Supplementary appendix of 'Preferences about future Alzheimer's disease treatments elicited through an online survey using the threshold technique'

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Table of Contents

Text 1. Information letter

Welcome to the study and thank you for your interest. Before you start the study, we would like you to read the information below.

Title of Study: Your views about benefits and risks of Alzheimer's disease treatments.

Name and Contact Details of the Principal Researcher: George Lankester, George.Lankester@alzheimersresearchuk.org

Invitation Paragraph
The survey aims to find out how people weigh up the benefits and risks of potential new Alzheimer's treatments that could stop or slow the disease process. You are being invited to take part in this study.

Before you decide whether you want to take part, it is important for you to understand why the research is being done and what taking part will involve.

Please take time to read this information carefully and discuss it with others if you wish. Contact us at George.Lankester@alzheimersresearchuk.org if there is anything that is not clear or if you would like more information.

Who is carrying out the study?
This survey is being carried out by Alzheimer´s Research UK, the University Medical Centre Groningen, and the European Medicines Agency.

What is the project's purpose?
It is very important to know what people living with the disease, carers, and the public think about potential new treatments. Understanding these views can:

Help researchers identify the treatment effects that matter most to people in the early stages of the disease.

Inform those who regulate and approve treatments about what people want from a treatment and what risks they will accept.

Help doctors and patients to choose the right treatment.

Do I have to take part?
Participation in this study involves completing an anonymous survey. Your participation is entirely voluntary. You can stop completing the survey at any time without giving a reason. There will be no negative consequences if you withdraw from the study.

Because the data is collected anonymously, it is not possible to delete your responses after you have partially or fully completed the survey.

What will happen to me if I take part?
The survey consists of three parts:

1. A short memory exercise and some questions about your beliefs about medicines.
2. Some questions about your views about hypothetical Alzheimer's treatments.
3. Some questions about you.

Part 1 of the survey aims to explore whether people's responses to these questions are linked to their views about future treatments. The memory exercise is not a medical test and like the rest of the responses, the answers are anonymous.

Completing the survey will take about 20 minutes. There is no time limit, so please take as long as you need. You can save your responses at any time and finish the survey later if you prefer to do so.

Within each part of the survey, you can go back to see your previous responses and change them if you wish to do so. However, once you have submitted your responses to proceed with the next part, you can no longer go back to the parts that you previously completed.

What are the possible disadvantages and risks of taking part?
Some people may feel uncomfortable thinking about different aspects of their brain health. You are free to stop completing the survey at any time.

If you have questions about dementia or want to know more about dementia research you can contact Alzheimer's Research UK's Dementia Research Infoline. You can contact us by calling 0300 111 5111 or by email at infoline@alzheimersresearchuk.org

What are the possible benefits of taking part?
We are unable to provide payment for your contribution to this study. Although there will be no immediate benefit to you, your answers will help us understand what people want from new Alzheimer's treatments, helping on the availability of future treatments.

What if something goes wrong?
To report a problem, you can contact us at policy@alzheimersresearchuk.org

Will anyone know I'm taking part in this project?
The survey is completely anonymous, meaning we cannot trace your responses back to you. The data we collect will be analysed by researchers at the University Medical Center Groningen (UMCG) in the Netherlands. We will store the data in a restricted-access folder on the UMCG network. In line with regulations in the Netherlands, we will store the data for a period of 15 years.

What will happen to the results of the research project?
We will use your survey responses for research purposes. By taking part in the study, you agree that we will publish the results in one or more scientific journals and include them as a chapter in a PhD thesis. We may also present the results at several scientific conferences. You will not be identified in any reports or publications. Publication is likely to take place about one year after we have finished collecting the data.

We will also publicise our findings, in an accessible format, via the Alzheimer's Research UK's website www.alzheimersresearchuk.org

Who is organising and funding the research?
This study is funded by Alzheimer's Research UK.

Contact for further information
If you have any questions, concerns, or complaints you can contact Alzheimer's Research UK. Please send an email to George.Lankester@alzheimersresearchuk.org

Thank you for reading this information and for considering taking part in this study.

If you agree with the statement below you can click 'Yes' and continue with the survey. Otherwise, please close the survey. Thank you for considering your participation.

By checking this box, I certify that I am at least 18 years old and that I give my consent freely to take part in this survey.

Yes

Table 1. Checklist for Reporting Results of Internet E-Surveys (CHERRIES)

Checklist Item	***Explanation***	***Page Number***
Describe survey design	Describe target population, sample frame. Is the sample a convenience sample? (In "open" surveys this is most likely.)	5
IRB approval	Mention whether the study has been approved by an IRB.	18
Informed consent	Describe the informed consent process. Where were the participants told the length of time of the survey, which data were stored and where and for how long, who the investigator was, and the purpose of the study?	5
Data protection	If any personal information was collected or stored, describe what mechanisms were used to protect unauthorized access.	5
Development and testing	State how the survey was developed, including whether the usability and technical functionality of the electronic questionnaire had been tested before fielding the questionnaire.	7,8
Open survey versus closed survey	An "open survey" is a survey open for each visitor of a site, while a closed survey is only open to a sample which the investigator knows (password-protected survey).	Open survey - 5
Contact mode	Indicate whether or not the initial contact with the potential participants was made on the Internet. (Investigators may also send out questionnaires by mail and allow for Web-based data entry.)	5
Advertising the survey	How/where was the survey announced or advertised? Some examples are offline media (newspapers), or online (mailing lists – If yes, which ones?) or banner ads (Where were these banner ads posted and what did they look like?). It is important to know the wording of the announcement as it will heavily influence who chooses to participate. Ideally the survey announcement should be published as an appendix.	5
Web/E-mail	State the type of e-survey (eg, one posted on a Web site, or one sent out through e-mail). If it is an e-mail survey, were the responses entered manually into a database, or was there an automatic method for capturing responses?	5
Context	Describe the Web site (for mailing list/newsgroup) in which the survey was posted. What is the Web site about, who is visiting it, what are visitors normally looking for? Discuss to what degree the content of the Web site could pre-select the sample or influence the results. For example, a survey about vaccination on a anti-immunization Web site will have different results from a Web survey conducted on a government Web site	5, 14
Mandatory/voluntary	Was it a mandatory survey to be filled in by every visitor who wanted to enter the Web site, or was it a voluntary survey?	Information letter
Incentives	Were any incentives offered (eg, monetary, prizes, or non-monetary incentives such as an offer to provide the survey results)?	Information letter
Time/Date	In what timeframe were the data collected?	5

Randomization of items or questionnaires	To prevent biases items can be randomized or alternated.	NA
Adaptive questioning	Use adaptive questioning (certain items, or only conditionally displayed based on responses to other items) to reduce number and complexity of the questions.	7
Number of Items	What was the number of questionnaire items per page? The number of items is an important factor for the completion rate.	From 1 to 13 items per page
Number of screens (pages)	Over how many pages was the questionnaire distributed? The number of items is an important factor for the completion rate.	Variable since it was an adaptative survey, maximally 21 pages.
Completeness check	It is technically possible to do consistency or completeness checks before the questionnaire is submitted. Was this done, and if "yes", how (usually JAVAScript)? An alternative is to check for completeness after the questionnaire has been submitted (and highlight mandatory items). If this has been done, it should be reported. All items should provide a non-response option such as "not applicable" or "rather not say", and selection of one response option should be enforced.	NA
Review step	State whether respondents were able to review and change their answers (eg, through a Back button or a Review step which displays a summary of the responses and asks the respondents if they are correct).	Back button available
Unique site visitor	If you provide view rates or participation rates, you need to define how you determined a unique visitor. There are different techniques available, based on IP addresses or cookies or both.	NA
View rate (Ratio of unique survey visitors/unique site visitors)	Requires counting unique visitors to the first page of the survey, divided by the number of unique site visitors (not page views!). It is not unusual to have view rates of less than 0.1 % if the survey is voluntary.	NA
Participation rate (Ratio of unique visitors who agreed to participate/unique first survey page visitors)	Count the unique number of people who filled in the first survey page (or agreed to participate, for example by checking a checkbox), divided by visitors who visit the first page of the survey (or the informed consents page, if present). This can also be called "recruitment" rate.	NA
Completion rate (Ratio of users who finished the survey/users who	The number of people submitting the last questionnaire page, divided by the number of people who agreed to participate (or submitted the first survey page). This is only relevant if there is a separate "informed consent" page or if the survey goes over several pages. This is a measure for attrition. Note that	NA

agreed to participate)	"completion" can involve leaving questionnaire items blank. This is not a measure for how completely questionnaires were filled in. (If you need a measure for this, use the word "completeness rate".)	
Cookies used	Indicate whether cookies were used to assign a unique user identifier to each client computer. If so, mention the page on which the cookie was set and read, and how long the cookie was valid. Were duplicate entries avoided by preventing users access to the survey twice; or were duplicate database entries having the same user ID eliminated before analysis? In the latter case, which entries were kept for analysis (eg, the first entry or the most recent)?	NA
IP check	Indicate whether the IP address of the client computer was used to identify potential duplicate entries from the same user. If so, mention the period of time for which no two entries from the same IP address were allowed (eg, 24 hours). Were duplicate entries avoided by preventing users with the same IP address access to the survey twice; or were duplicate database entries having the same IP address within a given period of time eliminated before analysis? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?	NA
Log file analysis	Indicate whether other techniques to analyze the log file for identification of multiple entries were used. If so, please describe.	NA
Registration	In "closed" (non-open) surveys, users need to login first and it is easier to prevent duplicate entries from the same user. Describe how this was done. For example, was the survey never displayed a second time once the user had filled it in, or was the username stored together with the survey results and later eliminated? If the latter, which entries were kept for analysis (eg, the first entry or the most recent)?	NA
Handling of incomplete questionnaires	Were only completed questionnaires analyzed? Were questionnaires which terminated early (where, for example, users did not go through all questionnaire pages) also analyzed?	9
Questionnaires submitted with an atypical timestamp	Some investigators may measure the time people needed to fill in a questionnaire and exclude questionnaires that were submitted too soon. Specify the timeframe that was used as a cut-off point, and describe how this point was determined.	NA
Statistical correction	Indicate whether any methods such as weighting of items or propensity scores have been used to adjust for the non-representative sample; if so, please describe the methods.	NA

Text 2. Survey

Part 1: Memory exercise and beliefs about medication

Question 1

The first part of this survey consists of a memory exercise.

Before you start, we would like to highlight that this exercise is not a screening or diagnosis tool. The only aim is to explore whether your views are in any way linked to your responses to the memory exercise. Like the rest of the responses, your answers are anonymous.

Below are three words. Please read them and memorise them. We will ask you these three words later in the survey.

Morning

Lamp

University

I have read the three words and I know that I will be asked to remember them later in the survey.

***

Question 2

Can you please write down the three words we have asked you to memorise?

_____

_____

_____

***

One more time!

Below are three new words. Please read them and memorise them. We will ask you these 3 new words later in the survey.

Window

Bottle

House

I have read the three words and I understand that I will be asked to remember them later in the survey

***

Before we ask for the three new words, can you complete the following questions? These questions are about your beliefs about medication.

***

- These are statements that other people have made about medicines in general.
- Please show how much you agree or disagree with them by ticking the appropriate box.

	Strongly disagree	*Disagree*	*Uncertain*	*Agree*	*Strongly agree*
Doctors use too many medicines					
People who take medicines should stop their treatment for a while every now and again					
Medicines help many people to live better lives					
Most medicines are addictive					
Natural remedies are safer than medicines					
In most cases the benefits of medicines outweigh the risks					
In the future medicines will be developed to cure most diseases					
Most medicines are poisons					
Medicines do more harm than good					
Medicines help many people to live longer					
Doctors place too much trust in medicines					
If doctors had more time with patients they would prescribe fewer medicines					

***

Coming back to the memory exercise, can you please write down the last three words we have asked you to memorise?

_____

_____

_____

***

Part 2: Your preferences about different Alzheimer's disease treatments

In this part of the survey, we will ask you to think about several different scenarios. We will be asking you to imagine that you have been diagnosed with Alzheimer's disease. If you are currently living with Alzheimer's, please think about how you would feel in each scenario.

The word 'dementia' describes a group of symptoms such as memory loss, confusion, mood changes and communication difficulties. Alzheimer's disease is the most common cause of dementia. It's a progressive disease that damages certain cells in the brain. As more cells become damaged, a person's symptoms get worse over time.

We can think of the disease as having three stages: early memory and thinking problems, mild to moderate dementia, and severe dementia. The symptoms that people may experience in each stage are explained in the table below, together with their impact on daily living and mood.

There are currently no treatments that can cure Alzheimer's disease. However, there are treatments under development that may help to slow the disease. But like all medicines, these potential treatments may also cause side effects.

Stages of Alzheimer's disease
Early memory and thinking problems Symptoms may include: • Forgetting specific episodes, dates (e.g. birthdays) and names. • Challenges with learning new information. • May need some help with complex tasks (e.g. taking care of finances). • Self-awareness of the onset of symptoms, depression and irritability.
Mild to moderate dementia Symptoms may include: • Loss of spatial awareness, difficulty finding words, or misunderstanding events and situations • Requires full assistance with complex tasks (e.g. taking care of finances). • No longer safe to travel alone or be left alone at home. • Mild depression or apathy, less often irritable/aggressive.
Severe dementia Symptoms may include: • No longer being able to hold conversations. • Loss of ability to use simple tools, dress, take care of hygiene, and to recognise people. • Becoming more apathetic over time with increasing irritability/aggression.

***

For the following questions, we want you to imagine that you have been living with early memory and thinking problems for some time. To slow the disease, you will be offered a choice between two hypothetical treatments. Your task is to select the one that you would prefer based on the information provided about:

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Exercise 1

Suppose that you could choose between the following two treatments:

Scenario 1

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	60% (60 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

**Reminder*

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	50% (50 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

****Reminder***

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent

medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	70% (70 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	40% (40 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

*****

Suppose that you could choose between the following two treatments: *Scenario 3b (only If **chosen B** in **scenario 2b)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	80% (80 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

****Reminder***

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

****

Exercise 2 - 4 years vs 8 years (option 1)– If for Scenario 1 in Exercise 1 treatment A was chosen

Suppose that you could choose between the following two treatments: *Scenario 1*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	8 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	60% (60 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

**Reminder*

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	8 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	50% (50 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

****Reminder***

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	8 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	70% (70 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	8 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	40% (40 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments: *Scenario 3b (only If **chosen B** in **scenario 2b)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	8 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	80% (80 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

***Reminder**

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

Exercise 2 - 4 years vs 5 years (option 2)– If for Scenario 1 in Exercise 1 treatment B was chosen

Suppose that you could choose between the following two treatments: *Scenario 1*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	60% (60 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

**Reminder*

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	50% (50 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	70% (70 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	40% (40 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

Suppose that you could choose between the following two treatments: *Scenario 3b (only If **chosen B** in **scenario 2b)***

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience periods of discomfort	30% (30 out of 100 people)	80% (80 out of 100 people)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience periods of discomfort

Percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment.

***

In the next set of questions, we will ask you to choose again between two hypothetical treatments to slow your disease progression. This time, please choose based on the following two characteristics:

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Exercise 3

Suppose that you could choose between the following two treatments:

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	6 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	40% (40 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	30% (30 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	6 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (1 out of 100 patients)	50% (50 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a**)*

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	6 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	20% (20 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

Scenario 3b (only If **chosen B** in **scenario 2b**)

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	6 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	60% (60 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

**Reminder*

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

*****

Exercise 4 - 4 years vs 8 years (option 1)– If for Scenario 1 in Exercise 3 treatment A was chosen

Suppose that you could choose between the following two treatments:

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	8 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	40% (40 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

**Reminder*

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

****

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	**Treatment A**	**Treatment B**

Number of years until more care and support is needed	4 years	8 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	30% (30 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	8 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (1 out of 100 patients)	50% (50 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a**)*

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	8 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	20% (20 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

Scenario 3b (only If **chosen B** in **scenario 2b**)

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	8 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	60% (60 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Exercise 4 - 4 years vs 5 years (option 2)– If for Scenario 1 in Exercise 3 treatment B was chosen

Suppose that you could choose between the following two treatments:

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	40% (40 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

***Reminder**

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

*Scenario 2a (only If **chosen A** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	30% (30 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

***Reminder**

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

*Scenario 2b (only If **chosen B** in **scenario 1**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (1 out of 100 patients)	50% (50 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments: *Scenario 3a (only If **chosen A** in **scenario 2a**)*

Treatment characteristics	Treatment A	Treatment B
Number of years until more care and support is needed	4 years	5 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	20% (20 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Suppose that you could choose between the following two treatments:

Scenario 3b (only If **chosen B** in **scenario 2b**)

Treatment characteristics	**Treatment A**	**Treatment B**
Number of years until more care and support is needed	4 years	5 years
Number of people who experience a side effect that could cause long-term or permanent disability	10% (10 out of 100 patients)	60% (60 out of 100 patients)

Which treatment would you choose? Treatment A Treatment B

Reminder

Number of years until more care and support is needed

How long it takes, on average, for people on the treatment to progress to the next stage of the disease.

Number of people who experience a side effect that could cause long-term or permanent disability

Percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke.

***

Thank you very much for completing the first two sections of the survey!
In this final section, we would like to ask you some questions about you and your personal situation. Your answers will help us understand whether people's views about treatments are in any way linked to different characteristics and personal situations. Like the rest of the responses, your answers are anonymous.

Part 3: General Questions

Question 1

What is your gender?

Female

Male

Other

Prefer not to say

Question 2

What age are you?

_____

Question 3

What is your highest level of education?

No formal qualifications

Secondary school or equivalent

A Level or equivalent

Degree or equivalent

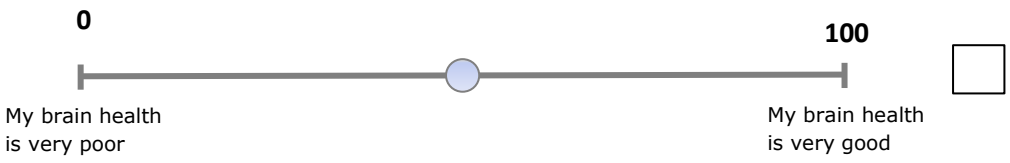
Postgraduate degree

Other

Prefer not to say

Question 4

How would you rate your brain health?



Question 5

Have you ever consulted a doctor about your brain health?

Yes

No

Not sure

Prefer not to say

Question 6

Have you ever cared for a relative, friend or neighbour with dementia?

Yes

No

Not sure

Prefer not to say

Question 7

Have you ever been given a diagnosis related to your brain health?*?*

Yes

No

Not sure

Prefer not to say

Question 8 *(Only if question 7 is 'Yes')*

Which diagnosis did you receive?

Mild cognitive impairment

Alzheimer's disease

Other diagnosis, please specify _____

Not sure

Prefer not to say

<u>Question 9</u> (Only if in Question 8 Alzheimer's disease is chosen)

Which of the following stages of Alzheimer's disease is closer to your current stage?

Pre-clinical

Early memory and thinking problems

Mild to moderate

Severe

Not sure

Prefer not to say

<u>Question 10</u>

Do you currently live alone?

Yes

No

Prefer not to say

<u>Question 11</u>

Do you need help from friends, family members or carers for any of these activities?

Cooking

Eating

Showering

Dressing

Doing groceries

Driving

Keeping finances

Taking my medication

Walking around my local area

I need help with activities not listed here*, for example,* _____

I do not need help with any activities

Prefer not to say

Question 12

Did anyone help you to fill out this survey?

Yes

No

Prefer not to say

Question 13

Where did you hear about this study?

Join Dementia Research (JDR)

Alzheimer's Research UK

Other, please specify _____

This is the end of the survey, thank you for your time and input. If you have any comments please add them here.

_____

***

Table 2. Differences in health-related questions between participants with and without memory problems.

Health-related questions		People living with memory problems (N=554)	People living without memory problems (N=3104)	P-value
Brain health (IQR)		70 (47 – 80)	85 (73 – 90)	<0.001
Help for daily activities (%)		127 (23)	111 (4)	<0.001
Help with the survey (%)		24 (4)	4 (0)	<0.001
Memory exercise				
Immediate recall (%)	<3 words correct	41 (7)	52 (2)	<0.001
Delayed recall (%)	<3 words correct	217 (39)	789 (25)	<0.001

IQR = Interquartile range

Text 3. Selection of attributes, attribute definitions, and attribute levels of the thresholding exercises

The selection, definition, and levels of the attributes were based on previous literature.

Attributes	Short definition	Complete definition	Attributes levels
Therapeutic benefits	Number of years until more care and support is needed	How long it takes, on average, for people on the treatment to progress to the next stage of the disease	4 years and 6 years
Moderate adverse events	Number of people who experience periods of discomfort	The percentage of people who have periods of discomfort that affect their ability to carry out daily activities. The discomfort is caused by side effects such as dizziness, nausea, diarrhoea, and headache. Urgent medical attention is not needed. However, a person may have the same side effects many times while receiving the treatment	30%, 40%, 50%, 60% 70%, and 80%
Severe adverse events	Number of people who experience a side effect that could cause long-term or permanent disability	The percentage of people who experience a severe side effect that stops them performing activities as usual. This type of side effect could cause a long-term or permanent disability. An example would be paralysis in half of the body or loss of speech, caused by a non-fatal stroke	10%, 20%, 30%, 40%, 50%, and 60%

The therapeutic benefit was estimated with a simulation based on the statistical model presented in the paper by Vermunt *(Vermunt et al, Alzheimers Dement 2019)*. The simulation uses a multi-state model to estimate the age-specific duration of the preclinical, mild cognitive impairment (MCI), and Alzheimer's disease (AD) dementia stages. Evaluating the fitted model at a starting age of 70 years, the authors found the average duration of the MCI stage to be about 4 years. To simulate the introduction of a hypothetical new AD treatment, a proportional hazards formulation to add a hypothetical treatment effect to the transition intensity from MCI to mild AD dementia was used. Different values of the hazard ratio (HR) were calculated and a 2-years delay in disease progression resulted in a HR=0.7: HRs > 0.7 are more conservative but may be too small to be detectable or measurable in a randomized clinical trial, while HRs < 0.7 represent more optimistic treatment effects with a lower chance of occurring. Considering the results of the estimations, 2-years delay in disease progression was considered appropriate for the elicitation exercise.

The moderate and severe adverse events were expressed in general terms because the survey was not directly linked to any existing treatment. In these cases, the use of standard attributes to which people can easily relate has previously been suggested in literature and has been followed in previous patient preference studies in this disease area *(Huys et al, PREFER IMI 2017; Johnson et al, Value Health 2019).*

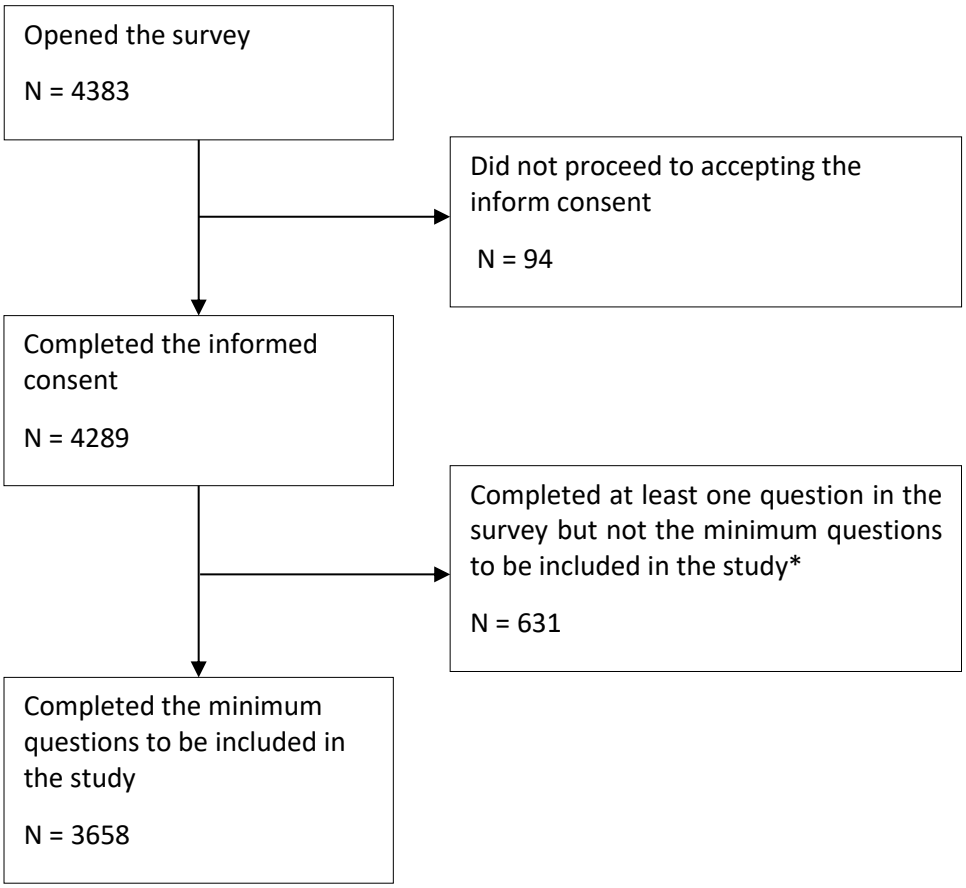


Figure 1. Flow chart of participants included in the study.

*The minimum questions to be included in the study were the two thresholding exercises and at least one individuals' characteristics question.

Table 3. Results of the mutually adjusted models showing the effect of the individuals' characteristics and beliefs about medicines on the MAR for the moderate and the severe adverse events. Effects are expressed in terms of acceleration factors.

	Moderate adverse events	*p*-value	Severe adverse events	*p*-value
Individuals' characteristics				
Age (per 10 years increase)	1.07 (1.10 – 1.04)	**<0.001**	1.07 (1.10 – 1.04)	**<0.001**
Females	1.16 (1.26 – 1.07)	**<0.001**	1.26 (1.37 – 1.16)	**<0.001**
High educational level	0.90 (0.97 – 0.83)	**0.008**	-	
Living alone	1.15 (1.25 – 1.05)	**0.001**	1.05 (1.15 – 0.96)	0.281
Experience as caregiver	-		-	
Living with memory problems	-		-	
Beliefs about medicines				
Benefits beliefs (per SD increase)	0.97 (0.98 – 0.95)	**<0.001**	0.98 (1.00 – 0.97)	0.064
Harm beliefs (per SD increase)	1.03 (1.04 – 1.01)	**0.004**	-	-
Overuse beliefs (per SD increase)	1.04 (1.06 – 1.02)	**<0.001**	1.01 (1.03 – 1.00)	0.063

Numbers below 1 indicate increase in the MAR and numbers above 1 indicate decrease in the MAR. For categorical variables, the reference groups were males, low/middle educational level, and not living alone. SD = standard deviation.