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Preference-Based Assessments

Something Is Better Than Nothing: The Value of Active Intervention in Stated Preferences for Treatments to Delay Onset of Alzheimer's Disease Symptoms

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ABSTRACT

Background: The objective of the study was to understand respondents' willingness to accept hypothetical treatment-related risks in return for the benefit of additional time with normal memory from potential Alzheimer's disease interception therapies.

Methods: A US web-based discrete-choice survey was administered to respondents ages 60 to 85 years with no Alzheimer's disease diagnosis and no cognitive symptoms. Choice questions required respondents to indicate whether they preferred a constant, no-treatment condition described as 4 years of normal memory followed by 3 years of cognitive impairment and 5 years of dementia or an interception treatment with chosen risks of disabling stroke and death, but with increased duration of normal memory. The study design included internal validity tests to verify data quality.

Results: On average, respondents were willing to accept a 5% to 13% risk of stroke or death in the first year for treatments that could provide 1 or more additional years with normal memory. Nevertheless, 30% of respondents failed a simple internal-validity test question where the treatment alternative offered no improvement in disease progression but had significant side effects. These respondents also were more likely to choose active treatment in the subsequent series of choice questions. This unexpected finding is consistent with hopeful attitudes of patients with debilitating and potentially fatal conditions.

Conclusion: Pro-treatment attitudes are clinically relevant and can affect the analysis and interpretation of stated-preference data. Internal-validity tests generally are underutilized in preference research. This study demonstrated how analysis of apparent validity failures can yield important insights about patient preferences.

Keywords: Alzheimer's disease, benefit-risk, patient preferences, treatment interception.

VALUE HEALTH. 2019; 22(9):1063–1069

Introduction

Biomarker evidence of amyloid beta deposits in the brain in cognitively healthy individuals is associated with an increased risk of Alzheimer's disease (AD).[1–3] Such pathological changes are observable a decade or longer before dementia symptoms are observed.[2] Currently, no available treatments modify underlying AD processes. Anti-amyloid medications and other disease-interception treatments in development may have significant therapeutic benefits; however, evaluating early interventions must account for exposure to possible screening and treatment-related risks years before onset of AD symptoms.

A previous study examining benefit-risk preferences in the context of AD that had already developed found high levels of risk tolerance with treatments that would arrest progression of disease. The objective of this study was to elicit patient preferences for preserving normal memory by delaying onset of cognitive impairment and Alzheimer's dementia using a discrete-choice experiment (DCE). The DCE surveys quantify the relative importance of benefits and risks of AD treatments from a patient's perspective, including the maximum acceptable risk for a given level of a benefit. This approach has been used to elicit willingness to accept benefit-risk tradeoff preferences in previous AD applications[4–8] and numerous other diseases.[9]

Conflict of interest: R.L.D., J.S., and B.L. are employed by Janssen Pharmaceuticals and are shareholders. Janssen develops medications to treat neurological conditions including Alzheimer's disease.

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https://doi.org/10.1016/j.jval.2019.03.022

Methods

Study Sample

Respondents were recruited from the Ipsos Observer's US consumer panel, where we included consenting English-speaking adults between 60 and 85 years of age with no prior diagnosis of or prescription medication to treat AD, dementia, cognitive impairment, or memory problems who were willing to provide informed consent. An institutional review board determined the study was exempt from formal review. Before the survey, respondents were presented with pertinent information about the goals of the study, the sponsor, the academic organization conducting the study, and what was required of participants, and were given the option to agree or not agree to participate. Panelists were recruited between December 18 and December 21, 2015 for initial pilot testing (n = 55) and between December 23 and December 30, 2015 for the remaining sample (n = 949), resulting in a total of 1004 respondents.

DCE Study Design

Good practices for conjoint analysis were followed, including face-to-face pretest interviews to evaluate survey content and presentation before survey implementation[10–13] (see Appendix A in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022 for details on the study-design qualitative research). The DCE elicitation format requires respondents to evaluate a series of pairs of constructed disease-outcome alternatives and indicate which of the 2 they would choose if those were the only options available. The alternatives are described using different levels of several salient treatment features or attributes.[14] Statistical analysis of the pattern of choices quantifies the preference weights, indicating the implicit relative importance of the attributes presented for each treatment alternative.

The constructed disease-progression profiles described time spent with normal memory, mild cognitive impairment, and progressively severe dementia symptoms. One treatment alternative (no medicine) appeared in each choice question and was designed to represent natural disease progression. Respondents were asked to assume that a brain scan had detected changes that would result in AD. There were 2 baseline cases used. Respondents aged 60 to 74 were randomly assigned either to the 12-year or 16-year version. Respondents aged 75 to 85 were assigned to the 12-year version in view of the shorter life expectancy of older respondents.

Without treatment, in the 12-year version they could expect to experience 4 years with normal memory, 3 years with mild cognitive impairment (worse memory), and 5 years with Alzheimer's dementia (need increasing help), with none of the possible side effects or risks associated with medication. The medicine alternative included varying durations of time over 12 or 16 years with normal memory, mild cognitive impairment, and Alzheimer's dementia, along with days per month with nausea, risk of disabling stroke, and risk of mortality, with both risks incurred in the first year of treatment. The adverse events (AEs) were selected in consultation with experts to encompass a range of potential AEs, but do not correspond to the AEs for any particular treatment to delay onset of AD. The treatment attributes were chosen in consultation with clinical experts and evaluated in interviews with older individuals with no diagnosis of AD, dementia, cognitive impairment, or memory problems.

A D-efficient experimental design generated in SAS version 9.2[15] determined the combinations of benefits, harms, and risks used to describe the treatment options that respondents evaluated[15–17] (see Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022 for outcomes and levels included in the study design). The 32 questions in the experimental design were divided into 4 survey variants with 8 randomly ordered choice questions each.

Figure 1 is an example choice question for the 12-year version. Respondents were presented with a total of 10 choice questions: 8 questions from the experimental design; 1 dominated-pair test question where the medication alternative had same benefits as no medication, but with side effects and risks; and 1 holdout question not included in the analysis (see Appendix B in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022 for survey instrument). The dominated-pair question provided an internal-validity test—we expected that all respondents would choose the no-treatment alternative because it provided the same benefits with no risks.[14,18]

Before the choice questions, the survey instrument obtained information on respondent characteristics, provided lower-literacy attribute definitions, and used training tasks to test and reinforce respondents' understanding of the constructs to be evaluated and the elicitation format used in the choice questions. To provide a plausible decision frame for considering treatment options, the following statement preceded the choice questions: "Suppose that you had a brain test and the result showed that you will develop Alzheimer's in the future even though your current memory is normal for people your age."

Statistical Analysis

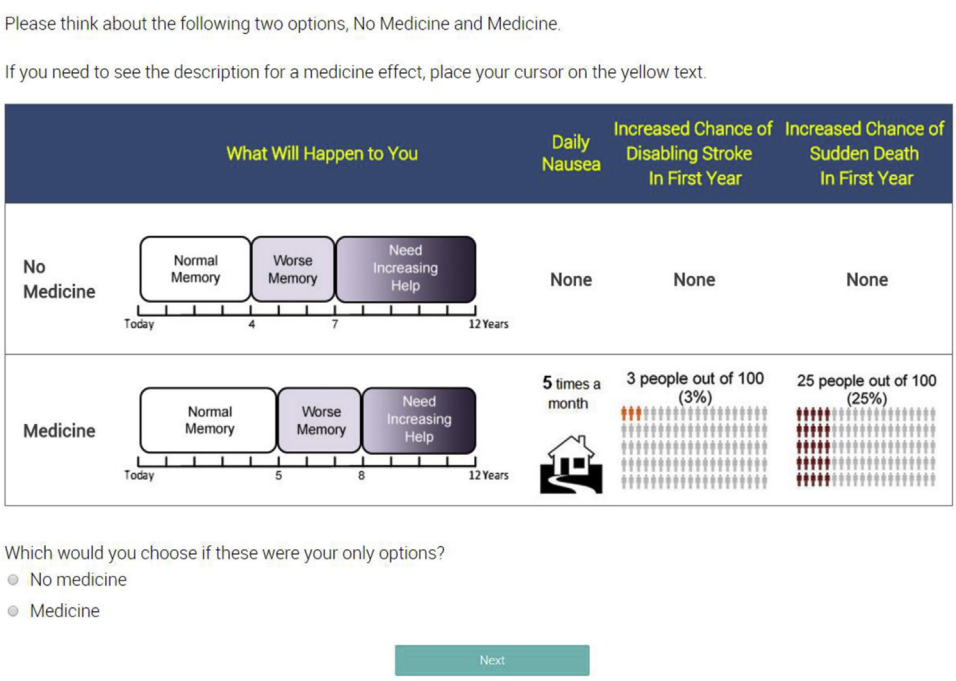
Preference weights were obtained using random-parameters logit (RPL) regression in Stata.[19] Unobserved preference heterogeneity among survey respondents was modeled in RPL as a continuous normal distribution of preferences for each model parameter using 500 Halton draws.[20,21] Box-Cox specification tests supported linear specifications for each attribute listed in Appendix Table 1 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022. An interaction term was included to account for nonlinearity between the number of years with mild cognitive impairment and the number of years with Alzheimer's dementia, and an alternative-specific constant was included to test for a pro-treatment label effect. A label effect is present when respondents perceive value or utility from the label attached to a choice alternative, apart from the utility explained by the mean attribute levels.[22,23]

The same RPL model specification was applied separately to data from the 12-year version among the 75- to 85-year-olds, the 12-year version among the 60- to 74-year-olds, and the 16-year version among the 60- to 74-year-olds. To facilitate interpreting the resulting relative preference-weight estimates, log-odds preference parameters were rescaled from 0 to 10, where 0 indicates the least important outcome level and 10 indicates the most important outcome level, and where benefits have a positive sign and harms have a negative sign. The maximum acceptable risk (MAR) is the largest treatment-related risk from disabling stroke or death in the first year that respondents would accept for a given improvement in normal memory.[24,25] The MAR is calculated as the preference utility of increased time with normal memory (and thus decreased time with cognitive impairment or dementia) scaled by the utility of a 1% decrease in risk. Specifically,

$$MAR[U(\Delta T_n)] = \frac{\Delta T_n \cdot (-\beta_i) + [(T_i - \Delta T_n) \cdot T_j] \cdot (-\beta_{ij})}{-\beta_r} \quad (1)$$

where T is years, β is a weight parameter, n is normal memory, and i and j are either cognitive impairment or dementia symptoms. If i is cognitive impairment, then j is dementia, and vice versa. β_{ij} is

Figure 1. Example choice question: 12 years of remaining life expectancy.



the parameter for the interaction term $(T_i \times T_j)$, $I \neq j$. $U(\Delta T_N)$ is the benefit of a ΔT change in years with normal memory. The benefit is the sum of the change times $-\beta_i$, benefit of 1 additional year of normal memory from a 1-year reduction in either cognitive impairment or dementia, and the interaction between the new level T_i - ΔT_n and the other symptom severity level T_j times the negative of the interaction parameter $-\beta_{ij}$. The weight parameter for a 1% decrease in risk is $-\beta_r$, where r can be either disabling stroke or death.

A binomial-probit model was used to evaluate associations between respondents' personal characteristics and their stated willingness to consider an interception AD treatment, as indicated by selecting Medicine in all answered choice questions. Analysis of rates of acceptance of the no-treatment alternative was used to evaluate preferences of respondents who failed the dominated-pair internal-validity test. We also explored the sensitivity of results to different assumptions about which respondents provided valid responses.

Results

Patient Characteristics

Across all 1004 respondents, the mean age was 70, and the sample was evenly divided by sex, mostly white (92%), and relatively well educated (46% with ≥4-year college degree). Sixty-four percent reported having had a friend or family member with AD, and of those, about 25% had provided some form of care for that person. Nevertheless, older respondents were less likely to have provided care for an AD patient (19% vs 28%, $P < .05$).

Preference-Weight Estimates

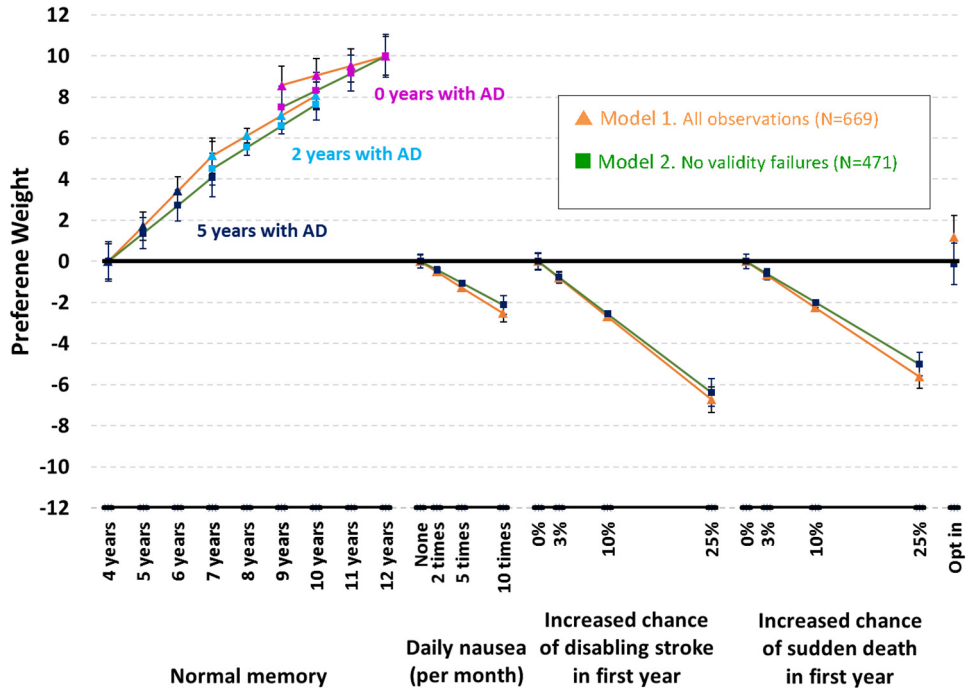
Given qualitative similarities in results, we report findings only for combined younger and older age groups in the 12-year version. Figure 2 compares estimated preference weights for all respondents (model A) with those who passed the dominated-pair validity test (model B). (For parameter estimates see Appendix Tables 2 and 3, and see Appendix Figure 1 for the 16-year version in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022). Preference weights are consistent with the natural ordering of the levels; that is, on average, respondents logically preferred fewer years with mild cognitive impairment and fewer years with Alzheimer's dementia, which equates to more years with normal memory. Negative preference weights for harms and risks indicated that they also wanted to avoid days with nausea or increased chance of disabling stroke or sudden death in the first year of treatment. The opt-in alternative-specific constant indicates the pro-treatment label effect for choosing the treatment alternative is positive for model B, but small and marginally insignificant (P = .058), indicating a negligible additional tendency to choose treatment after accounting for the effects of treatment attribute levels.

The incremental importance of an additional year of normal memory decreases as the number of years with dementia symptoms decreases from 5 years to 2 years and from 2 years to 0 years for the all-observation model. In contrast, the incremental importance is approximately constant when respondents who failed the validity test were excluded from the analysis. Slopes for nausea and risks are similar for both models. Indicated by the overall length of the lines, over the range of levels included in the study design, respondents regarded treatment risks in the first year of disabling stroke and mortality as similarly important.

Likelihood of Accepting Treatment

A surprising 30% of respondents unexpectedly chose the treatment alternative in the dominated-pair validity test, which had the same efficacy as no treatment, but had nausea and increased chances of stroke and death. The second column in Table 1 shows the distribution of the number of times the treatment alternative was selected out of 8 choice questions. For the

Figure 2. Preference weights: 12-year version. Each of the 4 points on the lines labeled as 5, 2, or 0 years of AD correspond to 3, 2, 1 and 0 years with MCI (from left to right). The vertical bars around the preference weights indicate the 95% confidence intervals for the estimates.



AD indicates alzheimer's dimentia; MCI, mild cognitive impairment.

combined-version distribution of number of times treatment was selected in Table 1, the weighted average was 4, indicating that the treatment and no-treatment alternatives were chosen an equal number of times. Nevertheless, in all 8 choices 147 respondents (about 15%) chose no treatment and 153 (also 15%) chose treatment. Eighteen percent of those who chose treatment fewer than half the time also failed the separate dominated-pair test, whereas more than twice that proportion (41%) of those who chose treatment more than half the time also failed the dominated-pair test.

Table 1. Number and percent of respondents in all survey versions and with validity failures by number of times treatment option chosen

Number of times treatment chosen	Number (%) of respondents in all survey versions	Number (%) of respondents with validity failures
0	147 (14.7)	7 (2.3)
1	73 (7.3)	14 (4.6)
2	107 (10.7)	33 (10.9)
3	108 (10.8)	26 (8.6)
4	124 (12.4)	43 (14.2)
5	103 (10.3)	34 (11.2)
6	111 (11.1)	30 (9.9)
7	77 (7.7)	26 (8.6)
8	153 (15.3)	90 (29.7)
Total	1003*	303

*1 respondent did not complete the choice questions.

Thus, participants who were more likely to select the treatment alternative also were more likely to fail the validity test. The correlation between counts of numbers of times treatment is chosen and the number of dominated-pair test failures for each level of treatment-choice frequency is 0.71.

Table 2 shows the results of a probit covariate analysis of the probability of always choosing the treatment alternative. The largest effect (23.9%, P = .006) was for respondents who had provided care for a person with AD in the last 3 years. The interaction between providing care and having a family member with AD reduced the effect of providing care somewhat, but was not statistically significant (−9.2%, P = .136). Answering all quiz questions correctly and being assigned to the 16-year survey version were both negatively related to always choosing treatment: −6.9% (P = .005) and −7.0% (P = .007). Age, sex, marital status, education, and health status had statistically insignificant effects on always choosing treatment.

Effects of Sample Definition on Estimated Label Effect and MAR

We evaluated the effects of deleting 3 kinds of respondents from the analysis of the 12-year version of the survey: those who failed the dominated-pair validity test, those who always chose the no-treatment alternative in all choice questions, and those who always chose the treatment alternative in all questions. None of the choice questions used in estimation contained the dominated pair. Table 3 compares the consequences of deleting particular groups of respondents for 2 estimates: the "do-something," pro-treatment label effect and the mortality MAR for an additional year of normal memory. Model 1 includes the full 12-year version sample of 669 respondents ages 60 to 85. There is a statistically significant pro-treatment label effect of 2.44 that is independent of the attribute levels shown in the treatment

Table 2. Probit analysis of effects of respondent characteristics on always choosing the treatment alternative

Survey respondents' characteristics	Mean value	Effect on likelihood of always choosing medicine (%)	*P* value
Age (years)	69.91	0.3	.14
Female	0.50	0.9	.69
Married	0.60	1.9	.41
Had at least an associate or college degree	0.56	1.8	.44
Had no self-reported health issues	0.15	3.5	.29
Provided care for a person with AD in the past 3 years	0.07	23.9	.006
Provided care for a person with AD ***and*** had family member with AD	0.05	−9.2	.14
Correctly answered all quiz questions on treatment efficacy and risks	0.29	−6.9	.005
Was assigned to the survey version with a 16-year time frame	0.33	−7.0	.007

AD indicates Alzheimer's disease.

alternatives. Thus, the estimated mean utility of the attribute profiles under-predicts the proportion of treatment choices. The incremental MAR for the full-sample model is 13%.

The pro-treatment label effect also is positive and significant or near significant for models 3 and 4, which omit respondents who always chose no treatment or respondents who always chose treatment, respectively. The 19% MAR for model 3 that excludes respondents who always chose no medicine is the largest among the 6 models, whereas the MAR for model 4 that excludes respondents who always chose medicine is about half that value. The remaining models 2, 5, and 6 have small, statistically insignificant label effects. All 3 models omit respondents who failed the dominated-pair validity test, and 2 of the 3 models omit respondents who always chose the treatment alternative. The 3% MAR for model 5 that excludes respondents who failed the validity test and who always chose medicine is the smallest among the 6 models, whereas models 2 and 6 have the same 7% MAR with the same CIs.

Risk Tolerance for Delaying Symptom Onset

Table 4 shows mean MAR estimates and 95% CIs for disabling stroke and death for years of additional normal memory and corresponding decreased time with dementia symptoms. For example, from the model excluding validity failures and using equation 1, the preference utility of 3 more years of normal memory obtained by reducing dementia symptoms by 3 years, holding cognitive impairment constant at 3 years, can be calculated from the direct and interaction marginal effects. From Appendix Table 3 (see Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022), the direct marginal effect of 1 year of normal memory is 0.72, the interaction marginal effect is 0.19, and the preference weight of a 1% decrease in stroke risk is 0.16. Thus, the mean maximum acceptable increase in stroke risk for a treatment that displaces 3 years of dementia symptoms with 3 years of normal memory is 2.73/0.16 = 17%. On average, respondents thus regarded the net benefit of 3 additional years of normal memory as positive for any stroke risk less than 17%.

Differences between type of risk are not statistically significant. See Appendix Table 4 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022 for MAR calculations for all possible reductions in cognitive impairment and dementia symptoms.

Discussion

Treating patients who are at risk, but asymptomatic, years in advance of their potential disease leads to complex benefit-risk questions: how much chance of short-term adverse events would at-risk patients be willing to accept in exchange for delaying disease years in the future? To answer this question, we estimated the relative importance of potential benefits and risks of constructed AD interception treatments. Preserving additional years of normal memory over remaining life expectancy, either by displacing years with mild cognitive impairment or years with

Table 3. Effects of sample definition on estimated label effect and MAR, 12-year version

Model	Exclusion criteria				Pro-treatment label effect	*P* Value	Mortality MAR for 1 more year of normal memory	95% CI
	Dominated pair failure	Always chose no medicine	Always chose medicine	Sample size				
1				669	2.44	.04	13%	(9-17)
2	Excluded			471	−0.14	.82	7%	(2-11)
3		Excluded		576	4.29	.00	19%	(15-23)
4			Excluded	548	1.93	.06	9%	(6-12)
5	Excluded		Excluded	417	−0.72	.26	3%	(0-7)
6	Excluded	Excluded	Excluded	328	−0.54	.19	7%	(2-11)

MAR indicates maximum acceptable risk.

Table 4. Maximum acceptable risks, 12-year version*

Risk	Additional normal memory (years)	All observations % (N = 669)	No validity failures % (N = 471)
Stroke	1	11 (7-14)	5 (2-9)
	2	17 (14-20)	11 (8-15)
	3	23 (20-27)	17 (13-21)
	4	Greater than 25	23 (18-28)
Death	1	13 (9-17)	7 (2-11)
	2	20 (16-25)	14 (10-19)
	3	Greater than 25	22 (16-28)
	4	Greater than 25	Greater than 25

*Calculations reduce number of years with dementia symptoms and hold mild cognitive impairment constant at 3 years. Calculations greater than the maximum death or disabling stroke probability of 25% used in the study design are shown as "greater than 25%." See Appendix Table 2 in Supplemental Materials found at https://doi.org/10.1016/j.jval.2019.03.022 for full set of results.

Alzheimer's dementia, was the most important treatment feature, followed by increased risk of stroke and then risk of death within the first year, conditional on the ranges of benefits and risks shown in the alternative treatment profiles. The high estimated MARs for deferring onset of AD symptoms, sometimes exceeding the 25% maximum level included in the study design, are consistent with high MARs obtained in studies of benefit-risk tradeoff preferences for hypothetical AD treatments.[5–8]

Many of our respondents were personally acquainted with AD. We found that 64% of respondents reported having had a friend or family member with AD, and of those, about 25% had provided some form of care for that person. According to an analysis of Medicare claims data, about one-third of all Medicare beneficiaries who died in 2014 had been diagnosed with AD or another dementia.[26] Because our respondents all were age 60 or older, the likelihood would be quite high that they were acquainted with at least 1 person with dementia.

There are competing hypotheses about why a proportion of respondents always choose either treatment or no treatment. Respondents could always choose the same alternative because they are unwilling to expend the effort of evaluating the choice alternatives. In that case we obtain no valid information about their actual preferences. Alternatively, it is possible that respondents either are highly risk averse or highly efficacy seeking. For these respondents, the study design never shows a treatment that would induce risk-averse respondents to trade away from the no-treatment alternative or discourage efficacy-seeking respondents to trade away from the treatment alternative. In that case, although we learn nothing about what levels would induce trading, the responses are a valid indication of preferences within the ranges of levels offered in the study design. A third possible explanation is that dread of experiencing the course of untreated disease progression leads some respondents to seek a "do something" strategy, perhaps hoping that their own efficacy, nausea, and risk outcomes would be better than the "average results" shown in the treatment alternatives. This strategy is a form of "scenario rejection." We simply do not know what such respondents were assuming about the outcomes in the treatment alternatives.

In addition to some respondents always choosing either treatment or no treatment, an unusual number of respondents apparently failed a simple validity-test question where the treatment alternative offered no improvement in disease progression but had a significant nausea side effect and serious risks of stroke and death in the first year of treatment. In a recent tabulation of internal validity tests for 55 DCEs, 23 datasets included a dominated-pair question.[27] The median failure rate was 7% compared to the 30% failure rate observed in this study. The 30% apparent failure rate suggests that there could be a "label effect" attached to the intervention alternative. Although the respondent sample was older and could have found the choice task difficult or confusing, we found that people who chose the intervention alternative in the test also were more likely to choose the intervention alternative in the choice-experiment questions than people who did not fail the test. We would not have observed such systematic behavior if respondents simply were confused. Instead, this result suggests doing something alone conveys additional utility, apart from clinical outcomes and risks. Respondents thus chose treatment more often than the net benefit of the average treatment profile would predict and quantitatively is identified as a positive treatment-label effect. This pattern is consistent with scenario recoding by respondents who assume their own results would be more favorable than the average patient. This "value of hope" has been observed in other terminal diseases.[28–30] There were few significant covariates to suggest possible competing hypotheses to that offered here. The largest effect size was for patient caregivers. The positive effect of experience on always choosing the active intervention is logical. Having at least a 2-year college degree also had a significant positive effect on propensity to fail the validity test, an indication that confusion related to low educational attainment was not a significant factor.

The model that excludes only respondents who failed the dominated-pair test (model 2) purges the label effect and provides a defensible basis for evaluating tradeoffs between benefits and risks in this group of respondents. This model excludes respondents who preferred the treatment option even when the treatment risks provided no benefits but includes some respondents who always chose no medicine and some who always chose medicine in the DCE questions but not in the validity test. This model yields risk-tolerance estimates similar to those for the model that includes the approximately half of the sample who at least sometimes accepted tradeoffs between no-treatment and treatment alternatives and also passed the validity test. The difference between the 7% mortality MAR for 1 additional year of normal memory in this model and the 19% MAR for the model with the largest label-effect parameter is 12%. That suggests that the average "value of hope" in this sample is equivalent to being willing to accept an additional 12% mortality risk.

The side effects that were used in the study design included up to a 25% chance of disabling stroke in the first year and up to a 25% chance of death in the first year of treatment. These levels are much larger than what regulators would ever consider approving for a medication. Nevertheless, AD is a dreaded condition. Our results suggest that respondents who understand the debilitating effects of Alzheimer's disease may be motivated to seek active interventions, possibly with risks that otherwise would be intolerable in other contexts. Although clinicians may be reluctant to accept such attitudes as valid, it is possible that the value of hope has a real impact on patients' tolerance for risk. Better understanding of the value of hope in stated-preference research could help inform patient-centric decision making that accounts for such preferences.

The usual limitations of stated-preference studies apply, including potential for hypothetical bias, measurement error resulting from the difficulty of evaluating the tradeoff questions, and poor understanding of treatment attributes and levels. In future research, it would be interesting to compare responses under a hypothetical diagnosis of early-stage AD with responses under an actual diagnosis. Because the sample consisted of older individuals who could find the choice questions especially

difficult, we simplified the task by including a no-treatment reference alternative that was held constant in every question. Only the features of the treatment alternative varied among questions. The study design successfully yielded preference estimates that were logically ordered with good statistical precision.

We defined the harmful treatment outcomes as number of events observed out of 100 patients treated and the no-treatment and treatment disease-progression profiles as deterministic ("what would happen to you"). Nevertheless, being amyloid positive does not mean a 100% chance that a person will get AD. Treating memory loss and dementia symptoms as deterministic makes the preference-elicitation questions less burdensome and reduces measurement error but biases MAR estimates upward to an unknown extent. We also asked respondents to assume they had received results from a hypothetical amyloid test that confirmed they would develop AD. It is possible that they would have responded differently if they had known their actual amyloid status. Repeating this study in a sample of actual patients with positive amyloid status would provide evidence on the role of hypothetical bias in stated-preference research.

The DCE questions can be challenging, particularly for older respondents. It is possible our high rate of dominated-pair test failure was a result of age-related cognitive decline. However, relative to respondents aged 60 to 74, respondents aged 75 to 85 had a slightly negative, but statistically insignificant, propensity to fail the test. Nevertheless, we are unable to rule out the possibility that failure rates for the same instrument would be lower in a younger sample.

The results of this study demonstrate that in a US sample of older individuals aged 60 to 85, respondents were more concerned, on average, about preserving additional normal memory than the risks presented from a hypothetical AD treatment. Nevertheless, some respondents were not willing to assume risks associated with treatment up to a decade before cognitive symptoms and functional decline. As we move into an era of screening and treating disease to preempt onset or modify the trajectory, individualized benefit-risk tradeoffs should be carefully considered before initiating screening and treatment for AD.

Acknowledgments

The authors thank Duke colleagues Juan Marcos Gonzalez and Angelyn Fairchild for comments and suggestions during the study. Financial support for this study was provided in part by a research agreement between Janssen R&D and Duke University. The funding agreement ensured the authors' independence in designing the study, interpreting the data, writing, and publishing the report. The following authors are (RLD, BL) or were (JS) employed by the sponsor.

Supplemental Materials

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2019.03.022.

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