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WP5: Integrated Assessment for Short to Medium term Policies and Measures

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ACRONYMS USED

CE	Choice Experiments
CV	Contingent Valuation
DALY	Disability Adjusted Life Year
DCE	Discrete Choice Experiment
QALY	Quality Adjusted Life Year
VSL	Value of Statistical Life
VLYL	Value of Life Year Lost
WTP	Willingness to Pay
COPD	Chronic Obstructive Pulmonary Disease
CVD	Cardiovascular Disease

1 Literature review on health outcomes valuation – the state of the art

1.1 Introduction

This review is based on a search of the existing systematic reviews of empirical studies on health valuation. For this purpose, three databases have been searched: Science Direct, Web of Knowledge and Pubmed. Keywords were "health", "valuation" and "review" and the research has been restricted to studies published after 2010.

The review has identified a number of studies, which offer a picture of the recent developments in stated preference (SP) techniques applied in health economics.

Elicitation methods for willingness to pay (WTP) for health improvements include contingent valuation methods (CV) and the use of discrete choice experiments (DCE).

1.1.1 Contingent Valuation

In CV methods, the respondent is asked to state how much he would be willing to pay for a certain health treatment, for improving health or for reducing mortality risk. WTP questions in CV methods take a number of forms, ranging from open-ended questions, to close-ended questions, double-bounded dichotomous models, bidding games, payment scales as well as card sorting games.

The use of CV methods can follow two approaches (described in detail by Donaldson et al. 2010 with reference to the QALY literature).

Within the *"direct method"*, the study directly presents a certain change in health and investigates the WTP of the respondent to avoid this scenario.

Within the second method – defined as the *"chained" method* – the quality (utility) of certain health states is first assessed by the respondent through an elicitation method, which can be an iterative *standard gamble*, a *time-trade off* exercise, the use of a *Visual Analog Scale* (VAS) as well as the use of the *EQ-5D* instrument[1]. Using one or more of these techniques, the utility associated to a health profile is first evaluated (this can be the current health state or a hypothetical previously described scenario). The second step of the chain is represented by the elicitation of the WTP for avoiding the adverse health scenario (or for benefiting of the health gain) using a CV technique.

1.1.2 Discrete Choice Experiment

Discrete choice experiments - also referred to as "conjoint analysis" - have increasingly been used in this literature.

In discrete choice experiments, respondents are asked to complete several choice tasks. In each task, they are asked which health scenario or treatment alternative they prefer. Alternatives are characterised by different attributes and different attribute levels. Within this context, preferences over the different alternatives are modelled using a random utility model (McFadden, 1984).

[1] Reviews of utility elicitation methods can be found, among others, in Peasgood et al. (2010), Chen and Ratcliffe (2015) and Jeong and Cairns (2016).

De Bekker-Grob et al. (2012) and Clark et al. (2014) have reviewed the economic literature using DCE over the period 2001-2008 and 2009-2012 respectively, discussing survey design issues, validity checks and econometric techniques usually applied to DCE data.

The econometric technique more commonly used to analyse choice experiment data is represented by the conditional logit model.
Following Lloyd et al. (2011), the probability of choosing alternative *j* from choice set C in choice task *i* is defined as:

$$P(J(C) = j) = P_j(C) = \frac{\exp\left(X'_{ij}\beta\right)}{\sum_{k \in C_i} \exp\left(X'_{ij}\beta\right)}$$

This model is the multinomial logit model. Given that attributes X represent alternative-dependent variables, this model is referred to as the conditional logit model. Given that the cost attribute is included, WTP for each of the attributes is easily computed by dividing the relevant attribute coefficient for the coefficient of the cost attribute[2].

DCE clearly offers an advantage as, when using CV "*respondents [are] asked to consider whole health states or scenarios [..] and decide how much they would like to pay. In reality, they might consider these health states or scenarios based on only some important attributes that were important to them*" (Nimdet et al., 2015, p. 16). Nevertheless, Lin et al. (2013a) points out that there is no conclusive evidence in terms of superiority of different WTP elicitation method in terms of accuracy of the values provided (both for CV vs. DCE and among different CV techniques).

1.1.3 Common issues in stated preference surveys

A number of problems on eliciting WTP using survey data have been pointed out by the literature.

- *"Framing effects"* (or "information bias") of the survey design are discussed by Ahlert et al. (2016) with the "*wording of the questions and the survey setting (personal or online interview)* [affecting the responses, as well as] *… simple design elements such as offering an explicit option to say "No" right away*" (p. 47).
  Lin et al. (2013b) show that how cancer survival rates are presented in the questionnaire can affect the respondent. In particular, they find that if expressed as median survival rates, WTP is lower than in the case of survival rates after one year from treatment.
  Another example comes from a study on cancer screening using a discrete choice experiment. Howard and Salkeld (2009) find that framing the question in a negative rather than positive way can have an impact on the results, with "number of cancer cases found" being valued higher than "number of missed cases avoided".
  De Bekker-Grob et al. (2010) show that also the labelling of the different options in a choice task may influence the respondent as it takes the focus off the attributes.

[2] If the cost attribute is not included, WTP cannot be estimated and DCE is usually used to analyse preferences and to elicit utility weights or quality of life weights (e.g. Ryan et al. 2006).

- Another issue discussed in these types of studies is the *"hypothetical bias"*. Kangethe et al. (2016) point out that when respondents consider the proposed scenario as very unrealistic, they may provide very unreliable and overestimated answers.
  Hultkrantz and Svensson (2012) suggest that WTP in a fictitious scenario may be 2 to 3 higher than real WTP. The use of "cheap talk" sections after the WTP elicitation exercise may help the respondent to better think about the scenario and his choices (Kangethe et al.. 2016).
  Olofsson et al. (2017) also suggest to include questions on how sure the respondent is about his choice.
- Moreover, different WTP elicitation methods suffer from different drawbacks. Soeteman et al. (2017) discuss the advantages of using payment scales. In particular, they point out the avoidance of starting point bias (although this is usually addressed in double-bound dichotomous choice models and bidding games by using different or random starting bids), the lower "cognitive burden" associated with this type of method (compared for example to open-ended questions), as well as the lower rate of missing responses. Davey et al. (1998) use an open-ended question followed by a "bid-up" exercise to elicit the maximum WTP and observe that this approach as well avoids starting point bias and that the respondent is able to answer the question as long as he is familiar with the topic.

In the following, we will review the most recent health economics literature analysing WTP for QALYs, VSLs and WTP for care in the context of asthma, cancer and diabetes.

1.2 WTP for a QALY

Ryen and Svensson (2015) and Nimdet et al. (2015) have carried out systematic reviews of the literature eliciting WTP for Quality-adjusted life years[3]. In this section, the papers included in these reviews will be presented[4], together with more recent studies[5].
Within this literature, Donaldson et al. (2010) have run a European project (EuroVaQ) aiming at reviewing the methods usually used to value a QALY and at proposing robust and consistent methods that should be used at the European level.

Two main approaches exist:

- The first involves estimating WTP for a QALY starting from existing studies on value of statistical life (VSL). To go from VSL to QALY, the value of VSL needs to be adjusted to take into account the age of the individual, a QoL weight for each remaining expected life year, and of course an appropriate discount rate. Examples are Hirth et al. (2000) on US data and Mason et al. (2009) for the UK.

[3] Ryen and Svenson carried out a systematic review on the databases Pubmed, Econlit and Google Scholar. Keywords used where "Willingness to pay", "WTP", "Value", "Monetary value", together with "QALY", "Quality-adjusted life year" and "Life year". They retrieved 24 studies published between 1998 and 2015.
Nimdet et al. (2015) searched Medline, Embase, Psyinfo, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Center of Research Dissemination (CRD) and EconLit. Their search queries where "(willingness to pay or contingent valuation or discrete choice experiment) AND (quality adjusted life year or QALY)" and "willingness to pay for (per) quality adjusted life year". Fourteen studies were extracted, published between 1995 and 2014.
[4] We have excluded studies published before the year 2000.
[5] These have been identified through the database Pubmed with similar keywords.

- The second approach is more relevant for us and involves the use of survey data to elicit WTP for a QALY using contingent valuation or choice experiment methods.

As suggested by Nimdet et al. (2015), CV methods used within this literature take different forms.

- Byrne et al. (2005), Nimdet and Ngorsuraches (2015) and Ahlert et al. (2017) use an *open-ended question* on the total amount of money the respondent would be willing to pay to achieve full health or to avoid an adverse health scenario.
- Gryd-Hansen (2003) and Gyrd-Hansen and Kjaer (2012) use *close-ended questions* to value two health scenarios, that have been previously evaluated by the respondent in terms of "best" or "worst" scenario.
- Shiroiwa et al. (2010 and 2013) use *double-bounded dichotomous choice* models to value a treatment from which the respondent would gain 1 QALY in the case of a serious illness (2010 paper) or in different health state scenarios (2013 paper). A double-bounded dichotomous choice is used also by Moradi et al. (2017) in a study on individuals with a cardiovascular problems. Within this framework, different starting bids are usually used in order to avoid starting point bias.
- Several studies follow an iterative *bidding method* to elicit the maximum WTP for a treatment which would allow the respondent to achieve perfect health or to overcome a specific health problem.

  Also in the case of bidding games, randomly drawn starting bids are usually used in order to avoid starting point bias.

  In the paper by Zhao et al. (2011), the initial bid was randomly drawn from three values, reflecting different income levels of the Chinese population. The bid was then halved or doubled depending on the answer to the previous bid. King et al. (2005) follow a similar approach, but use as initial value the monthly income of the household. The initial bid used by Martin-Fernandez et al. (2014) vary randomly from €1 to €8,192 per month. In a study on facial deformit (Dey et al., 2016) the initial bid is derived from a pilot study.

  Working along the same lines, Thavorncharoensap et al. (2013), Lieu et al. (2009) and Lim et al. (2017) also add an open-ended question after the bidding sequence, in the case the respondent is willing to pay more than the maximum price, or less than the minimum.
- A two-step approach is followed by Bobinac et al. (2010, 2012, 2013 and 2014). In the first step, a *payment scale* is used, where the respondent is presented with a set of monetary values, from which he is asked to select the maximum amount he would certainly pay for a treatment and the minimum amount he certainly would not. In the second *bounded open-ended* step, the respondent is asked to provide the maximum value he would pay within the previously defined range.
- Similarly, Robinson et al. (2013), Pinto-Prades et al. (2009) and Pennington et al. (2015) use a *card sorting* game to value health scenarios. In these papers, the respondent is asked to consider a set of payment cards and to decide what amount he would "definitely pay", "definitely not pay" to avoid a certain health state, and about which amounts he is "unsure". An open-ended question then allows to identify the respondent's actual WTP within this range.

As stated above, these different CV methods can be used either directly or within a "chained approach". Within the "direct method", the respondent is asked to value a certain change in QALY (which can be presented either in terms of QoL or life expectancy).
Within the "chained" method, the quality (utility) of certain health states is first assessed by the respondent who is then asked about his WTP for avoiding that scenario. Within the QALY literature, the chained method is the most widely used. It is in fact used in each paper listed above, with the following exceptions: Ahlert et al. (2017), Pennington et al. (2015) and Shiroiwa et al. (2010 and 2013).

Both approaches have their limits. In the direct approach, large changes in QALY are usually valued rather than small changes presented in percentage format. This is less challenging for the respondent, as it requires lower mathematical skills (Pennington et al. 2015, Haninger and Hammitt 2011).
On the other hand, the WTP associated with large changes in QALY are more likely to be affected by budget constraints (Robinson et al. 2013).
Along these lines, Ryen and Svensson (2015) and Sund and Svensson (2018) discuss the problem of scope sensitivity bias (or scale bias), i.e. non linearity between changes in QALY and changes in the WTP level (with WTP for a QALY being lower when larger QALY changes are valued).
This problem is quite common also in VSL studies as they are based on small mortality risk changes (Alberini, 2005; Lindhjem et al., 2011). It has been suggested that a good understanding of the concept of probability and risk change is associated with lower VSLs (Lindhjem et al., 2011) and it is therefore important to take this issue into account in questionnaire construction - for example visualizing changes in probabilities using grid squares (e.g. Scansi and Alberini, 2017).

1.3 The value of a statistical life

The OECD has recently compiled a large database of all studies published until 2008 that have used a stated preference approach to elicit VSL. The database and other material can be found at http://www.oecd.org/env/tools-evaluation/env-value-statistical-life.htm. The database contains approximately 70 studies and covers studies analysing WTP for mortality risk reduction in three contexts: health, transport and environment. These studies have been analysed through meta-analysis by Lindhjem et al. (2011).
Another review paper (by Hultkrantz and Svensson, 2012) has focused on VSL studies conducted for Sweden from 1996 until 2009[6].

The VSL is widely estimated using *discrete choice experiments*. Some of the most recent studies are presented in the following.

[6] The systematic review was carried out on the databases Pubmed, Econlit and Google Scholar. Keywords used where "value of statistical life", "value of prevented fatality" "mortality risk reduction", "willingness to pay", "stated preferences", "contingent valuation", "choice experiment" as well as "Sweden" or "Swedish".
They retrieved 12 studies published between 1996 and 2009.
For the purpose of this review, we have also carried out a literature search using the database Pubmed using similar keywords but not restricting the analysis to any country and including only papers published from 2005 onwards.

Guignet and Alberini (2015) elicit VSLs using a choice experiment in the context of house prices and air pollution levels, taking into account different levels of mortality risk reduction and different levels of house price premium. WTP for fatality risk reduction is estimated by Sčasný and Alberini (2012) using a discrete choice experiment. The different scenarios attributes include value of risk reduction, cost, latency and information on how many decades the reduction is going to last. Alberini and Ščasný (2018) develop a survey to estimate VSL in relation to risk of cancer. Their study adds to the literature by focusing not only on cancer fatality risks, but also including attributes such as level of pain and impact on daily life activities in the case of cancer. Interestingly, their results suggest that only level of mortality risk reduction but not the severity of the disease is significantly related to the estimated VSL.
Niroomand and Jenkins (2016 and 2017) analyse VSL in a road-safety context, respectively among drivers and pedestrians. The respondents are asked to choose among different routes in order to elicit WTP for higher road safety. For pedestrians routes are characterised by different speed limits, crossing types, walking time, number of injuries and fatality per year as well as increase in cost (in terms of municipality charges). For drivers, trips are characterised by the following attributes: speed limits, number of speed cameras, travel time, number of injuries and fatality per year as well as increase in travel cost. Also Yang et al. (2016) focus on transport safety using data on China and considering cost and fatalities for the different alternatives in a disctrete choice setting.

A number of papers have analysed the extent to which *VSL differ by cause of risk reduction*, with interesting results.
Carlsson et al. (2010) investigate VSL in Cyprus in three different risk contexts: road-safety, drowning and fire accidents. Discrete choice experiments investigate WTP for different risk reduction amounts and for different risk levels at baseline (attributes). Their results suggest a higher WTP for increasing road-safety, rather than reducing fatality risks from drowning and fire accidents. The rationale behind this appears to be that people tend to be more concerned about car accidents rather than drowning and fire. Moreover, people may consider the given baseline risk as not realistic and perceive the actual fatality risk as higher.
Carlsson et al. (2004) report that people are more willing to pay for reducing risk of dying when flying than when travelling by taxi.
Tekeşin and Ara (2014) suggest that differences in VSLs from different contexts of risk reduction depend also on "*pain, fear, and the duration of suffering*" (p. 6906). Their results suggest that VSL based on lung cancer risk reduction is 200% higher than VSL from increasing road safety.
A similar result is found by Viscusi et al. (2014) who use a similar choice experiment for reduction in mortality risk from cancer: WTP tends to increase the higher the perceived likelihood to be at risk of cancer. Moreover, they find evidence that the estimated cancer-related VSL is approximately 20% higher than the ones usually estimated for the US for other types of fatalities.

Hultkrantz et al. (2006) and Svensson and Johansson (2010) show that there may be a difference in VSL estimated for the same cause of risk reduction (road safety) but from different providers (public safety programme vs. privately purchased device) – the latter being considered by the respondent as more valuable than the former.

Contingent valuation methods have also been used in this literature. To the best of our knowledge, these have mainly been used following a "direct approach" rather than a "chained" approach. Among others,

Roldós et al. (2017) estimates WTP for reducing maternal mortality risk in Ecuador using a double-bounded model; Mofadal et al. (2015) use a payment card method in the context of pedestrian safety in Sudan. Svensson (2009a) uses an open-ended question to elicit WTP for a good that would reduce fatality risk from traffic accidents. His results interestingly suggest that VSL is independent from behaviours connected to risk aversion, such as use of seat belt, use of bicycle helmet or use of bicycle lights or respect of speed limits.

1.4 WTP for chronic respiratory diseases treatment

Zhou et al. (2017) provide a systematic review of studies focusing on valuation of respiratory diseases, with a particular focus on asthma[7]. In the following, we will focus also on chronic obstructive pulmonary disease (COPD).

Within this literature, a number of studies have used *discrete choice experiments* to elicit WTP for asthma and COPD treatments.

Lancsar et al. (2007) carry out a discrete choice experiment on a sample of adult asthma patients, who are asked to take into account the cost and nine other attributes of a hypothetical drug when making a choice regarding whether to take the new medication. Thanks to the presence of the cost component, the monetary value of each attribute can be valued. These attributes range from frequency and method of drug administration, through experience of asthma symptoms and side-effects, to impact on daily life activities. Attributes included in similar studies also include number of episode-free days (Walzer and Zweifel, 2007 and McTaggart-Cowan et al., 2008), risk of symptoms exacerbation and information on long-term side effects (Llyod et al., 2008). Kawata et al. (2014) assess the value of different maintenance medicine attributes on a sample of COPD patients, including, among others, extent and speed of symptoms relief, ease of use, need to use rescue medication and side effects. Their results suggest that WTP is highest for a medicine providing complete symptoms relief, followed by absence of side effects and avoidance of use of rescue medication. In a similar study on asthma and COPD patients, Svedsater et al. (2017) include among treatment attributes also the ability to engage in social and physical activities.

Bulcun et al. (2014) use a similar DCE for a treatment for COPD focusing also on patient-doctor relationship: attributes also include being seen always by the same doctor, whether the doctor spends enough time listening to the patient, and whether the doctor treats the patient as a whole person.

Along similar lines, a study by Hawken et al. (2017) explore the WTP for attributes relating to a new inhaler among asthma and COPD patients. Attributes include ease of use and read dose counter, hygiene of mouthpiece, possibility to use in case of breathing difficulties and costs.

Naik-Panvelkar et al. (2012) assess pharmacy-delivered asthma services focusing on cost of service, frequency and cordiality, effectiveness on symptoms and level of assistance.

[7] The systematic review by Zhou et al. (2017) was conducted on the databases Pubmed, Scopus and Google Scholar. Keywords used where "asthma", "carbon monoxide poisoning", "lead poisoning", "Willingness-to-Pay", "WTP", "cost-of-illness", "COI", "economic burden", "IQ" and "earnings", and. On WTP for asthma, 9 studies were identified published between 1998 and 2012.
Using similar keywords in the Pubmed database, and extending the research to chronic obstructive pulmonary diseases, several additional studies have been identified.

Direct CV methods to evaluate WTP for a cure for COPD have been used by Chen et al. (2016) and Stavem (2002) in studies on COPD patients. Chen et al. (2016) investigate WTP for a treatment for COPD in Taiwan using a closed-ended double-bounded model, finding that higher income level, presence of comorbidities as well as lower perceived quality of life are associated with an higher WTP. Along the same lines, Stavem (2002) use a payment-card method to asses WTP for a hypothetical cure for COPD among a sample of patients in Norway, finding instead little association between WTP and self-reported health level.

Another widely used approach in this field is the use of *CV methods within a chained framework*, which allows to separate the utility assessment exercise from the WTP elicitation exercise.
O'Conor and Blomquist (1997) and Blomquist et al. (2011) have used this approach for analysing the WTP for avoiding asthma morbidity and mortality. In the first step of their exercise, different drugs characterised by different level of risk and efficacy are presented to the respondent who is asked to choose the preferred drug. This reveals risk values accepted to avoid "symptoms-days". In the second step, the WTP for a medication that offers either higher safety or higher efficacy than the previously chosen drug is elicited by a closed-ended question. Blomquist et al. (2011) also allow for certain degree of uncertainty in the response (Definitely/Probably-Yes/No). Along the same lines, Zillich et al. (2002) first use the SF-36 questionnaire to elicit information on the quality of life of a sample of adults with asthma. WTP for a treatment able to offer the same utility as a life with no asthma is then measured with a single-bounded dichotomous model.

An interesting study by Guerriero et al. (2018) analyses children's capabilities to carry out WTP exercises taking into account their own budget constraint when stating their WTP for lowering the risk of experiencing asthma attacks. Results suggest that children are capable of answering rationally, and that their capability to understand the different elements of CV exercises increases with age.

1.5 WTP for diabetes treatment

A review of studies analysing patients' valuation of diabetes treatments is carried out by von Arx and Kjær (2014)[8]. Out of the 16 identified studies, three papers used CV techniques, with the remaining using discrete choice experiments. Out of the 13 studies using choice experiments, the cost of treatment was not included as a treatment attribute in six studies, making it impossible to compute WTP.

Contingent valuation studies
Davey et al. (1998) investigate diabetes patients' WTP for a new type of insulin using an open-ended question followed by a "bid-up" exercise to elicit the maximum WTP. They observe that this approach avoids starting point bias and that the respondent were able to answer the open question (due to the familiarity with the topic).

[8] The review was conducted on the databases MEDLINE, EMBASE, Biosis, Current Contents, Web of Science, CINAHL, PsycINFO, and EconLit. Keywords used included "diabetes", "diabetic", "stated preferences", "Willingness-to-Pay", "contingent valuation", "choice modelling", "choice experiment" and "conjoint analysis". The review identified 16 studies, published between 1998 and 2013.
Using similar keywords in the Pubmed database, four additional relevant studies published between 2015 and 2017 were identified.

Using a similar sample of diabetic patients, Sadri et al. (2005) examine WTP for inhaled or injected insulin. They employ a payment scale method with prices ranging from 0$ to 700$, followed by an open-ended question in case the respondent is willing to pay more than the maximum price. Valuation of inhaled insulin treatments is also the objective of the study by Pinto et al. (2009). Willingness to use and Willingness to pay were first elicited using a dichotomous question, followed by an (open-ended) question on maximum WTP.

Olofsson et al. (2016) conduct two different surveys in Sweden in order to compare the results of a WTP exercise with the results of a time trade-off method used to elicit information about the utility associated with different health states. The WTP for a number of attributes related to diabetes treatment is elicited using a card-sorting game, using an open-ended question if the respondent is willing to pay more than the maximum proposed amount. The utility levels derived from the TTO analysis are transformed into monetary values using a threshold of SEK500,000 per QALY. Their results suggest that, although the ranking of attributes is similar using the two techniques, the monetary values associated with the TTO analysis tend to be higher than the ones directly elicited through the WTP exercise.

Choice experiment studies

The studies using a discrete choice experiment approach are carried out on patients with type 1 and/or type 2 diabetes and investigate preferences and WTP for new treatments.

Table 2 in von Arx and Kjær (2014) summarizes attributes and levels included in each study of their review, together with WTP for the new treatment when the cost attribute is included (all studies are in Dropbox).

More recent papers analysing WTP for diabetes care include the studies by Fehrer et al. (2016), Janssen et al. (2017) and Morillas et al. (2015).

Besides cost of treatment, the attributes taken into account in these analyses include: frequency, mode and timing of administration, effectiveness of glucose control, need of glucose monitoring, number of hypoglycaemia events (nocturnal and/or during daytime), presence of side effects (particularly nausea and cardiovascular problems) and effect on daily life activities (e.g. having a driver's licence), weight change.

The studies included are quite homogeneous in terms of population analysed (mainly type 1 and/or type 2 diabetes patients) and attributes included in the choice experiment. The paper by Janssen et al. (2017) adds to this literature allowing for preference heterogeneity, which is achieved by estimating the model separately by educational level of the respondent.

1.6 WTP for cancer care

1.6.1 WTP for cancer screening

A large empirical research body on cancer has focused on valuation of cancer screening. Discrete choice experiments have been extensively used within this literature, which allow to analyse and compare the role of a number of attributes on the screening choice. These usually include features like screening cost, screening accuracy, screening frequency, risk of unnecessary treatments, avoided risk of more invasive tests. Examples of this literature include Wordsworth et al. (2006), de Bekker-Grob et al. (2013), Howard and Salkeld (2009). Studies eliciting WTP for cancer screening using CV methods are for example Yasunaga et al. (2011), Pedersen et al. (2011) and Frew et al. (2001).

A review of the literature using discrete choice experiments in the context of cancer screening can be found in Mansfield et al. (2016), while Lin et al. (2013a) also includes studies using contingent valuation techniques. These reviews highlight the impact of screening efficacy, cost, risk perception and family history on WTP levels. Nevertheless, non-conclusive evidence exists in terms of superiority of different WTP elicitation method in terms of accuracy of the values provided (Lin et al., 2013a).

Howard and Salkeld (2009) investigate colorectal cancer screening and include attributes such as screening efficacy, number of unnecessary colonoscopies avoided, as well as cost. Their analysis also offers a focus on "framing effects", showing that framing the question as number of cases found rather than number of missed cases avoided has a significant impact on the results. De Bekker-Grob et al. (2010) show that also the labelling of the different options in a choice task may influence the respondent as it takes the focus off the attributes.

1.6.2 WTP for HPV vaccine

Within the cancer literature, there has been an increasing interest in the Human Papillomavirus (HPV) vaccine (available since 2006). The literature has extensively analysed WTP for Human Papillomavirus Vaccine among women for themselves or for their daughters. In a study on the US, Brown et al. (2010 and 2014) carry out a discrete choice experiment and include cost, vaccine efficacy against cervical cancer and vaginal warts and length of protection period. Their results suggest that mothers are more willing to pay for each of the vaccine attributes for their daughters than the daughters for themselves. Similar studies have also been conducted in Thailand (Ngorsuraches et al., 2015) and Canada (Oteng et al., 2011), while CV methods have been used in studies on Nigeria (Umeh et al., 2016) and Thailand (Kruiroongroj, 2014).

1.6.3 WTP for cancer treatments

Johnson et al. (2014) and Muhlbacher and Bethge (2015) use discrete choice experiments to value different attributes of alternative cancer treatments. Attributes include severity of side effects, administration mode, administration frequency, risk of disruption of chemiotherapy schedule. Other studies have included treatment survival rates (Cho and Jo, 2015), cancer recurrence risk, surgery duration and travel time to the hospital (Essers et al. 2010). Lalla et al. (2014) use a discrete choice experiment to value in monetary terms the different side effects of cancer treatments (hair loss, nausea, diarrhoea, infection).

A chained method is used by Oh et al. (2012) to value breast cancer treatments. In this paper, the utility level associated with living with cancer is first estimated using the Quality of Life questionnaire developed by the European Organisation for Research and Treatment of Cancer. The WTP for a treatment which would allow complete remission of cancer is then measured using a bidding game followed by an open-ended question. A similar survey/questionnaire is also implemented by Thongprasert et al. (2015) in the context of lung cancer treatments. Along these lines, Lang et al. (2012) uses the EQ-5D tool to measure the quality of life of patients with cervical cancer. Their WTP for cancer remission is then investigated using a double-bounded dichotomous model.

Li et al. (2012) instead use a contingent valuation method – a bidding game – to directly measure WTP for a prostate cancer cure, with family members being willing to pay more than the patient himself. This is in line

with the result by Brown et al. (2010 and 2014) on mothers' higher WTP for HPV vaccine for their daughters than the girls themselves.
Another study on lung cancer uses a double-bounded dichotomous method followed by an open question to elicit WTP for a new treatment (Lang, 2010).

1.7 WTP for CVD prevention and treatment

WTP for CVD (Cardiovascular Disease) prevention and treatment has been explored in the literature using both DCE and CV methods[9].

Among the studies using DCE, Laba et al. (2015) analyse WTP for a CVD prevention pill among a sample of cardiovascular patients. Three different attributes are taken into account in the study, besides cost: number of pills per dose, frequency and time of day of administration, and frequency of doctor visits. In a similar setting, Ghijben et al. (2014) analyse WTP for an anticoagulant pill among a sample of individual at risk of atrial fibrillation (and hence stroke). The inclusion of the cost attribute in the DCE allows to measure WTP for stroke risk, bleed risk, blood test frequency, frequency of administration as well as whether food intake can influence drug assimilation.
Grisolia et al. (2018) evaluate a CVD prevention program framed in terms of a lifestyle change program. This study adds to the literature suggesting that the way health improvements are presented is likely to affect the respondent (framing effect). In particular, their results show that presenting the question in a positive way (i.e. increase in life expectancy rather than decrease in mortality) is associated with a higher program take-up. This is in line with the results by Howard and Salkeld (2009) in the cancer literature.A study by Whitty et al. (2013) analyse WTP for a home-program and a clinic-based program among a sample of individuals who have been previously hospitalized for Chronic Heart Failure. Attributes of the DCE include frequency of nurse visits, whether the patients is always seen by the same nurse, availability of a phone advice service, availability of support group sessions, as well as cost per nurse visit.
A DCE is also used to evaluate an electronic CVD management program in a study by Deal et al. (2014), taking into account both the patient and physician point of view. Attributes included in the DCE addressed to the patient are the following: cost, speed of information update, tasks carried out by nurse coordinator, frequency of nurse contact, frequency of doctor visits. Results suggest that for patients the most valued attribute relates to the tasks performed by the nurse coordinator, valuing in particular receiving phone and email reminders. Laver et al. (2013) investigates WTP for rehabilitation program among a sample of mainly stroke patients. Attributes in DCE include mode of therapy (i.e. group, individual or computer therapy), therapy time per day, specialists involved, percentage of recovery, and cost. Results show that patients particularly value and display a higher WTP for a higher amount of recovery, individual therapy compared to group or computer therapy, as well a shorter therapy time.

[9] A review was conducted on the Pubmed database using as keywords "Cardiovascular Disease", "CVD", "Acute coronary syndrome", "ACS", "heart disease", "stroke", "myocardial infarction", "angina", "heart failure", "heart attack", as well as "WTP", "willing* to pay", "contingent valuation", "Stated preferences", "monetary valuation", "monetary value", "conjoint analysis" and "choice experiment".

Another body of the literature analyzing WTP for CVD prevention has used CV methods.
Within this literature, Jacobs et al. (2011) focus on a sample of individuals which are offered a CVD prevention program using a closed-ended double-bounded dichotomous model. Pinto-Prades et al. (2008) investigates the use of single and double-bounded models to evaluate WTP for a new medicine reducing risk of death after myocardial infarction. Their results suggest that double-bounded models tend to give lower estimates than single-bounded models and to be more biased. Moreover, both an ex-ante and ex-post approach is followed: in the former, respondents are asked about their WTP higher taxes to access the medicine in the future, while in the latter the respondents are asked about their WTP in the case of an infarction. Results confirms that, as expected, individuals are willing to spend more ex-post than ex-ante. Willingness to pay for hypertension treatment is investigated by Yasunaga et al. (2006) using a payment card approach and by Tang et al. (2010) using a bidding approach. An open-ended question is instead used by Gleason-Comstock et al. (2017) in a similar study analyzing WTP for blood pressure control.

1.8 WTP for neurological diseases treatment

We have carried out a literature search using the database Pubmed to identify studies analyzing WTP for neurological diseases. The review has identified three main area of research: Multiple Sclerosis, epilepsy and dementia.

1.8.1 WTP for Multiple Sclerosis treatment

A large part of the literature focusing on WTP for neurological problems treatment focus on treatment for Multiple Sclerosis. Webb et al. (2018) review the Multiple Sclerosis literature using discrete choice experiment by conducting a search on the following databases: MEDLINE, Embase, PsycINFO, CINAHL, Cochrane Libraries, and Web of Science. Their analysis identifies 16 relevant papers and suggest that common attributes included in Multiple Sclerosis treatments DCE span from disease relapse and progression, to severity of side effects, as well as mode and frequency of drug administration and symptoms relief.
Not included in the review by Webb et al. are the papers by Hincapie et al. (2017) and Mansfield et al. (2017). The former evaluate Multiple Sclerosis treatment focusing on the following attributes: disease progression stabilization, risk of respiratory tract infection, risk of hospitalization from infection, mode and frequency of administration, and cost of treatment. Respondents are presented with a number of choice sets and asked to state how likely they would choose the treatment on a scale from 0 to 100. Mansfield et al. (2017) carry out a DCE distinguishing between Multiple Sclerosis patients according to different levels of disability. Their results suggest that for patients with low disability levels, the most valued attribute relates to avoidance of flu-symptoms after treatment followed by lower risk of progression, while for patients with high disability levels the most valued attribute is lower risk of progression followed by lower risk of serious infection. Iskedijan et al. (2009) use instead a CV method (bidding approach) to analyse a sample drawn from the Canadian general population to evaluate WTP for an insurance policy covering the expenses of a new drug for Multiple Sclerosis pain relief.

1.8.2 WTP for epilepsy treatment

Atkinson-Clark et al. (2018) use a discrete choice experiment to value different attributes of alternative management-programs for patients with epilepsy. Attributes include program focus (emotional management, disease management as well as self-monitoring), specialists involved (doctor, nurse etc.), meeting type (for

example face-to-face, support group, computer-based) time and cost. Lloyd et al. (2005) instead focus on drug treatment for epileptic patients. They use a DCE to place a monetary value on different drug's attributes, including symptoms reduction and a number of side effects. Their results show that avoidance of side effects such as hair loss and development of a rash are the most valued drug attributes.

WTP for a treatment for epilepsy is instead investigated using CV methods in a study by Stavem (1999). The study analyses a sample of epileptic patients in Norway. WTP is elicited using an open-ended question, which is replaced by a payment card method in the case the "cognitive burden" associated with the open-ended question is too high.

Within this literature, Gao et al. (2015) analyse WTP for a QALY among epileptic patients. As other QALY papers, this study uses a CV method following the chained approach. First, the utility associated to the current health profile is evaluated. Second, the WTP to achieve perfect health is elicited using a bidding game.

1.8.3 WTP for dementia care

Chester et al. (2016) focus on people with dementia and their carers to evaluate different care support options. To this end, they carry out a DCE to evaluate, among others, emotional support, availability of relaxation techniques, availability of information on coping with dementia and on use of memory aids, possibility to engage in social activities. Their results suggest that emotional support is the mostly valued attribute. Along similar lines, Nieboer et al. (2010) evaluate different characteristics of care services among a sample of people with dementia and frail people.

2 Design of survey in ICARUS

Key gaps in the literature include:

- Valuation of DALY/QALY under different health conditions, e.g. considering asthma and cancer as different outcomes (to test for “dread”)
- Valuation of DALY/QALY using air pollution as the key risk factor

The survey will hence focus on these issues – which also corresponds to the health effect estimation from Work Package 4 of ICARUS. The questionnaire will include demographics (based around the European Social Survey – the ESS) and health status, experience and attitude questions to cancer and asthma, discrete choice questions and follow up, and survey feedback.

A draft of the survey is included in the appendix.

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4 ANNEX 1: Valuation Questionnaire

Draft Survey Design

Version 2.1

July 2018

Part 1: Demographics

Gender

- o Male
- o Female

Age:

Ethnic group

- o White
- o Mixed
- o Asian/Asian British
- o Black/African/Caribbean/Black British
- o Other

Nationality:

Marital status

- o Single
- o Married/Civil Partnership/Living with partner
- o Divorced/Separated
- o Widow

Number of children

Highest Educational Level (From ESS)

1	Ph.D, D.Phil or equivalent
2	Masters Degree, M.Phil, Post-Graduate Diplomas and Certificates
3	5 year University/CNAA first Degree (MB, BDS, BV etc)
4	3-4 year University/CNAA first Degree (BA, BSc., BEd., BEng. etc)
5	Nursing certificate, Teacher training, HE Diploma, Edexcel/BTEC/BEC/TEC - Higher National Diploma (HND), OCR/RSA – Highe
6	Foundation Degree (FdA, FdSc etc)

7	Edexcel/BTEC/BEC/TEC - Higher National Certificate (HNC) or equivalent
8	HE Access
9	Vocational A-level (AVCE), GCE Applied A-level, NVQ/SVQ Level 3 GNVQ/SNVQ Advanced, Edexcel/BTEC/BEC/TEC (General/Ordina
10	(Modern) Apprenticeship, Advanced (Modern) Apprenticeship, SVQ/NVQ/Key Skills Level 1 and 2 City and Guilds Craft/Inter
11	None of these
5555	Other
7777	Refusal
8888	Don't know
9999	No answer

Employment status

- o Employed
- o Unemployed
- o Student
- o Retired
- o Other inactive

Household Income: (ESS)

- Income deciles

Health. How is your health in general?

- o Very good
- o Good
- o Fair
- o Bad
- o Very bad

Disability. Do you have any physical or mental health conditions or illnesses lasting or expected to last for 12 months or more? (ONS question)

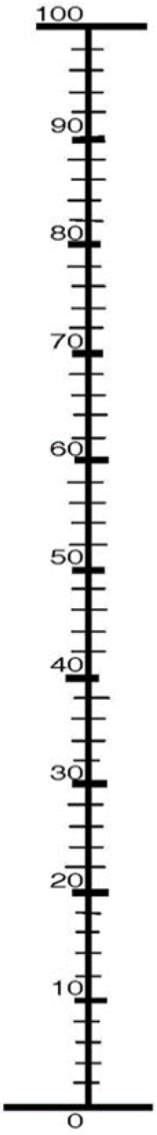
- o Yes
- o No

If yes, does this illness or disability reduce your ability to carry-out day-to-day activities? (ONS question)

- o Yes, lot
- o Yes, a little

Visual Analogue Scale (EQ VAS). On a scale from 0 to 100, where 100 means the best health you can imagine and 0 the worst health you can imagine, mark an X on the scale to indicate how your health is TODAY.

What is the number shown on the scale? ____



Part 2: Experience and attitudes questions

Experience with cancer and asthma (similar to Alberini and Scasny 2017)

Have you ever been diagnosed with cancer?

Have any of your immediate family members ever been diagnosed with cancer?

Have any of your closest friends ever been diagnosed with cancer?

Have you ever been diagnosed with asthma?

Have any of your immediate family members ever been diagnosed with asthma?

Have any of your closest friends ever been diagnosed with asthma?

Dread – worry and anxiety

On a scale from 1 to 5, where 1 indicates absolutely not worried and 5 extremely worried, how do you feel when thinking about cancer? (similar to Savage 1993)

On a scale from 1 to 5, where 1 indicates absolutely not worried and 5 extremely worried, how do you feel when thinking about asthma?

OR

From 1 ("not at all") to 4 ("a lot"), during the past month, how often have you thought about cancer/asthma? (Matro et al. 2014)

From 1 ("not at all") to 4 ("a lot"), during the past month, how often have thoughts about your chances of getting cancer/asthma affected your mood? (Matro et al. 2014)

Dread – Probability/comparative risk

On a scale from 1 to 5, where 1 indicates extremely unlikely and 5 the extremely likely, how likely do you think you will develop cancer in your life?

1-5

On a scale from 1 to 5, where 1 indicates extremely unlikely and 5 the extremely likely, how likely do you think you will develop asthma in your life?

OR:

Compared to other people your age, what are your chances of getting cancer/asthma, on a scale from 1 to 5, where 1 indicates "much lower" and 5 "much higher"? (Matro et al. 2014)

Feeling in control

From 1 ("none") to 4 ("a lot"), how much control do you feel you have over whether you develop cancer/asthma? (Matro et al. 2014)

Part 3: DCE – discrete choice experiments

Explanatory text – e.g. "Reducing certain air pollutants or reducing smoking can affect the risk of asthma and/or cancer, with differential impacts on the degree of health loss. We can measure the health loss attributable to changing the health risk using quality adjusted life years. If you were in perfect health, you would rate the Quality of your life in one year as being 100 points. Air pollution and smoking could have a longer term impact on quality of life – e.g. reducing quality of life by 25 points over a period of 4 years. Reducing air pollution and smoking is costly and you would need to contribute through increased taxes to pay for these policies."

Attributes	**Levels**
Type of health loss	Development of asthma Development of cancer
QALY loss	25 points for 4 years (QoL loss), 10 points for 10 years(QoL loss), life loss worth 1 QALY (life expectancy – number of months depending on own health level from EQ VAS)
Source of health risk	Air pollution exposure, Other controllable health risk (e.g. smoking)
Cost to prevent health loss	3,000 5,000 8,000 10,000 20,000 30,000 50,000 80,000 150,000 300,000

	(paid over a period of 10 years? or different payment periods)[1]
Payment period (discounting?)	4 years, 10 years, now
Certainty/Risk	0% risk (certainty); 5% risk, 10% risk

note:

[1] Scasny and ALberini (2012) say "We chose annual payment for 10 years, rather a one-time payment, because such an extended payment period was judged to be better compatible with the duration of the risk reductions, and because it allowed us to cover a greater range of possible VSL values"

FOLLOW UP QUESTIONS

1. **Reason for status quo choice (if all choices status quo)**

PART 4: SURVEY FEEDBACK (Lim et al. 2017)

(Time: ☐☐ ☐☐ ☐☐

hour minute AM/PM

How would you rate the difficulty of rating the health states on the visual analogue scale (thermometer scale)?

Would you say…

Very easy	☐	1
Easy	☐	2
Neither easy nor difficult	☐	3
Difficult	☐	4
Very difficult	☐	5
REFUSED/DON'T KNOW	☐	99

How would you rate the difficulty of the Choice experiment exercise (i.e., Part 3 - the exercise in which you are asked to choose between two different health outcomes)?

Would you say…

Very easy		1
Easy		2
Neither easy nor difficult		3
Difficult		4
Very difficult		5
REFUSED/DON'T KNOW		99

This is the end of interview. Thank you!

TIME INTERVIEW COMPLETED: ☐☐ ☐☐ ☐☐

hour minute AM/PM

PLEASE FEEL FREE TO ADD ANY ADDITIONAL COMMENTS ABOUT THE INTERVIEW.

5 ANNEX 2 – DESIGN NOTES

The following papers have used DCE for valuating QALYs (reported are attributes and levels used)

Lancsar et al. 2011

Table 2
Attributes and levels.

Description of attribute	Levels
Age at onset (years)	1 10 20 40 60 70
Age at death if untreated (years)	1 10 20 40 60 70 80
Qol if untreated (represented to respondents on a scale marked as %)[a]	0 30 60 90
Gain in life expectancy (years)	0 1 5 10 20 40 60 79
Gain in Qol with treatment (represented to respondents on a scale marked as %)	0 10 20 40 70 100

[a] This produces the equivalent variable quality of life lost = 1 – QOL untreated: 1, 0.7, 0.4, 0.1.

Linley and Hughes 2013 (only one with cost per QALY)

Main impact: survival or QoL

Number of patients treated

QALY gained: 0.1, 0.8, 1.6

cost per QALY gained: 4,000; 18,000; 40,000£

Uncertainty: Yes/No

Rowen et al. 2016

Table 1 Survey Attributes and Levels

Variant: Life Expectancy without the Condition, N	5 years	20 years	40 years	80 years
Attribute	Levels	Levels	Levels	Levels
Life expectancy without treatment, E	3 months 6 months 9 months 1 year 2 years 5 years	3 months 1 year 2 years 5 years 10 years	3 months 1 year 2 years 5 years 10 years 30 years	3 months 1 year 2 years 5 years 10 years 30 years 60 years
Life expectancy gain from treatment, S	0 1 month 3 months 6 months 9 months 1 year 3 years	0 3 months 6 months 1 year 3 years 10 years	0 3 months 6 months 1 year 3 years 10 years	0 3 months 6 months 1 year 3 years 10 years 60 years
HRQOL without treatment (%), H	10, 20, 40, 60, 80	10, 20, 40, 60, 80	10, 20, 40, 60, 80	10, 20, 40, 60, 80
HRQOL gain from treatment (%), Q	0, 2, 5, 10, 20, 30, 60	0, 2, 5, 10, 30, 60	0, 2, 5, 10, 30, 60	0, 2, 5, 10, 30, 60
Design				
Number of pairs	160	120	140	160
Combinations of pairs (card blocs)	16	12	14	16

Skedgel et al. 2013

Table 1 Attributes and levels

Attributes	Levels
Average age of patients (Age)	10, 40, 70
Quality of life without/before treatment (Initial utility)	0.1, 0.5, 0.9
Life expectancy without/before treatment (Initial life expectancy)	1 month, 5 years, 10 years
Quality of life with treatment (Final utility)	0.1, 0.5, 0.9
Change in life expectancy with treatment (Life years gained)	1 year, 5 years, 10 years
Number of patients that could be treated (Patients treated)	500, 2500, 5000

Aggregate QALYs gained was calculated for each choice scenario as [final utility 9 (initial life expectancy + life years gained) − initial utility 9 initial life expectancy] 9 total patients treated. The value of aggregate QALYs gained in the experimental design ranged from 54 to 45 373, with a mean of 10 591.

Van de Wetering 2015

Table 1 Overview of attributes and levels

Attributes	Levels
Quality of life without treatment (scale 0–100)	45, 65, 85
Age at death if untreated (scale 0–80)	30, 50, 70
Age group 10	50, 62, 74
Age group 40	73, 76, 79
Age group 70	
Gain in quality of life	5, 15, 25, 35
Gain in life expectancy	5, 10, 15, 20
Age group 10	2, 6, 10, 14
Age group 40	0.5, 1, 1.5, 2
Age group 70	
Increase of health insurance premium (euro)	6, 12, 18, 24
Affected people: 2000 in age group 10, 4000 in age group 40 and 12,000 in age group 70	

Donaldson and EuroVaQ study

WTP for a QALY (Stated preferences)

EuroVaQ. study

Direct method. Payment card method followed by open-ended question

The respondent is presented with 4/5 of the following scenarios:

Table 1
Overview of Decision Scenarios (see Donaldson et al., 2010, p.82).

Scenario	Health gain	Duration	QALY gain	When	Certainty/Risk
A	25 points	4 years	1	in 1 year's time	certainty
B	25 points	4 years	1	end of life	certainty
C	10 points	10 years	1	in 1 year's time	certainty
D	10 points	10 years	1	end of life	certainty
E	extra life	12+ months[b]	1	end of life	certainty
F	no coma	12+ months[b]	1	in 1 year's time	certainty
G	extra life (terminal illness)	12+ months[b]	1	in 1 year's time	certainty
H	25 points[a]	4 years	1	in 1 year's time	certainty
I	25 points	1 year	0.25	in 1 year's time	certainty
J	10 points	1 year	0.1	in 1 year's time	certainty
K	25 points	4 years	0.1	in 1 year's time	10% risk
L	10 points	10 years	0.1	in 1 year's time	10% risk
M	25 points	4 years	0.05	in 1 year's time	5% risk

[a] Scenario H differs from A in that in H the price is to be paid in 4 annual instalments, but in A in one amount.
[b] In scenarios E, F, and G 'additional life' is offered. The duration is adapted to the respondent's own health rating so that the gain at that health level amounted to one QALY (see also Donaldson et al., 2010, p.60).

For each scenario: payment card method

Valuing Health

Please use the mouse to click and drag each of the money amounts (shown below) into one of the three boxes below. Don't worry if you're not sure at first, you can move them about until you are happy with them.

To prevent you from experiencing a **25 point** drop in health for **4 years**, in 12 months' time.

Unwilling to pay	Unsure	Willing to pay
£ 20,000	£ 15,000	£ 10
£ 30,000		£ 50
£ 50,000		£ 100
£ 80,000		£ 200
£ 150,000		£ 500
£ 300,000		£ 1,000
		£ 1,500
		£ 2,000
		£ 3,000
		£ 5,000
		£ 8,000
		£ 10,000

The highest amount you said you **WOULD** be willing to pay was **£10,000**.

The lowest amount you said you **WOULD NOT** be willing to pay was **£20,000**.

What is the **MAXIMUM** amount you would be willing to pay? It could be **£10,000** or **£20,000**, or something in between.

16000