## RESEARCH ARTICLE



# Exploring sex and gender differences in the Alzheimer's disease patient journey: A survey study

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# Abstract

Introduction: The present study investigates differences between men and women in the Alzheimer's disease (AD) patient journey, aiming to improve early detection and patient care.

Methods: A sample of men and women (N = 142) at different stages of the AD journey were invited to complete an online survey. A series of logistic regressions and Cox regressions were used to examine sex and gender differences in diagnosis and treatment.

**Results:** Men showed greater awareness of sedentary lifestyle risks (p = 0.005). Diagnosis was more often by referral for women (p = 0.015). Women were more likely to be treated with reminiscence therapy (p = 0.029) and life story work (p = 0.025). Time to diagnosis was shorter when diagnosed directly by specialists (hazard ratio = 0.59, p = 0.022).

Discussion: This study reports sex- and gender-based differences in AD diagnosis and treatment. Expanding this research with diverse populations is essential to improve early detection and personalized care, ultimately enhancing patient outcomes.

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gender-sensitive health care, neurodegenerative diseases, patient journey in Alzheimer's disease, sex and gender differences in health

# Highlights

- · We identified sex- and gender-based differences in the Alzheimer's disease (AD) patient journey across diagnosis and treatment.
- · Shorter time to diagnosis was observed when a specialist directly diagnosed patients.
- Women showed stronger responses to life story work therapy and were diagnosed after primary care referrals.
- Men and women had comparable awareness of AD risk factors, but men were more aware of lifestyle risks.
- This study highlights the need for sex- and gender-specific diagnostic tools and personalized treatment approaches.

# **BACKGROUND**

Alzheimer's disease (AD) is a significant global public health challenge, with its prevalence increasing as populations age. 1 Characterized by progressive cognitive decline, AD affects memory, reasoning, and daily functioning. Early diagnosis is crucial for improving patient outcomes, enabling timely treatments, and facilitating effective care planning. Initiating treatment during the early stages of AD can help manage symptoms more effectively, potentially delaying progression to more severe stages and prolonging functional independence.<sup>2</sup> However, many individuals in the early stages remain undiagnosed due to subtle cognitive impairments, which are often mistaken for changes related to normal aging by patients, families, and health-care providers.3

Biological sex differences (male/female), referring to characteristics such as chromosomes, hormones, and reproductive anatomy, and gender-based differences (man/woman), referring to sociocultural roles, seem to play a significant role in AD symptom presentation, diagnostic accuracy, disease progression, and treatment responses.

Recent work has highlighted the pitfalls of conflating self-report identity categories with underlying biological or social mechanisms. Stites and Velocci argue that relying solely on male/female or man/woman labels can obscure causal pathways and reinforce normative assumptions about sexual diversity in AD research.<sup>4</sup> Because sex/gender was self-reported in this study, we therefore use the term "sex/gender" to acknowledge that these categories may reflect both biological and social influences.

Sex-specific factors in AD diagnosis and progression are well documented. For example, female patients tend to maintain stronger verbal memory than males in the early stages of the disease, potentially masking symptoms and delaying diagnosis. <sup>5</sup> Female patients also experience neuropsychiatric symptoms, like depression and psychosis, more often than males, while male patients are more likely to exhibit apathy, which

can lead to earlier but potentially inaccurate diagnoses.<sup>6</sup> Furthermore, female patients show faster cognitive decline after a diagnosis of mild cognitive impairment (MCI) or AD dementia.7 These differences highlight the need for sex-specific diagnostic and management strategies.

Sociocultural factors intersect with both sex and gender in the AD patient journey but have received less attention. For instance, women are less likely to engage in physical exercise, an important positive risk factor for dementia, and may receive less optimal medical care once diagnosed.<sup>8,9</sup> Data also indicate that women with dementia are more frequently prescribed antipsychotics, which have been linked to adverse outcomes. 10,11 These findings underscore the urgency of addressing sex/gender-based biases in health care to ensure equitable care for AD patients.

Beyond biological and clinical differences, research suggests that sex/gender may shape how patients are perceived by health-care professionals and caregivers, potentially influencing the accuracy and timeliness of diagnosis. Gender norms, biases, and expectations may cause identical symptoms to be interpreted differently depending on whether the patient is a man or a woman. For example, women's concerns may be dismissed as emotional or stress related, while similar presentations in men may prompt further investigation. This aligns with recent findings showing that the sex and relationship of the caregiver reporting patient symptoms significantly influences clinical dementia staging scores. 12 Such findings underscore that diagnostic outcomes are co-constructed, shaped not only by patients' symptoms, but also by how those symptoms are perceived and communicated by caregivers and interpreted by clinicians. These sociocultural dynamics remain underexplored in AD research and deserve focused investigation.

Despite increasing recognition of sex/gender differences in AD, significant gaps remain in understanding how these factors shape the

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patient journey. Our study aims to address these gaps by examining differences, between men and women, in key milestones of the AD journey, including symptom onset, diagnosis, treatment, and longterm care. By identifying these differences, this proof-of-concept study seeks to highlight opportunities for tailored diagnostic approaches and interventions that meet the unique needs of male and female patients, ultimately improving care and outcomes.

We conducted a survey comprising 79 structured questions created by a multidisciplinary team of scientists, with a focus on patient awareness, diagnosis, and treatment experiences (Supporting information). Our primary objective was to identify differences in how men and women experience AD in health-care settings in the United States and Germany. Information about the patient journey was reported either directly from individuals with AD, when feasible, or indirectly from their primary caregivers, who responded on behalf of the patient. Caregivers were instructed to report based on their knowledge of the patient's experience, and the survey was adapted to the respondent's role to achieve this objective. While acknowledging the limitations of proxy reporting, the study was designed to reflect the lived experience of individuals with AD. By integrating both patient- and caregiverreported data, this study lays the groundwork for more detailed investigations into the influence of sex/gender on the AD journey. While descriptive, it provides an essential foundation for future research into personalized and equitable care strategies for AD patients.

# **METHODOLOGY**

#### 2.1 Study design

We conducted an exploratory comprehensive survey-based study to understand the AD patient journey, from the initial suspicion of the disease, the observation of early symptoms, seeking medical advice, the experience of receiving an MCI or AD diagnosis, and postdiagnostic treatments/therapies. The survey included 79 structured questions related to various aspects of the patient journey, including patient awareness and attitude toward treatment choices, mode of diagnosis, therapies, and treatment. The survey questions were developed through a focus group involving 20 scientists with expertise in AD/neuroscience, neurology, and psychology, all affiliated with the Women's Brain Foundation. The process also included input from one patient with AD and two AD caregivers, as well as support from members of Alzheimer Disease International organization. Our protocol was reviewed by an institutional review board (Advarra IRB), which granted an exemption for the present study (Pro00063679). Before taking part in the study, participants were asked to provide informed consent.

#### 2.2 Sample size and procedure

The study sample comprised 142 participants, including patients (N = 10; F = 7, M = 3) and caregivers (N = 132; F = 73, M = 59),

#### RESEARCH IN CONTEXT

- 1. Systematic review: We conducted a survey-based study targeting individuals experiencing memory impairment and Alzheimer's disease (AD), exploring sex- and genderspecific differences in key milestones of the patient journey. The study aimed to investigate differences in symptom onset, diagnosis, treatment, and care, using structured questionnaires and logistic regression to identify sex/gender-related patterns. Previous work has highlighted sex and gender differences in cognitive decline, symptom progression, and treatment responses, but limited research has focused on these factors together throughout the entire AD journey.
- 2. Interpretation: Our findings confirm that sex and gender influence AD diagnosis and treatment pathways, with women more likely to be diagnosed after referral from a primary care physician and showing stronger responses to life story work therapy. These results contribute to understanding how sex and gender affect the AD experience and emphasize the need for sex- and gender-specific diagnostic and care strategies.
- 3. Future directions: Future research should directly explore the intersection of sex and gender in AD, accounting for the broader sociocultural factors influencing health care-seeking behavior and treatment outcomes. Additionally, larger, ethnically diverse cohorts are needed to confirm these findings across different health-care systems.

living in Germany (20 female, 20 male) and the United States (51 female, 51 male), all falling within the specified age range of 51 to 90 years (Table 1). Participants were either individuals diagnosed with MCI/AD or caregivers designated as the primary caregiver, responding on behalf of the patient and capable of providing insights into the patients' journey. The survey instrument was adapted according to the respondent's role-patient or caregiver-to ensure clarity and appropriateness of the questions. In most cases, primary caregivers served as proxies, providing responses intended to reflect the patient's experience with AD. While potentially introducing a bias, this proxy-based approach was necessary to ensure inclusion of individuals with cognitive impairment who may have had limited ability to complete the survey independently.

Before taking the survey, participants were asked to complete a set of screening questions to confirm study eligibility. Participants were asked to indicate their sex (Question: "What is your sex?" with options: "female," "male," or "other") to align with the study's focus on exploring sex differences specifically within the binary categories of male and female. Responses from individuals identifying outside the binary ("other") were not collected, as the anticipated sample size for this group was insufficient for robust and rigorous statistical analysis.

**TABLE 1** AD patient characteristics and disease severity distribution.

	Country				
AD Patient Characteristics	Germany		USA	USA	
Participants (N)	40		102		142
Women/Men (N)	20/20		51/51		71/71
Patient/Caregiver (N / %)	3/37		7/95		10/132
	7.5 / 92.5		6.9 / 93.1		7/93
	Women N (%)	Men N (%)	Women N (%)	Men N (%)	
Age Range (years)					
51-60	2 (100)	0 (0)	5 (55.5)	4 (44.5)	11
61-70	5 (45.4)	6 (54.6)	18 (41.5%)	23 (58.5)	52
71-80	6 (50)	6 (50)	16 (57.1%)	12 (42.9)	40
81-90	7 (47)	8 (53)	14 (58.3)	10 (41.7)	39
Ethnicity					
Caucasian/White	20 (50)	20 (50)	48 (54)	40 (46)	128
Black/Afro-Caribbean/African American	-	-	1 (14)	6 (86)	7
East Asian/Asian American	-	-	1 (100)	-	1
Native American/Alaskan native/Pacific Islander	-	-	1 (50)	1 (50)	2
Level of Education					
PhD, law/medical degree, Bachelor/Master's degree	9 (45)	6 (30)			15
Vocational/technical college	6 (30)	9 (34)			15
High School Graduate	2 (10)	2 (10)			4
Comprehensive School	0 (0)	0 (0)			0
Secondary modern school	2 (10)	3 (15)			5
Secondary school	0 (0)	1 (5)			1
PhD, law or medical degree			2 (4)	2 (4)	4
Master's degree			7 (14)	9 (18)	16
Some postgraduate			3 (6)	2 (4)	5
Bachelor's degree			12 (24)	17 (34)	29
Associate degree			8 (16)	4 (8)	12
Some college			9 (18)	6 (12)	15
High school graduate			8 (16)	8 (16)	16
Less than high school graduate			2 (4)	2 (4)	4
Insurance Type					
Public Insurance	18 (90%)	17 (85%)			35
Private Insurance	2 (10%)	2 (10%)			4
Other	0 (0%)	1 (5%)			1
Medicare			26 (51%)	20 (39%)	46
Health Insurance Plan			15 (29%)	23 (45%)	35
Medicaid			9 (18%)	6 (12%)	15
Other			1 (2%)	2 (4%)	3
Disease Severity Distribution (N = 142)			(,	,,	-
MCI/Prodromal AD	20 (28%)		24 (34%)		44 (31%)
Mild AD	34 (48%)		27 (38%)		61 (43%)
Moderate AD	17 (24%)		20 (28%)		37 (26%)

Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment.

However, it is important to note that this limitation reflects the study's specific scope rather than a disregard for the experiences of non-binary individuals, whose perspectives remain a critical area for future investigation. Furthermore, we acknowledge the importance of considering both sex and gender as distinct constructs. Nevertheless, due to the complex and multifaceted nature of gender and the limited sample size of our study, we decided to not collect patients' information about gender identity. For the purpose of this study, we used self-reported sex as a proxy for sex/gender, assuming that participants' reported sex (male/female) aligned with their gender identity (man/woman). We acknowledge that this assumption may not hold true for all individuals and that biological sex and gender identity are distinct constructs. However, because our survey did not include a separate measure of gender identity and due to the limited sample size, we were unable to examine these dimensions separately. Throughout the article, we therefore use the term "sex/gender" to reflect this methodological constraint and the likely overlap of biological and sociocultural factors in shaping the AD experience.

At the time of recruitment, participants were also asked to indicate their/the patient's formal diagnosis, as well as the level of independence and ability to perform daily activities. Based on the information provided, participants' disease severity was classified into (1) MCI/prodromal AD, (2) mild AD, (3) moderate AD, (4) moderatesevere AD. This last group was excluded from the study. This decision was made to ensure the reliability and interpretability of responses. While caregivers could act as proxies for these patients, the complexity and severity of symptoms in moderate-to-severe AD often lead to highly variable caregiving situations, increased burden, and limited insight into patients' subjective experiences. Including this group would have introduced greater heterogeneity and reduced the comparability of responses across stages of disease severity. Furthermore, participants were asked to indicate whether their/the patient's diagnosis had been confirmed by a lumbar puncture (cerebrospinal fluid testing) or a positron emission tomography scan (confirmed amyloid beta pathology). The screener also collected caregiver status and involvement (excluding professional caregivers and/or the ones who are not providing sufficient care), patient's age (excluding caregivers younger than 50 years), and additional details (if available) about formal diagnosis (excluding participants with familial AD or MCI due to other reasons).

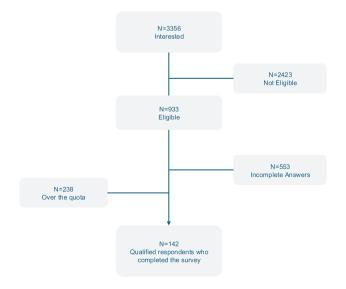
Participants were primarily recruited through a third-party market research vendor, Dynata LLC (https://www.dynata.com/), which used targeted online panels (i.e., pre-screened groups of individuals who have agreed to participate in research studies). These panels allow researchers to efficiently reach specific demographic, health-related characteristics or professional groups relevant to the study. The vendor contacted potential participants via e-mail or phone to gauge their interest in the study. Those who expressed interest were then directed to a screening process to confirm their eligibility. The study was also listed on the CenterWatch website, allowing interested patients or caregivers to request the survey screener. Eligibility was determined through a screening process, with participants informed of their privacy and data rights. Only those who consented to data use proceeded to the main study. Participants received a \$130 incentive upon

completion of the survey. Compensation was managed by the vendor. A summary of the recruitment process is provided in Figure 1.

A 45 minute online quantitative survey of 79 structured questions was administered as part of the research study. All participants completed the survey online at their own pace and in their own setting. No supervision was provided. The survey questions delved into various facets of disease progression, encompassing patient awareness, attitudes toward treatment options, diagnosis type, therapeutic interventions, and treatment modalities. The survey also included questions relative to the patients' emotional journey before and during the initial symptom presentation, while suspecting the illness, when formal diagnosis was achieved, and during the disease management. Quality control measures, such as removing respondents who completed the survey unusually quickly (based on the median, standard deviation, and expected completion time), verifying respondent location and uniqueness via IP address, and removing responses that were inconsistent or of low quality, were implemented.

# 2.3 | Statistical methodology

The analysis was performed using RStudio statistical software. The survey was divided into three sections: (1) "overall journey," including questions about experiences, feelings, process of time to diagnosis, order of events, tests, treatments/therapy, clinical trials, learning/awareness; (2) "milestone deep-dive," including disease awareness, risk factors, related memory topics, seeking help, noticing signs, doctor/specialist appointments, diagnosis, safety, support, impact of AD; and (3) "patient characteristics," including caregiver support, living situation, education levels, employment status, insurance, and medical conditions. Only a sub-selection of 14 questions of particular interest was tested statistically to reduce risk of type I error. These questions have been highlighted in the supporting information and in Table 2.



**FIGURE 1** Recruitment, eligibility, and inclusion. The flowchart displays our recruitment process.

TABLE 2 Results summary.

Question in supplement	Measurement	Women	Men	р
General awareness and underst	anding of Alzheimer's disease			
Q19	Awareness of Alzheimer's disease <sup>b</sup>			AII > 0.05
Q21	Awareness of potential risk factors for dementia (sedentary lifestyle)	28%	42%	0.005
Q65	Awareness of impact of MCI/AD on life			>0.05
Q60	Minimum acceptable safety for new treatments			>0.05
Diagnosis and the role of special	ists			
Computed	Time to diagnosis <sup>a</sup>			>0.05
Q3	Types of tests <sup>b</sup>			>0.05
Q4	Timing of the tests <sup>b</sup>			>0.05
Q5	How burdensome were tests <sup>b</sup>			>0.05
Patterns of referral and symptor	n presentation			
Q2	Diagnosed after referral from primary care physician	83%	65%	0.015
Q22	Recognition of cognitive symptoms at the time of diagnosis	80%	59%	0.007
Q20	Discussed memory-related topics			>0.05
Treatment approaches				
Q8	Reminiscence rherapy	38%	21%	0.029
	Life story work	28%	13%	0.025
	Other intervention <sup>b</sup>			>0.05
Q9	Therapeutic approach by timepoint			
	Reminiscence therapy after suspicion of the disease	24%	6%	0.011
Q10	Benefits from life story work <sup>b</sup>			0.044
	Not helpful at all—somewhat helpful	0%	11%	
	Somewhat helpful	16%	33%	
	Somewhat helpful—extremely helpful	42%	44%	
	Extremely helpful	42%	11%	

Abbreviations: AD, Alzheimer's disease; MCI, mild cognitive impairment.

A Cox proportional hazards regression analysis was performed to assess the association between the method of diagnosis and the time between symptom onset and diagnosis. Hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) were calculated.

Logistic regression was used to analyze questions with a binary outcome, such as mode of diagnosis direct from specialist/after referral. Separate logistic regression models were fitted for each outcome variable, with patient sex/gender as predictor and the respective diagnosis as the outcome variable. Significance was determined using the Wald test, with a significance level set at  $\alpha = 0.05$ .

## 3 | RESULTS

# 3.1 | Sample characteristics

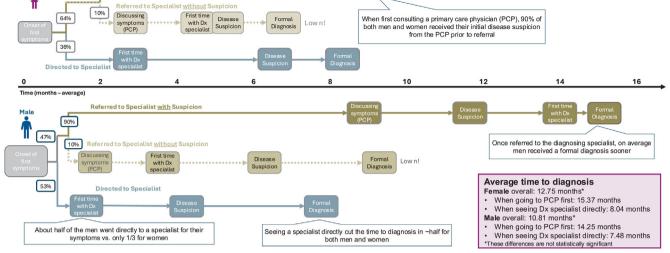
Disease severity distribution (Table 1) across sexes within the study revealed approximately one third experiencing MCI/prodromal AD (28%, N = 13 women; 33.8%, N = 15 men), approximately half diag-

nosed with mild AD (47.22%, N=23 women; 37.5%, N=23 men), and one quarter exhibiting moderate AD (23%, N=11 women; 28%, N=13 men). Approximately 93% of respondents overall were caregivers, completing the survey on behalf of a patient. Among these 132 caregivers, 89.4% identified themselves as family members and 10.6% as friends. Although the survey included an additional open-ended question asking caregivers to specify the exact nature of their relationship to the patient (e.g., daughter, spouse, grandchild), responses were often incomplete, heterogeneous, and inconsistently reported; therefore, we decided not to use this information.

Education attainment among study participants varied across the sample. In the US subgroup, 48% of women (N = 24) and 60% of men (N = 30) reported university-level education (bachelor's degree or higher). In the German subgroup, 45% of women (N = 9) and 30% of men (N = 6) reported university-level education, while 30% of women (N = 6) and 34% of men (N = 9) indicated vocational education. A summary of the results is presented in Table 1.

<sup>&</sup>lt;sup>a</sup>This variable was computed using dates provided by participants in the first part of the survey.

<sup>&</sup>lt;sup>b</sup>Please refer to supporting information to read the questions in full.



**FIGURE 2** Path to formal diagnosis. Overall, men received a formal diagnosis  $\approx 2$  months faster than women (this difference was not statistically significant). Directly seeing a specialist cut the time to diagnosis in approximately half.

# 3.2 | General awareness and understanding of AD

Referred to Specialist with Suspicion

90%

We first assessed general awareness of AD. We found no significant sex/gender differences in terms of awareness and understanding. Both men and women reported familiarity with the disease, possessing a general understanding of its nature, and having discussed it with a physician. Additionally, both men and women demonstrated similar levels of awareness regarding several major risk factors for AD, such as old age, a family history of dementia, hypertension, and loneliness (all p > 0.05). However, a notable group difference emerged in the awareness of lifestyle-related risks, with greater awareness of sedentary lifestyle as a risk factor among men compared to women (p = 0.005), suggesting potential variability in how risk factors are perceived and communicated based on sex or gender.

# 3.3 | Diagnosis and the role of specialists

Upon examining the diagnostic process, we observed that in our sample women were more frequently diagnosed by neurologists (34% for women vs. 24% for men), whereas being diagnosed by the first doctor consulted, which was not necessarily a specialist, was observed more often among men (68%) than women (32%). These results were, however, not statistically significant. Additionally, women were more likely to be diagnosed with MCI/AD after referral from a primary care physician (p = 0.015), highlighting a potential disparity in referral pathways and access to specialized care.

When looking at diagnostic pathways, men received a formal diagnosis  $\approx 10.81$  months after the onset of the first symptoms, while women received a diagnosis after  $\approx 12.75$  months; importantly, this difference did not reach significance (Figure 2). Overall, most

diagnoses (74%) were performed by specialists after a referral from another doctor. Our analysis revealed that the time between symptom onset and diagnosis was significantly shorter when patients, regardless of sex/gender, were directly diagnosed by a specialist (HR = 0.59, p = 0.022). This emphasizes the importance of specialist involvement in timely AD diagnosis.

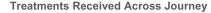
# 3.4 | Patterns of referral and symptom presentation

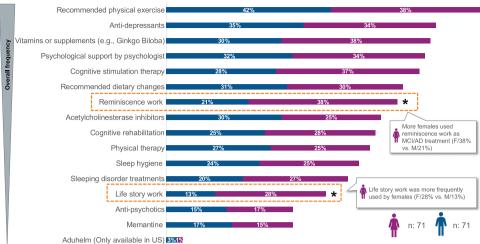
The pathway to a formal AD diagnosis differed based on sex/gender in terms of referral patterns and symptom presentation. Women were more frequently diagnosed with MCI or AD after a referral from a primary care physician (p=0.015). These diagnoses were often prompted by specific cognitive symptoms, such as forgetting recent conversations or events, which appeared to be more frequently recognized in women than in men (p=0.007). This finding suggests that sex/gender-based differences in symptom presentation and recognition may influence the referral and diagnostic process, potentially affecting the timeliness and accuracy of AD diagnoses.

# 3.5 | Treatment approaches

Our analysis revealed that standard pharmacological treatments were commonly used for both men and women (no significant differences; all p>0.05). However, this pattern was not consistently observed for non-pharmacological interventions. For example, across the journey, reminiscence therapy and life story work, though not the most common treatments overall, were more frequently used in the

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Treatment selection. Though not the most common treatments, reminiscence and life story work were more frequently used as treatments for women than men. AD, Alzheimer's disease; MCI, mild cognitive impairment.

treatment of women compared to men (p = 0.029, p = 0.025, respectively; Figure 3). When looking at treatment approaches at specific timepoints, we found that reminiscence therapy was more frequently used for treating women after suspicion of the disease compared to men (p = 0.011). Additionally, overall women reported deriving greater benefits from life story work compared to men (p = 0.044). This difference highlights the potential influence of sex/gender on treatment choices and preferences, suggesting that women may be more likely to engage in therapeutic activities that involve recalling and reflecting on personal memories.

#### 3.6 **Emotional journey**

When looking at the emotional journey of the patients throughout the disease, we observed that, after seeing a specialist for the first time, women reported heightened levels of anxiety. In contrast, men were more likely to feel grateful. An opposite pattern was observed after the formal diagnosis, with women generally feeling more relaxed, and men reporting to feel more anxious. Overall, feelings of helplessness or being overwhelmed were reported throughout women's patient journey. Men, on the other hand, seemed to feel more insecure and anxious throughout their journey. These results are displayed in Figure 4.

# **DISCUSSION**

The objective of this proof-of-concept study was to investigate sex/gender differences in the patient journey through stages of pre-conceived awareness of AD, diagnosis, post-diagnostic treatments/therapies, and quality-of-life markers. A growing body of research has highlighted sex/gender-related differences in AD symptom presentation, risk factors, biomarkers, and treatment

responses. 13-18 Understanding these differences is essential for developing sex/gender-informed prevention, diagnostic, and treatment strategies. Such advancements can contribute to precision medicine approaches, enhancing care measures by addressing AD heterogeneity. A sedentary lifestyle is associated with a higher risk of dementia and greater cognitive decline in older adults. 19,20 When reviewing patients' awareness of risk factors for AD, both men and women showed comparable levels of awareness overall, but men displayed significantly greater awareness about the impact of a sedentary lifestyle. This enhanced awareness among men may partially stem from historical focuses in health campaigns and education about various cardiovascular diseases (CVDs), such as hypertension, coronary heart disease, and stroke. Historically, these efforts were more directed toward men due to the long-held underestimation of heart disease in women.<sup>21</sup> Notably, CVD typically develops 7 to 10 years later in women than in men and remains the leading cause of death among women, particularly during post-menopause.<sup>22</sup> This misconception has led to an under-recognition of heart disease in women, resulting in less aggressive treatment strategies and lower representation of women in clinical trials.<sup>23</sup> Given that CVD and dementia share common genetic and biochemical risk factors, 24-26 the initial male-centric focus of health campaigns might partially explain why men exhibit higher awareness of the sedentary lifestyle risks associated with AD. Furthermore, increased physical activity has been shown to promote synaptic plasticity and enhance blood flow to the hippocampus, which supports brain health and improves brain functioning and cognitive performance.<sup>27,28</sup> Despite the well-known link between physical activity and brain function, sex/gender differences in physical activity engagement exist, 29,30 possibly due to women's greater caregiver duties, which often do not allow them to effectively look after their own well-being, among other factors. This evidence seems in line with our findings of a greater awareness in men compared to women, of the role of sedentary lifestyle as a contributing risk factor for AD. This

**FIGURE 4** Display of the emotional patient journey. Overall, women's journey was characterized by feelings of helplessness, frustration, or feeling overwhelmed; men mostly reported feeling anxious or insecure.

disparity in awareness may contribute to higher rates of AD prevalence in the female population, as currently, two thirds of AD patients are women,<sup>31</sup> underscoring the importance of targeted educational efforts that address all critical AD risk factors equally across men and women. Adapting health messages to bridge the awareness gap is crucial for promoting a broader understanding of lifestyle impacts on AD risk among all individuals, regardless of sex/gender.

The differences observed in the mode of AD diagnosis highlight important aspects of the patient journey that may affect timely and accurate diagnosis. While it was more common among men to receive a diagnosis from the first doctor they consulted, women were more likely to be diagnosed with MCI/AD after referral from another doctor, which suggests that their diagnostic pathway may involve additional steps compared to men. Although not statistically significant, our results indicating that women were diagnosed ≈ 2 months later than men seem to support this hypothesis. This aligns with existing research indicating that women often experience longer diagnostic pathways, potentially due to sex/gender biases in symptom recognition and reporting by health-care professionals.<sup>32</sup> Moreover, recent findings demonstrate that caregiver characteristics, such as sex, relationship to the patient, and cohabitation, can influence Clinical Dementia Rating Sum of Boxes (CDR-SB) scoring and diagnostic impressions, independent of patients' objective impairment. 12 Additionally, women may perform well on verbal memory tests even in the presence of similar AD pathology as men, leading to a diagnosis being delayed until more severe symptoms arise. 33,34 Recent digital biomarker research further supports the relevance of sex-specific patterns in AD detection, highlighting that sex-informed digital phenotyping can differentiate cognitive performance profiles in early disease stages, although these differences diminish as pathology progresses. 35 These differences may be partially explained by unintentional biases related to a patient's sex or gender.

For example, doctors may be more likely to associate women's memory problems to stress or emotional issues, which can lead to fewer referrals to specialists. Such biases can be reinforced by stereotype threat, in which women may doubt or downplay their cognitive difficulties under pressure, and by cultural assumptions that emotional factors predominately affect women. 36–38 These patterns are not necessarily the result of intentional discrimination but may come from long-standing habits in medical thinking and gaps in how women's symptoms are recognized. Addressing these influences will require targeted education and awareness initiatives to help clinicians recognize and counteract unconscious stereotypes in clinical decision making.

Our finding that women were more frequently prompted to seek diagnosis due to forgetting recent conversations or events seems to suggest that these specific symptoms might be more noticeable or concerning for women or their caregivers, thus triggering referrals. This observation aligns with previous research indicating that sex/gender differences in cognitive decline, particularly memory impairment, significantly influence the diagnostic process for AD.5 Women's more proactive health care-seeking behavior could lead to earlier diagnostic prompting,<sup>39</sup> although their verbal memory advantage can delay formal diagnosis until more pronounced symptoms appear.<sup>5</sup> Furthermore, social and caregiving roles may increase women's likelihood of seeking evaluation for memory-related concerns.<sup>40</sup> During menopause, the decline in ovarian hormones also contributes to memory decline and could mask AD-related symptoms in women.<sup>41</sup> Recognizing these differences is essential for developing sex/gender-sensitive diagnostic tools and pathways. For example, creating more sensitive memory tests that emphasize sex-specific cognitive domains associated with AD rather than menopause could enhance early detection in women.

Our findings revealed that non-pharmacological therapies were more frequently used by women. Specifically, reminiscence and life

Emotional responses to the AD journey also varied by sex/gender. After their first specialist consultation, women experienced heightened anxiety, likely driven by greater health-related concerns or more emotionally charged approaches to care. Conversely, men tended to express relief at taking proactive steps toward diagnosis. However, after a formal AD diagnosis, women generally felt more relaxed, while men reported heightened anxiety and insecurity. These emotional patterns align with previous studies showing higher levels of emotional distress and depressive symptoms in women and gendered caregiving role expectations.<sup>7</sup> Men's anxiety and insecurity may stem from cultural norms discouraging emotional expression, leading to internalized stress. 48 Emotional differences may also influence care-seeking behavior, coping strategies, and diagnosis timing. 33 It is also worth noting that neuropsychiatric symptoms often differ between men and women with AD, and this might have influenced our results. 6 Overall, tailoring psychosocial interventions to address these unique emotional challenges may foster resilience and improve patient satisfaction.

Taken together, our findings highlight the need for greater awareness among health-care providers of sex- and gender-specific AD symptomatology, diagnostic challenges, and treatment preferences. Enhancing direct access to specialists and refining diagnostic criteria to incorporate sex and gender differences may lead to earlier, more accurate diagnoses for women, ultimately improving their outcomes and care experiences.

#### 5 **LIMITATIONS**

This study has several limitations. First, the relatively small sample size limits the generalizability of the findings and necessitates further investigation with larger cohorts. Additionally, the study was conducted exclusively in Germany and the United States, representing two distinct health-care systems. As a result, the findings may not be applicable to other sociocultural contexts. The small sample size within each country further constrains the study's generalizability. Furthermore, we acknowledge that country-specific characteristics of health-care systems may influence the AD patient journey. While this study did not test specific hypotheses regarding how such systemic differences might interact with sex and gender, this remains an important question

for future, larger-scale investigations. Given the cognitive impairment associated with AD, most responses to our survey were provided by caregivers. While this approach is common in AD research, it inevitably reflects the caregivers' perceptions of the patient experience, which may not fully capture the patient's own perspective. This proxy-based method introduces potential bias, particularly in questions requiring subjective insight, such as perceived awareness of AD, the burden of diagnostic testing, or the emotional impact of the disease. Although the survey included questions about the caregiver's relationship to the patient beyond the distinction family/friend (e.g., spouse, son/daughter, grandchild), the information was often fragmented or inconsistently reported, limiting our ability to examine how caregiver characteristics, such as sex, gender, relationship type, or duration of caregiving, may have influenced the diagnostic process. 49 Notably, most proxy respondents identified as family members rather than friends, reflecting traditional caregiving roles. However, this distinction does not necessarily indicate differences in emotional closeness or caregiving quality. A friend acting as a primary caregiver may suggest a lack of available family or, alternatively, the presence of a strong and supportive non-familial bond. These variations underscore the complexity of caregiving dynamics and highlight the need for inclusive approaches that recognize diverse caregiver roles beyond family structures. Another key limitation is the study's focus on sex differences within the binary categories of male and female. Responses from individuals identifying outside the binary ("other") were excluded due to small sample size for appropriately powered statistical analysis. Furthermore, participants were asked to report their sex (male/female/other), but not their gender identity. As a result, we inferred gender based on sex, assuming correspondence (e.g., male = man), which may not reflect all individuals' identities or lived experiences. While practical for statistical clarity in this limited sample, this approach conflates sex and gender and does not account for people whose gender does not align with their sex assigned at birth. This limits the inclusivity of our study and underscores the importance of future research that explicitly distinguishes and includes a broader range of gender identities. Finally, the questionnaire was not administered in a standardized or controlled environment, which may have affected respondent's attention and focus, whether it was a patient or a caregiver. These factors introduce potential variability that was not accounted for in this study, warranting further exploration in future research.

# **CONCLUSION**

This study provides preliminary insights into sex/gender-based differences in the AD patient journey, from initial suspicion of the disease to diagnosis and post-diagnostic treatment. As a proof-of-concept study, our findings emphasize the need for further research with larger, more diverse cohorts that encompass different sociocultural backgrounds.

Recognizing both sex and gender differences is essential for healthcare providers to tailor patient and caregiver support, education, and early detection strategies. Understanding the influence of both sex and gender on the AD patient journey may also help improve patient experiences and lead to more effective interventions. Continued research is needed to further elucidate these differences and inform the development of targeted, sex- and gender-informed approaches to care.

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## **CONFLICT OF INTEREST STATEMENT**

Maria Teresa Ferretti is an employee of Syntropic Medical GmbH; in the past 2 years, she has received consultancy and speaking fees from Angelini Pharma, Prodeco, EPH Health, and Biogen, unrelated to the present work. All other authors reported no conflicts of interest. Author disclosures are available in the supporting information.

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# SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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