

MASTER THESIS

PREFERENCES FOR PROGNOSTICATION OF PATIENTS IN COMA AFTER CARDIAC ARREST: A PILOT STUDY AMONG DUTCH CITIZENS

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Preface

Foremost, I would like to thank my first supervisor dr. J.A. van Til for her great knowledge, motivation and support during my master thesis and for the nice cooperation we had. She helped me develop my research and professional skills and helped me lift my work to a higher level. Also, I would like to express my sincere thanks to my second supervisor dr. M. Boenink for her ethical and philosophical perspective on my research. She challenged me to look from another perspective to my research and see it in a broader context. Furthermore, I would like to thank the other members of the project team, of which I could be a part for the last seven months, for their knowledge and experience. Lastly, I want to thank my family and friends for their untiring and unconditional support during my master Health Sciences.

Abstract

Background

In the Netherlands approximately 5,000 patients are admitted to the ICU in a post-anoxic coma every year. Prognostication of these patients is difficult and for a vast majority of patients the prognosis remains uncertain in the first few weeks. This leads to a painful lasting uncertainty for the family. Recently, a new prognostic test was developed using the EEG, which provides more certainty, since it can predict both poor and good outcome in a larger portion of comatose patients at an earlier moment after the admission. The implementation of the EEG as prognostic test has multiple implications for clinical practice.

Objective

The objective of the current study is to contribute to societally acceptable implementation of the EEG as a new prognostic test for patients in post-anoxic coma. Therefore, preferences were identified for (1) receiving prognostic information, (2) minimally required certainty of a test for withdrawal of life support, (3) family involvement in the decision to withdraw life support and (4) the relationship between quality of life after post-anoxic coma and willingness to live.

Methods

In this study a web-based survey was developed and extensively pilot tested among a convenience sample in two phases. The first phase consisted out of a 'think aloud' pilot test (n=10) and was conducted to ensure feasibility, readability and comprehension of the questionnaire. The second phase consisted out of a web-based survey (n=56) and was conducted to ensure validity of the questionnaire. The questionnaire contained a combination of preference elicitation methods, namely the DCE, direct questioning and rating.

Results

For receiving a poor prognosis, the accuracy was perceived most important (relative importance (RI) 0.479), second-most important was the timing of test result (RI 0.396) and least important was the type of test (RI 0.125). For receiving good prognosis, the accuracy was also perceived most important (0.669), the timing of test result was perceived less important (RI 0.331). With regard to the trade-off between the probability of receiving a prognosis and the accuracy of this prognosis, the sample attached most importance to the probability of receiving a prognosis (RI 0.624), the second-most important was the accuracy of good prognosis (RI 0.269) and least important the accuracy of poor prognosis (RI 0.107). The minimally required quality of a test should be 95% (Range 80-100) according to the study sample. Shared decision making on the withdrawal of life support is preferred by 57% of the study sample. 25% of the sample was willing to live in a conscious state with both severe cognitive and physical impairments. 68% of the sample was willing to live in a conscious state with severe cognitive impairments. 78% of the sample was willing to live in a conscious state with severe cognitive impairments.

Conclusion

The preferences in this study are promising for the societal acceptation of the implementation of the EEG as a prognostic tool in clinical practice. Prognostic information is preferably provided as soon as possible with an accuracy as high as possible. Receiving any information is considered more important than the actual accuracy of the prognosis. For decisions on withdrawal of life support, a 100% certainty about the poor prognosis is not thought

necessary. This indicates that the sample is willing to accept the death of some patients who would otherwise have a good outcome. Shared decision making is preferred concerning the withdrawal of life support, where most respondents prefer to leave the final say to the family. The perception of a poor outcome in this study sample differs from the one in the medical and scientific community. If this is also true for the general Dutch population, it can have far stretching implications for clinical and scientific practice. Further research is needed in order to confirm whether the findings in the current study are representative for the Dutch population.

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List of acronyms

CPC	Cerebral Performance Category
CPC-E	Cerebral Performance Categories – Extended
DCE	Discrete Choice Experiment
EEG	ElectroEncephaloGraphy
Eq.	Equation
GOS	Glasgow Outcome Scale
ICU	Intensive Care Unit
MAX	Maximal value
MIN	Minimal value
MRS	Marginal Rate of Substitution
n	sample size
NPV	Negative Predictive Value
NYHA	New York Health Association Classification
PPV	Positive Predictive Value
RI	Relative Importance
SD	Standard Deviation
SFP	Self-Fulfilling Prophecy
SSEP	SomatoSensory Evoked Potential

1. Introduction

Every year, there are approximately 5,000 patients admitted to the intensive care unit (ICU) with a post-anoxic coma in the Netherlands [1]. In Europe, this figure is around 176,000 [2]. Patients in a post-anoxic coma are successfully resuscitated after an out of hospital cardiac arrest, however, the blood circulation was impaired for too long, leading to a state of (temporary) unconsciousness and potential brain damage [3]. To limit the brain damage the patient in post-anoxic coma is often cooled and sedated within the first few days after the cardiac arrest [1].

Of all patients with post-anoxic coma admitted to hospitals, between 40-66% never regain consciousness [4-6]. Most of these patients will die within 14 days after cardiac arrest. Only a small part will remain in a prolonged coma or vegetative state¹ [3]. Such vegetative state can last for months or even years, while the chance of regaining consciousness decreases while the vegetative state lasts [9]. The remainder of the patients in post-anoxic coma will regain consciousness, however, physical and cognitive impairments are common in this group. These can vary from minor disabilities to severe disabilities or even a minimal state of consciousness [10, 11]. A patient in a minimal state of consciousness has "a severely altered consciousness in which minimal but definite behavioral evidence of self or environmental awareness is demonstrated" [12].

The most used tests to determine the expected outcome (prognosis) of patients in post-anoxic coma in clinical care are the somatosensory evoked potential (SSEP) test and the pupillary light reflex test [13]. The SSEP-test measures the response of the brain to the stimulation of nerves with electric shocks. During the test multiple electrodes are placed on the patients head to measure the response of the brain upon stimulation of the nerves in the wrist. The test takes about 60-90 minutes and is non-invasive [14]. The pupillary light reflex test measures the constriction and subsequent dilation of the pupil in response to light. The test takes only a few minutes and is also non-invasive [15]. The Dutch guidelines of 2011 indicated that the absence of SSEP responses 24 hours after resuscitation or the absence of pupillary or corneal reflexes 72 hours after resuscitation are reliable predictors of a poor outcome in patients in post-anoxic coma, due to their high positive predictive values [13].

However, only a small portion of the patients in post-anoxic coma with a poor outcome has absent SSEP responses at 24 hours after resuscitation or absent pupillary or corneal reflexes at 72 hours after resuscitation, which indicates a low sensitivity of these tests [16-18]. Furthermore, these tests can only predict a poor outcome in patients in post-anoxic coma. Consequently, the prognosis of a vast majority of patients in post-anoxic coma remains uncertain in the first few weeks after resuscitation. This might result in ongoing but futile² treatments of patients in post-anoxic coma leading to high medical costs. Moreover, it leads to a lasting uncertainty for families of patients in post-anoxic coma [20]. This uncertainty is painful for families and can lead to an increase in anxiety [21].

Early identification of both good and poor outcome in more comatose patients can reduce this uncertainty for families [2, 16]. Recently, Hofmeijer et al. established that electroencephalography (EEG) patterns within the first 24 hours after cardiac arrest, can robustly contribute to predicting poor and even good outcome in patients with

¹ There is an international debate on this term and more often there is made a distinguish between 'unresponsive wakefulness syndrome' and 'minimally states of consciousness' [8, 9]. In this report the term 'vegetative state' is still used with as main reason to connect to the neurological outcomes used in the other studies within the project in which the current study is carried out.

² Futility is a concept with both medical and normative considerations. When naming futility in this report, we refer to medical futility defined as "a clinical action serving no useful purpose in attaining a specified goal for a given patient" [19].

post-anoxic coma. The EEG test measures the brain activity of the patient for a minimum period of 24 hours. To measure the brain activity, EEG patches are placed on the head of the patient and connected to a machine that measures the activity. A continuous EEG pattern within 12 hours predicts a good outcome. An EEG pattern that is persistently isoelectric or low voltage at 24 hours predicts a poor outcome. Also, EEG patterns with pronounced alterations in amplitudes indicate a poor outcome [22].

These results were confirmed in the largest published cohort study of patients with post-anoxic coma on continuous EEG monitoring in the Netherlands [2]. In the same study was also found that the use of EEG patterns in comatose patients could lead to small reductions in cost of hospitalization. Thus, the EEG provides more certainty on prognosis of patients in post-anoxic coma on a populational level, since is it able to predict poor and good outcomes in a larger portion of comatose patients at an earlier moment after the cardiac arrest. As of the spring of 2019, the use of the EEG is recommended in the current Dutch guideline on post-anoxic coma [23].

The introduction of the EEG as a prognostic test has multiple implications for clinical practice. Where before no good outcome could be predicted, the EEG enables the prediction of a good prognosis. This reduces the uncertainty for families of patients in post-anoxic coma but also raises questions for clinicians on how and when to share this information with the family. Moreover, when a good outcome is predicted by the EEG at 12 hours after the resuscitation, one could imagine that more proactive treatment decisions will be made, like early awakening of the patient by stopping the cooling process and sedation, resulting in change in medical practice.

The EEG also has implications for clinical practice for poor prognosis. Nowadays, the treatment of patients with a poor prognosis is often discontinued in the Netherlands. In these cases, treatment to prolong life is seen as futile. Since the EEG can predict a poor outcome for a larger portion of the patients, one could imagine that the decision to withdraw life support³ will increase in frequency. Furthermore, the EEG's ability to predict a poor outcome at 24 hours after resuscitation can cause the decision to withdraw life support to be made earlier.

In making the decision to withdraw life support, the clinician should consider two important factors, namely the perceived (dis)utility of the outcome and the (un)certainty of the test result. The perceived (dis)utility of an outcome can differ for individuals. It is important that the predicted poor outcome is also perceived as poor by the family, otherwise withdrawing life support could result in conflicts between clinicians and family members.

To determine whether the outcome is poor, the most commonly used measure is the Cerebral Performance Categories (CPCs), where CPC 1 represents the best possible outcome and CPC 5 represents death. The CPCs were derived from the Glasgow Outcome Scale (GOS) [24]. Even in the scientific community there is debate about what consist of a poor outcome. Before 2006, a poor outcome was generally represented by CPC 4-5 (vegetative state and death), and a good outcome was represented by CPC 1-3 (good neurological outcome, moderate disability and severe disability). However, from 2006 onwards most studies included CPC 3 into poor outcome [25]. This represents a change in values and preferences with respect to the outcome of post-anoxic coma in the medical and scientific community. The focus of a good outcome seems to have shifted from regaining consciousness as a priority, towards the recovery of mental and physical ability to allow societal participation [24]. It is unclear whether this change in focus also has occurred in society.

³ Life support interventions include oxygen, mechanical ventilation, dialysis and medications that support the heart.

The other factor that needs to be considered in the decision to withdraw life support, is the (un)certainty of a test result. Switching of life support in case of poor prognosis, leads to the death of three groups of patients. First, patients will die who would have died anyway, but now suffer for a shorter amount of time. Second, patients will die who would otherwise have lived in a vegetative state or with severe disability. Since these outcomes are currently perceived as poor by the medical and scientific community, as described in the prior paragraph, the death of this group is intentional. Third, some patients could die, who would otherwise have a good outcome and for whom the poor prognosis was a false positive. This third group should be the focus in considering the uncertainty of a test result, since the death of this group is unintentional. Ideally we have zero false positives, meaning that this third group does not exist [24]. However, in clinical practice this is not feasible. Therefore, the question remains how many false positives are accepted when the decision to withdraw life support is made.

The number of false positives is unknown in the Netherlands, since we cannot determine after the patient has died, which outcome the patient would have had. This is called the self-fulfilling prophecy: the patients expected to have a worse outcome, will indeed die, since we withdraw life support based on this expectation [26]. However, waiting until the outcome of a patient is known to prevent any false positives is also undesirable, because in these cases life cannot be ended any longer by withdrawing life support when the outcome is seen as poor and not a life worth living [27].

Decision making on the withdrawal of life support for patients in prolonged anoxic coma (>3 days) must be done within the first week after resuscitation. The first 3 days most patients are still unconscious and have not regained the basic life sustaining functions. Therefore, they are on life support. However, between 3 and 7 days after the cardiac arrest the basic life sustaining functions will come back in some patients, of whom most will have a good outcome, but also in some patients who will have a poor outcome [28]. When these functions have come back, a life considered futile cannot longer be ended by withdrawing life support, meaning that the patient must live with a poor outcome. This leaves the clinician, but also policy makers and society, with a difficult dilemma: how many false positives are allowed, to prevent suffering and a life not worth living in other patients. Although the EEG provides more certainty on a populational level, it also emphasizes this moral dilemma, because more patients with a poor outcome can be identified in an earlier stage after the resuscitation.

So, multiple questions regarding responsible implementation of the EEG-test as a prognostic tool in clinical practice remain. A societal perspective on these questions about clinical implications, cut-off points for good and poor outcome and the willingness to accept false positives can add to responsible use of the EEG by the clinician.

The objective of the current study is to contribute to societally acceptable implementation of the EEG as a new prognostic test for patients in post-anoxic coma. The research questions answered in this study are:

- 1. Which prognostic information would the Dutch public like to receive at which time after the cardiac arrest if they were a close family member of a patient in post-anoxic coma?
- 2. What is the Dutch public perception of the minimally required certainty of a test that is needed to support decision making regarding withdrawal of life support in patients with post-anoxic coma?
- 3. To what extent does the Dutch public like to be involved in the decision to withdraw life support in patients with post-anoxic coma if they were a close family member?
- 4. What are the Dutch public perceptions of "a life worth living" after post-anoxic coma?

Within this master thesis an extensive pilot-test was performed. The goal of the pilot-test was to develop a questionnaire that is valid, feasible, readable and comprehensible. Surveying a sample of the Dutch population was outside the scope of this master thesis, due to a lack of time. In the context of the broader project a web-based survey will be conducted in the autumn of 2019 in the Netherlands.

This broader project, in which this study is carried out, is named *Prognosticating of patients in coma: towards a responsible practice*. In this project the EEG-based prognostic technology is developed in such a way that it contributes to good prognostic practice for comatose patients after cardiac arrest. Knowledge about the preferences for prognostic information from a societal perspective can contribute to a good prognostic practice in which clinicians have to share prognostic information with the family and must made decisions concerning the withdrawal of life support based on outcome predictions. In this study the individual preferences of members of the Dutch population are used to paint a picture of the Dutch society's preferences.

2. Theoretical framework

This chapter starts with an explanation of medical concepts and evidence relevant for the methods of this study and interpretation of the results. In this first section the self-fulfilling prophecy is explained, evidence on measuring neurological outcome is presented and the test characteristics of the available prognostic tests for post-anoxic coma are explained. The chapter ends with an overview of the available knowledge concerning preferences for health states after post-anoxic coma in relation to the withdrawal of life support. To this purpose a literature review was conducted. The results from this review were used in selecting the proper methods and as context of the results of this study.

2.1 Relevant medical context and evidence

2.1.1 Self-fulfilling prophecy

The self-fulfilling prophecy (SFP) influences almost all studies concerned with poor prognosis and withdrawal of life support [2]. Wilkinson defines the SFP as "a prediction (that a certain outcome is likely or inevitable) that independently increases the probability of the outcome actually occurring" [26]. In case of predicting outcomes in patients with post-anoxic coma the prediction of a poor prognosis might be self-fulfilling if life support is withdrawn and thus the patient dies.

The SFP might lead to multiple issues for different stakeholders. Firstly, it makes it difficult to get the facts around prognosis. Because life support is withdrawn based on a poor prognosis, it is impossible to get the actual figures of (1) patients that will die, (2) patients that will live with a poor outcome, and (3) patients that will live with a good outcome, despite a prediction of a poor outcome. So, the SFP makes it difficult to determine the true mortality and morbidity rates [26].

The second issue, related to the first, is that the SFP might increase mortality, since also patients that will otherwise live with a good outcome die because life support is withdrawn. These are the so-called false positives. Since the poor prognosis in patients in post-anoxic coma is never hundred percent certain, the SFP increases mortality. However, it is the question whether this is necessarily problematic or it is just a consequence of decision making in the face of uncertainty, because waiting till the outcome is known can also be undesirable [26].

Thirdly, the SFP might also cause physicians to feel responsible for the death of patients. This is not necessarily a bad thing, since the physicians are responsible for making the decision to withdraw life support according to the law. The SFP can help them to be cautious, however, it can also make them feel guilty. Their fear to cause unnecessary death, can make them too cautious in their decision making on the withdrawal of life support. Because of this people could stay alive with poor quality of life, which is just as undesirable [26].

Fourthly, the SFP may cause physicians to, unintentionally, not fully inform patients' families about the survival chances of the patient. They might only tell the probability of dying when life support is withdrawn, while they don't know the probability of dying when life support is continued, due to the first issue mentioned. So, the SFP might limit the ability of physicians to inform the family of the patient in post-anoxic coma [26].

Lastly, the SFP can also emphasize the uncertainty in poor prognosis. This might lead to people holding on to this uncertainty causing unnecessary continuation of life support. This can result in patients living with outcomes perceived worse than death [26].

The consequences of SFP can be limited by carefully collecting and appraising prognostic evidence. Also, doctors need to recognize the uncertainty around and limits of knowledge in front of patients' families. In the end, the SFP is inevitable in decision making on the withdrawal of life support [26].

2.1.2 Measuring neurological outcomes

There are multiple instruments to classify the neurological outcomes. Examples are the New York Health Association Classification (NYHA), the Glasgow Coma Scale (GOS), and the EQ-5D. However, as mentioned in the introduction, the CPCs is most commonly used for assessing neurological outcomes in patients after cardiac arrest [24]. The CPCs are also used in the other studies within the broader project of this study, where CPC 1-2 indicated a good outcome, and CPC 3-5 indicated a poor outcome [2, 20, 22, 29].

CPC 1 represents a good cerebral performance. The patient in this category is conscious, alert, able to work and can have a normal life, although minor impairments, like mild dysphasia, are common. CPC 2 represents moderate cerebral disability. The patient in this category is conscious and has enough cerebral function to live independently, although more severe impairments, like seizures, are common. CPC 3 represents severe cerebral disability. The patient in this category is dependent on others for all daily activities and has limited cognition. There is a wide range of cerebral abnormalities in this category, from ambulatory patients with severe memory disturbances to patients with locked-in syndrome. CPC 4 represents coma or vegetative state. Patients in this category are unconscious, have no cognition and are unaware of their environment. CPC 5 represents death or brain death [30].

However, the CPCs are criticized. One criticism is the subjective, poorly defined criteria, where some criteria include multiple domains. The second criticism is that the instrument is never validated. Thirdly, the instrument has poor connections to measures of quality and disability of life [31, 32]. Therefore, the Cerebral Performance Categories Extended (CPC-E) was developed [33].

The CPC-E instrument was developed and validated by Balouris et al. [33]. The CPC-E redefined the different domains of the CPC and included quality of life measures. The instrument gives more detailed descriptions of outcomes after cardiac arrest. The content validity of the CPC-E was established by identifying the current domains in the CPC and adding new domains following from a literature review and expert panels. In the end, ten domains were identified: alert, short term memory, logical thinking, attention, motor, basic activities of daily living, mood, fatigue, complex activities of daily living, and return to work. The feasibility of the CPC-E was tested by performing a prospective study in the hospital, by which the time to complete the CPC-E was tested, the distribution of CPC-E scores was examined and the comprehensiveness of the collected data was tested. The interrater and the intra-rater reliability was tested by performing a retrospective study reviewing the electronical medical records. The feasibility of the CPC-E was excellent. Also, the reliability of the CPC-E was good to excellent. From the study can be concluded that the CPC-E is a clinically feasible and a valid instrument to describe impairments and disabilities after cardiac arrest [33]. The CPC-E is included in Appendix A.

2.1.3 Test characteristics

As mentioned in the introduction, there are currently three tests which can be used to identify outcomes of patients in post-anoxic coma. The quality of a prognostic test in scientific research depends on two factors, the sensitivity and the specificity [34].

The sensitivity of a test is the ability to correctly classify a person with the disease. So, the sensitivity is the percentage of true positives within the population that has the disease. It is calculated by dividing the true positives by the sum of true positives and false negatives. Specificity is the ability of a test to correctly classify a person who does not have the disease So, the specificity is the percentage of true negatives within the population that does not have the disease. It is calculated by dividing the true negatives by the sum of true negatives and false positives. "Sensitivity and specificity are inversely proportional, meaning that as the sensitivity increases, the specificity decreases and vice versa" [34]. When a test with a high specificity is positive you can be more certain that you have the outcome. When a test with high sensitivity is negative you can be more certain that you do not have the outcome.

However, the sensitivity and specificity are measures used in scientific quality testing of tests, but not in clinical practice, since you do not know the actual outcomes. Other measures are the positive predicted value (PPV) and the negative predicted value (NPV), although the NPV is hardly used in clinical practice. The NPV gives the probability that a patient does not have the disease when the test result is negative. It is calculated by dividing the true negatives by the sum of true negative and false negatives. The PPV gives the probability that a person has the disease when the test result is positive. It is calculated by dividing the true positives by the sum of true positive. It is calculated by dividing the true positives [34]. But for the tests for prognosis of post-anoxic coma we cannot really know the portion of false positives due to the SFP. For both scientific quality testing of the tests and clinical practice the quality of the tests are influenced by the SFP.

So, in summary, the sensitivity of a test is the portion of people with the predicted outcome in which the test gives a positive test result. The specificity is the portion of people with no predicted outcome in which the test gives a negative test result. The PPV is the portion of people with a positive test result who has the predicted poor outcome. The NPV is the portion of people with a negative test result who do not have the predicted outcome. These four test characteristics are presented in Table 1 for the three available prognostic tests for patients in post-anoxic coma.

Positive test outcome	Time since	Predicted	Specificity	Sensitivity	PPV	NPV
	cardiac arrest	outcome	Specificity			
Favorable EEG pattern	12h	Good	95 (87-99)	54 (42-65)	92 (80-98)	65 (55-74)
Unfavorable EEG pattern	24h	Poor	100 (95-100)	28 (21-35)	100 (91-100)	54 (48-61)
Absent pupillary light responses	48h	Poor	100 (97-100)	17 (12-25)	100 (86-100)	52 (45-58)
Absent SSEP	72h	Poor	100 (90-100)	44 (34-54)	100 (92-100)	39 (29-50)
Unfavorable EEG at 24h, a	absent pupillary					
light responses at 48h, or 6 72h	absent SSEP at	Poor	100 (97-100)	50 (41-58)	100 (95-100)	63 (56-70)

Table 1: Characteristics and outcomes of the available prognostic tests for patients in post-anoxic coma [29].

2.2 Overview of available knowledge concerning preferences

The available knowledge concerning preferences for health states after post-anoxic coma in relation to the withdrawal of life support was investigated using a mini-review as conducted as developed by Griffiths [35]. The objective of the literature review was twofold. On the one hand, it aimed to create an overview of the current state of the preference literature regarding stakeholders' perspectives on quality of life and prognosis of patients in post-anoxic coma. On the other hand, it aimed to identify possible preference elicitation methods for the survey.



Figure 1: Flow diagram mini-review

A literature search was performed in Scopus, PubMed, Web of Science and Cochrane library using a combination of words equal or similar to "coma", "withdrawal of life support", "quality of life", "preferences", "health states" and "measurement". Detailed information on the search terms used, can be found in Appendix B. The relevance of the literature was assessed in three rounds, according to the inclusion and exclusion criteria, presented in Table 2.

In the first round all literature was screened based on title, not relevant articles were excluded. In the second round the remaining articles were screened on their abstracts, not relevant articles were excluded. In the third round, the full text of the remaining articles was screened. For all articles, of which the full text was screened, the authors, year of publication, title, study design, aim, conclusions and whether they were included, are listed in a table in Appendix B. In total eight articles were included that met the inclusion criteria. This screening-process is depicted in a flow-diagram presented in Figure 1.

Study	Inclusion criteria	Exclusion criteria
characteristics		
Population	Patients in coma	Other specific illnesses
	Patient/physician/social perspective	
Study design	Preference elicitation method	
	Preference study	
	(Systematic) Review including preference	
	studies	
Outcomes	Preferences for/value of/attitude towards:	
	- withdrawal life support	
	- health states	
	- quality of life	
Timing	30 years back	
Report criteria	Articles in English or Dutch	Articles in language other than English or
		Dutch
		Abstract/full text not found

Table 2: Inclusion and exclusion criteria of the mini-review

2.2.1 Findings regarding preferences

The decision to withdraw life support seems dependent on physicians' preferences. The decision to withdraw life support for physicians is influenced by the type of life support. Physicians are for example two times more likely

to withdraw hemodialysis or blood products, compared to antibiotics. Also withdrawing mechanical ventilation, tube feedings and intravenous fluids are half times more preferred than antibiotics. The choices physicians make on withdrawing life support reflect certain moral, social and clinical goals. Artificial, expensive or scarce life support is more likely to be withdrawn [36]. The decision of a physician to withdraw life-support is also dependent on their own personal preference, i.e. whether they would want treatment for certain conditions [37].

Previous literature also suggests that the preference for continuation or withdraw life support is dependent on the expected outcome (quality of life) if treatment is continued. This is valid from the perspective of actual patients, physicians and the general public [38-40]. In end-of-life care the quality of life is more important than the length [40]. Actual patients are more supportive of withdrawing life-support if the expected outcome is perceived worse [38]. Also the majority of physicians would want life support withdrawn for themselves in case the expected outcome does not lead to meaningful survival (poor prognosis) [39]. Coma or a vegetative state as expected outcome leads to high numbers of treatment rejection [38, 40], which makes sense since a coma/vegetative state is valued equal to or worse than death by patients [41]. Physicians see the quality of life of patients in a vegetative state as 'no quality of life' or 'extreme low' [42].

Both the general public and intensive care professionals are willing to withdraw ventilator use in comatose patients. Although the intensive care professionals were more inclined to withdraw the ventilator, while the general public was more prone to continue the ventilator [43]. The extent to which a physician is inclined to withdraw life support can differ for countries [42]. Long term prognosis was more important in the decision to withdraw the ventilator for the intensive care professionals, compared to the general public. Age of the patient seemed not to influence the decision to withdraw life support. The attitude towards ventilator treatment was correlated with having discussed one's own preferences for life support [43]. However, only few patients discussed life support preferences with their physician. A portion of the patients does not desire such conversation, but there is also a large portion that would want such conversation but had not had such conversation [38].

2.2.2 Findings regarding preference elicitation methods

The included articles used different ways to elicit preferences. Where most explicitly mentioned the method they used, there was one article from which it was not clear which preference elicitation method was used. Explicit named designs were DCE [40], BWS case 1 [40], rating [37, 38, 41, 43], ranking [36, 41], standard gamble [41], time-trade off [41] and case vignettes [42].

The DCE was used in combination with BWS case 1 to elicit preferences for end-of-life care scenarios and to elicit attitudes in order to understand whether there was broad agreement between attitudes and preferences. For the DCE hypothetical clinical scenarios were created, defined by levels of three attributes (decline in cognitive health, health impairment and lifesaving treatment). For each scenario respondents were required to state whether they wish the lifesaving treatment or not. For the BWS case 1 13 attitudes were formulated towards medical treatment. A balanced incomplete block design was used and the respondent was asked with which attitude he agreed most and which one he agreed least [40].

Rating was used to examine (1) the relationship between personal preferences for life-sustaining treatment and medical decision making among pediatric intensivists; (2) the attitudes of the general public in Sweden in respect of the use of ventilator treatment for severely ill patients, and compare these attitudes with those of intensive care

professionals; (3) preferences for health states near to or worse than death; and (4) inpatients' preferences for life sustaining treatment. All studies using rating formulated multiple health states or clinical scenarios and asked the respondent to what extent he wanted life sustaining treatment on a 5-point Likert scale [37, 38, 41, 43].

Ranking was used to identify which attributes of life-sustaining treatment are important to physicians and to quantify preferences for health states near to or worse than death [36, 41]. Standard gamble and time-trade-off were also used to quantify preferences for health states near to or worse than death [41]. Case vignettes were used to compare the understanding of and attitudes towards vegetative state of German and Canadian specialty physicians [42].

These methods with their advantages and limitations were examined in the light of the aims of the current study, in order to choose the right preference elicitation methods for the survey. All methods with their possible advantages and limitations are outlined in one table for each research question. These tables are included in Appendix B.

A DCE was considered best to answer research question one, since a DCE can simulate the complex situations for prognosis of post-anoxic coma as in real life and it can show the explicit trade-offs we are looking for in this study between timing of test result, accuracy of a test and probability of receiving a prognosis.

To answer research question two also a DCE was considered. One similar to the one Flynn et al used was considered, with multiple clinical scenario's with poor prognosis and different accuracies followed by the question whether the respondent would withdraw life support. However, in the end direct questioning seemed more appropriate to reduce the length of the questionnaire and prevent respondent fatigue.

To answer question three the best preference elicitation method seemed the BWS Case 1, similar to what Flynn et al did. It was considered to formulate multiple attitudes concerning the involvement in decision making, create multiple choice sets with these attitudes and ask respondents which one they find best and which one they find worst. Again, in the end direct questioning seemed more appropriate to reduce the length of the questionnaire and prevent respondent fatigue.

To answer the fourth research question both ranking and rating was considered. In the end rating seemed more appropriate, since it shows clearly the strength of the preference and it is a relatively simple exercise for respondents.

3. Methods and materials

A survey was developed to determine the societal preferences for the prognostication of patients in post-anoxic coma. This survey contained a combination of methods in order to answer all four research questions. The performed literature review, as described in the previous paragraph, was used to select the proper methods together with an expert on eliciting preferences, dr. J.A. van Til. In selecting the proper methods, a careful consideration was made between different methods, taking statistical and response efficiency into account.

In the remainder of this chapter the multiple study designs, the questionnaire, study population, statistical analysis and ethical considerations are discussed.

3.1 Study design

3.1.1 Receiving prognostic information

A Discrete Choice Experiment (DCE) was used to elicit preferences for receiving prognostic information, since it can show the explicit trade-offs, which we are looking for in this study. A DCE is defined by Carson and Louviere as "a general preference elicitation approach that asks agents to make choice(s) between two or more discrete alternatives where at least one attribute of the alternative is systematically varied across respondents in such a way that information related to preference parameters of an indirect utility function can be inferred" [44]. DCE's are increasingly being used to determine preferences for medical treatment. The method is based on the random utility method, which assumes that a medical treatment can be described by its characteristics, so called attributes. The attributes are operationalized in multiple levels, these levels describe the possible outcomes for an attribute. Clinical scenarios are created by combining the levels of different attributes. These scenarios are presented to the respondent in pairs with the question which one he prefers (=choice task) [44, 45].

To construct the DCE, possible attributes and levels were identified from the literature and from a meeting with the expert group of the project. Only the most important attributes were selected, considering the respondents' burden. It was decided to construct three experiments within the questionnaire with only a few attributes to make sure all different aspects of receiving prognostic information were covered and to reduce complexity of the trade-offs for the respondents. Relevant attributes with the corresponding levels for all three experiments are presented in Table 3. Accuracy is operationalized as the PPV in this study.

Attribute	Level 1	Level 2	Level 3	Level 4
DCE Poor prognosis				
Timing of test result	12 hours	24 hours	48 hours	72 hours
Type of test	SSEP-test and pupillary	SSEP-test, pupillary light	-	-
	light reflex test	reflex test and EEG		
Accuracy of poor prognosis	80%	90%	95%	98%
DCE Good prognosis				
Timing of test result	12 hours	24 hours	48 hours	72 hours
Accuracy of good prognosis	80%	90%	95%	98%
DCE Probabilities				
Probability of receiving	20%	30%	50%	60%
prognosis (sensitivity)				
Accuracy of good prognosis	80%	90%	95%	98%
Accuracy of poor prognosis	80%	90%	95%	98%

Table 3: Attributes and levels

The full factorial design for poor prognosis contains 2x4x4 = 32 scenarios, while for the good prognosis the full factorial design contains 4x4 = 16 scenarios. The full factorial design for the probability of receiving a prognosis is 4x4x4 = 64 scenarios. A fractional factorial design is used to reduce the number of choice tasks. To minimize the sample size and the number of choice tasks, an efficient design was developed for the three DCE's.

For the DCE with poor prognosis and the DCE with good prognosis the software of Survey Engine was used to develop an efficient design. Both the DCE for poor prognosis and the DCE for good prognosis consisted of 16 unique choice-tasks. For the DCE with the probability of receiving a prognosis a blocked design was developed with 48 unique choice-tasks. Dominant scenarios were excluded from this design. A dominant scenario is "a scenario with a "better" level on at least one attribute and no "worse" level on all other attributes" [46]. In all designs level balance and orthogonality were maintained. Level balance means that "all the levels of each attribute occur with equal frequency" [46]. Orthogonality means that "the levels of each attribute vary independently of each other" [46], so in an orthogonal design each pair of levels appears equally often across all pairs of attributes within the design.

The respondent was presented with two alternatives for each question. For the DCE for poor prognosis and the DCE for good prognosis an opt-out was given ("I rather receive no information"). Each respondent received four choice-tasks for poor prognosis, four choice-tasks for good prognosis and four choice-tasks for the probability of receiving a prognosis. The respondents received detailed information concerning definitions of a good outcome and a poor outcome, the meaning of all the attributes and levels and the completion of a choice task, to make sure the respondents do not make default assumptions to fill in information gaps.

3.1.2 Certainty of a prognostic test

Direct questioning was used to measure the respondent perception on the minimally required certainty of a test before the decision to withdraw life support can be made. To this purpose one single choice question was developed with a drop-down with multiple answer alternatives. To make sure the respondent understood the question, the concept of test certainty was explained as the PPV before the question was asked.

3.1.3 Involvement in decision making

Direct questioning was also used to identify the preferences regarding the involvement in decision making about the withdrawal of life support as a close family member. To this purpose four single choice questions were developed concerning the topics who should start the conversation on withdrawal of life support and who should be responsible for making the final decision.

3.1.4 Quality of life after post-anoxic coma

To identify the public perceptions on a life worth living after post-anoxic coma, a design similar to the one of Frankl, Oye and Bellemay [38], Needle et al. [37], Sjokvist et al. [43] and Patrick et al. [41] was used. They formulated health states and asked respondents to rate their agreement with continuing/withdrawing life support on a 5-point Likert scale (ranging from definitely withdrawing life support to definitely not withdrawing life support).

From the literature it seemed most appropriate to formulate the health states based on either the CPC or the CPC-E. After discussion with the expert group it was decided to use the CPC-E, since the level of detail on health states was higher and it was felt that these descriptions would be easier to relate to for the respondents. It was assumed that everyone would want to live in case of CPC-E 1 and CPC-E 2, and everyone would want to die in case of CPC-E 5. Based on CPC-E 3-4 four health states were formulated to be rated by the respondents, where the focus was on CPC-E 3, because in recent years this has been the grey area with regard to what is considered a poor prognosis [24].

3.2 Questionnaire

The questionnaire consisted of six sections. The first section consisted of two questions concerning demographics and background. The second section consisted of the three DCE's as explained in paragraph 3.1.1, with twelve questions. The third part consisted of four questions concerning the preferred involvement in the decision making of life support as explained in paragraph 3.1.3. The fourth part consisted of the rating of the four health states as explained in paragraph 3.1.4. The fifth section consisted of some questions concerning costs and the withdrawal of life support. In this section also the question was asked about the required certainty of a test for withdrawal of life support as explained in paragraph 3.1.2. The questionnaire ended with some additional questions on background and demographics. This last section consisted out of six questions.

The questionnaire was completed individually by the respondents. The mode of administration of the questionnaire was a web-based survey. The questionnaire took 23 minutes to complete on average. The questionnaire can be requested from the researcher.

3.3 Study population

As said before, this study is the pilot study for a web-based survey to be conducted in the autumn of 2019 in the Netherlands. In that study, the study population will consist of members of the general population of the Netherlands. Survey Engine will recruit respondents for this sample. For sample size estimation the rule of thumb as proposed by Johnson and Orme was used. A sample size estimation of 250 complete responses is sufficient, according to this rule, to estimate all necessary parameters in this study. The intended sample size is estimated at 500 responses to make sure a proper subgroup analysis can be performed and the aforementioned power of 250 is achieved (since some of these 250 respondents may choose the opt-out in the DCE).

The goal of this pilot-test was twofold. On the one hand, the pilot-test was performed to ensure feasibility, readability and comprehension of the questionnaire. On the other hand, the pilot-test provided data for first analysis of preferences to see whether the research questions can be answered with the data the questionnaire provides and ensure in this way the validity of the questionnaire. A visual overview of the survey testing plan is depicted in Figure 2.

The first phase of the pilot-test took place among a convenience sample consisting of relatives, acquaintances and other members of the social network of the researcher. This first phase of the pilot-test consisted of 'think aloud' tests (n=10), during which the respondent completed the questionnaire reading out loud, while the researcher was present. The mean age of this sample was 35 years old (MIN=19, MAX=54). The ratio man-women in this sample was fifty-fifty. This 'think aloud' pilot-test mainly confirmed feasibility, readability and comprehension of the questionnaire, but also resulted in some revisions in the design of the questionnaire.

The major revises were within the design of the DCE's. Where first follow-up questions were asked about the receival of the information in the scenarios and the permission to withdraw life support in the chosen scenarios, in the final version these questions were omitted. Reason for this was that the questions about receiving information were seen as unnecessary. In the questions about withdrawal of life support additional trade-offs came to light, causing inability in determining the minimally required quality of a test. Also, where first only a DCE for poor prognosis and a DCE for good prognosis were included in the questionnaire, the DCE with the probability of receiving a prognosis was added to the final version, as described in paragraph 3.1.1. Instead of indirect questioning whether the life support may be withdrawn in different scenarios, a direct question was formulated to measure the minimally required test quality for the final version. See also paragraph 3.1.2. Last some questions about the costs were added to include a more societal perspective. For other changes following from this first pilot-test see the report included in Appendix C.

After this 'think aloud' pilot-test, the questionnaire was adapted and pilot-tested in a larger sample (n=56). For this test a system of the University of Twente was used, called SONA. SONA is a test subject pool system, which is used to recruit students as respondents for the questionnaire. Also, the social network of the researcher was used to recruit respondents for the questionnaire and a message was placed on Facebook to recruit respondents. The data this pilot-test provided was used for further analysis and the results in the next chapter.



Figure 2: Visualization of the pilot testing plan

3.4 Statistical analysis

The analyses of the pilot data were performed using a combination of the programs R and Excel. The significance level was set at 0.05.

The background characteristics and demographics of the sample were analyzed by descriptive methods. For continuous variables the mean, minimal value (MIN), maximal value (MAX) and standard deviation (SD) were calculated. For categorical variables frequencies and percentages were calculated.

Data of the three DCE's were analyzed using the Cox regression model, where the attributes were the independent variables and the respondent's choices the dependent variables. Cox regression applies a logistic regression analysis over the utility (U) equation, by which the following formulas could be formulated from the analysis (Eq. 1-3):

$$U_{DCE \ Poor \ prognosis} = V(\beta, X_i) + \varepsilon = \beta * timing \ test \ result + \beta * type \ of \ test \ (SSEP,$$

$$pupil \ and \ EEG) + \beta * accuracy \ good \ prognosis$$
(1)

 $U_{DCE \ Good \ prognosis} = V(\beta, X_i) + \varepsilon = \beta * timing \ test \ result + \beta * accuracy \ good \ prognosis$ (2)

 $U_{DCE\ Probability\ of\ receiving\ prognosis} = V(\beta, X_i) + \varepsilon = \beta * chance\ of\ receiving\ test\ result + \beta * (3)$ accuracy good prognosis + \beta * accuracy poor prognosis

Dummy coding was applied to the non-ratio scaled attributes. The reference levels were set to zero to be able to estimate the remaining levels. With the Cox regression the relative importance of the attributes was calculated. Also, the overall value and the share of preference (Eq. 4) were determined of the former clinical situation and the new clinical situation. This shows the predicted share of the population choosing each situation [46]. Lastly, to analyze the trade-offs respondents were willing to make between timing of test result, accuracy of test result and the probability of receiving a prognosis, the Marginal Rate of Substitution (MRS) (Eq.5) was calculated. The MRS calculates the ratio between the coefficients of two attributes. The MRS shows how much of one attribute the respondent is willing to give up in order to gain in another attribute. This allows different attributes to be easily compared [47].

$$P_{set} = \frac{e^{(\sum \beta_{ij})}}{\sum_{k} e^{(\sum \beta_{ij})}}$$
(4)

$$MRS_i = \frac{\beta_i}{\beta_{fixed-attribute}} \tag{5}$$

The data of the other questions of the questionnaire were analyzed using means, frequencies and percentages, depending on the type of variable. The Chi-squared test was used to test for statistically significant differences between the four health states.

There was no subgroup analysis performed, since the pilot sample is too small for this purpose. In the final sample, a subgroup analysis will take place. Also, the representativeness of the study sample for the Dutch population will be tested for the final sample.

3.5 Ethical considerations

Since there was participation of respondents in this study, there were some ethical considerations that had to be considered. Therefore, the study had to meet the ethical guidelines as laid down in the Declaration of Helsinki. Main ethical concerns in this study were the respondents' burden and the anonymity of the respondents.

Participation in this study was completely voluntary and the respondent could stop at all times if he wanted to. There were no consequences connected to participating or refusing to participate in this research. The respondent was informed about the goals of this study and processing of the results in advance of his participation. The burden of the respondent was kept as low as possible. There were no risks connected to participating in the study and the respondent did not need to travel long distances or anything of the sort. The only burden for the respondent was the time it took to complete the questionnaire. For this reason, no test-subject-insurance was needed, nor any form of reward was given. Furthermore, the respondent was actively asked to confirm whether he wanted to participate in the study.

The law on privacy was kept in mind during the study. The questionnaire was completely anonymous, which means the data of the questionnaire and the results of the study cannot be traced back to the respondent. The data of the questionnaire were used exclusively for analysis.

The Institutional Review Board of the University of Twente gave ethical permission for this study and advised that formal testing by a medical ethical committee was not necessary as the current study is no medical ethical research, since respondents were only required to complete an anonymous questionnaire once with a low burden, which is in accordance with the guidelines laid down in the Declaration of Helsinki.

4. Results

In this chapter the results of the pilot test are presented. In the first paragraph the characteristics of the study sample are described. In the second paragraph the preferences are presented for (1) receiving prognostic information, (2) required quality of a test before deciding to withdraw life support, (3) family involvement in the decision to withdraw life support and (4) relationship between quality of life after post-anoxic coma and willingness to live.

4.1 Study sample

The sample was recruited through multiple channels, namely through Sona, Facebook and the direct network of the researcher. In total, 212 respondents started the questionnaire, of which 57 respondents (27%) completed the questionnaire. 12 respondents (21%) were recruited via Sona, 8 respondents (14%) were recruited via Facebook and 37 respondents (65%) were recruited via the direct network of the researcher. One of these respondents needed to be excluded, due to invalid responses. Table 4 presents the different characteristics of the study sample.

Characteristic		(n = 56)
Age, mean (MIN-MAX; SD)		36 year (18-77; 16.59)
Gender, <i>n</i> (%)	Men	25 (45%)
	Women	31 (55%)
Education, n (%)	Low	3 (5%)
	Medium	18 (32%)
	High	35 (62%)
Relationship, n (%)	Yes	35 (62%)
	No	21 (38%)
Children, n (%)	Yes	25 (45%)
	No	31 (55%)
Religion, $n(\%)$	No religion	12 (21%)
	Christianity	43 (77%)
	Islam	0 (0%)
	Other	1 (2%)
Experience, <i>n</i> (%)	Yes	2 (4%)
	No	54 (96%)
Perceived health, mean (MIN-MAX; SD)		8.16 (6-10; 1.06)

Table 4: Ch	aracteristics of	of the stu	idy sample
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4.2 Sample preferences

4.2.1 Receiving prognostic information

The results of this study indicate that the study sample attach highest importance to the accuracy of a test result in case of receiving a poor prognosis (importance weight 0.479) (Table 5). The timing of the test result was the second-most important attribute (importance weight 0.396). The type of test was considered the least important (importance weight 0.125).

In case of receiving a good prognosis, the results indicate that the study sample attach also highest importance to the accuracy of a test result (importance weight 0.669) (Table 5). The timing of test result was considered as less important (importance weight 0.331).

Regarding the trade-off between getting a test result and the accuracy of the test result, the results indicate that the study sample attach highest importance to receiving a prognosis (importance weight 0.624) (Table 5). The accuracy of good prognosis was the second-most importance attribute (importance weight 0.269), and the accuracy of poor prognosis was the least important attribute (importance weight 0.107).

Table 5: Coefficients following from the regression analysis and the relative importance of attributes

Attribute and levels	Coefficients	SE	P-value	Relative importance
Poor prognosis				-
Timing of test result				0.396
12h, 24h, 48h, 72h	-0.019	0.005	0.000	
Type of test				0.125
SSEP-test and pupillary light reflex test	0	-	-	
SSEP-test, pupillary light reflex test and EEG	0.364	0.155	0.019	
Accuracy of poor prognosis				0.479
80%, 90%, 95%, 98%	0.078	0.016	0.000	
Good prognosis				
Timing of test result				0.331
12h, 24h, 48h, 72h	-0.027	0.007	0.000	
Accuracy of good prognosis				0.669
80%, 90%, 95%, 98%	0.181	0.027	0.000	
Sensitivity and specificity				
Probability of receiving a prognosis				0.624
20%, 30%, 50%, 60%	0.067	0.009	0.000	
Accuracy of good prognosis				0.269
80%, 90%, 95%, 98%	0.064	0.016	0.000	
Accuracy of poor prognosis				0.107
80%, 90%, 95%, 98%	0.026	0.016	0.102	

If we compare the share of preference between the new clinical situation, in which the EEG is introduced, with the former clinical situation with only the SSEP-test and the pupillary light reflex test, a higher percentage of respondents would prefer the new situation to the current situation (resp. 78% and 22%) (Table 6).

Further analysis showed that the respondents are willing to wait 4.0 hours longer to gain 1% of additional accuracy in the poor prognosis and 6.7 hours longer to gain 1% additional accuracy in the good prognosis. This confirms the importance of accuracy over the timing of the test result. Looking at the probability of receiving a prognosis, the respondents are willing to give up 2.6% in the accuracy of poor prognosis if the probability of receiving a prognosis increases with 1% and they are willing to give up 1% in the accuracy of good prognosis if the probability of receiving a prognosis increases with 1%. See also Table 7.

In the scenarios describing the option to receive information on poor prognosis in 9 questions (3 respondents) no preference ("opt out") was selected. Reasons for not expressing a preference and choosing for receiving no information were mainly that the respondents felt they couldn't do anything with the information. "The only thing you can do in such a situation is wait, hope and pray that it will get better", according to the respondents who opted out of receiving information a poor prognosis. One-time personal social circumstances were given as reason for not expressing a preference.

Situation	Timing of test	Type of test	Accuracy of	Overall	Share of
	result		test result	utility	preference
Former clinical	72 hours	SSEP-test and pupillary light reflex	99%	6.311	22%
situation		test			
New clinical	24 hours	SSEP-test, pupillary light reflex	99%	7.600	78%
situation		test and EEG			

Table 6: Share of preference in case of poor prognosis

Note: Utility equation as in Eq. 1 (par. 3.4) used with the relevant coefficients following from the regression analysis

Table 7: Marginal Rates of Substitution (MRS)

t 2	Additional hours respondents are willing to wait to gain 1% additional accuracy	Accuracy respondents are willing to give up to gain 1% additional probability of receiving a prognosis
Poor prognosis 4	4.0 hours (0.078/0.019)	2.6 % (0.067/0.026)
Good prognosis	6.7 hours (0.181/0.027)	1.0 % (0.067/0.064)

Note: Coefficients of relevant attributes displayed between brackets ()

In the scenarios describing the option to receive information on good prognosis in 8 questions (2 respondents) no preference ("opt out") was selected. The reason for not expressing a preference and choosing for receiving no information was here also that the respondents felt they couldn't do anything with the information.

4.2.2 Quality of a prognostic test

According to the respondent sample, the required quality of a prognostic test, before the decision to withdraw life support would be allowed, should be 95% (Range = 80-100; median = 98; SD = 5.77). The distribution of the answers is illustrated in Figure 3. Withdrawing the life support of patients in post-anoxic coma with a poor prognosis from a cost-perspective is justified according to a small majority of the study sample (59% (33/56)).

4.2.3 Involvement in decision making

The results indicated that the majority of the respondent sample (71% (40/56)) prefers the clinician to start the conversation about the withdrawal of life support in case of a predicted poor outcome (Figure 4). However, the majority of the respondent sample thinks the actual decision to withdraw life support should be a joined decision of the medical team and the family together (57% (32/56)) or a decision by only the family after they are advised by the medical team (25% (14/56)) (Figure 5).

In case of disagreement between the medical team and the family, the majority of the respondent sample thinks the opinion of the family should be decisive (67% (22/32). A minority of the respondent sample (15% (5/32)) had other opinions (Figure 6). Some thought it was important to not make any decisions concerning the withdrawal of life support if there was any doubt with any of the parties. Others thought third parties should be involved in case of disagreement, like the pastor. One respondent assumed the insurance company had the last say.

The majority of the study sample agreed (58%) with the current line of law, which states the clinician is responsible for the decision to withdraw life support, in case the clinician thinks that further treatment is futile (Figure 7).



Figure 3: Distribution of answers required test quality



Figure 6: Responsible in case medical team and family disagrees

Figure 7: Consensus with the law

4.2.4 Quality of life after post-anoxic coma

68% (38/56) of the respondent sample would (probably) not want to stay alive when the outcome after post-anoxic coma would be a vegetative state (Health state 1, Box 1). When the outcome after post-anoxic coma would be a minimal state of consciousness with both severe physical and cognitive disabilities (Health state 2, Box 1), the portion of the study sample that would (probably) not want to stay alive (45% (26/56)) was about the same as the portion of the study sample which would (probably) want to stay alive (43% (24/56)). In case the outcome comprises only severe cognitive disabilities (Health state 3, Box 1) 68% (38/56) of the study sample would (probably) want to stay alive. See also Figure 8. These differences in wanting to stay alive between the four health states are statistically significant (p = 0.00).

The majority of the study sample (77% (43/56)) did not consider the costs of care in their preferences for staying alive or not in these health states. Again, the majority of this portion (79% (34/43)) indicated they would not have different preferences when considering the costs of care.

Box 1: Health states as presented to the respondents in the questionnaire (translated)

Health state 1:

You are unconscious. The only movements you make are reflexes. Meaning you cannot eat, dress, move and go to the toilet independently. Also you do not have cognitive function, due to your unconsciousness. This means you do not respond to stimulus from your environment and communication is not possible. Due to your disabilities you stay in a nursing home.

Health state 2:

You are conscious, but you are physically disabled. You are bedridden and you can only sit with support. You cannot eat, dress, move or go to the toilet independently. You are also cognitively disabled: your short-term memory is disturbed, you are less concentrated, you cannot plan your day and you are less attentive to your environment. You are limited in your communication with your environment and it is unclear whether you understand what you are being asked and therefore whether your answers are correct. Due to your disabilities you stay in a nursing home.

Health state 3:

You are conscious and your physical functions are well recovered. You can sit and walk without assistance. You can eat, dress, move and go to the toilet independently. However, you are cognitively disabled: your short-term memory is disturbed, you are less concentrated, you cannot plan your day and you are less attentive to your environment. You are limited in your communication with your environment and it is unclear whether you understand what you are being asked and therefore whether your answers are correct. Due to your cognitive disabilities you stay in a nursing home.

Health state 4:

You are conscious, but you are physically disabled. You are bedridden and you can only sit with support. You cannot eat, dress, move or go to the toilet independently. However, your cognitive functions are well recovered: your short-term memory works just fine, you are well concentrated, you can plan your day and you are attentive to your environment. You are able to communicate with words with your environment. Due to your physical disabilities you stay in a nursing home.

Figure 8: Perceived quality of life after post-anoxic coma

5. Discussion

In this chapter the results of the current study are discussed. Firstly, the findings regarding the preferences for the prognostication are presented and put in a broader context using the literature. Secondly, the strengths and limitations of this study are elaborated on. Thirdly, some implications for methodology are discussed for the final survey in the autumn of 2019 in the Netherlands.

5.1 Preferences for prognostication of patients in post-anoxic coma

The objective of the current study was to contribute to societally acceptable implementation of the EEG as a new prognostic test for patients in post-anoxic coma by identifying preferences for prognostication of these patients from a societal perspective. The results of this study indicate that the respondents in this study prefer more prognostic information about good and poor outcomes at an earlier moment after cardiac arrest. A shorter amount of waiting time, a higher accuracy and a higher probability of receiving prognostic information have all a positive impact on the utility of a test. These are all promising outcomes regarding the societal acceptation of EEG test results in clinical practice.

Although the respondents of this study would like to receive the test results as soon as possible, they are willing to wait longer to increase the accuracy of the prognosis according to the results. However, they are willing to give up some of the accuracy of the prognosis if the probability of receiving prognostic information increases. A qualitative study, within the research project in which the current study is carried out, found that family wants to receive some information, any information when their family member is in a post-anoxic coma. This tendency, i.e. that the family rather receives any information regarding the status of their family member than dealing with the incremental effects of uncertainty, is also known within literature [21, 48, 49]. This might explain the preference of the study sample for a higher probability of receiving prognostic information to a higher accuracy of the prognostic information.

Looking at the importance of the accuracy of prognosis, we see that the respondents in this study find the accuracy of good prognosis more important than the accuracy of poor prognosis. This might be related to the difference between the perceptibility of the consequences of false positives in poor prognosis and false positives in good prognosis. The consequences of a poor prognosis are quite significant, i.e. they have a far stretching impact on withdrawal of life support and consequently possible death. However, the false positives in poor prognosis don't have that far stretching impact, since they simply cannot be identified as such by families and clinicians, due to the SFP [26]. On the contrary, for good prognosis a false positive becomes painfully clear, leading to disappointment for the family if the outcome turns out to be poor, despite earlier good prognosis. Furthermore, the 'think aloud' pilot test found that people might prefer a less accurate poor prognosis, because in such case the thought is that the probability that this prognosis is false and the patient has a good outcome, is higher. So, a less accurate prognosis might also represent hope for the family of a patient in post-anoxic coma [21]. However, the respondents may be unaware that the less accurate prognosis of poor outcome can nevertheless impact the outcome in such a way, that the unreliability becomes a threat to the patients' potential to prove the test wrong. To clarify, the less accurate prognosis can still be the basis for the decision to withdraw life support, causing the patient to pass away before the false positive can be detected. Another issue is that these 'confirmed' tests (the poor prognosis

led to a poor outcome) go on informing new prognosis afterwards, which further impacts the measured accuracy of the test.

The respondents in this study apparently prefer a mean certainty of 95% in a poor prognosis, before making the decision to withdraw life support. Looking at the scatter of the answers, most of the respondents prefers a certainty between 95% and 100%. Only a few respondents prefer a certainty around 80%. So, the 95% might be relatively low due to these few extreme answers and therefore not accurate, nonetheless, it shows that some uncertainty in the prognosis is acceptable for the respondents in this study. A low probability of prematurely ending the life of people who would have had a good outcome might be undesirable, but so is delaying the decision to withdraw life support until an outcome is hundred percent certain, since it leads to expensive futile care, but, above all, it is emotionally burdensome for both health care professionals and the family [27]. Health care professionals also accept some uncertainty in the poor prognosis. Health care professionals with more experience accept more uncertainty compared to professionals with less experience. Furthermore, palliative care professionals are more tolerant of uncertainty in prognosis when making the decision to withdraw life support [27]. Also other studies acknowledge that an accuracy of 100% is impossible for a prognostic test, although in an ideal situation premature withdrawal of life support in patients with a chance of good outcome is avoided [21, 24]. That from a societal perspective some uncertainty might be acceptable, can be a reassurance for health care professionals in their clinical practice and can ease possible feelings of guilt that some might have related to the SFP [26]. Taking this accepted uncertainty in a prognostic test together with the preference for a higher probability of receiving prognostic information, it promises a good societal acceptation of the EEG test. It might also point to a direction in scientific research with a focus on increasing the sensitivity of a test, instead of reaching for an impossible hundred percent specificity.

The respondents preferred the clinician to start the conversation on the withdrawal of life support. This seems in clinical practice also the case, since the clinician is more likely to initiate the conversation on withdrawal of life support than the family members of the patient [50-52]. Furthermore, most of the respondents in this study preferred shared decision making for the withdrawal of life support, where most respondents think the final say should be left to the family. Fortunately, for most decisions to withdraw life support the preferences of the family are taken into account by the medical team [52, 53]. The majority of studies on the involvement in decision making as family members report a satisfactory degree of involvement [54-56], although there are also results reporting insufficient involvement of family members [57]. This preference of the respondents in this study for involvement in the decision making concerning withdrawal of life support as a family member, is comparable to preferences of family members of patients in the ICU in Canada [56].

Although most of the respondents in this study indicate that the family should be responsible for making the decision to withdraw life support, also a small majority indicates it is good that the clinician is responsible for making this decision in accordance with the law. This seems contradictory; however, the law can have this natural authority which can change the respondent's opinion. Also, the statement of the law can change the respondent's perspective from a personal perspective, in which a hypothetical family member was in coma, to a more general perspective. Since the law reflects the policy of the country, respondents might think from a more general perspective that the law is right, while from their personal point of view, in which a hypothetical family member

is in coma, they might disagree. The contradictory response to this question might also indicate that the preferences are subject to external influences and can be shaped.

A clinical expert stated that the main reason for clinicians making the final decision was that the family finds it too difficult to decide on the withdrawal of life support for their close family member. However, it remains important that the clinician actively involves the family in the decision-making process. Especially since the clinician is influenced by his own preferences for treatment withdrawal [37]. Preferences of the family could help in making the right decision. Although both family members and clinicians often misjudge the preferences of the patient, research shows that family members can better estimate patient's wishes for withdrawal of life support than clinicians can [58, 59]. This misjudgment of preferences indicates a need for more expressed preferences of individuals themselves concerning the withdrawal of life support if they end-up in a post-anoxic coma after cardiac arrest. It is known from the literature preferences for withdrawal of life support are not often discussed [38].

The withdrawal of life support is closely connected to the perceived value of the outcome after post-anoxic coma. A vegetative state is clearly considered as poor by the respondents in this sample, which relates to previous research categorizing a vegetative state (CPC 4) as a poor outcome [24]. Previous research found that a vegetative state was valued worse than death [41], life support was not preferred in a vegetative state [38, 40], and a vegetative state was seen as having no or extreme low quality of life [42].

The three health states formulated for CPC 3 in this study where not necessarily considered as poor by the respondents. Where there is some variety within the CPC 3, generally speaking most of the respondents in this study considered this category as a life worth living. This contradicts most studies on this subject over the last years, because from 2006 onwards most studies categorized CPC 3 as a poor outcome [25]. The change in focus of a poor outcome from regaining consciousness as a priority towards the recovery of mental and physical ability to allow societal participation, where Sandroni, D'Arrigo and Nolan [24] write about, did apparently not occur in the sample of the current study.

Although the perception of CPC 4 as 'not worth living' is corresponding to other research, the difference in categorizing CPC 3 as poor or good between the current study and previous research means that the perception of the respondents on 'a life worth living' after post-anoxic coma is not comparable to previous research. This might be related to the high portion of Christians in the sample. In general, it is expected that Christians are more inclined to want to stay alive in these health states out of religious believes. When the study sample would be representative for the Dutch population it is possible that the majority of the Dutch public categorizes CPC 3 as a poor outcome. However, it is also important to consider that physicians are more inclined to withdraw life support than the general public [43]. There is a possibility that the general public also does not categorizes CPC 3 as a poor outcome but sees it as 'a life worth living', which is illustrated by the sample of the current study. When this is the case, it shows a discrepancy between the clinical/scientific perspective and the societal perspective with major implications for both the sensitivity and the specificity of the prognostic tests. Further research is needed to see if this discrepancy between the clinical and scientific community and the society really exists.

5.2 Strengths and limitations

One point to consider in any DCE is the relevance of the attributes and whether all relevant attributes were selected for the trade-offs between situations. This could be a source of uncertainty. In the current study attributes were chosen by the project team, based on the known literature and experience from previous and ongoing research of members within the team. In the 'think aloud' pilot test respondents were asked to make their trade-offs between scenarios out loud to see if attributes were missing. The results did not bring to light any other factors influencing respondents' trade-offs. This indicates that all relevant attributes were selected.

The second point to consider is risk communication of attributes. In most DCE's, as in the three DCE's of the current study, risk is an important attribute (accuracy of prognosis, probability of receiving prognosis). It is known that interpretation of numerical information including risks is difficult for respondents. There are also several characteristics influencing the ways respondents interpret the risk, like personal experience and the context of the risk. Transparency in reporting of risk presentation lacks in most studies using a DCE [60, 61]. It is questionable whether in the current study the risk presentation is sufficient for respondents to understand the risk. This is because the respondents stated they preferred a lower accuracy, because the probability that the test result is wrong, would then be higher. This trade-off the respondents made concerning the accuracy of poor prognosis, indicates the context of the risk (withdrawal of life support in case of poor prognosis) was not clear to the respondents. It is also questionable whether the translation of the PPV as the certainty of a test is sufficient, or that also other measures should be included, like the NPV, sensitivity and specificity.

The third point to consider is possible respondent fatigue. Although we tried to keep the questionnaire as short as possible, the length and the information density was quite high, which could have led to fatigue among respondents. The mean time to complete was 23 minutes, however, the time alone does not provide information on the burden of the questionnaire leading to respondent fatigue. A shorter time to complete can mean a reduced motivation to engage in the questions, while a longer time to complete can reflect more motivation of the respondent, meaning that the respondent was less burdened [62]. The results of the 'think aloud' pilot test indicated that, despite respondents had a high time to complete (about 45 minutes), they did not have the feeling the questionnaire was too long, due to the interesting topic of the questionnaire. However, the low portion of complete questionnaires in the larger sample (27% (56/212)) might indicate some respondent fatigue or lack of motivation. For 46% (98/212) of the entries to the questionnaire the consent question was left blanc, meaning the respondent dropped out while reading the introduction. 3% (6/212) did not give consent for their participation and dropped out after this. 51% (108/212) gave their consent for participating in the study, of which 30% (32/108) tried to fill out the questionnaire on their mobile phone. These respondents were automatically screened out. Of the remaining respondents 25% (19/76) dropped out during the remainder of the questionnaire. The high drop-out rate indicates there is indeed respondent fatigue or lack of motivation. Whether this has influenced the respondent's answers in the completed questionnaires and to what extent remains unknown.

The fourth point to consider is whether the preferences from an individual perspective are sufficient in painting a picture of the preferences of Dutch society. The question concerning the consensus with the law indicates it matters from which perspective the respondent is answering the questions. One could argue that only the sum of individual perspectives is not enough to identify the societal perspective. It might also include public debate and political decision making.

The fifth point to consider is the generalizability of the study results. The study sample is not representative for the Dutch population. Although this was not the aim of the pilot study, it still limits the generalizability of this study. The results of this study are therefore not representative for the general Dutch society.

5.3 Methodological implications for further research

The analysis of the extensive pilot test has multiple methodological implications for the web-based survey to be conducted in the autumn of 2019 in the Netherlands. These implications are important to name here and change before the web-based survey is conducted, to guarantee the questionnaire is valid, feasible, readable and comprehensible. Some implications are not directly changing the questionnaire but are important for the context of the later study.

Firstly, there is a need for a more extensive literature review than the performed mini-review in the current study. In this mini-review there was a focus on preferences for health states related to the decision to withdraw life support. To place the results of the web-based survey in the right context later on, a more extensive literature review is needed that also includes preferences for receiving prognostic information, preferences for the minimally required quality of a prognostic test before the decision to withdraw life support is made and preferences for the involvement in decision making concerning the withdrawal of life support. Some literature on these topics was already found and used within the current study. However, to create a proper context all relevant literature should be mapped in September 2019.

Secondly, the high drop-out rate in the current study is concern for the later study in the autumn of 2019. Although there are some explanations for this rate, like the exclusion of mobile phones and respondents opening the questionnaire without the intension to finish it at that moment, it is an indication of respondent fatigue. Therefore, it is recommended to look at the introduction and try to find ways to shorten it as first course of action. Furthermore, it might be a solution to reduce the number of choice tasks per respondent. There is room for such methodological change, without the sample size needed to be increased. It is also recommended to critically look at the relevance of every single question.

Thirdly, there needs to be taken another look at the risk presentation within the DCE's, but also at the question concerning the minimally required quality of a test. The analysis of the pilot test indicates that at least the context of the risks is not clear (i.e. withdrawal of life support as result of poor prognosis) for the respondent. Furthermore, the accuracy and certainty (risks) are in the current study operationalized as the PPV of a test. It needs to be discussed within the project team, whether NPV, sensitivity and specificity also need to be included. Whether this is needed for the DCE's is a trade-off between completeness and cognitive feasibility for the respondent. However, it is recommended to at least expand the question for the minimally required certainty of a test with questions about accepted false positives and negatives, since the one question that is asked in the current study seems not sufficient. Risk grids can be used to visually present the risks to the respondent. Steinberg et al. performed a study investigating the minimally required certainty of a test for withdrawal of life support from a health care providers perspective [27]. This study could serve as an example on how to measure the minimally required certainty of a test. It would also be interesting to measure it the same way, so the perspective of society on the minimally required certainty of test can be compared to the health care providers' perspective.

Fourthly, the contradictory response on the question about agreement with the law, indicates that preferences of respondents can be shaped by information they get. It illustrates the importance of information which is presented to respondents in the questionnaire. By presenting or withholding information to the respondents, their preferences can be shaped, resulting in an invalid picture of the preferences of the study sample. This finding is important to

keep in mind for the whole questionnaire in deciding which information respondents are presented with and which information is withheld.

Lastly, it is important to discuss with the project group whether the individual preferences of respondents together are sufficient for painting a picture of the preferences of Dutch society. The contradictory response on the law question illustrates that the perspective from which the respondent answers the questions matters and the preferences might be influenced by nationwide policies. If individual preferences are not sufficient for painting a picture of the preferences of Dutch society, the perspectives and information given in the questionnaire need to be changed.

6. Conclusion

In the current study, the preferences of the study sample regarding provision of prognostic information and discontinuation of life sustaining treatment are the following:

- Prognostic information is preferably provided as soon as possible with an accuracy as high as possible.
- Receiving any information is considered more important than the actual accuracy of predictions.
- For decisions on discontinuation of life sustaining treatment, 100% certainty about poor prognosis is not necessary.
- Shared decision making in withdrawal of life support is preferred, where most respondents prefer to leave the final say to the family.
- CPC 3 is generally considered a poor outcome in other studies, but not by the respondents in the current study.

Most of these preferences are promising for the societal acceptation of the implementation of the EEG as a prognostic tool in clinical practice. Further research is needed in order to confirm whether these findings are valid for the Dutch population. This will be done in a web-based survey to be conducted in the autumn of 2019 in the Netherlands. The current study indicates there are some improvements to be made, considering the feasibility and the comprehension of the questionnaire. It is necessary that these improvements are made before conducting the web-based survey, to ensure validity, feasibility, readability and comprehension of the questionnaire.

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Appendix A: Cerebral Performance Categories – Extended

			ASSESSED PRIOR TO DISCHARGE						ASSESSED POST DISCHARGE			
		1.1	1.2	13	1.4	1.5	1.6	1.7	1.8	1.9	1.10	
Domain Levels	i.	Alert	Short Term Memory [*]	Logical Thinking	Attention	Motor	Basic Activities of Daily Living (BADLs)	Mood	Fatigue	Complex Activities of Daily Living (CADLs)	Return to Work	
Best Indicator	1	Spontaneously orients or responds to person entering room	4 words recalled	Correctly answers all 4 questions	No errors	Ambulates without assistance	Independent in 4/4 (eating, dressing, transferring and toileting)	I feel positive and hopeful most of the time	I feel fatigued none of the time	Independent in 4/4 (medication management, food preparation, shopping and transportation)	Currently performing 100% pre CA ^{\$} work tasks ^{ée}	
	2	Requires only verbal stimulus to orient or respond to observer	3 words recalled	Correctly answers 3/4 questions	1 error	Ambulates with assistance	Independent in 3/4 (eating, dressing, transferring or toileting)	I feel positive and hopeful some of the time	I feel fatigued rarely	Independent in 3/4 (medication management, food preparation, shopping or transportation)	Currently performing 75% pre CA [§] work tasks ⁶⁶	
	3	Requires light touch and verbal stimulus to orient or respond to observer	2 words recalled	Correctly answers 2/4 questions	2 errors	Needs assistance to stand	Independent in 2/4 (eating, dressing, transferring or toileting)	I feel positive and hopeful occasionally	I feel fatigued occasionally	Independent in 2/4 (medication management, food preparation, shopping or transportation)	Currently performing 50% pre CA [§] work tasks ⁶⁶	
	4	Requires noxious stimulus to orient or respond to observer	1 word recalled	Correctly answers 1/4 questions	3 errors	Needs assistance to sit	Independent in 1/4 (eating, dressing, transferring or toileting)	I feel positive and hopeful rarely	I feel fatigued some of the time	Independent in 1/4 (medication management, food preparation, shopping or transportation)	Currently performing 25% pre CA ^{\$} work tasks ^{¢¢}	
Worst Indicator	5	No response to voice or physical stimulation; may observe abnormal reflex or posturing	No words recalled	0/4: Does not answer any question correctly	4 errors	Only moves in bed	0/4: Not independent in any BADLs	I feel positive and hopeful none of the time	I feel fatigued all of the time	0/4:Not independent in any CADLs	0%: Currently unable to perform any pre CA [§] work tasks ⁶⁶	
	6	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	Not Reported	
	7		Not Testable	Not Testable	Not Testable							

Abbreviated Scoring Sheet: Impairment and Disability Domains of the CPC-E Circle Ratings

* Scoring is based on the delayed 4 min recall trial (Refer to directions on page 2).

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1

§CA: Cardiac Arrest ^{\$\$} Includes retiree or homemaker.

CPC-E SUBJECT ID: _____ Date: __/__/20___ Data Collected By: _____

Appendix B: Mini-review

B.1 Search strategy Licht blauwe = goede resultaten

Donkerblauwe = alle zoektermen samengevoegd per database.

Database	Search term	# of records	Action	Result	Final search term
Scopus	TITLE-ABS-KEY (withdrawal AND life AND support AND coma)	221	Add 'preferences' to search term	5	TITLE-ABS-KEY (withdrawal AND life AND support AND coma AND preferences)
Scopus	TITLE-ABS-KEY (health AND state AND (preferences OR valuation))	12,274	Add 'withdrawal life support' to search term	24	TITLE-ABS-KEY (health AND state AND (preferences OR valuation) AND withdrawal AND life AND support)
Scopus	TITLE-ABS-KEY (health AND state AND (preferences OR valuation) AND quality AND of AND life)	2567	Add 'instrument OR measuring' to search term	547	TITLE-ABS-KEY (health AND state AND (preferences OR valuation) AND (instrument OR measuring) AND quality AND of AND life)
Scopus	TITLE-ABS-KEY (health AND state AND (preferences OR valuation) AND coma)	38			
Scopus	TITLE-ABS-KEY (measuring AND preferences AND withdrawal AND life AND support)	0			
Scopus	TITLE-ABS-KEY (measuring AND preferences AND health AND states)	272			
Scopus	TITLE-ABS-KEY ((measuring AND preferences AND health AND states) OR (health AND state AND (preferences OR valuation) AND ((withdrawal AND life AND support) OR ((instrument OR measuring) AND quality AND of AND life)))) AND (LIMIT-TO (DOCTYPE, "ar") OR LIMIT-TO (DOCTYPE, "re")) AND (LIMIT-TO (LANGUAGE, "English")) AND (EXCLUDE (PUBYEAR, 1988) OR EXCLUDE (PUBYEAR, 1987) OR EXCLUDE (PUBYEAR, 1983) OR EXCLUDE (PUBYEAR, 1973))	620			
PubMed	Search (withdrawal life support) AND coma Field: Title/Abstract	26	Add 'preferences' to the search term	1	Search (withdrawal life support) AND coma AND preferences Field: Title/Abstract
PubMed	Search (health state preferences) OR health state valuation Field: Title/Abstract	1438	Add 'withdrawal life support' OR 'quality of life' OR 'coma' to search term	469	Search ((health state preferences) OR (health state valuation)) AND ((withdrawal life support) OR (quality of life) OR coma) Field: Title/Abstract
			Add 'instrument' OR 'measuring' to search term	95	Search (((health state preferences) OR (health state valuation)) AND ((withdrawal life support) OR (quality of life) OR coma)) AND ((instrument) OR (measuring)) Field: Title/Abstract

PubMed	Search ((measuring) AND preferences) AND health states Field: Title/Abstract	61			
PubMed	Search (((measuring) AND preferences) AND health states) OR ((((health state preferences) OR (health state valuation)) AND ((withdrawal of life support) OR (quality of life) OR coma)) AND ((instrument) OR (measuring))) Sort by: Best Match Filters: Journal Article; Publication date from 1989/12/31 to 2019/02/20; English; Dutch; Field: Title/Abstract	136			
Cochrane library	(withdrawal life support):ti,ab,kw AND (coma):ti,ab,kw" (Word variations have been searched)	5			
Cochrane library	(health state preferences):ti,ab,kw OR (health state valuation):ti,ab,kw" (Word variations have been searched)	819	Add 'measuring' OR 'instrument' to search term Add 'withdrawal life support' OR 'quality of life' OR 'coma' to	409	((health state preferences) OR (health state valuation)):ti,ab,kw AND (measuring OR instrument):ti,ab,kw" (Word variations have been searched) ((health state preferences) OR (health state valuation)):ti,ab,kw AND (measuring OR instrument):ti,ab,kw AND ((withdrawal life support) OR (quality of life) OR (coma)):ti,ab,kw"
Cochrane library	(measuring):ti,ab,kw AND (preferences):ti,ab,kw AND (health states):ti,ab,kw" (Word variations have been searched)	351	Add 'withdrawal life support' OR 'quality of life' OR 'coma' to search term	146	(word variations have been searched) (measuring):ti,ab,kw AND (preferences):ti,ab,kw AND (health states):ti,ab,kw AND ((withdrawal life support) OR (quality of life) OR (coma)):ti,ab,kw" (Word variations have been searched)
Cochrane library	(((health state preferences) OR (health state valuation)) AND (measuring OR instrument) AND ((withdrawal life support) OR (quality of life) OR (coma))):ti,ab,kw OR ((measuring) AND (preferences) AND (health states) AND ((withdrawal life support) OR (quality of life) OR (coma))):ti,ab,kw (Word variations have been searched)'' in Cochrane Reviews, Trials (Word variations have been searched)	173			
Web of Science	(TS=(withdrawal life support AND coma*)) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years	73	Add 'preferences' to search term	7	(TS=(withdrawal life support AND coma* AND preferences)) AND LANGUAGE: (English OR Dutch) Timespan: All years. Indexes: SCI- EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI.
Web of Science	(TS=(health AND state AND (preferences OR valuation))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years	7,673	Add 'withdrawal life support' OR 'quality of life' OR 'coma' to search term	2,340	(TS=(health AND state AND (preferences OR valuation) AND ((withdrawal of life support) OR (quality of life) OR (coma)))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
			Add 'measuring' OR 'instrument' to search term	1,377	(TS=(health AND state AND (preferences OR valuation) AND ((withdrawal of life support) OR (quality of life) OR (coma)) AND (measuring OR instrument))) AND LANGUAGE: (English OR Dutch)

					Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
			Change 'Topic' into 'Title'	3	(TI=(health AND state AND (preferences OR valuation) AND ((withdrawal of life support) OR (quality of life) OR (coma)) AND (measuring OR instrument))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
Web of Science	(TS=(measuring AND preferences AND (health states))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years	2,069	Add 'withdrawal life support' OR 'quality of life' OR 'coma' to search term	1,069	(TS=(measuring AND preferences AND (health states) AND ((withdrawal life support) OR (quality of life) OR (coma)))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
			Change 'Topic' into 'Title'	1	(TI=(measuring AND preferences AND (health states) AND ((withdrawal life support) OR (quality of life) OR (coma)))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years
Web of Science	(TI=(measuring AND preferences AND (health states))) AND LANGUAGE: (English OR Dutch) Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years	29			
Web of Science	((TI=(measuring AND preferences AND (health states))) OR (TI=(health AND state AND (preferences OR valuation) AND ((withdrawal of life support) OR (quality of life) OR (coma)) AND (measuring OR instrument))) OR (TS=(withdrawal life support AND coma* AND preferences))) AND LANGUAGE: (English OR Dutch) Refined by: DOCUMENT TYPES: (ARTICLE OR REVIEW) AND [excluding] PUBLICATION YEARS: (1982) Timespan: All years. Indexes: SCI- EXPANDED, SSCI, A&HCI, CPCI- S, CPCI-SSH, ESCI.	28			

B.2 Full text screening

Author (vear)	Title	Study design	Aim	Conclusions	Inclusion
Asch, D.A., & Christakis, N.A. (1996).	Why Do Physicians Prefer to Withdraw Some Forms of Life Support over Others? Intrinsic Attributes of Life- Sustaining Treatments Are Associated with Physicians' Preferences	Combination of Delphi survey to identify relevant attributes and a mail survey to elicit preferences. Method to elicit preferences was ranking.	To identify which attributes of life- sustaining treatment are important to physicians, so we can learn what physicians value in this area, and how these values influence their choices among forms of life support.	Physicians have distinct and consistent preferences for withdrawing certain forms of life support over others. These preferences are associated with physicians' age. In the context of withdrawal of life support are able to agree on a series of underlying characteristics that distinguish different forms of life support. This study suggests that even when physicians may have agreed that life support should be withdrawn, the choices they make about the manner of withdrawing life support reflect other moral, social, and clinical goals. These goals include a desire to withdraw treatment they perceive as expensive, scarce or artificial.	Yes
Badia, X., Díaz-Prieto, A., Rué, M., & Patrick, D. L. (1996).	Measuring health and health state preferences among critically ill patients	Case-control design (retrospective), EuroQol questionnaire used to rate the health states of patients in in SDU, and a control group of healthy individuals.	The objectives of this study were: a) to determine whether the EuroQol instrument a preference-based measure of health- related quality of life (HRQoL)- can be used to assess the patient's previous health state when the patient is admitted to the ICU; b) to assess changes in HRQoL in the period before the onset of the condition leading to ICU admission and at discharge and c) to obtain preferences for a "common core" of EuroQol health states, including death, from critically ill patients, and to compare their preferences with those obtained from a sample of healthy individuals.	The EuroQol can be reliably used with proxies to determine the state of health of patients prior to the onset of the condition, intervention or accident that leads to the ICU admission. Additionally, knowledge of the previous health state of patients (whether conscious or not) admitted to the ICU could be used to provide information that might be important when making decisions regarding treatment. Healthy individuals and ICU patients place different values on the "common core" of EuroQol health states. This is especially true in the case of the worst health states, which ICU patients tended to value more highly than healthy individuals. Moreover, ICU patients rated no state as being worse than death. The degree of difference is low for preferable health states and is greatest for the worst health states. The results from this study suggest that ICU patients are willing to spend some time in even the worst health states rather than die: in other words, within the EuroQol descriptive system, there are no health states worse than death for such patients	No → Not about coma/ withdrawal of life support and no preference elicitation method
Bryce, C. L., Loewenstein, G., Arnold, R. M., Schooler, J., Wax, R. S., & Angus, D. C. (2004).	Quality of death: Assessing the importance placed on end- of-life treatment in the intensive- care unit.	Time-tradeoff experiment in the general population with 1 baseline scenario and 5 alternative scenarios for End of Life (EOL) care.	The objectives of this study were to test whether people would trade healthy life expectancy for better EOL care, to understand how much life expectancy they would trade relative to domains of good care, and to determine the association of respondent characteristics to time traded.	Most respondents were willing to trade substantial durations of healthy life for a better EOL experience supports the contention that EOL care matters 24 and suggests that traditional methods to calculate QALYs will underestimate the true societal value. Good EOL care encompasses both medical and nonmedical domains. Preferences for EOL care varied for respondent demographics and prior loss. Older respondents, blacks, and those with children traded less time for higher-quality EOL care. Exposure to the ICU setting through a loved one's death increased the value of EOL care relative to longevity, especially if the loved one's treatment was perceived to be neutral or uncaring.	No → not about coma/ withdrawal of life support.

Dmertzi, A., et al. (2011)	Attitudes towards end- of-life issues in disorders of consciousness: A European survey	European Survey among professionals visiting medical and scientific conferences/ meetings	The aim of the study was to update the end-of-life attitudes towards vegetative state and to determine the end-of-life attitudes towards minimally conscious state.	Two-thirds of the surveyed participants reported that it was acceptable to withdraw life support from these patients and most (82%) preferred not to be kept alive if they imagined themselves in a chronic vegetative state. Concerning chronic MCS, there were clear differences in opinions as compared to permanent VS: although almost 70% would not wish to be kept alive in this state, recognizing it to be worse than VS, less than one-third of our respondents supported treatment withdrawal from these patients. The majority of the study sample (80%) considered chronic VS worse than death especially from the family's point of View. For the recently defined MCS, there seems to be a strong dissociation between what we want for ourselves (most caregivers do not wish to be kept alive in this condition) and what we consider acceptable in patients (only a minority considered it acceptable to stop treatment in chronic MCS). Healthcare professionals' views are dependent on geographic and religious variables. Residents from Northern and Central Europe, as compared to Southern Europeans, were more likely to agree with ANH withdrawal in chronic VS whereas religious respondents, older respondents, and women were less likely to find it acceptable	No → no preference elicitation method.
Frankl, D., Oye, R. K., & Bellamy, P. E. (1989).	Attitudes of hospitalized patients toward life support: A survey of 200 medical inpatients	Prospective survey of inpatients about their preferences using a rating method.	Identify inpatients' preferences for life sustaining treatment	Ninety percent of patients either "strongly agreed" or "agreed" with life support if their health could be restored to its usual level; 30 percent favored life-sustaining therapies if they would be non-independent upon discharge; 16 percent favored life support given a hopeless prognosis; and only 6 percent would desire such therapy if they would remain comatose. Thus, preferences for aggressive care were modified by perceived outcome.	Yes (not specifically in case of coma)
Kind, P., & Macran, S. (2005).	Eliciting social preference weights for functional assessment of cancer therapy-lung health states	Postal survey using scaling method. Visual Analogue Scale	To develop a set of utility weights that could be used to convert the FACT-L into a single index capable of being used in the economic analysis of clinical trial data	This study demonstrates a practical method of converting a standard condition-specific measure into a form that has the requisite properties to legitimize its use in cost-utility analysis. The methodology used here is not unique to FACT-L and might be considered appropriate for use in converting similar instruments.	No → not about coma/ withdrawal of life support
Marik, P. E., Varon, J., Lisbon, A., & Reich, H. S. (1999).	Physicians' own preferences to the limitation and withdrawal of life-sustaining therapy	Survey among a sample of attending physicians in a spectrum of medical facilities in the US. Not clear what kind of preference elicitation method is used. "The respondents provided basic demographic data, do-not-	To determine physicians own preferences with regards to the limitation and withdrawal of life- sustaining therapy as well as active euthanasia.	In this study the majority of physicians who responded to the survey would not want cardiopulmonary resuscitation (CPR) to be performed on themselves and would want life-sustaining therapy withdrawn should the prognosis for meaningful survival be poor. A significant number were in favor of active euthanasia. It is therefore unlikely that physicians' personal beliefs result in the failure of communication between patients and their physicians as regards end-of-life issues.	Yes (about withdrawal of life support, but scenarios in question- naire did not include coma)

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		resuscitate preferences should they suffer a cardiac arrest under various circumstances as well as a response to a number of case vignettes. The questions required a yes or a no answer."			
Mushlin, A. I., Kern, L. M., Paris, M., Lambert, D. R., & Williams, G. (2005).	The value of diagnostic information to patients with chest pain suggestive of coronary artery disease	Prospective cohort study, using willingness to pay and time trade-off for eliciting preferences	To measure the value of stress testing to patients with chest pain suggestive of coronary artery disease (CAD) and to improve methods for measuring the value of diagnostic information.	This study found that a group of patients with chest pain suggestive of coronary artery disease experienced psychological benefits after a diagnostic workup with treadmill-based stress tests. Furthermore, most patients said they were willing to pay out of pocket for the test and would have requested it if their physicians had not ordered it. One week after testing and receiving the results, patients' perceived life expectancy increased, their anxiety about their symptoms decreased, and their uncertainty about their illness also decreased. For many patients, their symptoms were less bothersome after testing than before.	No → not about coma/ withdrawal of life support, nor relevant method for eliciting preferences
Needle, J. S., Mularski, R. A., Nguyen, T., & Fromme, E. K. (2012).	Influence of personal preferences for life-sustaining treatment on medical decision making among pediatric intensivists	Cross- sectional national anonymous mail survey; using Personal Preference Score	To examine the relationship between personal preferences for life-sustaining treatment and medical decision making among pediatric intensivists.	Pediatric intensivists are more likely to offer and recommend treatment when it is similar to their own preferences for care at the end of life. Personal preferences may influence how and what physicians offer and recommend to families of critically ill children.	Yes (not about coma)
Norman, R., Cronin, P., & Viney, R. (2013).	A pilot discrete choice experiment to explore preferences for EQ-5D-5L health states	Pilot discrete choice experiment	To test the plausibility and acceptability of estimating an Australian algorithm for the newly developed five-level version of the EQ-5D using a DCE	The study has demonstrated that a choice experiment approach, which has been used to estimate QALY weights for the EQ-5D-3L, is also feasible for a larger multi-attribute instrument that covers more health states.	No → the study is to general, not about coma or withdrawal of life support.
Patrick, D. L., Starks, H. E., Cain, K. C., Uhlmann, R. F., & Pearlman, R. A. (1994).	Measuring Preferences for Health States Worse than Death	Case-control study. Interview, preference elicitation methods: rank order, category scaling, time trade-off and standard gamble	The specific aims of this inquiry were 1) to adapt existing measurement methods and evaluate them for the ability to identify and quantify preferences for health states near to or worse than death; and 2) to evaluate the cognitive burdens and respondents' levels of understanding of these preference- measurement methods for states	The study indicates that current methods for eliciting health-state preferences can be adapted successfully for quantitative assessment of states considered worse than death. All four methods evaluated in this study were able to distinguish preferences for health states better than or worse than death at the group level. For individuals, however, significant inconsistencies in preferences occurred when comparing judgments obtained using different methods. The majority of respondents considered the health state describing severe constant pain better than death on all four methods. For the health state describing dementia, fewer respondents assigned a value better than death. Only the health state describing coma was rated	Yes

			considered worse than death.	as equal to or worse than death by a majority of respondents.	
Singer, P. A., et al. (1995).	Life-sustaining treatment preferences of hemodialysis patients: implications for advance directives				No → full text not found
Sjokvist, P., Berggren, L., Svantesson, M., & Nilstun, T. (1999).	Should the ventilator be withdrawn? Attitudes of the general public, nurses and physicians	Survey for general public and ICU personnel. Not clear which preference elicitation method. Two hypothetical clinical scenarios in which the respondent is asked whether treatment should be withdrawn, answers used a 5-point Likert scale ranging from 'yes, absolutely' to 'no, absolutely not'.	To examine the attitudes of the general public in Sweden in respect of the use of ventilator treatment for severely ill patients, and compare these attitudes with those of intensive care professionals	a majority or near majority of all respondents were willing to discontinue ventilator treatment both in the case of a conscious cancer patient and in the case of a comatose patient. However, the magnitude of the difference in attitudes between the general public and the ICU professionals varied between the scenarios. In the case of the patient who had been comatose for a month following a head injury the public were more prone to continue ventilator treatment than were the health care professionals. In contrast, there was only a moderate difference in attitudes of the public and the professionals towards continued use of ventilator treatment when the respondents were asked to imagine themselves as a patient with severe cancer. The willingness of intensive care personnel to discontinue ventilator treatment is more pronounced than that of the public when faced with identical scenarios. The ICU professionals also emphasize long term prognosis and dementia as determinants for life support as compared with the general public. Consequently, physicians and nurses cannot assume that patients and their family members share their opinions about the use of life support. It is therefore important to carefully explore the patients view, either directly or through the family, before deciding about whether to withdraw life support. Respondents attitudes towards the use of ventilator treatment were correlated with having discussed their own preferences for life support. This indicates the importance of such discussions. Health care professionals have a special obligation to encourage individuals to discuss their preferences for life support.	Yes
Trafford Crump, R., & Llewellyn- Thomas, H.	Characterizing the public's preferential attitudes toward end-of- life care options: A role for the threshold technique?	During personal interviews, participants considered four EOL scenarios, each presenting a choice between a less intense and more intense care option.	To assess the Threshold Technique's (TT) feasibility in community-wide surveys of U.S. Medicare beneficiaries' preferences for end- of-life (EOL) care options.	84 percent of the respondents favored no respirator over the use of a respirator to extend their life. Given the potential advantages of using the TT in wide-scale surveys to elicit strength-of- preference scores for care at the end of life, further methodological research is needed to specify the kind of TT designs that would work best in this context. In particular, these methodological investigations should focus on identifying which care-relevant attributes are most salient and meaningful to work with in the TT. This understanding could help investigators interested in collecting empirical data about the public's preferential attitudes toward health care delivered at the end of life.	No → More about methods, also not connected to coma / (active) withdrawal life support
Yepes- Núñez, J. J.,	Preferences of states of health				No → Not in English

i.						
	& García, H. I.	and measurements of utility				
	Flynn, T.N., Huynh, E., & Corke, C. (2015).	BWS object case application: attitudes towards end- of-life care	DCE, case 1 BWS	To elicit preferences for end-of-life care scenarios and to elicit attitudes in order to understand whether there was broad agreement between attitudes and preferences.	Imagining living with pre-existing dementia was associated with lower acceptance rates generally, and experiencing irreversible coma caused a large number of treatment rejections. The older age group consistently rejected treatment more often than the younger age group. There were four groups in the population: (1) strongly opposed to any intervention that prolongs life in poor health or quality of life state, (2) in favor of medical interventions no matter what the chance of success or degree of impairments, (3) mildly anti treatment, but willing to trade-off aspects of treatment and outcomes, (4) very weak preferences with no discernible patterns. On average the sample agreed that quality of life should take precedence over life extension and believe that their view should not be overridden. Attitudes towards treatment can in general usefully predict treatment preferences among those with anti-treatment attitudes.	Yes
	Flynn, T.N., & Huynh, E. (2015).	BWS profile case application: preferences for quality of life in Australia	DCE, case 2 BWS	To produce population average tariffs for the ICECAP-O instrument and to investigate heterogeneity in preferences for wellbeing and ascertain the extent to which any differences were related to current well-being.	Low levels of social empowerment are associated with worries about the future, as is a lack of independence. Increased age is associated with a switch towards a preference for independence and away from relationships. Por health is associated with a switch towards a focus on independence and worries about the future and away from relationships and enjoyment. Extreme worry about the future is a particularly insidious impairment, since people experiencing it cannot easily be compensated via other attributes; they focus all the more on the effect that attribute has on their capability.	No → not about coma, nor about withdrawal of life support.
	Kuehlmeyer, K., Palmour, N., Riopelle, R.J., Bernat, J.L., Jox, R.J., & Racine, E. (2014).	Physicians' attitudes toward medical and ethical challenges for patients in the vegetative state: comparing Canadian and German perspectives in a vignette survey	Survey, case vignette	To compare the understanding of and attitudes towards vegetative state of German and Canadian specialty physicians.	The Canadian participants were more likely to favor limiting life sustaining treatment (LST) than the German participants The willingness to limit LST in specific circumstances (e.g., patient's will is opposed to LST; patient suffers from fatal disease; surrogate refuses consent to LST; no chance of recovery of consciousness; no improvement > 1 year) varied considerably. However, there was a trend: Canadian participants were more likely than German participants to favor the limitation of LST in almost all circumstances. Quality of life of VS patients was rated by 33% as 'no quality of life' and 28% as 'extreme low'. 14% was not able to rate the quality of life. Striking similarities were found in the participants' medical knowledge with high diagnostic accuracy rates. However, important differences were found in the attribution of capabilities to the patients and attitudes toward limiting LST. Different hypotheses could explain this difference such as societal and medical practice contexts (e.g., distribution of resources for the long-term-care for these patients), religiosity, and underlying moral theories.	Yes

B.3 Examination of preference elicitation methods

Research question 1:

AIM: To identify preferences for the receival of prognostic information as a close family member of patient in post-anoxic coma. With a focus on trade-offs between probability of receiving a prognosis, timing of the prognosis and the accuracy of prognosis.

Method	Used for	Advantages considering the aim	Disadvantages considering the aim
DCE	Used to elicit preferences for end-of-life care	 Can simulate the complex situations for prognosis of post-anoxic coma as in real life It can show the explicit trade-offs we are looking for in this study between timing of test result, accuracy of a test and probability of receiving a prognosis 	 Respondent fatigue, especially since the length of the questionnaire is substantial due to the multiple research questions Much information can be retrieved from responses, but analysis is complex and results are hard to interpret. Especially since the researcher has almost no experience with this method
BWS case 1 (object case)	Used to elicit attitudes towards end-of-life care	 Can show explicit trade-offs we are looking for Might be an easier choice- task than a DCE, although this is questioned in some studies 	 Cannot estimate the overall utility of scenarios Asking for the best and worst attribute provides no information about the attractiveness of a situation itself Only multiple objects which are compared. No levels within these objects. Low theoretical precision regarding the weights of objects
Ranking	Used to distinguish preferences for health states better or worse than death and to identify attributes of life- sustaining treatment important to physicians	 Can show explicit trade-offs Allows respondent to rank all attributes Simple data-analysis 	 Attributes have no different levels Dependent on number of attributes, but could be difficult to complete for respondent if many attributes More abstract exercise, not easy to relate to real life
Rating	Used to elicit the preferences for withdrawing life support and health states better or worse than death	 Strength of preference clearly expressed Simple exercise for respondents 	 No explicit trade-offs Scale can be interpreted in different ways by different respondents
Standard gamble	Used to distinguish preferences for health states better or worse than death	• Way to incorporate uncertainty	• No explicit trade-offs
Time trade off	Used to distinguish preferences for health states better or worse than death		• No explicit trade-offs
Case vignettes	Used to compare the understanding of physicians of the vegetative state and attitudes of physicians towards the vegetative state		More like a case-studyLess known about

Research question 2:

AIM: To identify the minimally required quality of test before withdrawing life support.

Method	Used for	Advantages considering the aim	Disadvantages considering the aim
DCE	Used to elicit preferences for end-of-life care	 Can simulate the complex situations for the withdrawal of life support in patients in post-anoxic coma as in real life It can show the explicit trade-offs we are looking for in this study between the quality of a test and the choice to withdraw life support 	 Respondent fatigue, especially since the length of the questionnaire is substantial due to the multiple research questions Much information can be retrieved from responses, but analysis is complex, and results are hard to interpret. Especially since the researcher has almost no experience with this method
BWS case 1 (object case)	Used to elicit attitudes towards end-of-life care	 Can show explicit trade- offs we are looking for Might be an easier choice- task than a DCE, although this is questioned in some studies 	 Cannot estimate the overall utility of scenarios Asking for the best and worst attribute provides no information about the attractiveness of a situation itself Only multiple objects which are compared. No levels within these objects. Low theoretical precision regarding the weights of objects
Ranking	Used to distinguish preferences for health states better or worse than death and to identify attributes of life-sustaining treatment important to physicians	 Can show explicit trade- offs Allows respondent to rank all attributes Simple data-analysis 	 Attributes have no different levels Dependent on number of attributes, but could be difficult to complete for respondent if many attributes More abstract exercise, not easy to relate to real life
Rating	Used to elicit the preferences for withdrawing life support and health states better or worse than death	 Strength of preference clearly expressed Simple exercise for respondents 	 No explicit trade-offs Scale can be interpreted in different ways by different respondents
Standard gamble	Used to distinguish preferences for health states better or worse than death	• Way to incorporate uncertainty	• No explicit trade-offs
Time trade off	Used to distinguish preferences for health states better or worse than death		• No explicit trade-offs
Case vignettes	Used to compare the understanding of physicians of the vegetative state and attitudes of physicians towards the vegetative state		More like a case-studyLess known about

Research question 3:

AIM: To identify preferences for the involvement in the decision to withdraw life support as a close family member of a patient in post-anoxic coma

Method	Used for	Advantages considering the aim	Disadvantages considering the aim
DCE	Used to elicit preferences for end-of-life care	• Can simulate the complex situations for the withdrawal of life support in patients in post-anoxic coma as in real life	 Respondent fatigue, especially since the length of the questionnaire is substantial due to the multiple research questions Much information can be retrieved from responses, but analysis is complex, and results are hard to interpret. Especially since the researcher has almost no experience with this method
BWS case 1 (object case)	Used to elicit attitudes towards end-of-life care	 Might be an easier choice-task than a DCE, although this is questioned in some studies Instead of attitudes towards end-of-life care, attitudes towards involvement 	 Cannot estimate the overall utility of scenarios Asking for the best and worst attribute provides no information about the attractiveness of a situation itself Only multiple objects which are compared. No levels within these objects. Low theoretical precision regarding the weights of objects
Ranking	Used to distinguish preferences for health states better or worse than death and to identify attributes of life-sustaining treatment important to physicians	 Allows respondent to rank all attributes Simple data-analysis 	 Attributes have no different levels Dependent on number of attributes, but could be difficult to complete for respondent if many attributes More abstract exercise, not easy to relate to real life
Rating	Used to elicit the preferences for withdrawing life support and health states better or worse than death	 Strength of preference clearly expressed Simple exercise for respondents 	• Scale can be interpreted in different ways by different respondents
Standard gamble	Used to distinguish preferences for health states better or worse than death		• No real gamble in involvement
Time trade off	Used to distinguish preferences for health states better or worse than death		• No real time trade off in the preferences for involvement in decision making
Case vignettes	Used to compare the understanding of physicians of the vegetative state and attitudes of physicians towards the vegetative state		More like a case-studyLess known about

Research question 4:

AIM: To determine the	public perce	ption of a life w	orth living after	post-anoxic coma.
				P

Method	Used for	Advantages considering the aim	Disadvantages considering the aim
DCE	Used to elicit preferences for end-of-life care	• Can simulate the complex situations for different health states after post-anoxic coma as in real life	 Respondent fatigue, especially since the length of the questionnaire is substantial due to the multiple research questions Much information can be retrieved from responses, but analysis is complex and results are hard to interpret. Especially since the researcher has almost no experience with this method
BWS case 1 (object case)	Used to elicit attitudes towards end-of-life care	 Might be an easier choice-task than a DCE, although this is questioned in some studies 	 Cannot estimate the overall utility of scenarios Asking for the best and worst attribute provides no information about the attractiveness of a situation itself Only multiple objects which are compared. No levels within these objects. Low theoretical precision regarding the weights of objects
Ranking	Used to distinguish preferences for health states better or worse than death and to identify attributes of life-sustaining treatment important to physicians	 Allows respondent to rank all attributes Simple data-analysis Different health states can be ranked from best to worse 	 Attributes have no different levels Dependent on number of attributes, but could be difficult to complete for respondent if many attributes More abstract exercise, not easy to relate to real life Not clear what is worth living and what not
Rating	Used to elicit the preferences for withdrawing life support and health states better or worse than death	 Strength of preference clearly expressed Simple exercise for respondents Aim of studies using this method comparable to aim of current research question 	• Scale can be interpreted in different ways by different respondents
Standard gamble	Used to distinguish preferences for health states better or worse than death	 Way to incorporate uncertainty Aim of studies using this method comparable to aim of current research question 	 More difficult for respondent to complete (compared to rating), since probabilities are involved
Time trade off	Used to distinguish preferences for health states better or worse than death		 More difficult for respondent to complete compared to rating Not sure whether it can be use proper in asking when life support should be withdrawn
Case vignettes	Used to compare the understanding of physicians of the vegetative state and attitudes of physicians towards the vegetative state		More like a case-studyLess known about

Appendix C: Report 'think aloud' pilot-test

In de pilottest 'think out loud' zijn tien respondenten benaderd in de omgeving van de onderzoeker met de vraag of ze de vragenlijst wilden test. Bij het vragen van de respondenten is gelet op leeftijd geslacht en opleidingsniveau om zo de vragenlijst in verschillende groepen te testen.

Descriptives

De gemiddelde leeftijd van de respondenten was 35 jaar (MIN=19; MAX=54). De verdeling man/vrouw in de steekproef was 5 om 5. Er was 1 respondent laag opgeleid, 4 respondenten waren middelbaar opgeleid en 5 respondenten waren hoogopgeleid. 8 van de 10 respondent hadden een levenspartner, 2 respondenten hadden geen levenspartner. 4 van de respondenten had kinderen, 6 van de respondenten had geen kinderen. Wat betreft religie waren 8 respondent christelijk, 2 respondenten gaven aan geen religie te hebben. Geen van de respondenten had ervaring met een post-anoxisch coma.

Samenvatting per onderdeel van de vragenlijst

Hieronder wordt per onderdeel van de vragenlijst kort samengevat, wat de algemene observaties waren van de onderzoeker en opmerkingen/vragen door respondenten.

Inleiding

Bij de inleiding werden over het algemeen weinig vragen en opmerkingen geplaatst door de respondenten. De inleiding leek te worden ervaren als duidelijk en goed leesbaar. Tevens werd de inleiding als interessant ervaren, waardoor de lengte werd gerelativeerd.

Belangrijkste punten die naar voren kwamen tijdens het lezen van de inleiding waren:

- 1. Wat gebeurt en na een post-anoxisch coma (dus na twee weken)?
- 2. Door wie wordt de vegetatieve toestand en zware handicap als slechte uitkomst gezien?
- 3. De zin 'Deze twee testen die op dit moment beschikbaar zijn, geven maar bij 2 op de 10 (20%) van de patiënten die uiteindelijk een slechte uitkomst hebben, daadwerkelijk een slechte uitkomst aan' is een moeilijke zin.
- 4. Wat betekent post-anoxisch?
- 5. Wat kan de EEG identificeren in vergelijking met SSEP en pupilreflex die 20% kan identificeren.
- 6. Is het niet post-anoxisch<u>e</u>?

DCE

Over het algemeen snapten de respondenten wat ze moesten doen bij de DCE en werden er overwegingen gemaakt in de keuze voor een scenario zoals verwacht. Respondenten wogen de tijd af tegen de zekerheid van de test, waarbij soms verrassende inzichten werden opgedaan door de onderzoeker. Zo was er één respondent die het liefst zo lang mogelijk wachtte op een testuitslag en het zelf wou aankijken, waarbij de zekerheid van de test niet van belang was. Deze respondent koos dan ook voor het niet-dominante scenario. Ook andere respondenten noemden soms dat ze het liever niet zo snel zouden willen weten, naast dat ze zekerheid ook heel belangrijk vinden. We kunnen dus niet de aanname maken dat zo snel mogelijk informatie ontvangen een dominante keuze is over langer wachten. Door andere respondenten werd de vraag met het dominante scenario vaak als strikvraag ervaren en leidde het in sommige gevallen tot verwarring. Ook de situatie met meer testen en minder zekerheid werd soms als onlogisch ervaren.

Bij de slechte uitkomst werd ook het type test daadwerkelijk meegenomen in de overweging van respondenten. Sommige respondenten kozen dan ook liever de situatie met de EEG terwijl de aangegeven betrouwbaarheid in deze situatie lager was dan in de andere situatie. De redenatie van sommige respondenten was dat ze liever extra testen hadden, terwijl anderen noemden dat ze in de inleiding hadden gelezen dat de EEG betrouwbaarder was.

Sommige respondenten noemen ook de kosten in hun redenering en dat ze dat missen in het scenario. Desondanks konden ze wel een keuze maken.

"Stel, een direct familielid ..." wat aan het begin staat van elke DCE vraag in het persoonlijk perspectief wordt na een aantal vragen niet meer gelezen. Echter wordt wel aangegeven dat het niet storend is dat het er staat. Een aantal respondenten ervaarden het ook als fijn dat het er stond.

Wat betreft de vragen vanuit het maatschappelijk perspectief, is het de vraag of hier onderscheidt in moet worden gemaakt. Vier van de vijf respondenten noemden nadrukkelijk dat ze de vragen betrokken op een direct familielid. De redeneringen achter de keuzes van respondenten verschilden ook niet voor het maatschappelijk en persoonlijk perspectief.

De aanvullende vraag of de respondent ook daadwerkelijk de informatie in de aangegeven situatie zou willen ontvangen werd door alle respondenten beantwoord met "ja, natuurlijk". Sommige respondenten gaven aan dit een rare vraag te vinden, omdat het volgens hen vanzelf sprak. Een aantal respondenten raakten gefrustreerd doordat ze het logisch vonden en het wel elke keer weer moesten beantwoorden. Eén van de respondenten vroeg of mensen wel een voorkeur zouden hebben voor een situatie als ze het niet willen weten.

De vraag over het ontvangen van informatie, als de voorspelde uitkomst achteraf anders blijkt te zijn, was voor sommige respondenten verwarrend. Na twee keer lezen, snapten de respondenten wel wat er wel bedoeld werd. Ook bij deze vraag vonden de respondenten het antwoord vanzelfsprekend, want "het is toch logisch dat je die informatie wil ontvangen, ook als het later anders uitpakt. Als de informatie maar genuanceerd wordt gegeven en inderdaad wordt gezegd dat er een kans is dat het ook anders is".

De vraag over het stopzetten van de levensverlengende behandeling wordt gesteld met als doel te achterhalen hoe zeker een test moet zijn voordat de levensverlengende behandeling mag worden stopgezet. In de pilot test kwam naar voren dat dit niet het enige is wat respondenten meenemen om deze vraag te beantwoorden. Een aantal respondent noemden (zoals verwacht) dat ze op basis van de zekerheid wel of niet de levensverlengende behandeling wilden stopzetten. Ook werd de overweging genoemd dat zoveel procent niet onterecht mocht komen te overlijden. Echter namen een aantal respondenten ook de tijd en het aantal testen mee in de overweging. Hierbij werd soms gezegd bij bijvoorbeeld een situatie met 12 uur en 98% zekerheid dat ze niet wilden stopzetten, omdat ze 12 uur te snel vonden om die beslissing te maken. Twee respondenten gaven ook aan graag informatie te willen hebben over wanneer basisfuncties terugkeren en hoelang familie heeft om de keuze te maken om de levensverlengende behandeling stop te zetten. Deze info zorgt dat ze de vraag anders willen beantwoorden.

Huidige vs. nieuwe situatie

Over het algemeen gaf deze informatie met bijbehorende vraag verwarring onder de respondenten in plaats van dat het verduidelijkend was. 7 van de 10 respondenten snapten de informatie niet zonder nadere uitleg van de onderzoeker. De conclusie dat in de nieuwe situatie een onzekere prognose slechter nieuws is, werd door bijna geen van de respondenten begrepen. Reden was dat de meesten de verschillende getallen en percentages niet goed begrepen. 2 snapten niet waarom het slechter nieuws was. "Er is toch minder onzekerheid? En onzeker is onzeker, dan maakt die kans niet uit."

De alinea waarin werd verteld dat bij beide situaties de uiteindelijke uitkomsten hetzelfde zijn, leidde ook tot onbegrip. Sommige respondenten snapten daardoor het stuk erboven ineens niet meer. Anderen vroegen zich af waarom de nieuwe situatie dan een verbetering zou zijn. Eén van de respondenten opperde om deze alinea aan het begin van het stuk informatie te plakken. Daarnaast werd het door sommige respondenten ook als verwarrend gezien dat het ineens over een maand gaat, terwijl voor de rest het over 2 weken gaat.

Verder werden nog de volgende vragen gesteld over de huidige en nieuwe situatie:

- Is de nieuwe situatie alleen de EEG of de drie testen samen?
- Hoe zeker is die 20% slechte uitkomst/25% slechte uitkomst/25% goede uitkomst?

Betrokkenheid

De meerkeuze vragen met betrekking tot de gewenste betrokkenheid werden over het algemeen vlot ingevuld en er was geen verwarring over wat er bedoeld werd met de vragen. Er waren dan ook weinig opmerkingen en vragen van de respondenten. De vragen vanuit het maatschappelijk perspectief betrokken de respondenten ook weer op hun directe familie ("wat zou ik willen als …"). Een opvallende observatie was, dat respondenten twijfelden of ze optie drie moesten kiezen bij de vraag wie de keuze moet maken om de behandeling stop te zetten, omdat ze gelijk bedachten dat de familie en het medisch team ook niet eens konden worden. Als de onderzoeker dan noemde dat dit een vervolgvraag was, dan kozen ze gelijk voor optie drie. Misschien moet in de antwoordoptie worden verwerkt dat er een vervolgvraag is.

De vragen/opmerkingen die verder werden genoemd zijn:

- De wetvraag bevat een erg lange zin. Wellicht opdelen in twee zinnen.
- Wat is medisch onwenselijk/zinloos?
- Eén van de respondenten overweegt ook onenigheid binnen de familie in het beantwoorden van vraag 15 en vraag 16.

Gezondheidstoestanden

De vragen over de gezondheidstoestanden werden over het algemeen goed ontvangen door de respondenten en er waren dan ook weinig vragen. Echter kon één respondent de vragen niet invullen, ook na uitleg wat de bedoeling was, kon de respondent de vragen niet beantwoorden. De respondent had wel begrepen wat de bedoeling van de vraag was, maar het was voor de respondent niet relevant wat de verwachte uitkomst was om de keuze te maken om de behandeling stop te zetten. Het ging bij de respondent erom hoe de patiënt op het moment van keuze eraan toe was en niet wat later als uitkomst wordt verwacht.

Daarnaast was het voor het maatschappelijk perspectief verwarrend dat het ineens over de voortzetting van de behandeling gaat, terwijl in de voorgaande vragen het gaat over het stopzetten van de behandeling. Ook zouden respondenten het fijn vinden als de gezondheidstoestand in de toekomende tijd zou worden geformuleerd (omdat het de <u>verwachte</u> uitkomst is) en de belangrijkste punten worden onderstreept.

De meeste respondenten vonden het ook vanzelfsprekend om in leven te blijven/dat de patiënt in leven werd gehouden in de laatste twee gezondheidstoestanden. Hierdoor moeten we ons wellicht afvragen of het werkelijk zinvol is om deze uit te vragen in het kader van het project. Een aantal respondenten vroegen zich ook in eerste instantie af of de laatste twee gezondheidstoestanden wel van elkaar verschilden, na een tweede keer lezen, zagen ze het verschil.

Wat betreft de intro van de gezondheidstoestanden voor het maatschappelijk perspectief werd door twee respondenten benoemd dat ze algemeen patiënten prefereerden boven het specifiek noemen van een groep patiënten (bv. Kinderen met astma).

Twee respondenten van het maatschappelijk perspectief gaven aan de vragen hetzelfde te beantwoorden als werd gevraagd of ze zelf in die gezondheidstoestanden wilden blijven leven. De andere drie respondenten is dit niet gevraagd. Dit roept het dilemma op of het relevant is om onderscheid te maken tussen een persoonlijk en maatschappelijk perspectief.

Conclusies

Overall kan worden geconcludeerd dat de pilottest een positieve bevestiging geeft van de vragenlijst, wel zullen een aantal punten moeten worden aangepast om de vragenlijst te optimaliseren.

- Inleiding is goed, op wat kleine aanpassingen na.
- DCE meet wat de DCE moet meten.
- Aanvullende vraag over ontvangen van informatie wordt als overbodig gezien.
- Vraag over stopzetten van levensverlengende behandeling meet niet wat de vraag zou moeten meten. Deze moet worden aangepast en eventueel opnieuw worden getest.
- De uitleg over de huidige en nieuwe situatie leidt tot veel verwarring. We moeten ons afvragen of dit nodig is om erin te benoemen of dat we het er misschien beter uit kunnen laten. Als we het erin willen hebben, moet het drastisch worden aangepast. Dit zou ook opnieuw moeten worden getest, om te kijken of het dan wel duidelijk is.
- Vragen over de betrokkenheid zijn goed en duidelijk. Er kunnen nog wat kleine puntjes worden aangepast, maar overall is het goed.
- Vragen over gezondheidstoestanden werden ook goed ontvangen. Gezondheidstoestanden moeten nog wel in de toekomende tijd worden geformuleerd en hoofdzaken moeten worden onderstreept.
- Over het algemeen moet een overweging worden gemaakt of het daadwerkelijk zinvol is om een onderscheid te maken tussen een persoonlijk en maatschappelijk perspectief.

Besluiten naar aanleiding van de pilottest (bespreking 6 mei)

Dat er een aantal spelfouten moet worden verbeterd en sommige zinnen moeten worden herschreven moge duidelijk zijn en er zal verder niet worden uitgelegd welke woorden/zinnen het hierbij precies om gaat en waarom dit moet gebeuren. Daarnaast wordt ook enkele informatie in de inleiding toegevoegd op verzoek van respondenten, hier wordt ook geen nadere toelichting op gegeven.

In onderstaande alinea's zijn de 'grotere' besluiten beschreven en is beargumenteerd waarom. Het gaat hierbij om aanpassingen in de DCE en de huidige vs. nieuwe situatie. Wat betreft de betrokkenheid en de gezondheidstoestanden zijn er geen drastische veranderingen nodig. Allereerst wordt nog een algemeen besluit genoemd met betrekking tot de twee perspectieven van de vragenlijst.

Er is besloten om de vragenlijst enkel te maken voor het persoonlijk perspectief en geen scheiding te maken tussen maatschappelijk en persoonlijk perspectief. Deze keuze is gebaseerd op de observatie dat respondenten die het maatschappelijk perspectief invullen de vragen automatisch betrekken op hun directe familie. Daarnaast kan het argument worden gevoerd dat alle meningen van individuen gezamenlijk de mening is van de maatschappij. Wel moet worden overwogen of er bij de gezondheidstoestanden nog moet worden benoemd dat er een beperkt budget is in de gezondheidszorg en geld maar één keer kan worden uitgegeven. Aan de ene kant kan dit van invloed zijn op het besluit van de respondent of hij in een bepaalde gezondheidstoestand wil blijven leven (voor mij persoonlijk wel, maar ik ben geen gemiddelde denker), aan de andere kant zou dit respondenten ook voor het hoofd kunnen stoten. Dit zal worden besproken op de eerstvolgende meeting met de projectgroep.

Op basis hiervan zal een besluit worden genomen wat betreft het al dan niet noemen van de kosten bij de gezondheidstoestanden. \rightarrow Naar aanleiding van de meeting met de projectgroep is besloten om de kosten niet te benoemen voorafgaand aan de gezondheidstoestanden. Wel werd benadrukt dat het van belang was om iets met deze vraag te doen. Daarom is besloten om aan het einde van de vragenlijst de kosten te benoemen en de respondent te vragen of hij/zij rekening heeft gehouden met de kosten in zijn antwoorden. Zo niet, zou de respondent dan de vragen anders hebben beantwoord. Dit kan worden gesplitst voor de DCE en de gezondheidstoestanden. Als laatste vragen of de respondent het gerechtvaardigd vindt om na twee weken de behandeling stop te zetten vanuit een kostenperspectief. Deze vragen zijn simpele ja/nee vragen.

Wat betreft de DCE is besloten ook een aantal aanpassingen te doen naar aanleiding van de pilottest. Allereerst wordt de vraag of de respondent ook daadwerkelijk de informatie wil ontvangen achterwege gelaten. In plaats hiervan wordt naast de twee gepresenteerde situaties een opt-out gepresenteerd met 'ik wil geen informatie ontvangen'. Deze aanpassing wordt gedaan op basis van meerdere observaties. Ten eerste, kan men zich afvragen of respondenten die geen informatie wel ontvangen, wel een voorkeur hebben voor één van de situaties. Er wordt aangenomen dat dit inderdaad niet het geval is. Ten tweede, werd de observatie gedaan dat respondenten het een vanzelfsprekende vraag vonden. "Natuurlijk wil ik die informatie ontvangen". Na enkele vragen begonnen respondenten zich dan ook te ergeren dat elke keer deze vraag werd gesteld. Om deze twee redenen is besloten de vraag achterwege te laten en de optie 'geen informatie ontvangen' toe te voegen voor degenen die inderdaad geen informatie willen ontvangen. Bij de optie 'geen informatie ontvangen', wordt wel gevraagd waarom de respondent geen informatie wil ontvangen. \rightarrow Projectgroep eens, vonden het een mooie oplossing. \rightarrow Verder is later ook nog besloten een extra experiment toe te voegen waarin de sensitiviteit als attribuut is meegenomen in combinatie met de accuracy van zowel slechte als goede prognose.

De vraag waarbij wordt gesteld dat de daadwerkelijke uitkomst achteraf anders blijkt dan de voorspelde uitkomst en of de respondent dan ook de informatie wel had willen ontvangen, werd ook door respondenten gezien als vanzelfsprekend. Daarom is besloten om deze vraag ook achterwege te laten bij de DCE. Met de projectgroep zal de eerstvolgende bespreking worden overlegd of zij deze vraag wel willen behouden. Mocht dit het geval zijn, dan zal deze vraag worden losgetrokken van de DCE. → Tijdens de bespreking met de projectgroep werd in eerste instantie gezegd dat zo'n soort vraag wel moest worden gesteld. Na wat discussie heen en weer, is toch tot de conclusie gekomen dat het niet van belang is voor het maatschappelijk perspectief, omdat ervan wordt uit gegaan dat hierin vooral mensen zitten die geen ervaring hebben met coma en daarom automatisch zeggen, natuurlijk wil ik die info ontvangen. In de interviews van Mayli kwam naar voren dat dit verandert als mensen het pas echt meemaken.

Uit de pilottest bleek dat de vraag over het stopzetten van de levensverlengende behandeling in de DCE niet meet wat de vraag zou moeten meten. Daarom wordt besloten om deze vraag ook achterwege te laten. Wegens het tijdsbestek van de masterthesis wordt voor de pilottest in de grotere sample deze vraag ook niet op een andere manier toegevoegd. Dit betekent dat onderzoeksvraag 2 niet zal kunnen worden beantwoord en welke vraag we dan moeten stellen in de vragenlijst, zodat in de uiteindelijke sample van de Nederlandse maatschappij deze vraag wel kan worden meegenomen en uiteindelijk onderzoeksvraag 2 kan worden beantwoord. De twee opties waar nu aan wordt gedacht zijn (1) direct uitvragen of (2) meerdere situaties presenteren met verschillende zekerheden, waarbij wordt gevraagd of de levensverlengende behandeling mag worden stopgezet. Belangrijk bij beide opties is dat de respondent de benodigde informatie wordt gegeven om de keuze te kunnen maken. Hierbij moet ook worden gedacht aan informatie over wanneer basisfuncties terug keren en op wat voor termijn zo'n besluit moet worden genomen. Dit miste in de huidige vragenlijst. \rightarrow Wel van belang om mee te nemen voor de landelijke sample, om twee redenen. (1) Interessante vraag om te weten, wellicht kan daardoor specificiteit worden aangepast. (2) De testen lijken een specificiteit van 100% te hebben, maar de praktijk wijst uit dat dit niet het geval is. Dit komt door de selffulfilling prophecy. Daarom wel belangrijk om te weten. Hoe dit meenemen de komende weken goed over nadenken. \rightarrow Uiteindelijk toch als directe vraag meegenomen in de extensive pilot test.

Naar aanleiding van de pilottest is besloten om de vraag over de huidige situatie versus de nieuwe situatie achterwege te laten. Deze vraag was te ingewikkeld voor bijna alle respondenten en heeft geen toegevoegde waarde voor het beantwoorden van de onderzoeksvragen. De sensitiviteit van de EEG zal in plaats daarvan worden benoemd in de inleiding. Aan het einde van de DCE zal nog wel kort worden beschreven voor de respondent hoe de klinische praktijk nu is met de testen en hoe de EEG daaraan bijdraagt. Dus welke timing van testresultaten daadwerkelijk het geval is en welke zekerheid, zodat de respondent uiteindelijk wel weet hoe het in werkelijkheid zit. \rightarrow Projectgroep was het hiermee eens. Met Jeannette overleggen hoe het wel te formuleren. Mayli noemde dat het misschien toch niet relevant meer is om te benoemen voor de respondent. \rightarrow Uiteindelijk niet meer bijgevoegd, om dat het niet als relevant werd gezien.

Verder is besloten in overleg met de projectgroep om niet alle acht gezondheidstoestanden uit te vragen, maar enkel de eerste vier, omdat die gaan over CPC 3. Voor CPC 2 mag duidelijk zijn dat mensen in deze gezondheidstoestand willen leven.

Actiepunten

- 1. Inleiding
 - a. Toevoegen wat er gebeurt na twee weken coma
 - b. Slechte uitkomst vanuit medisch perspectief toevoegen.
 - c. Kijken of zin met sensitiviteit van SSEP en pupilreflextest kan worden ingekort.
 - d. De sensitiviteit van de EEG in de inleiding benoemen (huidige vs. nieuwe situatie achterwege laten in vragenlijst).
 - e. Zekerheid van de EEG achterwege laten (immers is zelfde als SSEP/pupilreflex)
 - f. Post-anoxisch<u>e</u>??
- 2. DCE
 - a. Efficiënt design maken voor DCE
 - b. Vraag over informatie ontvangen \rightarrow achterwege laten. Opt-out toevoegen met 'geen informatie ontvangen
 - c. Vraag over als achteraf uitkomst anders dan voorspelt, dan informatie ontvangen \rightarrow achterwege laten
 - d. Vraag over stopzetten levensverlengende behandeling aanpassen → achterweg laten, directe vraag voor formuleren
 - i. Zodat het gaat over zekerheid en tijd niet mee wordt genomen.
 - ii. Lostrekken van DCE
 - iii. Info toevoegen over terugkeer basisfuncties en tijdsbestek waarin keuze moet worden gemaakt
- 3. Huidige vs. nieuwe situatie
 - a. Achterwege laten!
 - i. Voor onderzoeksvragen niet per se toegevoegde waarde. Bracht veel verwarring bij respondenten en kost veel tijd. Zonder uitleg niet duidelijk.
 - ii. Korte omschrijvende tekst toevoegen i.p.v. dit, om respondent te informeren hoe het in werkelijkheid zit.
- 4. Betrokkenheid
 - a. Benoemen in optie drie van vraag 15 dat er een vervolgvraag is over als medisch team en familie oneens zijn.
- 5. Gezondheidstoestanden
 - a. Hoofdzaken onderstrepen
 - b. Maatschappelijk perspectief:
 - i. Aanpassen astmatische kinderen in patiënten met betere prognose.
 - ii. Voorgezet \rightarrow stopgezet?
 - iii. Gezondheidstoestanden in toekomende tijd formuleren voor maatschappelijk perspectief
- 6. Algemeen
 - a. Paar spelfouten eruit halen
 - Bespreken of het zinvol is om maatschappelijk perspectief te scheiden van persoonlijk perspectief → Niet zinvol. Alleen persoonlijk perspectief.

Aantekeningen per respondent

Respondent 1:

- Inleiding:
 - Wat komt er na post-anoxisch coma? Wat gebeurt er na twee weken?
 - Doe wie is vegetatieve toestand en zwaar gehandicapt als slechte uitkomst gezien?
 - De zin met 'er zijn 2 testen beschikbaar en 20% kans' \rightarrow moeilijke zin
- DCE:
 - 'Gedane' is te deftig
 - o Als mensen het niet willen weten, hebben ze dan wel een voorkeur voor een scenario?
 - Verwarring na het beantwoorden van meer vragen. De respondent gaat anders denken over z'n voorkeur door de vraag over het stopzetten van de levensverlengende behandeling.
 - "Stel, een direct ..." wordt niet meer gelezen (maar wel fijn dat het er staat, na gevraagd te hebben)
 - Het aantal testen verbindt de respondent aan kosten
 - Gebruikte testen zijn volgens respondent niet relevant voor zijn voorkeur
 - Wat is goed en wat is slecht? Niet bewust van wat precies een slechte uitkomst is, de aanname is dat de medische mening daarin overeenkomt met de persoonlijke mening in het beantwoorden van de vragen.
- Huidige vs. nieuwe situatie
 - Is de nieuwe situatie alleen EEG, of alle drie testen samen?

- Moet niet bij dat 20% een slechte uitkomst heeft, met 100% zekerheid? Respondent mist de zekerheid van de uitkomsten en onzekere prognose
- Betrokkenheid
 - Wetvraag lange zin
 - Gezondheidstoestanden
 - Strepen onder tekst in gezondheidstoestanden

Respondent 2:

- Inleiding:

- Wat is post-anoxisch?
- DCE:
 - Leest niet alles letterlijk meer na aantal vragen, alleen onderstreepte gedeeltes
 - Bij vraag over "als achteraf de uitkomst toch slecht blijkt te zijn" even verwarring → "of ik toch liever de andere situatie had gehad?"
 - Neemt testen mee in overweging. "SSEP en pupilreflex zijn minder betrouwbaar dan de EEG heb ik gelezen in de inleiding"
 - Lastig iets te zeggen over het stopzetten van de behandeling omdat het hypothetisch is. Respondent verwacht anders te antwoorden als hij/zij daadwerkelijk in de situatie zou zitten.
 - EEG weegt zwaarder, omdat die betrouwbaarder zou zijn volgens de inleiding, terwijl de betrouwbaarheid in de aangegeven situatie lager is dan in de situatie zonder EEG.
 - Informatie ontvangen \rightarrow JA NATUURLIJK
 - o "Ik wil het liever ook niet te snel weten. Lijkt me heftig om zo snel na opname al een uitslag te hebben".
- Huidige vs. nieuwe situatie
 - Telt percentages van verschillende onderdelen bij elkaar op, wat niet kan. Misschien toch percentages weglaten?
 - Uitleg nodig over het 'slechter nieuws' als onzekere prognose is nieuwe situatie.
 - Moeilijke vraag huidige vs. nieuwe situatie \rightarrow informatie niet makkelijk te begrijpen.
- Betrokkenheid
 - Wat is medisch onwenselijk/zinloos?
- ACHERAF
 - Vragen over de levensverlengende behandeling toch anders willen invullen geeft de respondent achteraf aan, nadat hij/zij iemand anders de vragen hoorde invullen. Niet over de situatie specifiek nagedacht, bv qua tijd.

Respondent 3:

- Inleiding:
 - Hoe kan ik iets zeggen over de meerwaarde van de EEG? SSEP en pupilreflextest kan 20% identificeren.
 Wat kan EEG? Respondent wil eigenlijk gelijk de onderzoeksvraag beantwoorden. Na uitleg over dat dat later in de vragenlijst komt, zegt de respondent dat hij graag een zin zou willen toevoegen in de inleiding waarin staat dat de info wat EEG kan later in de vragenlijst aan bod komt.
- DCE:
 - o "Ik weet niet of de situatie duurder is ofzo, maar op basis van deze info, deze situatie betrouwbaarder, meer zekerheid wenselijk" → Respondent geeft aan behoefte te hebben aan informatie over kosten
 - "EEG verbetert natuurlijk wel accuratie, maar ik ga toch voor situatie 2, want die geeft meer zekerheid" (vr.8)
 - Omwille v.d. 2% moet je toch niet de levensverlengende behandeling stopzetten als het gaat om je familie.
 Die 2% kans moet je dan nemen.

Respondent 4:

- DCE:
 - Deze situatie → de door u gekozen situatie
 - Respondent neemt tijd mee in de keuze om de levensverlengende behandeling wel/niet stop te zetten. Dus los van hoe zeker de testuitslag is, ook tijd nodig om de keuze te bepalen.
- Huidige vs. nieuwe situatie:
 - Respondent heeft uitleg nodig. Het 'slechter nieuws' snapt de respondent niet
- Betrokkenheid:
 - Respondent overweegt ook onenigheid binnen de familie in de keuze voor een antwoord bij vraag 15/16
- Gezondheidstoestanden:
 - Wel veel info en lange zinnen

• Verschillen de laatste 2 gezondheidstoestanden?

Respondent 5:

- Inleiding:
 - "Moet ik alle info lezen?"
- DCE:
 - Respondent heeft even moeite met de overweging tussen situaties en haalt tekst uit de inleiding erbij. Uiteindelijk begrijpt hij/zij het wel.
 - Bij een slechte uitkomst, noemt de respondent bij 1 van situaties dat hij/zij liever minder zekerheid heeft, want dan kan hij/zij hoop houden.
 - Respondent neemt aantal testen mee in overweging.
- Huidige vs. nieuw situatie:
 - Respondent heeft uitleg nodig.

Respondent 6:

- Inleiding:
 - Post-anoxisch<u>e</u>??
- DCE:
 - Respondent betrekt vragen automatisch op eigen familie en vriend (ook voor vragen over betrokkenheid en gezondheidstoestanden)
 - Huidige vs. nieuwe situatie:
 - Respondent heeft uitleg nodig om het te snappen. Laatste stuk over uiteindelijke uitkomsten is verwarrend
 → misschien juist als eerste noemen.
- Betrokkenheid
 - o Gesprek beginnen, keuze uiteindelijk voor arts, maar respondent zat ook te denken aan verpleegkundige.
- Gezondheidstoestanden
 - o Niet kinderen met astma, maar gewoon patiënten noemen met betere prognose
- Achtergrondkenmerken
 - Vraag naar ervaring. Volgens respondent weten mensen dit niet. Mensen weten hooguit coma (ja/nee). En dan kan de ene respondent denken wel coma, maar of dat post-anoxisch was weet ik niet, dus nee. Terwijl een andere respondent juist ja kan zeggen.

Respondent 7:

- DCE:
 - Op één na laatste zin van de introductie snapt respondent niet goed. 2^{de} zin kost moeite. Respondent vindt het ook raar dat alleen bij slechte uitkomst testen worden genoemd.
 - De respondent ging veel te moeilijk denken over true negatives bij de afweging tussen de situaties \rightarrow De respondent had iets sturing nodig.
 - De respondent snapt de vraag niet over info ontvangen. Het is toch logisch dat mensen die info moeten krijgen?
 - o Situatie met meer testen en minder zekerheid voelde als onlogisch voor de respondent
 - ∨ Voor levensverlengende behandeling stopzetten wil de respondent graag aantal patiënten weten dat per jaar wordt opgenomen en voor die keuze komt te staan. → Absolute getallen
- Huidige vs. nieuwe situatie:
 - o Mist de fout-positieven
 - o "Slechter nieuws? Hoezo is minder onzekerheid slechter nieuws?"
- Gezondheidstoestanden:
 - Niet astmatische kinderen noemen
 - Gezondheidstoestand is in tegenwoordige tijd \rightarrow toekomende tijd van maken
 - Hoezo goed hersteld, maar de patiënt kan niet zelfstandig eten maken?

Respondent 8:

- DCE:
 - o "Ja, NATUURLIJK moet familie info ontvangen"
 - Dominant scenario geeft verwarring
 - Zekerheid is belangrijk voor respondent
 - Achteraf, ook NATUURLIJK wel info, info moet echter wel genuanceerd gegeven worden.
 - Nee, op levensverlengende behandeling stopzetten, 2% mag niet onterecht dood.
 - o Aantal testen is heel belangrijk voor respondent

- Respondent betrekt de vragen automatisch op directe familie.
- Huidige vs. nieuwe situatie
 - o Moest worden uitgelegd was onduidelijk. Snapt het slechter nieuws niet.
 - Voor wie onzeker, blijft onzeker. Waarom maakt die kans dan uit?
- Gezondheidstoestanden:
 - \circ 'Verwachte' onderstrepen.
 - Gezondheidstoestand in toekomende tijd formuleren.
 - \circ Voortgezet? \rightarrow Het ging de hele tijd over stopzetten, nu ineens andersom denken.

Respondent 9:

- DCE:
 - Meer tijd is belangrijk voor respondent in de overweging voor een keuze van één van de situaties. Dan heeft de patiënt tijd om te herstellen. Daardoor ook keuze voor de niet dominante situatie!
 - Respondent betrekt de vragen automatisch op directe familie.
 - De testen worden meegenomen in keuze om levensverlengende behandeling stop te zetten. Evenals tijd. 72 uur is te kort om die keuze te maken.
 - Respondent gaat terug naar de inleiding om te kijken wat de EEG doet, halverwege het beantwoorden van DCE.
 - o EEG zou keuze voor stopzetten levensverlengende behandeling kunnen motiveren voor respondent.
 - De respondent zou willen weten wanneer basisfuncties terug keren en wanneer de keuze moet worden gemaakt om de levensverlengende behandeling stop te zetten
 - Hoelang heeft de familie om over de keuze na te denken om levensverlengende behandeling stop te zetten?
 24 uur? 48 uur?
- Huidige vs. nieuwe situatie:
 - Respondent heeft uitleg nodig om het te snappen
 - o De respondent kan geen keuze maken tussen de situaties, omdat respondent het niet uit maakt.
 - Hoezo ineens na een maand alles gelijk?
 - De informatie is niet relevant voor de respondent
- Gezondheidstoestanden
 - 'Verwachte' onderstrepen o.i.d.
 - Respondent kan de vragen niet beantwoorden. Ook niet na uitleg en discussie. Volgens respondent ligt de keuze ervoor en maakt de verwachte uitkomst niet uit voor de keuze. Mag iemand nog overlijden? Wat die uren voor dat moment gebeurt is belangrijk en hoe de patiënt in die eerste uren zich ontwikkelt/herstelt.

Respondent 10:

- Inleiding:
 - Postanoxisch<u>e</u>??
- DCE:
 - Waarom zou je niet info willen ontvangen? \rightarrow Overbodige vraag!
 - \circ Dominant scenario \rightarrow gevoel dat het een strikvraag is
 - $\circ \quad \ \ \, Vraag \ over \ levens verlengende \ behandeling$
 - Niet mijn keuze, arts keuze
 - Misschien info geven over dat stopzetten binnen die eerste dagen moet plaatsvinden en niet na twee weken nog kan. Dan veranderen de antwoorden van respondent.
- Huidige vs. nieuwe situatie:
 - Respondent had bijna geen uitleg nodig
- Betrokkenheid
 - Vraag over gesprek beginnen. Respondent denkt dat het beter is als familie begint, maar als die het niet doen, dan moet de arts beginnen. Daarom keuze voor arts.
 - o De keuze voor stopzetten is voor familie, want die moeten zorgdragen en er mee kunnen leven.
- Gezondheidstoestanden:
 - $\circ \quad \text{Voortgezet?} \rightarrow \text{Stopgezet}$
 - Antwoorden veranderen niet als de respondent de gezondheidstoestanden voor zichzelf beoordeelt.