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Why would caregivers not want to treat their relative's Alzheimer's disease?

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Abstract

Objectives: To determine family caregivers' willingness to use Alzheimer's disease (AD)-slowing medicines and to examine the relationships between this willingness, dementia severity, and caregiver characteristics.

Design: Cross-sectional survey.

Setting: In-home interviews of patients from the Memory Disorders Clinic of the University of Pennsylvania's Alzheimer's Disease Center.

Participants: One hundred two caregivers of patients with mild to severe AD who were registered at an Alzheimer's disease center.

Measurements: Subjects participated in an in-home interview to assess their willingness to use a risk-free AD-slowing medicine and a medicine with 3% annual risk of gastrointestinal bleeding.

Results: Half of the patients had severe dementia (n=52). Seventeen (17%) of the caregivers did not want their relative to take a risk-free medicine that could slow AD. Half (n=52) did not want their relative to take an AD-slowing medicine that had a 3% annual risk of gastrointestinal bleeding. Caregivers who were more likely to forgo risk-free treatment of AD were older (odds ratio (OR)=1.7, P=.04), were depressed (OR=3.66, P=.03), had relatives living in a nursing home (OR=3.6, P=.02), had relatives with more-severe dementia according to the Mini-Mental State Examination (MMSE) (OR=2.29, P=.03) or Dementia Severity Rating Scale (DSRS) (OR=2.55, P=.002), and rated their relatives' quality of life (QOL) poorly on a single-item global rating (OR=0.25, P=.001) and the 13-item quality-of-life (QOL)-AD scale (OR=0.38, P=.002). Caregivers who were more likely to forgo a risky treatment were nonwhite (OR=6.53, P=.005), had financial burden (OR=2.93, P=.02), and rated their relative's QOL poorly on a single-item global rating (OR=0.61, P=.01) and the QOL-AD (OR=0.56, P=.01).

Conclusion: These results suggest that caregivers are generally willing to slow the progression of their relative's dementia even into the severe stage of the disease, especially if it can be done without risk to the patient. Clinical trials and practice guidelines should recognize that a caregiver's assessment of patient QOL and the factors that influence it affect a caregiver's willingness to use AD-slowing treatments.

Comments

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CLINICAL INVESTIGATIONS:

Why Would Caregivers Not Want to Treat Their Relative's Alzheimer's Disease?

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Objectives: To determine family caregivers' willingness to use Alzheimer's disease (AD)-slowing medicines and to examine the relationships between this willingness, dementia severity, and caregiver characteristics.
Design: Cross-sectional survey.
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Participants: One hundred two caregivers of patients with mild to severe AD who were registered at an Alzheimer's disease center.
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Results: Half of the patients had severe dementia (n=52). Seventeen (17%) of the caregivers did not want their relative to take a risk-free medicine that could slow AD. Half (n=52) did not want their relative to take an AD-slowing medicine that had a 3% annual risk of gastrointestinal bleeding. Caregivers who were more likely to forgo risk-free treatment of AD were older (odds ratio (OR)=1.7, P=.04), were depressed (OR=3.66, P=.03), had relatives living in a nursing home (OR=3.6, P=.02), had relatives with more-severe dementia according to the Mini-Mental State Examination (MMSE) (OR=2.29, P=.03) or Dementia Severity Rating Scale (DSRS) (OR=2.55, P=.002), and rated their relatives' quality of life (QOL) poorly on a single-item global rating (OR=0.25, P=.001) and the 13-item quality-of-life (QOL)-AD scale (OR=0.38, P=.002). Caregivers who were more likely to forgo a risky treatment were nonwhite (OR=6.53, P=.005), had financial burden (OR=2.93, P=.02), and rated their relative's QOL poorly on a single-item global rating (OR=0.61, P=.01) and the QOL-AD (OR=0.56, P=.01).
Conclusion: These results suggest that caregivers are generally willing to slow the progression of their relative's dementia even into the severe stage of the disease, especially if it can be done without risk to the patient. Clinical trials and practice guidelines should recognize that a caregiver's assessment of patient QOL and the factors that influence it affect a caregiver's willingness to use AD-slowing treatments.

Alzheimer's disease (AD) causes substantial morbidity for patients and their family caregivers,[1,2] the annual costs of care range from $51 billion to $88 billion,[3,4] and in the next 50 years, the current

prevalence of four million patients is projected to quadruple.[5] Current treatments such as vitamin E and cholinesterase inhibitors affect the progression of functional losses.[6,7] Treatments that could definitively slow progressive decline hold great promise,[5] but the promise of AD-slowing treatments also presents a challenge: When is slowing AD no longer valued?[8] Family caregivers' answer to this question provides an important perspective. They are largely responsible for making treatment decisions for patients, especially patients with moderate to severe AD.[9] Hence, their decisions will influence the distribution of the costs and benefits of dementia treatments and the prevalence of the disease. It will also suggest what clinical factors influence treatment decisions. These, in turn, can be useful guides for clinicians, researchers, and policy makers to develop patient- and caregiver-sensitive treatment and research guidelines.

Previous research has shown that caregivers' willingness to slow AD and to take risk to achieve this are associated with their assessment of the patient's quality of life (QOL),[10] but this study included only caregivers of patients with mild to moderate dementia, and all the caregivers were willing to slow the patients' dementia with a risk-free medicine.

In the current study, caregivers' willingness to treat AD in patients with a wider spectrum of dementia severity was examined. The authors hypothesized that three factors would be associated with the decision not to treat AD: increasing dementia severity, increasing caregiver distress, and decreasing ratings of the patients' QOL.

Methods

Eligibility Criteria

Caregivers of patients who met National Institute of Neurological and Communicative Disorders and Stroke/Alzheimer's Disease and Related Disorders Association criteria for probable or possible AD[11] were recruited from the caregiver cohort of the Memory Disorders Clinic of the University of Pennsylvania's Alzheimer's Disease Center (ADC) to participate in an in-home interview. Eligible caregivers had to live within a 1.5 hour driving distance from the ADC and had to be knowledgeable informants about disease severity and response to treatments, make decisions for or with the patient, and—except in the case of patients in residential long-term care—to assist the patient with activities of daily living.

Caregiver Measures

The caregivers' age, years of education, employment, and finances were recorded using the single-item Established Populations for Epidemiologic Studies of the Elderly financial burden measure.[12] Caregivers' depressive symptoms were measured using the 15-item Geriatric Depression Scale (GDS) and were assigned a score of 6 or more as depression,[13] and caregiver burden was measured using the Screen for Caregiver Burden (SCB).[14] This 25-item scale includes an objective measure of the presence of potentially distressing patient behaviors and caregiving tasks (range 0–25) and a subjective measure of the degree of distress the caregiver experiences from the event (25–100).

Patient Measures

The same demographic information was recorded for the patients as for their caregivers; in addition, the severity of the patient's dementia was assessed using the Mini-Mental State Examination (MMSE)[15] and the Dementia Severity Rating Scale (DSRS).[16] The DSRS is a caregiver-completed

version of the Clinical Dementia Rating scale.[17] Higher scores indicate increasing severity of cognitive and functional impairment.

Measures of QOL

Caregivers' rating of patients' QOL was determined using a single-item rating of the patient's overall status ("How would you rate your relative's overall quality of life?" poor, fair, good, very good, or excellent), and the Quality of Life in Alzheimer's Disease Scale (QOL-AD).[18] The QOL-AD assesses 13 items (physical health, energy, mood, living situation, memory, family, marriage, friends, self as a whole, ability to do chores around the house, ability to do things for fun, money, and life as a whole) with the answer choices of poor, fair, good, and excellent for each item. Scores range from 13 to 52. Higher scores indicate better ratings of QOL.

Measures of Caregivers' Treatment Preferences

Caregivers participated in an interview that assessed their willingness to allow their relative to take each of two AD-slowing medicines: a medicine without risks and a medicine with a 3% annual risk of gastrointestinal bleeding severe enough to require hospitalization, transfusion, and possible surgery. The order of questions was the 3% risk medicine, a series of questions to assess the patient's involvement in the decision to use the medicine, and then the risk-free medicine. Both medicines' benefits were described as "once-a-day medicine that slows down Alzheimer's disease and memory loss by 1 year." A study of the medicine showed the following benefits: patients live 1 year longer, a 1-year delay before needing 24-hour nursing care, and a 1-year delay before problems in recognizing family." The interviewer explained that a disease-slowing medicine does not restore abilities the patient has already lost but delays the time before other abilities are lost. These benefits and risk were chosen because previous research by the authors of caregivers' treatment preferences identified them as important benefits, and caregivers readily understood the risk of gastrointestinal bleeding.[10] To minimize the framing effects the risk was presented as: "The chance of this risk is 3%. This means that if 100 people take it for 1 year, three of them will have this bleeding ulcer and 97 will not." Caregivers were also asked to explain their decision not to use a risk-free medicine. These answers were tape- recorded and transcribed. Content analysis was used to generate codes that explained the meaning of the caregiver's answers.[19] Two research assistants collectively reviewed these codes to generate a consensus-based set of codes that they used to independently code all of the answers. Agreement between the coders was 85%.

Assessment of Treatment Preferences Reliability and Validity

A pilot test of the interview on 23 caregivers showed that the caregivers' decisions had good test/retest reliability with kappa of 0.64 for a risk-free AD-slowing medicine and 0.56 for a medicine with risk. Comparing the patients' current AD treatments with the caregiver's decisions supported the validity of the measure. The decision not to take either AD-slowing medicine was strongly associated with the patient not taking a cholinesterase inhibitor (no risk: chi-square ($\chi 2$)=8.6, P=.003, risk-free: $\chi 2$=7.13, P=.008). Although a similar association was not found with the use of vitamin E ($\chi 2$=0.43, P=.5; $\chi 2$=2.3, P=.13), only 19% of the caregivers thought that vitamin E slows dementia, whereas 49% thought that a cholinesterase inhibitor slows dementia.

Statistical Analyses

Logistic regression was used to examine univariate and multivariate associations between caregiver and patient demographics, the caregiving experience, patient disease severity, and ratings of QOL as

summarized in Tables 1 and 2. Continuous measures were separated into categories based on accepted cutpoints (MMSE, GDS) or by quartiles (age, SCB, DSRS, QOL-AD). For the decision to take an AD-slowing medicine, a coding of a "yes" as 0 and a "no" as 1 was used. Hence, unless otherwise indicated, an odds ratio (OR) greater than 1.0 indicates that an independent variable is associated with not wanting to slow AD. Multivariate models were constructed using all univariate associations with a type I error of 0.20 or less and assessed the significance of a variable's contribution to a multivariate model using the likelihood ratio test and the P-value of its z score.20 A significance was defined as type I error of 0.05 or less. Stata 6.0 was used to perform statistical analyses (Stata Corp., College Station, TX).

Table 1. Caregiver and Patient Demographics

Demographic Measure	Caregivers (n = 102)	Patients (n = 102)
Sex, n (%)		
Female	67 (66)	70 (69)
Male	35 (34)	32 (31)
Age,* mean ± SD (range)	61.4 ± 13.2 (24–88)	77.7 ± 8.4 (46–96)
Age, n (%)	< 50 25 (25)	< 75 30 (29)
	50–59 27 (26)	75–79 19 (18)
	60–74 29 (28)	80–84 32 (31)
	≥ 75 21 (21)	≥ 85 21 (21)
Race, n (%)	84 (82.4)	84 (82.4)
White	17 (16.7)	17 (16.7)
African American	1 (0.1)	1 (0.1)
Hispanic†		
Education, years, mean ± SD (range)	14.7 ± 2.9 (8–20)	13.2 ± 3.5 (4–20)
Employment, n (%)		
Not working	57 (55.9)	102 (100)
20–39 h/wk	15 (14.7)	
≥ 40 h/wk	30 (29.4)	
Relationship to patient, n (%)		
Spouse	45 (44.1)	
Not spouse (52 adult children)	57 (55.9)	
Financial burden, n (%)‡		
Some money left over	62 (68.1)	
Just enough money	24 (26.4)	
Not enough money§	5 (5.5)	
Where patient lives, n (%)		
Alone or with caregiver	72 (71.3)	
Nursing home or assisted living	29 (28.7)	

* Age categories based on percentages.
† Category combined into "African American" for analyses.
‡ Numbers do not sum to 102 because of missing data.
§ Category combined into "just enough money" for analyses.
SD = standard deviation.

Table 2. Patient Disease Severity, Caregiving Experience, and Caregiver Ratings of Patient Quality of Life

Parameter	Outcome
Mini-Mental State Examination score, mean ± SD (range)	11.9 ± 9.8 (0–29)
Severity, n (%)	
Mild (20–30)	31 (30)
Moderate (12–19)	19 (19)
Severe (0–11)	52 (51)
Dementia Severity Rating Scale, mean ± SD (range)	28.7 ± 14.0 (2–54)
0–16, n (%)	28 (26)
17–27, n (%)	30 (27)
28–37, n (%)	24 (22)
38–54, n (%)	27 (25)
Geriatric Depression Scale score >5, mean ± SD (range)	2.8 ± 2.9 (0–12)
Not depressed, n (%)	85 (83)
Depressed, n (%)	17 (17)
Caregiver objective burden, mean ± SD (range)	8.4 ± 4.2 (2–19)
0–4, n (%)	21 (21)
5–7, n (%)	27 (27)
8–11, n (%)	30 (30)
12–19, n (%)	23 (23)
Caregiver subjective burden, mean ± SD (range)	33.7 ± 8.4 (25–61)
25–27, n (%)	26 (26)
28–30, n (%)	23 (23)
31–37, n (%)	24 (24)
38–61, n (%)	28 (28)
Quality of life–Alzheimer's disease, mean ± SD (range)	30.6 ± 6.7 (15–50)
13–26, n (%)	29 (28)
27–30, n (%)	23 (23)
31–36, n (%)	29 (28)
37–50, n (%)	21 (21)
Global rating of patient quality of life, n (%)	
Poor	17 (17)
Fair	39 (38)
Good	31 (30)
Very good	14 (14)
Excellent	1 (1)*

*Category "excellent" combined with "very good" in analyses.
SD = standard deviation.

Human Subjects Protections

All caregivers provided verbal informed consent, and patients provided assent or consent to participate in this institutional review board–approved research.

Results

One hundred two (60%) of the 171 eligible caregivers agreed to participate. The dominant reason for nonparticipation was lack of time. Comparing the available demographic data of refusers with subjects showed no significant differences in patient or caregiver race, relationship, or age. Tables 1 and 2 summarize the characteristics of the patients and their caregivers. Using standard cutpoints of the MMSE, half of the patients had severe AD (n=52, 51%) and half had mild (n=31, 30%) or moderate (n=19, 19%) AD. Nearly three-quarters (n=72, 71%) lived alone or with family members, and the rest lived in an assisted living facility or nursing home. Two-thirds of the caregivers were women (n=67, 66%). Their average age was 61, but the range of 24 to 88 years reflects that 51% were adult children and 44% were spouses. Nearly two-thirds reported that they

were not experiencing financial distress (n=62, 68%). The majority was Caucasian (n=84, 82%).

Willingness to Use a Risk-Free AD-Slowing Medicine

Only 17 (17%) of the 102 caregivers would forgo a risk-free medicine that could slow AD. Broken down by MMSE-defined dementia stage, one of 31 (3%) caregivers of patients with mild AD, four of 19 (21%) caregivers of patients with moderate AD, and 12 of 52 (23%) caregivers of patients with severe AD would forgo the risk-free medicine. Most (76%) of these 17 caregivers explained that treatment was not of value to the patient, as the following quote illustrates, "It's too late. She already needs 24-hour nursing care; she already doesn't recognize anyone. For her it's just too late." In contrast, the 85 caregivers who wanted to use the medicine offered three reasons: the medicine presented no risk (67%) and provided specific benefits (46%), and taking it was an obvious choice (31%). The most common specific benefits they described were prolonged survival, slowing dementia progression, and maintaining an acceptable patient QOL.

Univariate analyses showed that caregivers who were older (OR=1.71, 95% confidence interval (CI)=1.01–2.89, P=.04) or depressed (OR=3.66, 95% CI=1.13–11.9,P=.03), whose relative lived in a nursing home (OR=3.60, 95% CI=1.23–10.57, P=.02), or who had a patient with more severe dementia according to the MMSE (OR=2.29, 95% CI=1.07–4.90, P=.03) or DSRS (OR=2.55, 95% CI=1.39–4.64, P=.002) were more likely to forgo risk-free treatment of AD. In contrast, the higher a caregiver rated the patient's QOL on a single-item global rating (OR=0.25, 95% CI=0.11–0.55, P=.001) and the 13-item QOL-AD scale (OR=0.38, 95% CI=0.2–0.7, P=.002), the more likely they were to be willing to slow AD. There was a marginal association between greater financial burden and being more likely to forgo treatment (OR=2.99, 95% CI=0.96–9.29, P=.06).

The small number of caregivers who declined this medicine limits the number of predictors in multivariate models. Bivariate analyses that examined the effects of QOL paired with each of the six objective measures of the patient (MMSE, DSRS, and residence) and caregiver (depression, age, and financial burden) were performed. Because there was a strong association between the global QOL measure and the 13-item QOL-AD (rs=0.7), these analyses were performed separately with each QOL measure. In addition, analyses for collinearity among univariate predictors showed an association between the functional severity of dementia (DSRS) and QOL (r=–0.63). Using the QOL-AD scale, only QOL was associated with the decision to forgo risk-free treatment in all bivariate models, except in the model with caregiver age, in which both were significant. The same results were found using the global measure of QOL. In both models, the effect of DSRS greatly attenuated the association between QOL and the willingness to use the medicine, as shown by a 33% reduction in the QOL log OR. To better understand the relationships between DSRS, QOL, and the willingness to treat, an exploratory analysis of dementia severity (DSRS) and QOL in patients with severe AD was performed. It showed that the ratings of QOL were better associated with the decision to forgo the medicine (QOL-AD OR=0.13, 95% CI=0.02–0.96, P=.05; global QOL OR=0.21, 95% CI=0.05–0.83, P=.03) than the measure of dementia severity (OR=5.77, 95% CI=0.6–55.9, P=.13 in both models).

Willingness to Use an AD-Slowing Medicine with Risk

Half (n=52) of the caregivers chose to forgo an AD-slowing medicine that had a risk of gastrointestinal bleeding. Broken down by MMSE-defined dementia stage, 15 of 31 (48%) caregivers of patients with mild AD, 11 of 19 (58%) caregivers of patients with moderate AD, and 26 of 52

(50%) caregivers of patients with severe AD would forgo the medicine that had a risk of gastrointestinal bleeding. All of the 17 caregivers who chose to forgo a risk-free AD-slowing medicine also chose to forgo this medicine.

Univariate analyses showed that caregivers who were nonwhite (OR=6.35, 95% CI=1.71–23.6, P=.005) and had financial burden (OR=2.81, 95% CI=1.12–7.04, P=.03) were more willing to forgo the medicine. In contrast, caregivers rating their relatives' QOL higher on the single-item global rating (OR=0.61, 95% CI=0.4–0.95, P=.03) and the QOL-AD (OR=0.57, 95% CI=0.39–0.84, P=.004) were more willing to use the medicine. Marginally significant associations existed between forgoing the medicine and caregivers who were female (OR=0.51, 95% CI=0.22–1.17, P=.11) and patients who were male (OR=2.15, 95% CI=0.91–5.0, P=.08) and older (OR=1.27, 95% CI=0.89–1.81, P=.18).

A multivariate model that excluded the 11 subjects with missing financial burden data showed that caregivers' decision to forgo treatment was associated with lower ratings on measures of patient QOL (global QOL OR=0.6, 95% CI=0.37–0.94, P=.05 and QOL-AD OR=0.56, 95% CI=0.36–0.88, P=.02) and with being nonwhite (OR=6.6, 95% CI=1.7–25.1, P=.005. Models that included financial burden showed essentially the same results. The relationship between patient and caregiver (spouse vs not spouse) may confound the marginally significant associations between patient and caregiver sex and the caregiver's willingness to forgo treatment. Male patients were more likely than female to have a spousal caregiver (exact P=.001). Models that examined the effects of sex adjusted for spousal status showed that caregivers of male patients were more willing to forgo treatment (OR=3.47, 95% CI=1.2–10.0, P=.02). Eighty-one percent of these caregivers were female spouses.

Associations Between Treatment Preferences and Caregivers' Assessments of Patient QOL

Associations between treatment decisions and the subscales of the QOL-AD after adjusting for multiple comparisons (P-value of .004=.05/13) showed that the decision to forgo a risk-free medicine was associated with lower caregiver ratings on the subscales assessing the patient's life as a whole, self, and mood. In contrast, the decision to forgo a medicine that presented risk was associated with lower ratings on the physical health subscale. Table 4 shows that the proportion of caregivers that forgo each of the two AD-slowing treatments increases as the caregivers' global assessment of patient QOL declines. In both decisions, a marked increase occurs when global ratings are fair or poor.

Table 3. Associations Between Patient and Caregiver Characteristics and Caregiver Decision to Use Alzheimer's Disease–Slowing Medicines

Characteristic	No Risk	Risk of Gastrointestinal Bleeding
	OR (95% Confidence Interval) *P*-value	
Caregiver demographics		
Sex: female versus male	1.05 (0.35–3.14) .93	0.51 (0.22–1.17) .11
Age	1.71 (1.01–2.89) .04	1.17 (0.81–1.68) .40
Race: white versus other	1.0 (0.26–3.92) 1.00	6.35 (1.71–23.6) .006
Education	0.99 (0.83–1.18) .92	0.95 (0.83–1.09) .49
Employment		
Not working	1	1
20–39 hrs/wk	0.30 (0.04–2.52) .27	2.07 (0.63–6.83) .23
>40 hrs/wk	0.84 (0.26–2.68) .76	0.91 (0.27–2.20) .83
Caregiver relationship to patient: spouse versus not spouse	0.87 (0.30–2.49) .79	0.73 (0.34–1.61) .44
Financial burden: some money left over versus just enough/not enough money	2.99 (0.96–9.29) .06	2.81 (1.12–7.04) .03
Patient demographics		
Sex: female versus male	1.17 (0.39–3.50) .78	2.15 (0.91–5.04) .08
Age	1.10 (0.67–1.76) .69	1.27 (0.89–1.81) .18
Education	1.05 (0.90–1.22) .55	0.98 (0.88–1.10) .77
Where patient lives: nursing home or assisted living versus alone or with caregiver	3.60 (1.23–10.57) .02	1.50 (0.63–3.58) .36
Dementia severity		
Mini-Mental State Examination	2.29 (1.07–4.90) .03	1.02 (0.65–1.58) .95
Dementia Severity Rating Scale	2.55 (1.39–4.64) .002	1.15 (0.81–1.63) .43
Caregiving characteristics		
Caregiver depressed: yes versus no	3.66 (1.13–11.9) .03	1.97 (0.67–5.80) .22
Caregiver objective burden	1.11 (0.68–1.83) .44	1.10 (0.78–1.59) .61
Caregiver subjective burden	1.17 (0.74–1.85) .50	1.10 (0.78–1.55) .58
Caregiver ratings of patient quality of life		
QOL-AD scale	0.38 (0.20–0.70) .002	0.57 (0.39–0.84) .004
Global rating of QOL	0.25 (0.11–0.55) .001	0.61 (0.40–0.95) .03

Note: Odds ratio (OR) >1 denotes an association with decision not to use the AD-slowing medicine; OR <1 denotes an association with the decision to use the medicine.
QOL = quality of life.

Table 4. Proportions of Caregivers Not Wanting to Use Alzheimer's Disease (AD)-Slowing Treatments for Each Level of the Global Assessment of Quality of Life

Caregiver Global Rating of Patient Quality of Life	Forgo a Risk-Free AD-Slowing Medicine	Forgo an AD-Slowing Medicine with Risk of GI Bleeding
	% (n/N)	
Very good (n = 14) or excellent (n = 1)	0 (0/15)	40 (6/15)
Good (n = 31)	6 (2/31)	35 (11/31)
Fair (n = 39)	18 (7/39)	61 (24/39)
Poor (n = 17)	47 (8/17)	64 (11/17)

GI = gastrointestinal.

Discussion

The development of AD treatments has placed increased focus on the need for stage-specific treatment goals.[21] This study begins to define the caregiver perspective on these goals. Caregivers are generally willing to slow the progression of their relative's AD even into the severe stage of the disease and to expose the patient to risk to achieve this. Below, four specific findings about how caregivers will formulate treatment goals are discussed.

First, for both risk-free and risky AD treatments, QOL is a key factor in a caregiver's decision as to whether to allow their relative to use that treatment. A single global rating that is poor or fair may signal that a caregiver no longer values slowing disease progression and that a discussion of palliative care is warranted. The associations between the QOL subscales and the decision not to treat suggest that caregivers who decline a treatment that they perceive as risky are likely to perceive the patient's overall health as poor. The association between forgoing this treatment and increasing patient age supports this conclusion, because older patients are likely to accumulate comorbidity. These results emphasize the need for AD treatment guidelines to include overall assessments of the patient's health and suggest that comorbidity influences willingness to treat AD. Future studies should examine the influence of patients' comorbidity on caregivers' treatment decisions. In contrast, caregivers who decline a treatment that they perceive as safe or even risk-free are addressing fundamental issues about the patient as a person. Finally, a decision not to treat warrants identifying and addressing sources of burden. Although caregiver burden was not directly associated with the decision not to treat, greater degrees of caregiver burden are associated with lower ratings of patient QOL. (In this cohort, associations between the measures of QOL and burden ranged between 0.34 and 0.45.[22,23]) This illustrates how QOL is a composite measure that incorporates aspects of dementia severity, burden, and caregiver depression.

Second, the decision to forgo treatment is more likely as dementia severity increases, but this depends on the risk of the treatment and the caregiver's assessment of patient QOL. The decision not to use a risk-free medicine was most strongly associated with functional (DSRS) rather than cognitive (MMSE) measures of dementia severity, but adjusted analyses suggest that the assessment of patient QOL diminishes the significance of dementia severity. The addition of risk to a treatment choice shows this even more clearly. The decision to forgo a risky treatment was not associated with functional or cognitive measures of dementia severity but with caregivers' assessment of patients' QOL.

Third, caregivers' mental health may influence their decisions to forgo AD treatment. Greater depressive symptoms in caregivers were associated with less willingness to treat with a no-risk treatment, but greater scores on the objective and subjective measures of burden were not associated with treatment decisions. These findings support the view that depression is the final common path of the many aspects of caregiver burden.[24] Clinical trials and practice should recognize the caregiver as a potential second patient and focus on caregiver mood as an endpoint and goal of treatment. Further research should investigate whether treatment of caregivers' depression will alter their choices about AD treatment.

Fourth, specific patient and caregiver characteristics were associated with treatment decisions. Caregivers who were older were less willing to use a risk-free medicine. Because none of the disease-severity or QOL measures were associated with caregiver age, this suggests a unique association

between the willingness to slow AD and the caregiver's age. Caregivers who were nonwhite were less likely to use a risky treatment. This association warrants further research to investigate potential ethnic and cultural differences in concepts of risk taking, surrogate decisions, and AD. The relationship between financial burden and the decision not to treat reiterates the finding that families of seriously ill patients with financial stress are more likely to express a preference for comfort care over life-extending care.25 This study's results may reflect caregivers' concerns that harm to the patient caused by a treatment's side effects will increase their care needs and thus the out-of-pocket costs of health care or that living longer with AD extends costs. It also suggests that the price of AD medicines may affect caregivers' willingness to use them. In this study, medication cost was not disclosed, and caregivers who asked for that information were instructed to work with the information presented. Finally, the associations between the decision to use a risky treatment and patient and caregiver sex suggests that the relationship between patient and caregiver or their sexes may influence caregivers' willingness to take risk to treat their relative's AD.

Limitations of this study include the difficulty in enrolling caregivers who reported that they did not have enough time to participate in an interview. This may explain the failure of this study to identify an even greater effect of depression on decision-making. In addition, although this sample reflects a diverse severity of AD, it came from patients and caregivers who attended a university-based ADC. People in this kind of cohort are unique in terms of their understanding of AD and the information and attitudes they receive from clinicians. Future research should investigate the treatment preferences of more-diverse caregiver cohorts to examine variability in the decision to use AD-slowing treatments and patient, caregiver, and clinician factors associated with these decisions. Finally, the associations between the willingness to take risk to slow AD and patient and caregiver factors may depend on the magnitude or probability of the risk.

Caregivers are largely responsible for making treatment decisions for patients, especially patients with moderate to severe AD.9 Understanding how they make these decisions can guide the development of patient- and caregiver-sensitive treatment and research guidelines. Caregivers' decisions not to treat AD are to some degree associated with functional measures of dementia severity, but their assessment of patient QOL, demographic, and cultural factors largely attenuates this effect. These results suggest that objective measures of dementia severity cannot be the sole guide for the use of these drugs.

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