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ORIGINAL RESEARCH

Living at Risk: The Sibling's Perspective of Early-Onset Alzheimer's Disease

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Abstract Early-onset Alzheimer's disease (EOAD) is an increasingly diagnosed condition and is associated with genetic risk factors. This is one of the first studies exploring the lived experience of siblings of individuals with EOAD. We used structured questionnaires and semi-structured interviews to assess a broad range of siblings' experiences with and beliefs about EOAD, including knowledge, perceptions of personal risk, level of worry, and effects on life decisions. Participants (n=24) were predominantly female (62.5%) and middle-aged (mean = 56.8 years; range 37–83). When asked about risk factors, genetics was cited most frequently (62.5%). Several potential means of reducing AD risk were endorsed, with 54% reporting engagement in behaviors for this purpose (e.g., keeping mentally active). Participants ranged widely in their perceived personal risk of AD (range: 0–100; mean = 35.6%), with higher perceived risk associated with worry about AD (p<0.01). Understanding siblings' experiences with EOAD can inform how genetic counselors and healthcare professionals work with this population to facilitate risk communication and decision-making about testing and healthcare.

Keywords Early-onset Alzheimer's disease · Sibling · Risk · Lived experience · Worry · Genetics · Decision-making

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Introduction

Early-onset Alzheimer's disease (EOAD) is a neurodegenerative disease, and common form of dementia, with onset of symptoms prior to age 65. EOAD is estimated to affect approximately 250,000 Americans (Alzheimer's Association 2007) and may account for up to 5% of all cases of Alzheimer's disease (Bertram and Tanzi 2004; Brickell et al. 2006). Multiple genetic risk factors have been associated with both early-onset and late-onset Alzheimer's disease, and many unknown genetic and environmental components are likely involved (Bertram and Tanzi 2004; Bird 2005). There are three genes known to cause early-onset familial Alzheimer's disease (*APP, PSEN1,* and *PSEN2*), which are implicated in less than 2% of Alzheimer's disease cases (Bird 2005). All are inherited in an autosomal dominant pattern and show complete penetrance (Bertram and Tanzi 2004; Bird 2005).

The most powerful risk factor for late-onset Alzheimer's disease, on the other hand, is an individual's age, with the prevalence in the general population increasing from 3% at age 65 to 50% by age 85 (Lautenschlager et al. 1996). Interestingly, 25% of individuals with late-onset Alzheimer's

disease have a relative who also had dementia, and more than 100 genetic loci are being considered as low penetrance risk factors for developing Alzheimer's disease (Bertram and Tanzi 2004; Bird 2005). In addition, homozygosity for the apolipoprotein E (APOE) ε4 genotype, presumably in conjunction with several other unidentified genes, has been shown to put an individual at a higher risk for developing Alzheimer's disease at an earlier age, increasing one's risk by 3–4 times and shifting the age of onset by as much as 10 to 15 years (Bird 2005; Farrer et al. 1997; Lautenschlager et al. 1996). An individual's *APOE* genotype is not, however, sufficient to cause Alzheimer's disease, making genetic counseling for this genetic testing fraught with complications. As a result of this genetic and phenotypic heterogeneity, some cases of early-onset Alzheimer's disease are clearly familial with understood genetic causes and modes of inheritance. Others arise in families where the genetic contributions are less clear, for example, a family with no history of disease or with a history of late-onset Alzheimer's disease (Brickell et al. 2006). Individuals in such families are considered at increased risk but are not certain to develop Alzheimer's disease, making this condition similar to other multifactorial adult diseases.

Risk Perceptions

The general public's perception of risk for common multifactorial adult diseases such as heart disease, cancer, and diabetes, is molded by an individual's experience with the disease, the patterns of disease in the family, and how an individual compares him or herself to an affected relative (Sivell et al. 2008; Walter et al. 2004). A recent study by Suhr and Kinkela (2007) found that individuals with a family history of Alzheimer's disease reported a higher perceived threat of developing the disease than individuals who had no personal experience with the disease or whose experience was with non-related individuals. One's risk perceptions are further interpreted through one's beliefs of disease causation and fatalism, and depend upon one's coping skills and personal control needs (Walter et al. 2004). These findings are consistent with current theoretical models of illness representation and risk perception across multiple disease types (Shiloh 2006; Sivell et al. 2008). Furthermore, an individual's risk perception has been linked to changes in health behaviors and uptake of various services (e.g., purchase of long- term care insurance) (Decruyenaere et al. 2000; Zick et al. 2005).

Once a close relative has been diagnosed with Alzheimer's disease, personal risk becomes a clear concern for family members (Roberts and Connell 2000; Suhr and Kinkela 2007). However, efforts to understand the risk perceptions of individuals with a family history of Alzheimer's disease have largely been limited to the children of affected individuals (Gershenson Hodgson and Cutler 2003; Roberts and Connell 2000). Previous studies of siblings at genetic risk for adult-onset disorders have centered on the genetic testing process and an individual's decision about or response to testing (Broadstock et al. 2000). While this is helpful for understanding clinical outcomes, it does not adequately address the "lived experience" that an individual has with a disease (Etchegary 2006). The way individuals experience a disease in their family influences their beliefs about the disease, the coping strategies they may adopt, and possibly important life decisions regarding self-care, family planning, and financial planning (Etchegary 2006; Sivell et al. 2008; Walter et al. 2004).

The Sibling Experience

In general, siblings are an important and understudied group. The majority of genetic risk studies have focused on children of affected individuals or how risk perceptions relate to genetic testing uptake (Broadstock et al. 2000). Studies of disease experiences tend to focus on youth or carrier status and caregiver studies usually focus on spouses or children. There are, however, many reasons to learn about an individual's experience with a sibling with EOAD. Not only are these individuals at an increased risk for Alzheimer's disease themselves (Green et al. 2002; Lautenschlager et al. 1996), their experience with EOAD may have personal psychosocial ramifications.

Very little is known about how brothers and sisters respond to a siblings' disease. Studies of adults who have lost a sibling in childhood to cystic fibrosis, ataxia telangiectasia, or X-linked severe combined immunodeficiency have uncovered many inaccurate beliefs about genetic inheritance, feelings of guilt and burden, and communication barriers between family members (Fanos 1999; Fanos and Gatti 1999; Fanos and Johnson 1995; Fanos et al. 2001). For an individual whose sibling is affected with Alzheimer's disease, these responses could be complicated by physical or emotional distance between siblings, assuming the role of caregiver, and the additional responsibilities that come with adulthood, such as work and family.

Factors that influence communication in the family may impact how an individual experiences a sibling's disease, particularly one with genetic components (Etchegary 2006; McAllister et al. 2007). Social stigma has been associated with several neurological and psychological conditions and can impair an individual's and a family's ability to talk about a disease and how it is inherited. A lack of communication may lead to myths, misconceptions, or ignorance of the risk for developing the condition (Fanos 1999; Fanos and Gatti 1999; Fanos and Johnson 1995; McAllister et al. 2007). This could potentially interfere with the difficult or painful task of talking about a genetic risk in the family or with communicating needs as a caregiver.

The unique nature of an individual's experience with Alzheimer's disease is likely to be interwoven with the risk he or she perceives, the openness of communication within the family, and the level of control that the individual feels as a result of this risk. One measure of disease-related anxiety is symptom-seeking, or searching for evidence of a disease in oneself. Symptom-seeking has been associated with first-degree relatives of individuals with genetic diseases such as Huntington's disease, and Gershenson Hodgson and Cutler (2003) have demonstrated that children of individuals with Alzheimer's disease often exhibit symptom-seeking behavior. The early-onset nature of a sibling's disease may lead to more fear and anxiety than if the disease onset were later. Furthermore, younger individuals may also experience greater concern for their own risk of developing Alzheimer's disease than older people, leading to a higher interest in genetic susceptibility testing (Beebe-Dimmer et al. 2004; Roberts et al. 2004; Suhr and Kinkela 2007).

Purpose of this Study

The objective of this exploratory study was to gain an understanding of the experiences of adults who have a sibling with early-onset Alzheimer's disease, their sense of risk, and the impact of their sibling's illness on life decisions. Within this larger objective, we examined differences based on age and gender between specific measures, including: 1) Alzheimer's disease-related anxiety as measured by symptom-seeking behavior, 2) worry about Alzheimer's disease, 3) beliefs about developing Alzheimer's disease, and 4) perceived risk. Based on previous studies, we anticipated that younger individuals would indicate a higher sense of risk than older individuals (Roberts et al. 2004; Suhr and Kinkela 2007). We believe that learning about these experiences can provide insight for genetic counselors and other healthcare professionals who will encounter these individuals as patients, as well as identifying possible improvements in healthcare resources or areas of future study.

Methods

Participants and Procedures

Individuals were eligible for participation if they had a sibling, living or deceased, who was diagnosed with early-onset Alzheimer's disease (as defined as onset before the age of 65), and if they were not personally experiencing symptoms of dementia. Multiple siblings from the same family were eligible. This study was approved by the University of Michigan Medical School Institutional Review Board.

Twenty-five individuals participated in this study and were recruited through five sources: 1) the Michigan Alzheimer's Disease Research Center's (MADRC) patient registry (n=12); 2) the Adult Medical Genetics Clinic and the Neurology Clinic at the University of Michigan (n=1); 3) support groups of the Michigan Great Lakes and Greater Michigan Chapters of the Alzheimer's Association (n=6); 4) websites focused on Alzheimer's disease research and clinical trials recruitment (e.g., www.alzforum.org, n=4); and 5) word of mouth (n=2).

Once contacted by a participant, we mailed an informed consent form and a 48-item questionnaire to the participant's home. The questionnaire consisted of four sections: a) demographics, b) experience with Alzheimer's disease, c) perceptions of Alzheimer's disease, and d) response to Alzheimer's disease. The format was modeled after the Alzheimer's Disease Treatment and Illness Perceptions Survey from Boston University which has been used in previous studies of adult children and siblings (Roberts 2000; Roberts and Connell 2000). Each participant was also given the opportunity to participate in an optional telephone interview. Semi-structured interviews, ranging from 30 to 90 min, were conducted by phone with those participants who chose to continue with the study. Interviews were audio taped and transcribed verbatim.

A total of 29 individuals originally made contact and agreed to participate. One participant decided later not to participate because of concerns for his spouse's health, and two others failed to return their questionnaires. Due to late enrollment, one participant was interviewed but did not fill out a questionnaire. Twenty-five participants from 17 different families returned questionnaires (response rate = 86%); 16 participants were interviewed. One participant filled out the questionnaire incorrectly and was excluded from the statistical analysis; however, some of the qualitative questionnaire responses were utilized. Therefore, there were 25 participants with 24 questionnaires and 16 interviews considered for analysis.

Measures

Demographics and Health History

General demographic information was elicited, as well as the physical distance the participant lived from the affected sibling and the amount of time since the sibling's diagnosis. Family history information was elicited through a list of relatives (e.g., mother, father…), including current age or age at death and age at diagnosis if affected. Participants were asked to rate their physical health, mental health, and memory (1=Poor; 5=Excellent).

Experience with Alzheimer's Disease

In the quantitative questions, participants were asked to indicate: 1) when they were informed of their sibling's

diagnosis (1=Same day; 6=More than a year), 2) what their relationship with their sibling was like before and after the diagnosis (1=Very close; 4=Not close), and 3) what types of caregiving roles they have provided for their sibling from a given list (e.g., manage finances, prepare meals).

Qualitative questionnaire and interview questions explored the relationship between the participants and their affected siblings by asking for a description of what growing up together was like and what their relationship as adults was like. Participants were asked to describe when they first suspected/learned about the diagnosis, who they talked to about their concerns, how they felt, and what it was like to talk to their sibling and other family members about it. Participants were also asked to describe how the relationships within their family have changed when their sibling was diagnosed.

Perceptions of Alzheimer's Disease

Measures regarding perceptions of Alzheimer's disease were taken from the Alzheimer's Disease Treatment and Illness Perceptions Survey from Boston University (Roberts 2000; Roberts and Connell 2000). This survey includes subscales measuring: 1) knowledge of basic facts about Alzheimer's disease, 2) beliefs about Alzheimer's disease risk factors and possible preventive measures, and 3) perceptions of personal risk of developing Alzheimer's disease. Knowledge was assessed with a series of 13 Yes/No or True/False questions (e.g., "*Which of the following are symptoms of Alzheimer's disease?*") (Roberts and Connell 2000). Beliefs and concerns about Alzheimer's disease were assessed by asking the participants to respond to a series of statements (e.g., "*I believe I will get AD someday.*") (1=Strongly disagree; 5=Strongly agree). They also assigned a level of importance to a list of risk factors and preventive measures (1=Not important; 5=Extremely important), and provided an estimated percentage for their risk for developing Alzheimer's disease during their lifetimes (0–100%). Qualitative questionnaire and interview questions expanded on participants' thoughts about their personal risk for developing Alzheimer's disease and what they believe may impact this risk.

Response to Alzheimer's Disease

Time spent worrying and the effects of worrying about Alzheimer's disease were assessed with scaled responses (1=Very often; 4=Not at all), and participants were asked about any memory checks they have. One question regarding symptom-seeking behavior was used in a previous study of children of individuals with Alzheimer's disease (Gershenson Hodgson and Cutler 2003). Participants were asked if they had made any behavior changes in order to reduce their risk, and if so, to describe them. Participants were asked to indicate any plans made to prepare for the development of Alzheimer's disease from a given list with "Yes/No" responses.

Qualitative questionnaire and interview questions invited participants to describe their feelings about Alzheimer's disease, how Alzheimer's disease has affected their life decisions, any positive outcomes from their sibling's illness, and any other thoughts or experiences that they would like to share. Interviews ended with the participants describing how the siblings' illnesses have changed their lives, whether any life decisions would have been made differently if their sibling had not developed Alzheimer's disease, any changes in self-perception, any positive experiences, and any other thoughts or experiences that were felt to be important.

Data Analysis

Quantitative Analysis

The responses from the questionnaire were coded, entered into a Microsoft Access database, and analyzed using SPSS 13.0. Descriptive statistics were used to characterize sample demographics and responses to questionnaire items. Chi-square analyses with or without a Fisher exact two-tailed test were performed to identify age-related differences in: symptom-seeking behavior, worry about Alzheimer's disease, and answers relating to beliefs and concerns about developing Alzheimer's disease someday. Five-item scaled response categories were collapsed into three for analysis: disagree (containing strongly disagree and disagree), neutral, and agree (containing strongly agree and agree). Correlational analysis was performed to identify an association between age and risk estimation. For all analyses of age effects, the participant data were dichotomized as either "younger" (56 years or below) or "older" (57 years and above). This division was based on a mean participant age of 56.8 years.

Qualitative Analysis

Analysis of qualitative data was based on constant comparative analysis within the grounded theory approach proposed by Glaser and Strauss (Heath and Cowley 2004). This approach allowed the data from the questionnaires and the interviews to be considered together and has been used in the fields of sociology, nursing, and genetic counseling. Open-ended questionnaire responses were considered in combination with related interview responses, and interview-specific questions were considered independently. Participants could offer multiple responses to each question.

Qualitative responses to each question were analyzed for the emergence of themes and recurrent responses by the lead author. These themes were then further subdivided or combined as appropriate into response categories. For example, emotional responses such as sadness, feelings of loss, and grieving were combined into a category of grief, and expressions of concern were divided into concern for self and concern for other family members. The number of individuals who gave responses in the most common categories was totaled.

Table 1 Participant Demographics (n=24)

Age: Range (37–83), Mean (56.8)	*n*	%
30–39	2	8.3
40–49	4	16.7
50–59	11	45.8
60–69	2	8.3
70–79	4	16.7
80–89	1	4.2
Gender		
Female	15	62.5
Male	9	37.5
Marital status		
Married	17	70.8
Divorced	5	20.8
Widowed	1	4.2
With partner	1	4.2
Education level		
High school/GED	5	20.8
Some college	8	33.4
Bachelor's degree	5	20.8
Graduate degree	6	25
Number of children		
None	4	16.7
One	4	16.7
Two	9	37.5
Three or more	7	29.1
Distance from sibling		
One hour drive	11	45.8
Two hour drive	3	12.5
More than five hour drive	10	41.7
Personal health estimates		
Physical health:		
Excellent/Very good	9	37.5
Good	10	41.7
Fair/Poor	5	20.8
Mental health:		
Excellent/Very good	14	58.3
Good	8	33.3
Fair/Poor	2	8.3
Memory:		
Excellent/Very good	11	45.85
Good	11	45.85
Fair/Poor	2	8.3

Results

Demographics and Family History

Demographic data are summarized in Table 1. Participants' ages ranged from 37 to 83 years, with a mean age of 56.8 years and a median age of 55.5 years. Participants were predominantly female, Caucasian, and married. Educational backgrounds were evenly divided across high school and higher levels of education. The majority of participants lived in Michigan (n=15), while the remainder lived across eight states throughout the United States.

The majority of participants (n=14, 58%) had no affected family members, other than their sibling. Six individuals (25%) had one or more first-degree relatives with Alzheimer's disease, in addition to their affected sibling. Most of the affected siblings were living (62.5%) and were female (70.8%). The age at diagnosis for the affected siblings ranged from 29 to 62 years, with a mean of 49.6 years.

Experience with Alzheimer's Disease

Receiving the Diagnosis

Forty-six percent (n=11) of participants were informed of their sibling's diagnosis on the same day that the diagnosis was made. Six participants were actually at the doctor's appointment with their sibling. Seven individuals (28%) noted the difficulty in obtaining an accurate diagnosis and described years of testing and resistance from the medical community in believing that a person could have Alzheimer's disease at a young age. An overall lack of resources was noted, and four individuals (16%) wished they had been given better information regarding the disease, how it progresses, and what to expect.

> "Her family doctor was pretty insistent it was the depression and he kept treating her for that… but we had to push really hard because nobody up in our area would see her and evaluate her."
>
> - 41 year old woman, affected sister 56 years old

One woman reported that the diagnosis for her father and eventually her sister was delayed because of a lack of communication of the disease in her family.

> "We had taken my sister to many doctors before we found out what was wrong with her. And it was a relief when we did. But of course we didn't know a lot about it. When my dad got sick they misdiagnosed him with MS, so that's why we had a hard time finding out what was wrong with my sister. My grandma, aunts, and uncles never said anything about

the other family members that were also sick, it was just called the "family curse."

- 52 year old woman, affected sister deceased

There were also differences in how individuals reacted to their siblings' diagnoses when this sibling was the only affected family member as opposed to individuals with other affected family members as well. The 14 participants with no other affected family members often discussed their family history as a source of confusion:

"So it's like, where is this coming from; I can't imagine. You know, it's one thing if your mother has breast cancer and then you get breast cancer and your aunt has breast cancer, you kind of expect it."

- 49 year old woman, affected sister 51 years old

For individuals with a family history beyond the affected sibling, a sense of dread and fear was more often reported than confusion. These individuals were more likely to be aware that Alzheimer's disease was a possibility.

Relationship with Sibling and Caregiving

For the majority of participants (n=15, 62.5%) there was no reported change in how close they felt to their sibling before and after the diagnosis of Alzheimer's disease was made. Five individuals (20.8%) felt less close to their sibling, and four individuals (16.7%) felt closer. Eight individuals (33.3%) reported talking with their sibling more often after the diagnosis (including all four individuals who reported feeling closer to their sibling). Fourteen participants (58.3%) reported no change in contact, and two individuals (8.3%) indicated that they talked to their sibling less frequently. Only one individual who reported feeling less close to his sibling had decreased the frequency of contact with her. One participant stated that a factor in her changing relationship with her sister was that her sister's friends were no longer willing to spend time with her, while another noted that her increased contact was due to her sibling's care needs.

"[Her friends are] just not there. So… that affects the siblings because then she doesn't have them to do things with anymore and so she wants you to do them. And she does feel bad because we don't spend much time with her but it's really hard to try to find some things that you can do."

- 54 year old woman, affected sister 56 years old

"From all the research I had done, I knew how incredibly stressful full time care-giving to an Alzheimer's patient is. I decided that I would have to be involved in my sister's care in order to take care of my parents and make sure that they did not over do it. This has not been easy on many levels."

- 41 year old woman, affected sister 56 years old

Women tended to be involved more often than men in all types of care, except for contributing financially. Women were significantly more likely to prepare meals for their sibling (p=0.02) and to provide "other" care (p=0.01). Examples of "other" care provided include: supporting other family members and encouraging involvement with care, childcare, coordinating living arrangements and medical care, and taking their sibling to support groups. There were no differences in caregiving roles based on age or how far the participant lived from the affected sibling, and 92% of individuals reported providing emotional support.

Communication and Conflict Within the Family

Some participants shared the way that their sibling's condition was discussed within the family. Nine participants (36%) disclosed that there was or is some difficulty talking about Alzheimer's disease in the family. In addition, seven individuals (28%) mentioned that the response to their sibling's illness from some family members was to back away and avoid involvement.

"You know, I haven't really talked to him about it because I haven't known what to say. So we all, in fact, we're all just kind of tip-toeing around it."

- 63 year old woman, affected twin brother

Seven individuals (28%) reported conflict within their family, sometimes resulting in concern over the quality of their sibling's care. In contrast, eight participants (32%) indicated that they had grown closer as a family.

"Our whole family dynamic has changed and not for the better. We said that we would act as a team, but that just isn't happening. When we do get together to discuss things, no decisions get made. Nobody really says anything of importance. We all sit around and pretend that we're on the same page. There are so many negative undercurrents."

- 41 year old woman, affected sister 56 years old

"My siblings and I have developed a closer bond and growth through this painful experience. Areas of disconnect have been strengthened and I feel we have discovered things about each other that we never knew. In addition, there have been opportunities to care for each other as well as for my brother."

- 59 year old woman, affected brother 56 years old

Perception of Alzheimer's Disease

Knowledge

The average knowledge score was 86.9% correct. Women (average knowledge score = 91.5%) scored significantly higher than men (average knowledge score = 78.5%) ($p<0.01$). The association between knowledge scores and education level approached significance ($p=0.06$), and may have been significant in a larger sample. There were no significant associations between knowledge scores and coping by information gathering ($p=0.39$) or treatment seeking ($p=0.08$), the number of affected family members ($p=0.76$), or categorical age ($p=0.19$).

Beliefs and Concerns

Participants' beliefs and concerns about developing Alzheimer's disease are summarized in Table 2. There were no significant associations between any of these measures and gender or age. Siblings who reported changing their behavior to reduce their personal risk ($n=13$, 54%) cited improving their health via better diet and exercise ($n=11$) and increased mental activity ($n=5$). There were no associations between behavior change and age. Participants who had made behavior changes were more likely to agree that treatments to prevent or delay Alzheimer's disease will be available in the next 5 years ($p<0.01$) and were more likely to agree that they worry about developing Alzheimer's disease someday ($p=0.04$). Participants who stated that they worry about developing Alzheimer's disease often or very often ($n=13$) were more likely to believe that they will develop Alzheimer's disease someday ($p=0.001$) and were more likely to agree that they would like to know if they will develop Alzheimer's disease ($p=0.04$). Participants who acknowledged symptom-seeking ($n=14$) were more likely to believe that they will develop Alzheimer's someday ($p=0.004$), and were more likely to acknowledge worrying about developing Alzheimer's disease someday ($p=0.01$). Individuals whose affected sibling was living tended to be more likely to agree (somewhat or strongly) that they worry about developing Alzheimer's disease someday, though this was not statistically significant.

Participants' responses regarding risk factors and preventive measures for Alzheimer's disease are summarized in Table 3. Genetics/heredity was rated more often as an important risk factor than any other risk factor. Keeping mentally active was the most commonly endorsed preventive measure, followed by spending time with friends and maintaining a healthy diet.

Risk Perception

When participants were asked to estimate their own risk for developing Alzheimer's disease, the mean response was 35.5%, with a range of 0–100% and a mode of 50% (Fig. 1). Of the six participants who estimated their risk to be 50%, three had no other affected family members, two had other family members who may have had Alzheimer's disease at older ages, and one had a history of known autosomal dominant early-onset Alzheimer's disease.

> "The reason I put 50% was because I look at it as I'm either going to get it or I'm not. It's a fifty/fifty shot."
>
> - 41 year old woman, affected sister 56 years old (no other family members with AD)

Ten participants (41.7%) stated that they have talked to their physician about this risk, and three (12.5%) have had genetic testing. However, two of these three individuals were enrolled in a research protocol and tested on a research basis only. They did not know the genes tested

Table 2 Beliefs and Concerns About AD ($n=24$)

Personal concern about AD	*% Disagree*	*% Neutral*	*% Agree*
I believe that I will get AD someday[b,c]	50.0	29.2	20.8
I worry about getting AD someday[a,b,c]	45.8	0.0	54.2
I worry about getting AD in the next few years[b,c]	75.0	4.2	20.8
If I got AD, it would be extrememly stressful for my loved one and me	12.5	8.3	79.2
AD is just part of growing older	91.7	4.2	4.2
AD is one of the worst diseases I can think of	20.8	4.2	75.0
I would like to know if I am going to get AD at some point later in my life[b]	20.8	33.3	45.8
Treatment optimism			
A cure for AD will be found in the next 5 years[c]	54.2	33.3	12.5
Treatments to prevent or delay AD will be developed in the next 5 years[a,c]	8.3	16.7	75.0
Treatments for the symptoms of AD will be greatly improved in the next 5 years	4.2	20.8	75.0

[a] Denotes association with making behavioral changes ($p<0.05$).
[b] Denotes association with frequency of worry ($p<0.05$).
[c] Denotes association with symptom seeking ($p<0.05$).

Table 3 Perceived Importance of Risk Factors and Preventive Measures (n=24)

Risk factor	*% Indicated important*
Genetics/heredity	62.5
Old age	50.0
Head injury	45.8
Exposure to toxins	45.5
Stress	39.1
Mental illness	34.8
Drinking too much alcohol	26.1
God's will	21.7
Smoking too much	21.7
Preventive measure	
Keeping mentally active	91.7
Spending time with friends	75.0
Maintaining a healthy diet	75.0
Exercising	70.8
Avoiding head injuries	66.7
Avoiding smoking	45.8

or the results of the testing. The individual who did know her test result tested negative for a familial mutation in one of the three genes associated with autosomal dominant early-onset familial Alzheimer's disease. She described how having a sibling develop the disease was a different experience than when it had been another family member.

> "When you know a parent had a disease (but you were too little to remember) it seems like a sad fairy tale. However, caring for a brother with AD puts things in a different perspective. Then seeing him slowly get worse and worse and knowing it could be you in a few years was unbearable."
>
> - 35 year old woman (negative genetic testing), affected brother deceased

Response to Alzheimer's Disease

Emotional Response

Twenty-two participants (88%) responded with feelings of "grief", including feelings of loss and sadness. Eleven participants (44%) expressed "anger", including frustration, resentment, and the feeling that life is unfair. Eight participants (32%) expressed "distress", via statements of being upset, stressed, hurt, or in pain, and eight felt "vulnerable", as described by feeling personally helpless or that their life/health was uncontrollable. Seven participants (28%) felt "overwhelmed" and noted exhaustion, insufficiency, and powerlessness to help.

> "I often feel very overwhelmed with all of the responsibilities. Afraid I am going to make the wrong choices. Concerned about my mother's health because she is dealing with most of the day to day stuff. Terribly sad about the whole situation. Sometimes resentful about how it has changed my life."
>
> - 55 year old woman, affected sister 53 years old

> "Sad, angry, hurt, every emotion you can think of I have felt at one time or another. And I know this may sound crazy, but I was even happy when she passed and was not trapped inside her body anymore. And I miss her so much. I think of her every day."
>
> - 52 year old woman, affected sister deceased

Five participants (20%) gave "positive responses", including statements of thankfulness, admiration, happiness, or enjoying time. Statements of concern were divided into a category for concern about personal health/life (four responses) or concern for other family members (eight responses).

Worry and Symptom-Seeking

When asked how often they worry about developing Alzheimer's disease, five participants (20.8%) reported worrying "very often", two (8.3%) "somewhat often", 11 (45.8%) "not often", and six (25.0%) "not at all". Fewer individuals felt that worrying affected their life, with 11 (45.8%) reporting "not often" and eight (33.3%) reporting "not at all". Respondents who reported an impact of worry on their life noted increased anxiety/symptom-seeking (n=8), mental health effects (n=6), changes in personal life (n=4), and changes in financial planning (n=3). Personal risk estimation was positively correlated with level of worry and the impact of worry on life (p<0.01).

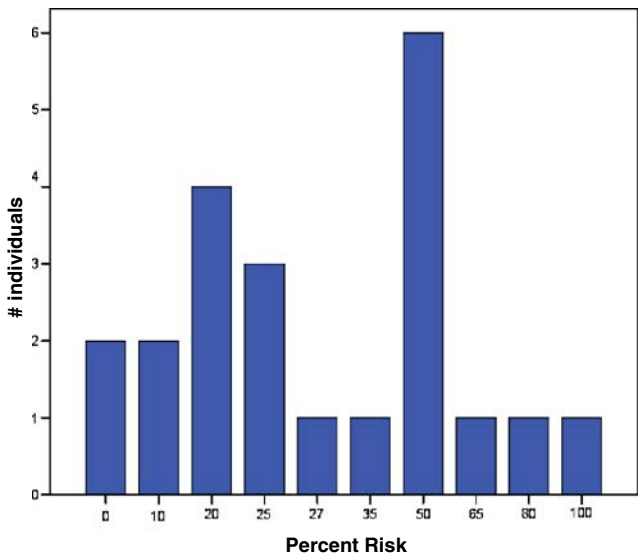

Fig. 1 Personal Risk Estimates.

"I worry about my sister's future and it takes up time and resources trying to learn and help. I worry about our parents, age 78 & 80, that care for my sister 24/7. It has taken a toll on them and the relationships with their other children and grandchildren. I worry about her next step—assisted living—and try to get her sons involved. I worry that I am next. I'm less than 2 years younger. I don't want to burden my kids or family."

- 54 year old woman, affected sister 56 years old

"On rare occasions that I have trouble sleeping at night, I tend to think worrisome thoughts, usually not about [AD]."

- 71 year old woman, affected sister deceased

Eight (33.3%) individuals reported some kind of memory check for themselves, and 11 (45.8%) compared themselves to their affected sibling. Five participants (20.8%) expressed vulnerability as a result of this comparison, four (16.7%) reported comparing their personal characteristics like physical appearance, personality, or life events to those of their sibling and relating this in some way to their risk, and two (8.3%) expressed feelings of personal fortune. Fourteen individuals (58.3%) looked for symptoms of Alzheimer's disease in their own behavior.

Impact of Alzheimer's Disease on Life Decisions

Participants were asked about any arrangements made in case they develop Alzheimer's disease and were given a list of eight possibilities. The most common arrangements made were: writing a living will (45.8%), writing an advanced directive (37.5%), and recontacting family and friends (29.2%). There were no statistically significant associations with gender, although women were more likely than men to have recontacted family and friends. Older participants were more likely to have written a living will ($p=0.04$).

Eight participants (32%) reported that they would have made decisions in their lives differently if their sibling had not developed Alzheimer's disease. Women and younger participants appeared to be most likely to be among this group, although these associations did not reach statistical significance. Six individuals (24%) stated that they would have made different work or financial decisions, and seven individuals (28%) stated that they would have made different decisions concerning their family and personal relationships.

"For example, my eldest went away to college, private, and I wonder if this is a waste of money (if he gets this disease—in his 40s) or will we be able to afford it if I get ill. Yes, I am not happy in my marriage and don't know if I want a divorce yet. Illness will play a role."

- 47 year old woman, affected sister 48 years old

Other responses included possible reproductive planning, attention to personal health, genetic testing, and relocation. Four participants (16%) would not have made any decisions differently.

"I may have neglected my own family. I was recently diagnosed and operated on for a brain tumor (meningioma) and my wife and I are battling infertility. While none of these issues were directly affected by my sister's disease, my focus on AD probably delayed my seeking treatment for meningioma and infertility on a more urgent basis."

- 42 year old man, affected sister 48 years old

When asked about how thoughts of developing Alzheimer's disease play a role in decisions for their future, eight participants (32%) stated that this has had no effect on decision-making or has not had an effect yet. Seven participants (28%) stated that thoughts of developing Alzheimer's disease have had an impact on financial/work decisions, including retirement decisions, long-term care insurance, and job security. Seven participants (28%) stated that their sibling's disease has made them decide to "make the most of life", including balancing the future with the present and hoping for the best.

"One never knows what is coming one's way, some things are under our control, others not. One learns to 'savor the moment' and to fully enjoy the time we have and the good health we enjoy *today*!"

- 83 year old woman, affected brother deceased

Three participants (12%) stated an impact on "end of life plans", including living wills and informing others of their wishes. And three participants (12%) stated that Alzheimer's disease was not a special concern, that aging or another disease was a more important factor in decisions.

"I don't think about having AD any more than I do any other disease. Several years ago we set up a trust fund and a living will. We also bought long term health insurance."

- 74 year old woman, affected brother deceased

Discussion

It is important for genetic counselors and other healthcare professionals to try to understand each patient's unique experience with early-onset Alzheimer's disease in order to provide optimal care. Learning about a patient's experience

includes understanding the events that led up to their consultation, what their particular questions are, what misconceptions they may have, and what genetic information may mean to them. This helps to facilitate rapport and trust, to ensure that the patient's agenda is addressed, to help the patient identify sources of support, and to facilitate communication with other family members. Understanding these experiences can also help to identify ways to expand genetic services and genetic education for other healthcare professionals.

The results of this study indicate that, not only are these individuals involved in their sibling's care despite physical distance, they also may be trying to understand their own risk for developing Alzheimer's disease and may be factoring this possibility into life decisions. A lack of a family history and a lack of communication within a family play roles in how siblings try to understand their personal risk as well as being a possible factor in the difficulty many families face in obtaining an accurate diagnosis. Similarly, the potential for family conflict and communication breakdown may create barriers to individuals receiving genetic counseling or other support services. Participants in this study were knowledgeable about Alzheimer's disease, perhaps due to attempts to obtain information about the diagnosis and understand their sibling's illness, although this was a generally well-educated sample. Women had higher knowledge scores than men, which may be explained by their being more likely to fulfill more caregiver roles than men.

Interestingly, genetics was ranked as the most important risk factor for developing Alzheimer's disease. However, almost all of the preventive measures were considered important, 75% of participants believed that treatments would be developed in the next 5 years, and roughly half of participants reported making behavior changes to reduce their risk. This optimism may indicate a sense of control or ability to modify any genetic risk. Although no behavior changes have been definitively proven to reduce an individual's risk for Alzheimer's disease, the public health campaigns driven by the Alzheimer's Association ("Maintain Your Brain") and the American Association of Retired People ("Staying Sharp") do advocate for better health habits and increased social and mental activity (Hendrie et al. 2006). Our findings also indicate that even though siblings may be very worried about their risk, or estimate their risk to be high, they may also feel fairly optimistic about the potential for risk reduction via health behavior changes.

The mean estimated personal risk was 35.5%, which is similar to published lifetime risk estimations for first-degree relatives (Green et al. 2002; Lautenschlager et al. 1996). However, the most common risk response was 50%. While it is possible that this reflects a general bias toward the midpoint in these types of questions, individuals' comments inform us that they came to this 50% risk because they were viewing their risk as "all or none", either they will develop Alzheimer's disease or they will not. This difficulty in understanding what personal risk may mean, as well as the factors influencing one's risk perception, should be considered during the genetic counseling session. Accurate risk awareness by both at-risk family members and their physicians is important for an individual's health. Early detection of Alzheimer's disease is considered increasingly important as treatments improve and an individual may benefit from having the opportunity to make decisions and participate in her or his own care (Bird 2005). Additionally, an accurate risk perception can help combat the stress, anxiety, and possible misdiagnosis brought on by the tendency to over-magnify one's risk (Sivell et al. 2008; Suhr and Kinkela 2007).

Fifty-eight percent of individuals reported symptom-seeking behavior. This proportion was higher than the 36% of participants (ages 40–60) who reported symptom-seeking behavior in a previous study of adult children of Alzheimer's disease patients (Gershenson Hodgson and Cutler 2003). It appears that either the nature of early-onset Alzheimer's disease and/or the fact that the affected person is a sibling causes higher anxiety about developing Alzheimer's disease. Because siblings are considered peers, it may be that a personal health threat posed by a sibling's illness seems stronger or more real than one posed by a parent's illness. Exploring an individual's anxiety by inquiring about symptom-seeking behavior can be helpful in anticipating potential reactions to genetic testing results (Decruynaere et al. 1999).

The fact that multiple participants expressed a variety of strong emotions concerning grief, frustration, vulnerability, being overwhelmed, and concern for themselves and others can serve as a reminder to clinicians that all members of the family are affected and that any number of these emotions may be experienced or discussed during a consultation. Furthermore, unaffected siblings may have already made important life decisions based on an inaccurate perceived risk regarding finances, family, or personal health needs.

Impact of Participant Age

We anticipated that younger individuals would feel a higher sense of risk than older individuals. We reasoned that older individuals may feel that they have passed the age where developing Alzheimer's disease is likely, whereas younger individuals have not. Although there was no significant age difference seen in risk estimation, level of symptom-seeking, or level of worry, younger individuals were more likely than older individuals to report making different life decisions based on their sibling's illness. It was notable

from the qualitative responses that older individuals were more likely to refer to old age or another health condition as a concern. Older individuals whose affected siblings had died years ago made more positive statements regarding their sibling's care and about the sibling's spouse than younger individuals. They tended to be able to look back on the experience with a sense of acceptance which was markedly different from the active grief that many of the younger individuals expressed. These qualitative data are consistent with a previous study which found a statistical association between younger age and perceived threat of Alzheimer's disease in individuals who had Alzheimer's disease experience with a genetically related family member (Suhr and Kinkela 2007). Similar findings have been published from a study of men with a brother with prostate cancer, where younger brothers had a higher perceived risk than older brothers (Beebe-Dimmer et al. 2004).

Impact of Caregiving

Caring for an individual with Alzheimer's disease (regardless of age of onset) has long been acknowledged as a particularly stressful and difficult responsibility for spouses and family members (Alzheimer's Association 2007). The results of this study inform us that siblings of individuals with early-onset Alzheimer's disease in particular are also susceptible to caregiver burden and its effects on one's personal life and family dynamics. The stress of actively caring for a sibling with early-onset Alzheimer's disease may exacerbate existing family conflict and communication difficulties. Personal decisions in life can be affected by caring for a sibling with early-onset Alzheimer's disease. About a third of participants felt that decisions in their lives would be different if their sibling had not developed Alzheimer's disease. Some individuals simply stated that they would have their sister or brother back, but many stated specific aspects of their personal life that would have been different, including moving to another state, changing jobs, marital decisions, spending time with family, and better mental or physical health. Women were also more likely to report making life decisions differently because of their sibling's disease, which may be explained by their greater involvement in the sibling's care, necessitating a greater sacrifice of their personal priorities. While it may not be possible to speculate with great accuracy about how one's life would be under different circumstances, these responses illustrate the sacrifices that siblings are experiencing in attempts to help their families. These sacrifices may have important implications for an individual, such as seeking medical or mental health care when appropriate, effects on personal relationships, and financial stability for the future.

Impact of Alzheimer's Disease

There is a distinct effect on siblings from the nature of Alzheimer's disease. The genetic components of early-onset Alzheimer's disease were referred to often by individuals who were worried for themselves or other family members and the majority of participants rated genetics as an important risk factor. This genetic risk has been reported previously as a concern for individuals with late-onset Alzheimer's disease as well (Roberts and Connell 2000; Suhr and Kinkela 2007). For most participants, the lack of a family history of Alzheimer's disease was a source of confusion, causing them to struggle to understand how their sibling could have developed Alzheimer's disease at such a young age. This confusion may have contributed to the sense of vulnerability that many individuals expressed; Alzheimer's disease was not considered a threat until their sibling developed it.

Confusion over the genetic nature of early-onset Alzheimer's disease may have contributed to the difficulties that many participants reported in communicating about the disease (Etchegary 2006). For example, one woman was astounded to find that she had an extensive family history of early-onset Alzheimer's disease on her deceased father's side, and that no one from that family shared this information until after her sister was diagnosed. This lack of communication may have been due to a sense of stigma in the family preventing family members from talking about the risk. It could also be influenced by lack of knowledge about the risk for extended family members and lack of skills in approaching extended family members with this information. For families with sporadic early-onset Alzheimer's disease or familial Alzheimer's disease without clear autosomal dominant inheritance, understanding this risk may be even more difficult. Individuals with and without a family history of Alzheimer's disease were clearly thinking about the possible genetic components and some indicated that they did not know how to gain access to genetic counseling services or clear information about their risk.

The progressive, neurological nature of Alzheimer's disease and the lack of experience with it was also a source of struggle for a number of individuals. Feeling powerless to help and the demands of constant patience with their sibling seemed to be related to watching their sibling lose cognitive ability. The loss of the sibling's personality, and therefore of the sibling as a friend or companion, was viewed by the majority as much worse than a physical decline. In particular, a number of participants felt that they did not know what to expect from the disease. It may be that these participants were more likely to seek out knowledge about Alzheimer's disease because of a sense of confusion and lack of information. A number of participants stated that they needed more guidance for what

to expect in their sibling's disease course and what hurdles to expect in their care. A need for more complete information regarding the disease and its effects has also been acknowledged by individuals with early-onset Alzheimer's disease (Alzheimer's Association, 2006).

Limitations

The findings of this study are limited by a relatively small convenience sample. Studies using convenience samples tend to report higher levels of caregiving for women compared to men than are reported in probability samples (Pinquart and Sorensen 2006). It is possible that due to sample bias and a small sample size, some of the gender differences reported here have been exaggerated. Similarly, sibling relationship (e.g., sister–sister) associations could not be conducted due to the small sample size. Although statistically significant associations were found, larger studies are recommended.

There is a lack of racial and ethnic diversity in this sample. Because grief, coping responses, and changes in family dynamics may differ strikingly among cultures, these findings should not be applied generally to individuals of diverse backgrounds. A sampling bias may exist as well, favoring individuals who are likely to want to share their experience, who are more highly involved with their affected sibling, who are seeking out research opportunities, who are highly educated, and who are seeking information. This may be a factor in the high knowledge scores and frequent request for more research in this field.

This exploratory study included individuals with various family histories; some with no other affected family members and others with known autosomal dominant inheritance. Therefore, the nuances of the effect of family history on a sibling's experience may have been underappreciated, as well as the impact of the affected sibling's age of onset on family members. Additional studies to determine the effect that different family histories have on disease experience are suggested. Although some measures were validated, it is also possible that some of the questions developed for this study were of suboptimal reliability and validity.

Conclusions

This study offers a description of the lived experiences of individuals with a sibling with early-onset Alzheimer's disease: their personal experience with their sibling's disease, how they understand the disease and the risk implications for other family members, and how they may have made behavior changes or life decisions based on this understanding. As public awareness of early-onset Alzheimer's disease increases, more individuals may be seeking information regarding their risk and genetic testing options. In order to provide optimal care to this population, it will be important for genetic counselors and other healthcare professionals to elicit an individual's personal experience with Alzheimer's disease and attempt to understand how they perceive their risk, how they are responding to this risk, and how their lives may have been changed by their sibling's illness.

These findings can serve to give genetic counselors and physicians insight into the feelings, experiences, and goals of individuals seeking a genetic consultation, by keeping the following main points in mind. The lack of other affected family members may create confusion as to what is happening to the sibling, for the sibling's relatives as well as possibly for clinicians involved in the affected sibling's care. Siblings of individuals with early-onset Alzheimer's disease may be highly involved in the care of their affected sibling, and their lives are likely to be impacted by this care and by the personal risk they perceive for themselves and other family members. This risk may impact levels of worry and anxiety as well as major life decisions, yet it may also be accompanied by optimism for the ability to modify one's risk through improved health behavior. Larger studies are clearly needed to better understand the effects of various family history differences, such as the impact of age of onset, the number of affected individuals, and the specific genetic background of different families. Similarly, studies examining differences in perceptions between adult siblings and adult children of affected individuals are suggested to clarify possible differences related to anxiety and symptom-seeking behavior.

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