & Zwerina (1996) have shown that the incorporation of the utility balance principle increases efficiency of the DCE.

3.3. Data Collection

This section involves all the remaining issues that need to be considered before the questionnaire is presented to the respondents (Kjaer,2005). This includes several decisions such as the lay-out, whether to include an opt-out alternative, the inclusion of socio-demographic questions and warm-up questions.

3.3.1. Opt-Out Choice

One important issue to consider while designing a DCE is whether to include or not an opt-out choice. Opt-out choice allows the possibility for the respondent not to choose any of the alternatives in the choice set, as demonstrated in figure1. There is literature supporting both decisions and the reasoning for the choice stands mostly on the nature of the experiment (Kjaer, 2005).

The inclusion of an opt-out alternative in DCE is becoming popular , as it allows for realism (deBekker-Grob et al., 2012). Ryan and Skatun (2004), explain that, in the health care context, individuals may prefer not to take-up certain treatments or services, whatever the level of attributes of the service, or prefer to participate only for certain levels of attributes.

FIGURE 1 - TEMPLATE OF A CHOICE SET INCLUDING AN OPT-OUT ALTERNATIVE

CHOICE 1			
	Treatment A	Treatment B	No treatment
Total treatment duration	4 years	6 years	0 years
Amount of relief	Little relief	Complete relief	No relief
Side effects	Yes	Yes	No
Total cost	350 €	900 €	0 €
Which treatment you prefer?	A ☐	B ☐	None ☐

Taking the example in Figure 1, if the maximum willingness to pay of a respondent is 300€, he would, in such choice set, opt for the "none" alternative. If the design did not allow for an opt-out choice, a forced answer would result in overestimates (identifying demanders that would opt-out) Ryan and Skatun, 2004). Nonetheless, the omission of the opt-out alternative is still considered in the heath care market DCEs. Firstly, respondents may tend to avoid difficult responses such as ethical ones, using heuristics to make the task easier. (Kjaer, 2005). Additionally, allowing respondents to select an opt-out option provides less information on respondents' relative preferences for the attributes in the hypothetical alternatives. Forced experiments constrain respondents to express a preference (i.e., make a trade-off among attributes) even when both

alternatives are unattractive (Mentzakis, Stefanowska & Hurley 2011). Hensher, Rose and Greene (2005), argue that such a design is preferred when the objective of the study is to examine the impact of the relationships different attribute levels have upon choice. For the present study, it was decided to design a forced-choice DCE as the investigation sets on ethical and policy principles.

3.3.2. Introductory Text

Before the respondents answer the DCE, it is important to firs introduct them to the task. The introductory text should define the aim of the study, the importance of the respondents' participation on such study and why he was selected to participate (Kjaer 2005).Then, an introduction to the task, including the time it takes to complete the questionnaire and the instructions should also be a part of the introductory text (Benett and Blamey 2001). Adding an example of an answered choice set and warm-up questions may increase the validity of the responses (Kjaer 2005)

3.3.3. Sampling

The sample design specifies the population of interest, the sampling frame, and the technique for drawing a sample from the sampling frame. How the survey is administered the survey mode – will impact how a sample is drawn (Champ & Welsh 2006).
The mailed questionnaire approach is – for good reason – by far the most widespread data collection method for DCEs in many research areas, including health economics. Some of the advantages with this method are the relatively small cost compared to the amount of information gathered and the fact that respondents can chose to complete the questionnaire when it suits them. However this method tends to result in low response rates and thus sampling bias. A postal questionnaire limits the complexity of the choice task as the respondents must be able to answer the questions without help. Furthermore, the questionnaire needs to be written in simple language in order not to discriminate against individuals who are unused to completing forms and understanding written material. (Champ & Welsh 2006. Kjaer, 2005)
The choice of sampling frame that is to be used to generate potential respondents (the

survey sample) will depend upon the nature of the particular application. The sampling frame defines the universe of respondents from which a finite sample is drawn to whom the data collection instrument will be administered (Louviere et al. 2000). If the study intends to examine the use value of asthma medication, then the most appropriate frame would be asthma patients. If the aim of the study is to examine use as well as non-use and option value, however, then the appropriate frame would be the general public.

Based on the sampling frame, the sampling strategy and sample size are determined. One sampling strategy is simple random sampling, in which all individuals from the sample frame have equal opportunity to be chosen as potential respondents; another sampling strategy might be dividing the frame into groups, each representing a portion of the population, depending upon characteristics such as sex, income, residential location etc. (Louviere et al. 2000). It is possible to determine the appropriate sample size by using of elementary statistics and can be calculated through online services. In a mailed survey, the size of the sample depends on the number of questions given each respondent, the size of the population, and the statistical power that is required of the model derived. Bennett & Blamey (2001) state that the minimum size of a sub-sample should be in the order of 50 respondents, depending on the statistical power that is necessary for the estimation procedure. Furthermore, the sample size will be highly dependent on the expected response rate. To increase sample size (when using postal questionnaires), it might be appropriate to send out a reminder in the event of non-response.

3.4. Data Analyses

3.4.1 Data input

After the data are collected, it needs to be organized and set into a computerized database. Each choice set contains two forms of information: the attribute levels of each alternative, and which of the given alternatives has been chosen. To estimate the model, each attribute is handled as a variable containing different levels and each level has to be coded in order to estimate the importance of each attribute, i.e. the marginal values and trade of ratios (Louviere and Hensher 2000). When designing a

DCE it is important to consider how the exploratory variables are going to be coded. Dummy variables are used to account for this approach, and the least desirable option defined acts as a reference case. A priori the coefficients for severity of the disease for which the treatment is indicated, prevalence of the disease and efficacy of the new pharmaceutical are expected to have a positive sign, indicating an increase in utility (probability of being chosen for funding) relative to the reference case (constant). The use of dummy variables is helpful in interpreting the findings of the study, at a policy level, providing a meaningful reference case for a health policy audience (Louviere and Hensher 2000 ; Green and Gerard 2009).

3.4.2 Econometric Analyses

In econometric literature conditional logit models are often employed estimate the choice models (Greene, 2003). It differs from ordinary logistic regression in that the data are divided into groups and, within each group, the observed probability of positive outcome is either predetermined due to the data construction (such as matched case–control) or in part determined because of unobserved differences across the groups (Gould, 2000). This is in line with the underlying RUT. Thus, the likelihood of the data depends on the conditional probabilities, that is, the probability of the observed pattern of positive and negative responses within group conditional on that number of positive outcomes being observed. Terms that have a constant within-group effect on the unconditional probabilities — such as intercepts and variables that do not vary — cancel in the formation of these conditional probabilities and so remain unestimated). In this model, an individual is faced with an array of alternatives and must choose one. Individual taste can be captured in conditional logit models as long as it varies systematically with respect to observed variables (McFadden, 1973).
Once a satisfactory model has been estimated, the results obtained can be used to simulate outcomes that can be used in policy analysis or as components of decision support tools.
Furthermore, DCE allow estimation of trade-offs that respondents make between attributes, defined as marginal rates of substitution (MRS) (Lancsar and Louviere 2008; Ryan 1999). Following the standard consumer theory, MRS is calculated comparing the estimated coefficients of two attributes. MRS indicates the trade-off between two attributes that characterize the good and thus the mutual importance of the attributes

in question. Holding the overall utility level constant:

$$\partial V_i = \beta \partial x_i = 0$$

(Eq.5)

And MRS is calculated through equation 6:

$$MRS_{12} = \frac{-d x_{i1}}{d x_{i2}} = \frac{\beta_1}{\beta_2}$$

(Eq.6)

When one of the attributes is a cost attribute, the MRS indicates the willingness-to-pay (WTP) for a change in the qualitative attribute, i.e. the marginal willingness-to-pay (MWTP). Let the price attribute be denoted as p. As income cancels out in linear price models (hence the negative sign of the cost variable in equation 7), marginal WTP is derived (Ryan et. al 2008):

$$MWTP_i = \frac{dx_i}{dU_{income}} = \frac{dx_i}{dp} = \frac{\beta_{x_i}}{-\beta_{co}}$$

(Eq.7)

Applications of DCE to economic policy (e.g. health and health care) are often targeted to predictions of behaviour, generating welfare measures or both. This is done by the comparison of the relative importance of the good attributes. The probability that respondents will choose each alternative in a choice set is calculated using equation 3, a conditional logit specification for the choice probabilities which allows comparison of the impact of each attribute in a common metric.

4. Discrete Choice Experiments In Pharmaceutical Funding Decisions: A Review Of The Literature

A comprehensive electronic search was carried out to identify published studies using DCEs within the pharmaceutical funding context. Portuguese and English language studies, between January 1992 and March 2013, were searched through MEDLINE, SCOPUS and RePEc database. Studies that matched the required criteria were selected, that is, that included a stated preference study to investigate preferences for funding decision of pharmaceuticals. Search strategies were formulated for individual databases using the following keywords: 'discrete choice' or 'discrete choice experiment' or 'discrete choice analysis' or 'discrete choice modelling' or 'conjoint' or 'conjoint analysis' or 'stated preference method' AND 'pharmaceuticals' or 'medicines' or 'drugs' or 'pharmaceutical funding' or 'pharmaceutical funding criteria' or 'pharmaceutical funding decisions' or 'reimbursement' or 'pharmaceutical reimbursement'. There are a limited number of DCE experiments eliciting preferences for pharmaceutical funding decisions. The few existing studies were, however, crucial in elucidating the suitable methods, some of the motivational factors behind choosing treatments and supporting the attributes selection and shaping the design.

Presented in table 5 are the four research articles found that matched the defined criteria. The table is organized according to the target population of the study.

The first presented study, conducted by Whitty et al. (2008), seeks to quantify criteria considered important by the Australian public for allocating resources for pharmaceuticals. A DCE was administered to two samples of adults in Australia. A total of four attributes were selected, based on the principal that public are willing to trade between the individual components of effectiveness (that is, survival, quality of life (QoL), and chance of success) for the treatment of others. Further, this study aims to investigate the importance of government costs in prioritizing healthcare, including a government cost attribute. According to their findings, the Australian public view the QoL after treatment, survival after treatment and chance of success associated with a new pharmaceutical to be important considerations when funding pharmaceuticals for the treatment of others suffering a severe disease. Furthermore, this study concludes that, when framed in terms of a government tax fund payment vehicle, the cost of the pharmaceutical is important to the respondents.

An interesting point of view is given by Diaby et al. (2011), with the investigation physicians' preferences when selecting reimbursable drugs and the analyzes of trade-offs

between criteria for formulary listing in Côte d'Ivoire. In order to do so, a DCE was administered, considering four attributes: cost effectiveness, severity of the disease for which the treatment is indicated, social class and age. Respondents' relative weightings of four criteria were to be significant in selecting reimbursable drugs, being cost effectiveness, severity of the disease and social class the more relevant, in this exact order. This work sets foundation on studies that have demonstrated the feasibility of simultaneously accounting for efficiency, equitity and social criteria in a way that allows a rank ordering of health interventions.

Another study focusing on elicitation of preferences of health care professionals was held by the All Wales Medicines Strategy Group (AWMSG), which is a Welsh Government-funded body consigned to appraise new medicines for use in NHS Wales when NICE guidance is not imminent. The primary aim of this DCE was to explore the preferences of AWMSG appraisal committee members for specific new medicines adoption criteria and their efficiency trade-offs. Moreover, it aims included exploration of the external validity of the DCE by comparing appraisal committee members' hypothetical recommendations against actual AWMSG recommendations for the use of new medicines in Wales. The conclusions set that QALY maximisation and economic efficiency are not the only considerations of committee members when making recommendations on the use of medicines in Wales, as respondents were willing to trade over other attributes.

Finally, Whitty et al., 2011, carried out a pilot DCE in Australia to test the concept of evaluating the consistency of public and decision maker preferences for the public subsidy of pharmaceuticals. Here the preferences of members of a pharmaceutical funding decision-making body are compared with those of the public on whose behalf decisions are made. The elicitation of preferences was based on the relative importance of gains in survival, quality of life (QOL), chance of response success and government costs in pharmaceutical funding decisions. The DCE was administered to a sample of the Australian public and members of the Pharmaceutical Benefit Advisory Committee and its Economic Subcommittee. For both samples, increased survival, QOL and chance of response success, and a reduction in costs and uncertainty (decision makers only), were relevant and increased the likelihood that a pharmaceutical would be chosen for funding. Moreover, both samples were more likely to fund a pharmaceutical that was used for the treatment of severe illness. Besides pointing out the relative importance of decision criteria, this study suggests the consistence of funding decisions for pharmaceuticals with the preferences of society.

TABLE 5 – SUMMARY OF THE LITERATURE REVIEW FOR THE DCE IN PHAMACEUTICAL FUNDNG DECISIONS

Study/country	Study focus	Attributes
Public Preferences		
Whtty et al. 2008. Australia	Public preferences for allocation resources for pharmaceuticals	Chance of success, Survival, Quality of life, Additional cost
Decision Makers/Health Professionals Preferences		
Diaby et al, 2011. Canada	Preferences of physicians in Côte d'Ivoire when selecting reimbursable pharmaceuticals	Cost effectiveness of treatments, severity of the disease, age and social class
W. Linley, D. Hughes, 2013. UK	Preferences of All Wales Medicines Strategy Group (AWMSG) appraisal committee and appraisal sub-committee (New Medicines Group) members ('appraisal committees') for specific new medicines adoption criteria	Main impact of disease before treatment, annual number of patients to be treated, QALYs gained per treated patient, incremental cost per QALY gained, uncertainty in cost effectiveness is thoroughly explored
Public Vs. Decision Makers Preferences		
Whitty et al. (2011) Australia	Evaluate the consistency of public and decision maher preferences for the publc subsidy of pharmaceuticals	Chance of response success, survival, quality of life (QoL), cost to government per person treated. Uncertainty around the chance of response success (only for decision makers)

	Study design and estimation method	Key findings and conclusions
	Fractional factorial additive main effects design obtained from SPSS. Multinominal logit (MNL) model.	Public consider QoL after treatment, survival after treatment and chance of success of a new pharmaceutical important attributes when funding pharmaceuticals for the treatment of others suffering a severe illness.
	Optimal design for proposed by Street et al, 2005. Binary logistic regression, STATA 8.0	Preferences of physicians in Côte d'Ivoire are based on cost effectiveness, severity of disease, and social class.
	Fractional factorial design, we therefore used an orthogonal main effects plan from Shaphira's catalogue, 1996. Conditional logit, main effects only, STATA10.1	A willingness to trade the cost effectiveness and QALY gains against other factors indicates that economic efficiency and QALY maximisation are not the only considerations of committee members when making recommendations on the use of medicines in Wales
	Orthogonal array from SPSS and Shifted Design technique. MNL and mixed logit (MXL)	For both samples, increased survival, QOL and chance of response success, and a reduction in cost and uncertainty (decision makers only), increased the likehood that a pharmaceutical would be chosen for funding. Pharmaceuticals used for the treatment of severe disease were also more likely to be funded.

Chapter 4. Method

1. Identification Of Attributes And Assignment Of Levels

In this section efforts were towards the definition of meaningful attributes, capable of defining a new pharmaceutical. These attributes were then decomposed in levels and to describe those attributes in manners of levels so that respondents can make choices as the levels vary. A preliminary selection of meaningful attributes is presented in Table 6. This choice draws mainly from a portuguese study that defined several attributes to develop and validate a new reimbursemnt system for pharamceuticals. Through a Delphi technique, Maria et al. (2007), asked a group of experts, mainly physicians, to identify which attributes they consider important when granting reimbursemnt for a new pharmaceutical.

TABLE 6 – FIRST SET OF ATTRIBUTES SELECTED (Maria et. al (2007)

Dimensions	Attributes	Levels
Disease	Probaility of causing definite incapcity	High (>70%), Moderate (50% to 70%), Low (<50%)
	Mortality	High (>10%), Moderate (5% to 10%), Low (<5%)
	Prevalence	High (>5%), Moderate (1% to 5%), Low (<1%)
Patient	Share of the expenditure with pharmaceuticals on the monthly income	High (>10%), Moderate (3% to 10%), Low (<3%)
	Monthly salary (MS)	High (>5MS), Moderate (2 to 5 MS), Low (<2MS)
	Number of chronic disease	High (>3), Moderate (2 to 3), Low (<2)
Pharmaceutical	Efectiveness	High (>70%), Moderate (50% to 70%), Low (<50%)
	Security	High (high Benefit/Risk ratio, Low (poor Benefit/Risk ratio)
	Exhisting alternatives	Yes, No

The number of attributes to include in the DCE is an important issues to balance. When individuals respond to the choices, it is assumed that they are considering all the attributes, and making trade-offs among them. It is this assumption that allows

such trade-offs to be estimated, and therefore monetary values to be estimated. If too many attributes and levels are included, individuals will not consider all the information, but adopt simple decision-making strategies (such as always choosing the option with the highest pay). If this is the case, estimated trade-offs will not be valid. The question is then raised: What is too many attributes? Applications of DCEs in health economics have included anywhere between two and 24, with a mode of six (de Bekker-Grob et al. 2012). Within the context of pharmaceutical funding the average number of attributes is five.

The levels presented in table 6 appear in both quantitative and qualitative scales. Although in the questionnare, both ways were presented in the explanatory text, only the qualitative scale was carried through th equestionnaire. The main reason for such decision was the goal to keep the task simple and not confuse repondents. When targeting general public it is important to count with respondent for every educational level and ability to comprehend (Champ & Welsh 2006 2006). Table 7 displays the attributes and levels assigned for this study. The chosen attributes represented criteria that were identified from a review of the literature as likely to be important to the public for funding decisions, and which addressed the study purpose (Diaby et al. 2011, Maria et al. 2007, Whitty et al. 2008, Whitty et al, 2011).

TABLE 7 - SELECTED ATTRIBUTES, ITS LEVELS AND SOURCES

Attributes	Levels	Source
Severity of the disease for which the treatments are indicated	Not severe Severe Very Severe	(Green and Gerard 2009; Koopmanschap, Stolk, and Koolman 2010; Maria et al. 2007)
Prevalence of the disease in Portugal	High Moderate Low	(Maria et al. 2007)
Efficacy of the new pharmaceutical	High Moderate Low	(Diaby et al. 2011, Maria et al. 2007, Whitty et al. 2008, Whitty et al, 2011).
Government cost (per person treated)	500, 1000, 5000, 10000, 50000, 100000	(Diaby et al. 2011, Maria et al. 2007, Whitty et al. 2008, Whitty et al, 2011).
Government savings		

1.1. Severity Of The Disease For Which The Treatments Are Indicated

On the literature, severity of a health condition can be defined as the likelihood of death or organ failure as a result of disease progression, independent of treatment (Mentzakis et al. 2011). Severity of health, the pre-treatment health state of patients, is identified in the current literature as a social value that is supported by respondents in a number of empirical studies reporting experimental data and in studies reporting attitudinal data. Severity of disease is consistently identified as a factor individuals consider important for resource allocation in health care (Mentzakis, et al. 2011). The quality of life descriptions were drawn from the health state levels of the EQ-5D classification system corresponding to the Mobility, Usual Activities, and Pain/discomfort health states (Dolan 1997). A simplistic scale was adjusted for the questionnaire, using "very severe disease", "severe disease" and "mild disease". Other things equal, we expected that respondents would prefer to fund a drug that treated those with a serious condition than those with a moderate condition. In the questionnaire, examples of diseases severity's classification were used to provide a clear definition of each level to respondents (Koopmanschap, Stolk, and Koolman 2010).

Whilst the Portuguese pharmaceutical policy does explicitly consider, the severity of the disease for which the treatments are indicated, the different reimbursement rates are defined according to the pharmacotherapeutic group. This comprises, indirectly, the severity of the disease criteria, assigning higher reimbursement rates for disease considered more life threatening. Table 8 presents the attribute and its levels, with an inclusion of the example used in the questionnaire.

TABLE 8 – SEVERITY OF THE DISEASE FOR WHICH THE TREATMENT IS INDICATED

Attribute	Label	QoL score (0-1)	Example
Severity of the disease for which the treatment is indicated	Not severe	0.94	eczema or non chronic, mild low back pain
	Moderate	0.65	heart failure or moderate rheumatoid arthritis
	Very severe	0.33	progressive multiple sclerosis

1.2. Prevalence Of The Disease In Portugal

Frequency of the disease treated by a drug is a primary attribute of interest. Maria, 2007, showed that the prevalence of the disease is an important attribute to consider for the pharmaceutical funding decisions. Drummond et al., 2009 raised some important questions on funding medicines for low prevalent diseases. In essence, there is a natural tendency to prefer to save the greater amount of individuals, keeping costs constant, and therefore to disregard the treatment for low prevalent diseases. The efficacy of these medicines is generally poorly stated as it is more difficult to set clinical trials. (Drummond et al. 2009) For these reasons, Drummond (2009), suggests that there should be a commitment to a fair decision- making process for drugs for rare diseases, recognizing that inevitably this has a value-based foundation. This process should, therefore, include appropriate community input, including patients and taxpaying citizens. Existing decision-making processes need to be reviewed to assess their suitability for dealing with the challenges posed by drugs for rare diseases, including some cancers. Promising initiatives, such as attempts to engage stakeholders, including patients and the public, or to undertake conditional field evaluations, need to be supported and built upon(Drummond et al. 2009). The attribute prevalence of the disease was presented to respondents followed by examples, as showed in table 9. Green (2009), on the conclusion of his study, states that the number of individual being treated is a desirable attribute to include while eliciting preferences on social issues.

TABLE 9 – PREVALENCE OF THE DISEASE IN PORTUGAL

Attribute	Label	Percent	Example
Prevalence of the disease	Low	< 1%	Renal failure
	Moderate	Between 1% and 5%	Bronchitis, malignant tumour
	High	>5%	Hypertension

1.3. Efficacy Of The New Pharmaceutical

The standard goal of the Portuguese regulatory agency, INFARMED, is to provide cost-effective pharmaceuticals and to assure its quality and efficacy. The efficacy of a treatment is defined as the probability of the pharmaceutical to produce the expected results. The efficacy is a criteria used by INFARMED to determine the therapeutic added value of a new pharmaceutical. In the assessment phase, the clinical, pharmacotherapeutic and pharmacoeconomic outcomes of a pharmaceutical are quantified and compared to available reimbursed drugs. The assessment thus determines (incremental) cost-effectiveness ratio of a pharmaceutical. In principle, the elements considered in the assessment phase can be broader, including also a description of ethical and organisational issues. In order to investigate if the public considers the same criteria the government does, or if they are willing to trade the maximization of efficacy on the outcomes for equitity, this was included in the study. The levels were defined according to Maria (2007). Each level was firstly presented in the questionnaire on an introductory text, with its description. Table 10 presents the levels that describe this attribute.

TABLE 10 – EFFICACY OF THE NEW PHARMACEUTCAL

Attribute	Label	Percent
Efficacy of the new pharmaceutical	Low	< 50%
	Moderate	Between 50% and 70%
	High	>70%

1.4. Government Costs/Government Saving

It was decided to frame the cost attribute in terms of government values (Table 11). There was little prior guidance in the literature on plausible levels for government costs, so levels were chosen to represent a wide range of costs that the public might be likely to associate with pharmaceuticals). Initially, we were keen to define the cost attribute as a government saving if the reimbursement was not granted to the pharmaceutical. Regarding the Portuguese economic context, it seem more relevant in a policy perspective to present respondents with the possibility of directly choose public savings. The question about if this cost attribute wouldn't compromise the easiness of the task arises. Therefore, on the pilot

study, each attribute was tested. Although, the scenario of government cost savings may reflect more accurately the Portuguese economic situation, the qualitative pilot test forced to chose the attribute government cost per person treated. This issue is further discussed.

TABLE 11 – GOVERNMENT COST PER PERSON TREATED

Attribute	Levels
Government costs per person treated	500, 1 000, 5 000, 10 000, 50 000, 100 000

Government costs per person treated was included and allowed us to identify respondents' views regarding the amount the government should be willing to pay at the margin for a pharmaceutical. Government costs per person treated took on six levels ranging from €500 to €100,000. A priori expectations were that, ceteris paribus, the lower the per-patient cost the higher the probability of choosing that particular alternative.

2. Experimental Design

Having decided the relevant attributes levels, hypothetical choices with different combinations of attributes and levels were formulated and presented to respondents. The selected attributes and levels resulted in 162 profiles (3 attributes with 3 levels and 1 attribute with 6 levels = 3^3 x 6^1), and 13041 pairwise choices (162*161/2). As it is not possible to present respondents with all the possible combinations of choices, the experimental design methods are used to reduce the numbers of choices for respondents. A fractional main effects design was chosen, where statistical efficiency of the design was maximized with orthogonality, level balance and minimal overlap. Orthogonality is assumed when there is a linear relationship between all attributes with no attribute having a dominant position within the design. An orthogonal experimental design was constructed using an orthogonal array from Sloan's website (Sloan, 2009) http://www.research.att.com/~njas/oadir) (Street, Burgess, and Louviere 2005). The orthogonal array was a multiple design and included a fractional factorial design with 18 choice sets, 5 attributes each at 3 levels and one with 6. Of this array, only four of the columns were used (Appendix A). The removal of columns is proven to be an effective approach (Hensher et al. 2005; Street et al. 2005 and Burgess & Street, 2008). The data was then converted using the levels identified in

Appendix C. Following Louviere et al. (2000), a "foldover" method was used to obtain consistent pairwise choices. A foldover design is defined as a systematic level change of the original design (0=1, 1=2, 2=3, and 3=0) which results in a design that has a higher efficiency (Street, Burgess, and Louviere 2005). Following this, the design was then tested for level balance acknowledging an equal number of levels to be assigned with each of the product attributes. Further, minimal overlap was assessed by checking that no attributes had the same level within a choice set.
Consistent with most applications of DCEs within health economics, only main effects were estimates (de Bekker-Grob, 2012). It is argued that such effects explain most of the variation in preferences, assuming that nonlinearities and interactions are negligible (Kløjgaard et al 2012; Ryan, Watson, & Gerard 2005). An unlabelled, forced-choice experimental design was chosen. Hence, for every decision, respondents faced a choice between two pharmaceuticals used to treat undefined disease with specified attribute levels for each.

2.1. Number Of Choices And Cognitive Fatigue

Even after using experimental fractional factorial design methods, a large number of choices may remain for presentation to respondents. The design selected resulted in eighteen choice sets. This raises the question of the number of choices subjects can respond to, before becoming tired, bored, or unmotivated. The number of choice sets that respondents are presented with in DCEs in health has increased, with the mean number at 14 (de Bekker-Grob et al. 2012).Acknowledging this, a design with 18 choice sets seemed plausible.

2.2. Inclusion Of A Validity Test In The Choice Task

The experimental design included one choice sets where one alternative unquestionably dominates the other(s) on all attribute (Appendix I, question 11). We decided to keep these questions in order to test the rationality of responses. 'Incorrect' responses can either be interpreted as a result of irrational respondents, a lack of understanding of the choice task, or a simple mistake on the part of the respondent (Kjaer 2005).

2.3. Checking Properties

Huber and Zwerina (1996), outlined four criteria to consider when constructing a survey; namely, orthogonality, level balance, utility balance and minimal overlap. However, obtaining a balance between the different criteria is a matter of judgment since improving some of the criteria can come at the expense of others. The main criteria adhered to in this study were orthogonality, level balance and minimal overlap. The constructed design allows for this three of the four principle of an efficient design, as shown in table in appendix B, table 17.

3. Data Collection

3.1. The Questionnaire

After obtaining the optimal experimental design, the task of constructing the survey instrument then moved on to designing the layout and overall presentation of the survey. Each survey contained a title page explaining to the respondents that the data was being collected as part of a postgraduate research project, was confidential, and would have no impact on actual policy making. The approximate time to complete the study was also provided, acknowledging the approximate length of completion. The second page included a likert scale, used as the warm-up questions. Here, respondents were asked to answer general questions about their view on the Portuguese reimbursement system. Page three comprised instructions about the scope and how to face the DCE. The purpose of the choice set was explained, stating that we would like to know how the respondent prefer to allocate public funds, when it comes to fund pharmaceuticals. We explained the real decision context, stating that the budget for pharmaceutical funding is limited and there are more drugs available than can be funded with the budget, so choices must be made regarding which drugs to fund. Respondents were then asked to imagine the decision was up to them, and to choose which pharmaceutical they prefer, considering all presented attributes. Page four described the selected attributes and levels, with tables and examples. Page five included an example of an

answered choice set and included the interpretation of such choice. The following pages were the DCE itself. The last section covered demographic, economic and health status information the collection of demographic and heath status information about the respondent. The questionnaire is divided three parts, being the 1st and the 3rd, supporting questions and the second part the DCE itself.

3.1.1. "Warm-Up" Questions: The Likert Scale

Respondents are expected to have different experiences with medicines along with a heterogeneous attitude facing the Portuguese reimbursement system. A bunch of generalist questions, shaped as a Likert scale, were firstly presented to respondents. These were attitude and experience questions, primarily asked to focus the respondent on the issue we study.

This first part included questions about how well respondents understand the Portuguese reimbursement system and generic questions about how the reimbursement should be granted (for example, only for people with low income or only for non expensive medicines).

Whilst economists have used rating scales to estimate quality weights or benefit scores, other social and behavioural scientists have tended to favour scales that are concerned with respondent's attitudes. A common technique used here is the Likert scale. This contains a series of opinion statements on a given issue. Respondents' attitudes are elicited by presenting them with a series of statements and asking them their level of agreement on an agree–disagree continuous scale. This is often an 'odd' number scale, with a neutral/undecided point in the middle.

Methodological evaluations of Likert scales have been limited in healthcare, outside of their use in satisfaction studies. The literature states good internal consistency and reliability. Construct validity is also supported in terms of convergent validity, Likert scales demonstrated good results. A major disadvantage of totalling up scores is that "while a set of respondents will always add up to the same score, the same total may arise from many different combinations of responses, which lead to a loss of information about the components of the scale score". Nevertheless, Likert scales are relatively easy to complete and seemed a good way to introduce the questionnaire.

3.1.2. DCE Section

Respondents faced a dichotomous choice (i.e. choose alternative A or B) as shown in Figure 2.

FIGURE 2 - DCE QUESTIONNAIRE (QUESTION TEMPLATE)

1. Please compare the following medicines and select which one you think should BE REIMBURSED:

	MEDICINE A		MEDICINE B
Severity of the disease	Very severe		Not severe
Prevalence of the disease	Moderate		Low
Medicine's efficacy	Low efficacy		Moderate
Government costs	10 000€		5 000€
	Medicine A		Medicine B
Please tick one box:	☐		☐

3.1.3. Socio-Demographic Questions

It is desirable to include some questions on socio-demographic variables (Champ, 2006). The inclusion of socio-demographic questions makes it possible for the researcher to split the sample into subgroups and to test whether different groups of respondents answer differently, e.g. to test for heterogeneity in preferences. In practice this is done by examining interactions between personal characteristics and the desired attributes (Kjaer 2005). Age, gender, qualifications, health status, professional status, income, monthly expenditure with medicines, private health insurance, benefits from any reimbursement subsystem or reimbursement special scheme were included.

3.2. Qualitative Work: Piloting

This study targets the general population, with a random sample of citiziens. Therefore it is important to assure that every respondent who could probably receive the questionnaire would understand the task and be willing to perform it. Regarding this, qualitative work was developed.

For a DCE, qualitative work can take many forms. Taking in account the context of this work, namely the time and budget available, a small pilot was conducted, with eight respondents.

Many reasons motivated the pilot: detecting possible errors and amending them before the main study, clarifying if the attributes are meaningful for respondents, identify any misunderstanding that could arise from the terminology used, evaluating the level of comprehension and difficulty of the proposed task, determining how long respondents take to complete the questionnaire.

The pilot consisted of asking the selected individuals to answer the questionnaire following a think aloud methodology. The respondents were recorded, with a camera, while they were answering the questionnaire. Before this, respondents signed an informed consent and were showed a template video to illustrate the think aloud method. This procedure was followed by careful analyses of the videos. Each video was seen in the day the task was performed. Amendments to the questionnaire were due at the end of each pilot and results are showed in table 13, page 53.

Think aloud data can be obtained in two ways: concurrent and retrospective. Concurrent think aloud asks respondents to verbalise their thoughts as they complete a task. Retrospective think aloud asks respondents to describe what they were thinking after the task has been completed. We used a concurrent think aloud method. Respondents were asked not to explain or plan what they were saying, but to act as if they were speaking to themselves. There is still some uncertainty around how individuals make their choices which may emphasize the need of planning qualitative work such as a verbal protocol. However, there is evidence that individuals use simplifying heuristics when faced with complex decisions, and that preferences may be constructed at the time rather than existing previous to the task. Individuals may also be unwilling to trade, making choices based on a single high priority attribute. It is not clear whether behaviour which does not correspond to the assumptions underlying economic theory reflects limitations in the decision maker or task- related demand characteristics.

3.2.1. Tested Features

A) Opt-Out Question

The pilot showed evidence on propensity for choosing the opt-out alternative. While performing the DCE, one respondent verbalized the will to choose none. The reasoning behind this was that so sensible from an ethical point of view that they would rather not make the choices at all. Since that the respondent did not avoid the task because he felt none of the options were plausible, but rather because he didn't felt comfortable on having to choose one pharmaceutical over other, we decided to keep the questionnaire as a forced task. There evidence that, when faced with sensitive hypothetical decisions, there is a trend of respondents to avoid answering.

B) Cost attribute

One important aim of the pilot was to investigate the best way to present the cost attribute to respondents. Table 12 highlights the framed question for each version and the number of respondents for each version.
Reactions to version 0, where the cost attribute was presented as government savings, revealed difficulty in understanding the question which resulted in 2 incoherent answers (respondents verbalized their answer as if the cost attribute was "government costs per person treated"). Another respondent had to go back several times to the introductory page where the cost attribute was described. After these pilot results, that denoted confusing over understanding the cost attribute when framed as "government savings", only version 1 was used to complete the qualitative work.

TABLE 12 – DIFFERNCE BETWEEN TWO VERSIONS OF THE QUESTIONNAIRE

	Version 0	**Version 1**
Code	P 0**0X**	P 0**1Y**
Question	Which of the following medicines you think should not be reimbursed?	Which of the following medicines you think should be reimbursed?
Cost attribute	Government cost saving	Government costs per person tretated
Number of respondents	3	5

C) The Likert Scale

Respondents reacted positively to the Likert Scale task. The think aloud method was the key for the researcher to understanding how respondents face the Portuguese funding pharmaceuticals. On distributive questions, respondents found interesting the set of questions presented, stating that they have never thought about these problems. Respondents took a fair time thinking and raising equity and ethical questions while responding. The Likert scale is presented in Appendix F.

D) Levels

Generally the respondents found the levels feasible and with an acceptable range, forcing them to make decisions. Respondents didn't seem confused about the presented levels nor about the way they were explained.

E) Framing

Although all respondents expressed that the framing of the questionnaire was clear and concise, the qualitative test resulted in some amendments on the framing (Table 13). They readily started to fill the questionnaire, just based on the provided instructions, and with no questions. At first, respondents were suprised of having to choose to fund one treatment over another. Most respondents have never realized this were actual choices and would prefer not to chose, or reimburse all the medicines.

TABLE 13 – PILOT RESULTS

Pilot Number	Pilot Version	Amendment	Section	Respondent Reaction/ Quote
1	0	Include the option " no monthly expenditure with pharmaceuticals"	Demographics	"I don´t have any expenditures in pharmaceuticals"
1	0	Change the question from "Which health subsystem do you benefit from "Do you have any health subsystem"	Demographics	Respondent seemed confused with the options available

TABLE 13 – PILOT RESULTS (CONT)

2	0	Shorten the description by simplifying it	DCE (instructions)	Skipped the description of economic evaluation
2	0	Remove example from the question	Lickert scale	"smokers shouldn´t benefit from co-payments? Why penalize them? What about the individuals who have other unhealthy habits?
3	0	Remove double word "studying"	Demographics	-
1	1	Question 14, cost value changed from 50 000€ to 5 000€	DCE	-

One respondent was reluctant to complete the DCE, stating that it was not fair to do such decisions. There was the need to explain the task and emphasize that although she was facing hypothetical scenarios, the choice involved in the decision reflected real choices done by decision makers when facing limited public budgets.

F) Attributes

All the respondents agreed that the chosen attributes reflected their concerns about the reimbursement of pharmaceuticals and that the questionnaire presented an easy task. However, through the analyses of the think loud records, we concluded that there were some obstacles to the conclusion of the questionnaires. This statement will be clarified through this section. Overall, the proposed design proved to be well accepted by the respondents. There was some confusing when the cost attribute was presented as government savings so this version was dropped before the main study.

3.2.2. Conclusions From The Pilot

The qualitative data from the verbal protocol analysis is a powerful tool that has been exploited to test response motivations in stated preference studies. Although in this study we just used it to provide information about the structure, design and terminology of the questionnaire, it can provide rich information about respondents' preferences. Ryan et al., 2009, used a verbal protocol analyses combined with a DCE to test if

respondents hold complete, monotonic, and continuous preferences and why some people fail standard applied quantitative test (Ryan te al. 2009).
Overall, the proposed design proved to be well accepted by the respondents. There was some confusing when the cost attribute was presented as government savings so this version did not followed to the main study.

3.3. Sample Design And Data Collection Method

Most of DCE applied to the health care market target a specific group of population such as patients, decision makers or health care practitioners (de Bekker-Grob et al. 2012). Due to the nature of the present study, it was decided to focus on the general population. Rather than elicit preferences for a defined pharmaceutical or for a given disease, this study covers the problem of public funding of pharmaceuticals, through the point of view of tax payer. This is in line with the shape of the cost attribute, which will, ultimately, allow us to conclude if there the public is a concern about how much should the government pay for health, and, more specifically, for pharmaceuticals.
The survey was administered to a probability sample, on the geographical area of São Vitor which in the Portuguese city of Braga. The parish has an estimated population of 29.642 inhabitants (Census, 2011) thus requiring a sample of 377 individuals, in order to be representative (95% confidence level and 5% and a confidence interval of 5%) (sample size obtained through online calculator: http://www.raosoft.com/ samplesize.html).
The parish was selected for being the biggest parish on the city and because it comprises a very heterogeneous population and a wide geographical area.
The aim is to obtain a probability sample, giving more value to statistical inference. To do so, there were made contacts with the post office to obtain the best service. The first idea was to determine the geographical limits (the ones of the referred parish) and they would distribute the surveys in random base. The only service the post office offers to do so, does not allow to get a record of the addresses. This was not convenient for our study as we aimed to send more than one correspondence.
A database with 218 streets was introduced into Excel®, 2007, and subsequently randomized till 40 streets were left. In each street, 10 questionnaires were delivered, resulting in 400 questionnaires.
Randomisation within an experimental design is a way of ensuring control over con-

founding variables and as such it allows the researcher to have greater confidence in identifying real associations between an independent variable (a potential cause or predictor) and a dependent variable (the effect or outcome measure).

The complete questionnaire is in appendix I. The advantages of paper surveys include the ability of respondents to complete the survey at their convenience and at their own pace. Respondents may also feel more comfortable offering honest responses to sensitive questions if they are not facing an interviewer while completing the questionnaire. The downside of paper surveys is the lack of control over the order in which the respondent answers the questions. Further, f the respondent doesn't have contact with the research, doubts about the questionnaire may arise while completing it, remaining unclear.

During 26th and 27th May, 400 questionnaires were administered through mail in S. Vitor's area. The envelope contained the main questionnaire, one post card, presenting the study and a response free of charge envelop.

After one week, a remembering post card (annex B) was delivered on the same addresses, thanking the response, if already done, or emphasizing the importance of replying if not yet done.

The first documentation outlined that we expected responses within two weeks. Nevertheless, few were the responses that got to the post office in time. Therefore, we extended the calendar for one month. Responses received after the 27th June were not considered.

4. Data Analyses

4.1. Data Input

After the data are collected, they need to be organized and set into a computerized database Statistical package STATA 10 ® was used to analyse the data. Each choice set contains two forms of information: 1) The attribute levels of each alternative, and 2) Which of the given alternatives has been chosen. Each attribute level has to be coded in order to estimate the importance of each attribute, i.e. the marginal values and trade of ratios. The coded data of the choice set and data input, is presented in Appendix C. For this task we used a dummy variable coding. Attributes are coded so

that the constant term is used to reflect what is expected to be the least desirable option (for funding) in the factorial design.

4.2. Econometric Analyses

The DCE was analysed with a conditional logit regression taking each choice among the two options (pharmaceutical A and pharmaceutical B) as an observation. Assuming that all attributes have an independent influence on respondents' preference, the following model was estimated:

$$V = \beta_0 + \beta_1 severity + \beta_2 prevalence + \beta_3 efficacy + \beta_4 governmentcost$$

Where:

- V represents the utility derived for the new pharmaceutical
- β0 is a constant reflecting the respondents' preference for pharmaceutical A over pharmaceutical B.
- β1 to β4 are the coefficients that indicate the relative importance of each attribute.

The signs of the coefficients reflect whether the attribute has a positive or a negative effect on utility. The value of a coefficient indicates the relative importance of the corresponding attribute. A priori we expected that only the cost attribute would have a negative significant coefficient. The trade-offs that the respondents were willing to make between the attributes were estimated by the ratios between the coefficients. The coefficient of the cost attribute is used to estimate the willingness to pay (WTP).

Chapter 5. Results And Discussion

1. Response Patterns

400 questionnaires were mailed and 39 of them were returned. Of these 39 respondents, 34 completed the DCE questionnaire, resulting in a response rate of 8.5%. The number of individuals providing responses for the regression analysis is 34, providing 612 choice responses and 1224 observations.

An additional set of 56 surveys were administered locally, on the headquarters of the Parish of São Vítor. These 56 individuals provided 2016 observations from 1008 choice responses.

In line with the findings of the pilot, it seemed that respondents understood the task and faced it as hypothetical scenarios that reflect a real decision. One of the respondents refused to answer writing that he couldn't decide on such a delicate question and that all pharmaceuticals should be funded.

2. Characteristics Of Respondents

Respondents were aged between 18–80 (mean 45.08), 74% were female. 45.05%, reported a good health status, while 13.64% declared a bad or very bad health status (table 14). The monthly expenditures with pharmaceuticals was reported to be between 6€ – 25.99€ for 40.7% of respondents and between 26€ and 50.99€ for 22.1% of respondents. Only 4% of the respondents have commissioned a private health insurance and 5.9% benefit for an additional reimbursement scheme, due to specific diseases.

Individuals in the non-random sample have, on average, a lower income and lower educational level than the random sample. Further, the non random sample has 30 % of individuals away from work ill, while none of the respondents from the random sample reported to be in this situation.

In order to test that both samples were equally distributed in terms of socio demo-

graphic characteristics, a chi-squared test was performed to compare them. The results showed that there is significant difference in some variables, namely income, education level and professional situation, at conventional levels (Appendice G). The results are, therefore, reported separately.

It is important to underline that this study was not intended to be representative of the Portuguese population. Nonetheless, we find of relevance to contextualize our sample in the pattern of the Portuguese population. Comparing to the Portuguese population (Census 2011), both samples are more likely to have female respondents. Further, high educated individuals are overrepresented comparing to the Portuguese population (15%). Most respondents (45.4%) state that they have a good health status. Only 25% reported one chronic disease while the statistic for the Portuguese population is 40.5%.

TABLE 14 - RESPONDENTS' CHARACTERISTICS

	Category	Random sample	Non random sample	Ch2
Age (mean)		47.3	43.4	0.2731
Gender (%)	Female	63.64	80.7	0.079
Education (%)	Higher education	69.7	32	0.009
	Secondary education	21.21	36	
	Basic education	3	24	
	Primary education	3	6	
	Never studied	3	2	
	Rather don't say	0	0	
Health status (%)	Very good	21.21	8.93	0.178
	Good	51.52	42.86	
	Fair	21.21	30.36	
	Bad	6	10.71	
	Very bad	0	7.14	
Chronic diseases (%)	No	66.67	66.07	0.375
	Yes, one	30.3	23.21	
	More than one	3	10.71	
Employment (%)	Unemployed	0	30.36	0.004
	Retired	27.27	30.36	
	Working	54.55	50	
	Studying	6.06	1.76	
	Disabled	3.03	1.79	
	Away from work ill	6.06	8.93	

TABLE 14 (CONT) - RESPONDENTS' CHARACTERISTICS

	Category	Random sample	Non random sample	Chi2
Income (%)	None	15.15	21.43	0.039
	Up to 485.99€]	3.03	12.5	
	[486€ ;900,99€]	21.21	30.36	
	[901€;1455,99€]	24.24	12.5	
	[1456€;1940,99€]	9.09	7.14	
	[1941€;2425,99€]	15.15	8.93	
	[2426€;3395,99€]	12.12	0	
	More than 3396	0	0	
	Rather not say	0	7.14	
Monthly expenditure with pharmaceuticals (%)	None	8.82	9.62	0.971
	Up to 5.99	11.76	7.69	
	[6€ ;25,99€]	38.24	42.31	
	[26€; 50,99€]	20.54	23.08	
	[51€;75,99€]	5.88	3.85	
	[76€;100,99€]	5.88	7.69	
	[101€; 150,99€	0	0	
	More than 151€	5.88	1.92	
	Don't know	2.94	3.85	
Benefits from special scheme of reimbursement (%)	Yes	2.94	3.92	0.414
	No	88.24	96.08	
	I don't know	2.94	0	
Private health insurance (%)	Yes	8.82	1.79	0.116
	No	91.18	98.21	

3. Model estimation and interpretation

The individuals were asked to choose between two alternatives (pharmaceutical A and pharmaceutical B).

Two of the respondents answers failed a 'consistency check' question, choosing the option that was dominated across all attributes by the alternative available and a third provided answers in a "geometric pattern". Therefore, in 8.8% of cases (3/34) the sample did not meet the requirement for consistent answers. Given the societal

context of the survey (Green and Gerard 2009), and a lack of clarity in the research literature on what might be classified as irrational response data (Lanscar and Louviere, 2006; Ryan et al 2009), the data from these respondents was included in the analysis.

As described on the method, the sample design resulted in two different groups of the same population, one selected randomly and the other handed personally. On both methods, as showed in appendix D, a random selection of the respondents was motivated by the request that one resident of the house, aged over 18 years old and whose birthday is closest to the current date, to respond to the questionnaire. The likelihood-ratio test (LR chi2(7)= 38.58; Prob > chi2 = 0.0000) reject the null hypothesis, that stated preferences are the same when samples are analyse as a whole or separately. Therefore the samples were reported separately. Table 15 reports the results of the conditional logit model, for analysis of main effects on both samples.

TABLE 15 – RESUTS FROM CONDITIONAL LOGIT MODEL FOR EACH RANDOM AND NON RAMDOM SAMPLES

Samples	Random	Non random	Whole sample
		Results	
Very severe (p value)	2.045199 (0.0001)	1.35059 (0.0001)	1.527974 (0.0001)
Severe (p value)	1.299507 (0.0001)	0.8244396 (0.0001)	0.9322099 (0.0001)
High prevalence (p value)	1.929115 (0.0001)	1.093388 (0.0001)	1.27659 (0.0001)
Moderate prevalence (p value)	2.035019 (0.0001)	1.184279 (0.0001)	1.368776 (0.0001)
1Very effective (p value)	2.645672 (0.0001)	1.253538 (0.0001)	1.621912 (0.0001)
Moderate effectiveness (p value)	1.68076 (0.0001)	0.893373 (0.0001)	1.10018
Government costs per person treated (p value)	-0.0000127 (0.0001)	-0.00000389 (0.010)	-0.000005.88 (0.0001)
Log_likelihood (intercept only)	-220.20122	-515.14322	-754.63669
Chi-squared statistic	408.01	367.1	736.52
Adj Mc Fadden's R^2	0.4809	0.2627	0.3280
Number of individuals	34	56	90
Number of observations	1224	2016	3240
Likelihood ratio test: LR chi2(7) Prob > chi2		37.56 0.00001	-

4. Model Fit

The pseudo R2, after adjustment for the degrees of freedom, was 48% for the random sample and 26% for the non random sample, indicating an acceptable fit for both models (Table 15) (Hensher et al., 2005). Furthermore, the models returned a high chi-squared statistic, 408.01 for the random and 367.1 for the non random sample, indicating that the estimated model has improved explanatory power over a model where only constant terms were included.

5. Importance Of Attributes

Table 15 presents the results from conditional logit model. As showed, all attributes were statistically significant at the level of 1% (alpha ≤0.01). Also, both samples reported a negative and significant coefficient for the government cost per person treated attribute, showing that respondents prefer these attribute to take lower levels. In other words, respondents showed that, other things equal, they prefer the government to fund less costly pharmaceuticals. The results were in line with expectations and provided support for the theoretical validity of the model. The attributes "very severe" and "very effective" had high and positive coefficients on each sample, although with different ranks of priority. This reflects that, status quo, respondents prefer the government to fund a pharmaceutical to treat a serious condition rather than a moderate condition, and a pharmaceutical with high efficacy. These results were expected and in line with previous studies (Diaby, et al. 2011, Whitty et al. 2011, Whitty et al. 2008). For the random sample, the regression coefficients indicated that "severity of the disease for which the treatment is indicated" had the strongest influence on respondent's choice behaviour, followed by efficacy of the pharmaceutical, prevalence of the disease and government costs per person treated. On the other sample, effectiveness of the pharmaceuticals had the higher positive coefficient, indicating that, for these respondents, a pharmaceutical with high efficacy seems to be the most important attribute for funding decisions. In this group, efficacy of the new pharmaceutical is followed by the severity of the disease for which the treatment is indicated and prevalence of the disease ranks as the least relevant attribute, although still significant.

Unexpectedly, the coefficient for moderate prevalence of the disease is higher than for high prevalence of the disease. Individuals may have showed concerns about distributional and equity principles, preferring pharmaceutical that may, ultimately be associated with a more rare disease. Also, respondents may have related the attribute prevalence of the disease with the attribute government costs per person treated, which may conduct them to choose a less prevalent disease in order to save public funds. Nevertheless, this result was not accounted while designing the experiment as the qualitative pilot did not revealed such potential relation. This issue requires further research, namely a depth qualitative work.

6. Socio Demographics Interactions

An interesting approach that the DCE methods is the investigation of the relation between the socio-demographics characteristics of the respondents and the utility they assign to each attribute by choosing an alternative. To allow for variation in preferences (therefore WTP values), interaction terms were created between the attributes and characteristics of respondents to test its ability to influence preferences. The whole sample was used for this estimation (table 15). The subgroups were defined a priori based on a review of the DCE literature. Income is assumed to change the way respondents weigh the cost attribute and the self-reported health status to influence the way they valuated the severity of the disease for which the treatment is indicated attribute (Green and Gerard, 2009). Nonetheless it is important to emphasize that, as the cost attribute in our study is framed as public costs, such relation wasn't expected, or at least it wasn't expected to be notorious. The results (chi2 (6) = 1.87 and Prob > chi2 = 0.931) show that income levels are not associated with the willingness to accept the government to fund pharmaceuticals.

Further, the hypothesis that respondents with a worse self reported health status would input increasing marginal utility on a pharmaceutical which is indicated to treat a very severe disease was tested. Contrary to what we expected, the result - chi2(4) = 6.69 and Prob > chi2 = 0.1530 – did not allow to conclude that the reported health status influences the choice. This may be related to the small size of the sample and to the overrepresented individuals that reported a good health status.

7. Marginal Willingness To Pay

The inclusion of a cost attribute is useful for the calculation of the marginal willingness to pay (MWTP) respondents indirectly showed through the task. The results for WTP and MWTP are presented in table 16.

Although we are not considering out-of-pocket money as the paying vehicle, the WTP was estimated in order to assess respondents' way of dealing with public funds.

On the random sample, everything else equal, respondents were willing to accept a public paying of 161 039€ for a pharmaceutical indicated for a very severe disease. The marginal willingness to pay (WTP) for a pharmaceutical indicated for a very severe disease, rather than for a pharmaceutical indicated for a moderate severe disease is 58.716€.

The non random sample indicated, everything else equal, that the respondents willingness to pay more, 347 195€ in terms of public funds for a pharmaceutical indicated for a very severe disease. The marginal willingness to pay was 135 257€ for a pharmaceutical indicated for a very rather than for a pharmaceutical indicated for a moderate severe disease.

On average, the marginal willingness to pay for a very effective pharmaceutical rather for a pharmaceutical with moderate effectiveness is 75 977€ for the random sample and 91 814€ for the non random sample.

TABLE 16 – WTP AND MWTP FOR EACH ATTRIBUTE

Samples	Random		Non random	
	WTP(€)	MWTP (€)	WTP(€)	MWTP (€)
Very severe (β_1)	161 039	58 716	347 195	135 257
Severe (β_2)	102 323		211 938	
High prevalence (β_3)	151 899	-8 339	281 077	-23 365
Moderate prevalence (β_4)	160 238		304 442	
Very effective (β_5)	20 8321	75 977	322 246	92 587
Moderate effectiveness ($\beta_{6)}$)	13 2343		229 659	

8. Interpreting The Choice Probability

At the level of the scenarios, perhaps a more policy-relevant perspective, it is important to consider how the data presented can be interpreted in terms of the relative desirability (attractiveness) of the alternative scenarios. The probability scale allows interpretation with ratio-level properties, and allows a judgment against a cardinal scale, indicating how much better or worse one option is, when compared with another. That is, when comparing estimates of the probabilities that each option will be chosen, it is possible to state how much worse (or better) one probability is compared with another (Green and Gerard, 2009)

Calculating the choice probability of selected scenarios is a useful tool to inform policy makers. This technique is able to turn the results of the regression model into a comparative analyse of two scenarios. It is therefore possible to support policy decisions, knowing which scenario is more likely to fit respondents' choice, over another. Taking equation 4 in chapter three, the probability of choosing between a set of scenarios was calculated. The results are presented in Appendix H. These probabilities provide a measure of preference, with higher probabilities (for funding the described scenario) showing which scenario is given higher priority (preference) compared with those with a lower probability of being chosen for funding (from the full set of scenarios available) (Whitty et al., 2008).

The attributes "severity of the disease for which the treatment is indicated" and "efficacy of the new pharmaceutical" had the strongest influence on respondents' choice behaviour on the random and non random sample, respectively. Therefore, this attributes were varied for both the pilot and main study models to provide an example of how the models can be used to estimate the probability of a respondents' choice to fund a hypothetical pharmaceutical. In the first hypothetical choice set, holding all attributes at their lowest level, except "severity of the disease for which the treatment is indicated", the probability the public would want a pharmaceutical to treat such severe disease was 89% for the random sample model and 79% for the non random sample model, when compared to a pharmaceutical indicated for a mild disease (for which the funding probabilities are 11% and 21% respectively) (Appendix H, table 19). In the second hypothetical choice set, we find that setting all other attributes to their best level compensates significantly for a low "severity of the disease for which

the treatment is indicated" level in both models, taking the funding probability for a pharmaceutical indicatedfor a mild disease to 75% in the random sample model (from 11%) and to 65% in the main study model (from 21%) (Appendix H). The same exercise was done for the attribute efficacy of the new pharmaceutical.

Chapter 6: Conclusion

This is the first DCE in Portugal extending the discussion of prioritization in the health care sector, namely on the pharmaceutical funding decision, to the general population. Whilst this study was undertaken in the Portuguese context and has deep exploratory nature, we found consistency between our findings and those comparable studies undertaken in the UK, Australia and Canada (Diaby et al. 2011, Whitty et al., 2008, Tappenden et al., 2007).

This experiment is useful to introduce a new approach to Portuguese policies design. It shows the potencial of DCE to inform both marketers in which way to address new products and public policy-makers to target resources towards services which are likely to give the greatest overall societal benefit (Whitty, 2008).

In line with other DCEs, this study supports the existence of equity versus efficiency trade-off as other studies (Green and Gerard 2009, Whitty, 2008, Diaby, et al. 2011) also report. The results suggest that, when considering resource allocation for the treatment of others with pharmaceuticals, the public value the efficacy of the pharmaceutical, the severity of the disease for which it is indicated, and the prevalence of the disease. This is, to some extent, consistent with the prioritization criteria INFARMED uses. The first funding decision consideres the therapeutic value and the economic profile of the new pharmaceutical. Further, the law accounts for vulnerable gorups, to assign different rate of financing (Chapter 2).
Additionally, the findings suggest that cost is of relatively little importance when compared to the other attributes. However, it is not irrelevant, and it appears that the public are willing to trade between cost and effectiveness, even when the costs are publicly supported. In other others, and in line with Whitty (2008), they do not expect the government to purchase health gain at any cost. (Whitty et al. 2008). Findings suggest that general public concerns to be both sided, balancing equity principles such as severity and prevalence with efficacy and costs, as all attributes were significant (Green and Gerard 2009).

Respondents from the pilot showed some reluctances in answering the DCE choices which suggests that they engaged with the choice task and its context and highlights their ability to weigh up the difficult choices presented, offering some confidence in the validity of the experiment (Green and Gerard 2009). Further, one respondent from the main questionnaire wrote that he noted the relevance of the study and would like it to be published in order to be informed of the results.

This study has some limitations that we assume fair considering its explorative nature. We identify two main constraints, the budget and scheduled time, to be the main sources of limitations.

Firstly, altough the importance of the qualitative work on a DCE has been aknowledge during the work, it was not possible to perform the ideal amount of it. Further qualitative work would have been beneficial for a more grounded selection of the attributes and its levels and for the consitency of the results (Klojgard 2012).

Secondly, the sample carries some limitations. The findings of this DCE may be limited by the sample design, which resulted in a low response rate (8.5%). A small sample doesn't seem to allow the accurate estimation of the interactions between socio-demographic characteristics of respondents and their choices. Besides, the sample is not representative of the selected population. Future research may be able to address this limitation, with face to face questionnaires to increase response rate and identify response errors (Whitty et al., 2008). It is also possible to send an additional post card or to reapeat the administration of the questionnaires, in order to incite individuals to respond to the mailed questionnaire.

Expecting such low response rate while designing the DCE, we decided to include an additional sample, which aimed to strengthen the main sample and give robustness to the results. However, the statistical analyses forced us to consider the samples separately which has limited the statistical efficiency of the model (as it resulted in two smaller samples). It may have been useful to design the study differently, e.g. using the non-random sample as a pilot sample and the random sample as the main study sample. Such study would require more time. Despite these limitations, the considerable similarities (in terms of coefficient significance, size and order of attribute importance) between the models for both samples, suggest that the findings are robust (Whitty et al., 2008).

The use of the conditional logistic model may be considered a limitation for its simplicity (Green and Gerard 2009). Altough this factor is able to make the findings policy-relevant and the presentation of findings policy friendly it represents potential limitations in the methodology. Nervertheless, these preliminary findings can be used to inform more detailed future study designs (Green and Gerard 2009).

This research suggests that the results are useful and indicative of what may be possible in future, through more comprehensive research. The results allow concluding that the public is willing and able to provide preferences to inform policy for pharmaceutical decision-making, setting foundations for further research.

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Appendices

Appendix A

Figure 3. The mixed-level orthogonal main effects plan MA 18.3.6.6.1 for the multinomial design, (Sloan, 2009)

Inside the dashed line box are the columns used for the experimental design

	A1	A2	A3	A4	A5	A6	A7
Choice 1	0	0	0	0	0	0	0
Choice 2	0	1	2	2	0	1	1
Choice 3	0	2	1	2	1	0	2
Choice 4	0	1	1	0	2	2	3
Choice 5	0	2	0	1	2	1	4
Choice 6	0	0	2	1	1	2	5
Choice 7	1	1	1	1	1	1	0
Choice 8	1	2	0	0	1	2	1
Choice 9	1	0	2	0	2	1	2
Choice 10	1	2	2	1	0	0	3
Choice 11	1	0	1	2	0	2	4
Choice 12	1	1	0	2	2	0	5
Choice 13	2	2	2	2	2	2	0
Choice 14	2	0	1	1	2	0	1
Choice 15	2	1	0	1	0	2	2
Choice 16	2	0	0	2	1	1	3
Choice 17	2	1	2	0	1	0	4
Choice 18	2	2	1	0	0	1	5

Appendix B

TABLE 17 – EXPERIMETAL DESIGN RESULT

Choice	MEDICINE A				MEDICINE B			
	Severity	**Preva-lence**	**Efficacy**	**Cost (€)**	**Severity**	**Preva-lence**	**Efficacy**	**Cost (€)**
1	Not severe	High	Low	100000	Severe	Moderate	Moderate	50000
2	Very severe	High	Moderate	50000	Not Severe	Low	High	10000
3	Very severe	Moderate	Low	10000	Not severe	Low	Moderate	5000
4	Not severe	Low	High	5000	Severe	Moderate	Low	1 000
5	Severe	Low	Moderate	1000	Very severe	Moderate	High	500
6	Severe	Moderate	High	500	Very severe	Moderate	High	100000
7	Severe	Moderate	Moderate	100000	Very severe	Low	High	50000
8	Not severe	Moderate	Moderate	50000	Severe	Low	Low	10000
9	Not severe	Low	Moderate	10000	Severe	High	High	5000
10	Severe	High	Low	5000	Very severe	Moderate	Moderate	1000
11	Very severe	High	High	1000	Not severe	Moderate	Low	500
12	Very severe	Low	Low	500	Not severe	High	Moderate	100000
13	Very severe	Low	High	100000	Not severe	High	Moderate	50000
14	Severe	Low	Low	50000	Very severe	High	Moderate	10000
15	Severe	High	High	10000	Very severe	Moderate	Low	5000
16	Very severe	Moderate	Moderate	5000	Not severe	Low	High	1000
17	Not severe	Moderate	Moderate	1000	Severe	Low	High	500
18	Not severe	High	Low	500	Severe	Moderate	Moderate	100000

Appendix C

TABLE 18 – CODING ATTRIBUTES

Attributes		**Levels**	
Discription	Code	Discription	CODE
Severity of the disease for which the treatment is indicated	**A1**	mild severe	0
		severe	1
		very severe	2
Prevalence	**A2**	high	0
		moderate	1
		low	2
Efficacy of the medicine	**A3**	low	0
		moderate	1
		high	2
Government costs	**A4**	100 000	0
		50 000	1
		10 000	2
		5 000	3
		1 000	4
		500	5

Appendix D

FIGURE 4. TEMPLATE OF INTRODUCTORY POST CARD (TRANSLATED)

Dear household,

Are you willing to help with research conducted at the University of Minho?

Within the scope of the Masters in Health Economics and Policy, it is our aim to study which criteria d you find important to decide pharmaceutical funding by the government.

We therefore ask that one resident of this house, aged over 18 years old and whose birthday is closest to the current date, to respond to this questionnaire. Such task will takes, approximately, 20 minutes.

The information collected is confidential and it won't be available for any other organization. This means you won't be identified by your answers.

Your participation is crucial for the success of this research.

We understand that your time is valuable and therefore, we are deeply thankful for you cooperation.

Appendix E

FIGURE 5. TEMPLATE OF REMEMBERING POST CARD (TRANSLATED)

Public Stated Preferences for pharmaceutical funding decisions

About 1 week you were sent a questionnaire seeking your opinion about public funding of pharmaceuticals.

If you have already completed and returned the questionnaire to us, please accept our sincere thanks.

If you haven't yet replied, we very much look forward to receiving your views. If you did not receive a questionnaire or it was misplaced, please contact Magda Aguiar: pg19509@alunos.uminho.pt or Paula Benesch: 253 604 549 for a replacement questionnaire.

Thank you for your help!

Appendix F

FIGURE 6. 1ST SECTION OF THE QUESTIONNAIRE - WARM-UP QUESTIONS

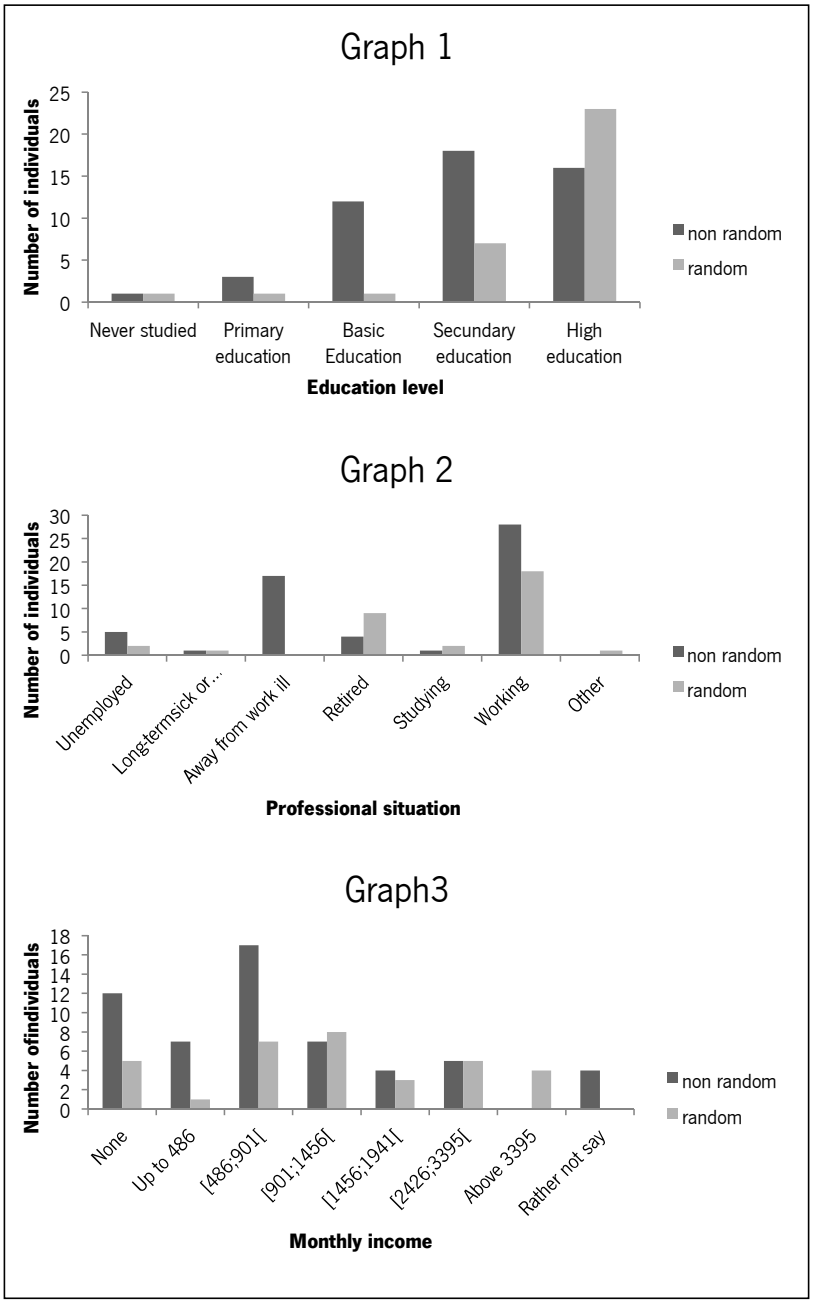
Part 1. The Portuguese reimbursement system - In this section we want to know what do you think about the Portuguese reimbursement system for pharmaceuticals. There are no right and wrong answers, is your opinion that counts for us!

Please select **(✓)**, in each row, one option:

	Totally disagree	Disagree	Uncer-tain	Agree	Totally agree
I understand the Portuguese reim-bursement system for pharmaceu-ticals	☐	☐	☐	☐	☐
The Portuguese reimbursement system for pharmaceuticals should simpler	☐	☐	☐	☐	☐
Only the most effective pharmaceuti-cals should be reimbursed	☐	☐	☐	☐	☐
The government spends too much money on the reimbursement of pharmaceuticals	☐	☐	☐	☐	☐
Only the cheaper pharmaceuticals should be reimbursed	☐	☐	☐	☐	☐
The reimbursement of pharmaceuti-cals should be granted just for those with lower income	☐	☐	☐	☐	☐
There should be a maximum limit of reimbursement per individual	☐	☐	☐	☐	☐
Reimbursement rates should be calculated based on the patient monthly expenditures (higher rates for those who spend more)	☐	☐	☐	☐	☐
Individuals with unhealthy habits shouldn't benefit from reimburse-ment	☐	☐	☐	☐	☐
All available medicines should be reimbursement	☐	☐	☐	☐	☐
Non prescription medicines should be reimbursed	☐	☐	☐	☐	☐

Appendix G

FIGURE 7. DISTRIBUTION OF EDUCATIONAL LEVEL (GRAPH1), PROFESSIONAL SITUATION (GRAPH 2 AND MONTLHY INCOME (GRAPH 3) FOR EACH SAMPLE.



APPENDIX H

TABLE 19 – PROBABILITY THAT A RESPONDENT IN RANDOM AND NON RANDOM SAMPLE WOULD CHOOSE A HYPOTHTICAL SCENARIO:

		RANDOM				NON RANDOM		
Alternatie	Severity	Other attributes leves	Systematic utility (V)	Prbability of funding (Pr)	Severity	Other attributes leves	Systematic utility (V)	Prbability of funding (Pr)
Choice set one								
1	High	low prevalence, low efficacy, 100 000€	3.315199	89%	High	low prevalence, low efficacy, 100 000€	1.73959	79%
2	Low	low prevalence, low efficacy, 100 000€	1.27	11%	Low	low prevalence, low efficacy, 100 000€	0.389	21%
Choice set two								
1	High	low prevalence, low efficacy, 100 000€	3.315199	22%	High	low prevalence, low efficacy, 100 000€	1.73959	35%
2	Low	High prevalence, high efficacy, cost 500€	4.4581137	78%	Low	high prevalence, high efficacy, 500€	2.348871	65%
Alternatie	Efficacy	Other attributes leves	Systematic utility (V)	Prbability of funding (Pr)	Efficacy	Other attributes leves	Systematic utility (V)	Prbability of funding (Pr)
Choice set three								
1	High	low severity, low prevalence, 100 000€	3.915672	93%	High	low severity, low prevalence, 100 000€	1.642538	78%
2	Low	low severity, low prevalence, 100 000€	1.27	7%	Low	low severity, low prevalence, 100 000€	0.38	22%
Choice set four								
1	High	low severity, low prevalence, 100 000€	3.915672	48%	High	low severity, low prevalence, 100 000€	1. 642538	31%
2	Low	high severity, high prevalence, 500€	3.980664	52%	Low	high severity, high prevalence, 500€	2.445915	69%

APPENDIX I

FIGURE 8 . QUESTIONNAIRE (ORIGINAL)

Universidade do Minho
Escola de Economia e Gestão

Caro cidadão,

Convido-o a participar numa investigação da Universidade do Minho. Para isso peço-lhe que responda ao questionário que encontra nas páginas seguintes. Esta investigação faz parte de uma tese de mestrado em Economia e Política da Saúde, sob o tema "*Preferências Sociais no financiamento de medicamentos em Portugal"*.

O objetivo deste estudo é recolher informação sobre as **preferências da população no que respeita ao financiamento dos medicamentos.**

Como sabe, em Portugal os cuidados de saúde são, na sua maior parte, financiados pelo estado, com recurso aos impostos que cada contribuinte paga. Assim queremos saber como acha que estes recursos deviam ser usados, nomeadamente na comparticipação de medicamentos

A sua colaboração é valiosa e imprescindível para que a que investigação prossiga.

Peço que leia com atenção toda a informação que fornecemos. Os textos que lhe apresentamos servem de introdução às perguntas e tornarão mais fácil a compreensão e conclusão deste questionário. O questionário tem impressão **frente e verso.**

Para facilitar a devolução do questionário à Universidade do Minho, enviamos-lhe nesta carta um envelope sem franquia **(não precisa de selo)**. Por favor, devolva o questionário devidamente preenchido neste envelope, **dentro de duas semanas.**

Os seus dados são confidenciais e manter-se-ão protegidos. Os resultados deste estudo serão utilizados apenas para esta investigação e **não** têm qualquer envolvimento político.

Agradeço desde já a disponibilidade. Para qualquer questão, por favor contacte-me através do endereço eletrónico **pg19509@uminho.pt.**

Atenciosamente,

(Magda Aguiar) (Paula Benesch)

Parte 1. O sistema de comparticipação de medicamentos

Queremos saber o que pensa do sistema de comparticipação de medicamentos português. Por favor selecione **(✓)**, em cada linha, uma opção:

	Discordo totalmente	**Discordo**	**Não tenho a certeza**	**Concordo**	**Concordo totalmente**
Compreendo o sistema de comparticipação de medicamentos	☐	☐	☐	☐	☐
O sistema de comparticipação de medicamentos devia ser mais simples	☐	☐	☐	☐	☐
Apenas os medicamentos mais eficazes deviam ser comparticipados	☐	☐	☐	☐	☐
O Estado gasta demasiado dinheiro com a comparticipação de medicamentos	☐	☐	☐	☐	☐
Apenas os medicamentos mais baratos deviam ser comparticipados	☐	☐	☐	☐	☐
Apenas se devia comparticipar os medicamentos aos indivíduos com mais dificuldades económicas	☐	☐	☐	☐	☐
Devia haver um limite máximo de comparticipação por indivíduo	☐	☐	☐	☐	☐
A comparticipação devia basear-se nos gastos mensais com medicamentos (ajudar mais quem gasta mais)	☐	☐	☐	☐	☐
Não se devia comparticipar medicamentos a indivíduos com hábitos pouco saudáveis	☐	☐	☐	☐	☐
TODOS os medicamentos deviam ser comparticipados	☐	☐	☐	☐	☐
Os medicamentos de venda livre (não sujeitos a receita médica) deviam ser comparticipados	☐	☐	☐	☐	☐

Parte 2. Escolher entre diferentes medicamentos

Por favor LEIA COM ATENÇÃO:

Nesta segunda parte, queremos saber como gostava de distribuir os recursos disponíveis para o financiamento de medicamentos em Portugal.

Perante um orçamento limitado, o Ministério da Saúde é forçado a fazer escolhas, incluindo sobre quais os medicamentos que devem ser comparticipados.

Os **critérios** atualmente considerados para apoiar esta decisão são a **eficácia** do medicamento e o **preço** do medicamento. Os medicamentos que não apresentam eficácia comprovada ou que sejam considerados caros, em comparação com os que já existem no mercado, não recebem comparticipação.

Nas próximas perguntas, pedimos-lhe que **imagine** que lhe cabe a si esta decisão. Assim, deve escolher, em cada pergunta, que medicamento acha que o governo **DEVE COMPARTICIPAR,** tendo em conta as características que considera mais importantes. Lembre-se que apenas um dos medicamentos pode permanecer na lista de medicamentos comparticipados. Cada pergunta é independente o que significa que ao longo do questionário os medicamentos A e B são diferentes

Entendemos que algumas respostas serão difíceis mas lembre-se que não existem respostas certas nem erradas. É a sua opinião que conta!

NA PÁGINA SEGUINTE ESTÃO DESCRITOS OS CRITÉRIOS A TER EM CONTA PARA A SUA DECISÃO.

POR FAVOR LEIA CUIDADOSAMENTE A PÁGINA SEGUINTE ANTES DE RESPONDER AO RESTO DO QUESTIONÁRIO.

Critérios apresentados

Para que possa escolher entre os dois medicamentos, descrevemos-lhe as características que deve ter em conta:

- **Gravidade da doença -** Grau de incapacidade provocado pela doença. Quanto mais incapacitante for a doença, mais grave ela é.

NÍVEIS	EXEMPLOS
Doença ligeira	Eczema, dor de costas passageira (aguda), enxaqueca
Doença grave	Tuberculose, artrite reumatoide moderada
Doença muito grave	Esclerose múltipla progressiva, cancro.

- **Prevalência da doença -** Número total de casos, numa dada população, num determinado tempo.

NÍVEIS	DESCRIÇÃO	EXEMPLOS
Elevada (mais de 5%)	Mais de 5 em cada 100 pessoas têm esta doença	Hipertensão arterial Doença reumática
Moderada (entre 1% e 5%)	Entre 1 e 5 pessoas em cada 100 têm esta doença	Tumor maligno Bronquite
Baixa (menor de 1%)	Menos de 1 em cada 100 pessoas têm esta doença	Insuficiência Renal Enfarte Agudo Miocárdio

- **Eficácia do medicamento -** corresponde à capacidade de o medicamento produzir os resultados pretendidos.

NÍVEIS	EXEMPLOS
Muito eficaz	Este medicamento faz, na maioria das vezes, o efeito pretendido
Moderadamente eficaz	Nem sempre este medicamento faz o efeito pretendido
Pouco eficaz	Muitas vezes este medicamento não faz o efeito pretendido

- **Custo para o Estado** - quanto o Estado gasta, por pessoa tratada, ao decidir comparticipar o medicamento (500€,1.000€, 5.000€, 10.000€, 50.000€, 100.000€)

EXEMPLO

Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença ligeira
Prevalência	Moderada	Elevada
Eficácia do medicamento	Moderadamente eficaz	Moderadamente eficaz
Custo para o Estado	1 000€	500€
Por favor marque uma das opções	**Medicamento A** ☐	**Medicamento B** ☑

Apenas um dos medicamentos pode entrar na lista de medicamentos comparticipados.

Ao escolher o medicamento B, este indivíduo prefere comparticipar um medicamento **com eficácia moderada** para tratar uma **doença ligeira** (mínima gravidade). Esta doença tem **elevada prevalência**. A decisão de comparticipar este medicamento vai custar ao estado **500€ por pessoa tratada**.

Ao selecionar o medicamento B este indivíduo escolheu não comparticipar o medicamento A.

1. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Alta	Moderada
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	500 €	1 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

2. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Alta	Baixa
Eficácia do medicamento	Moderadamente eficaz	Muito eficaz
Custo para o estado (por pessoa tratada)	1 000€	10 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

3. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Moderada	Baixa
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	5 000€	10 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

4. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Baixa	Moderada
Eficácia do medicamento	Muito eficaz	Pouco eficaz
Custo para o estado (por pessoa tratada)	10 000€	50 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

5. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença muito grave
Prevalência	Baixa	Moderada
Eficácia do medicamento	Moderadamente eficaz	Muito eficaz
Custo para o estado (por pessoa tratada)	50 000€	100 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

6. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença muito grave
Prevalência	Moderada	Baixa
Eficácia do medicamento	Muito eficaz	Pouco eficaz
Custo para o estado (por pessoa tratada)	100 000€	500€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

7. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Grave	Doença muito grave
Prevalência	Moderada	Baixa
Eficácia do medicamento	Moderada	Muito eficaz
Custo para o estado (por pessoa tratada)	500€	1 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

8. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Moderada	Baixa
Eficácia do medicamento	Moderadamente eficaz	Pouco eficaz
Custo para o estado (por pessoa tratada)	1 000€	5 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

9. **Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:**

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Baixa	Alta
Eficácia do medicamento	Moderadamente eficaz	Muito eficaz
Custo para o estado (por pessoa tratada)	1 000€	50 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

10. Por compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença muito grave
Prevalência	Alta	Moderada
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	10 000€	50 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

11. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Alta	Moderada
Eficácia do medicamento	Muito eficaz	Pouco eficaz
Custo para o estado (por pessoa tratada)	50 000€	100 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

12. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Baixa	Alta
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	100 000€	500€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

13. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Baixa	Alta
Eficácia do medicamento	Muito eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	500€	1 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

14. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença muito grave
Prevalência	Baixa	Alta
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	1 000€	50 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

15. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença grave	Doença muito grave
Prevalência	Alta	Moderada
Eficácia do medicamento	Muito eficaz	Pouco eficaz
Custo para o estado (por pessoa tratada)	5 000€	10 000€
Por favor selecione uma opção	**Medicamento A** ☐	**Medicamento B** ☐

16. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença muito grave	Doença ligeira
Prevalência	Moderada	Baixa
Eficácia do medicamento	Moderadamente eficaz	Muito eficaz
Custo para o estado (por pessoa tratada)	10 000€	50 000€

	Medicamento A	**Medicamento B**
Por favor selecione uma opção	☐	☐

17. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Moderada	Baixa
Eficácia do medicamento	Moderadamente eficaz	Muito eficaz
Custo para o estado (por pessoa tratada)	50 000€	100 000€

	Medicamento A	**Medicamento B**
Por favor selecione uma opção	☐	☐

18. Por favor compare os seguintes medicamentos e selecione qual acha que deve ser COMPARTICIPADO:

	Medicamento A	**Medicamento B**
Gravidade da doença	Doença ligeira	Doença grave
Prevalência	Alta	Moderada
Eficácia do medicamento	Pouco eficaz	Moderadamente eficaz
Custo para o estado (por pessoa tratada)	100 000€	500€

	Medicamento A	**Medicamento B**
Por favor selecione uma opção	☐	☐

Parte 3. Sobre si: (Para melhor compreendermos as suas respostas, gostaríamos de lhe colocar algumas perguntas mais pessoais)

1. **Que idade tem?**

☐ Prefiro não dizer

2. **Qual é o seu género?**

Masculino ☐ Feminino ☐

3. **Que habilitações literárias possui? Por favor selecione (✓) apenas uma opção.**

- ☐ Ensino Superior
- ☐ Ensino secundário (até ao 12º
- ☐ Ensino Básico (até ao 9º ano)
- ☐ Ensino Primário (até à 4ª classe)
- ☐ Nunca estudei
- ☐ Prefiro não dizer

4. **Como classifica o seu estado geral de saúde? Por favor selecione (✓) apenas uma opção.**

Muito bom ☐ Bom ☐ Razoável ☐ Mau ☐ Muito mau ☐

5. **Sofre de alguma doença crónica? Por favor selecione (✓) apenas uma opção.**

Sim, uma ☐ Sim, mais do que uma ☐ Não ☐

6. **Neste momento está: Por favor selecione (✓) as opções que se aplicam.**

- ☐ Profissionalmente ativo
- ☐ A estudar
- ☐ Reformado
- ☐ Outro. Por favor diga-nos qual: _____
- ☐ Desempregado
- ☐ Incapacitado para trabalhar por doença
- ☐ De baixa/licença médica

7. **Qual destas opções representa o seu salário mensal, incluindo todos os benefícios e depois de todas as deduções (salário mensal líquido)? Por favor selecione ✓**

- ☐ Não tenho rendimentos
- ☐ Até 485,99€
- ☐ Entre 486€ e 900,99€
- ☐ Entre 901€ e 1455,99€
- ☐ Entre 1456€ e 1940,99€
- ☐ Entre 1941€ e 2425,99€
- ☐ Entre 2426€ e 3395,99€
- ☐ Mais de 3396€
- ☐ Prefiro não dizer

8. **Em média, quanto gasta por mês na compra de medicamentos? Por favor selecione ✓**

- ☐ Não tenho gastos com medicamentos
- ☐ Até 5,99€
- ☐ Entre 6€ e 25,99€
- ☐ Entre 26€ e 50,99€
- ☐ Entre 51€ e 75,99€
- ☐ Entre 76€ e 100,99€
- ☐ Ente 101€ e 150,99€
- ☐ Mais de 151€
- ☐ Não sei

9. **Beneficia de algum subsistema de saúde? Por favor selecione ✓ apenas uma opção**
(Nota: exemplos de subsistemas são: ADSE, SAMS, ADM, SADPSP/GNR, entre outros)

Sim	Não	Não sei
☐	☐	☐

10. **Possui algum seguro privado de saúde que cubra despesas com medicamentos? Por favor selecione (✓) apenas uma opção.**

Sim	Não
☐	☐

11. **Beneficia de algum regime especial de comparticipação (pensionistas, lúpus, paramiloidose, artrite reumatoide)? Por favor selecione (✓) apenas uma opção.**

Sim	Não	Não sei
☐	☐	☐