

Dilemmas in diagnosing Alzheimer's disease: The peril and promise of self-fulfilling prophecies

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Abstract

To date, there are limited empirical data to inform various approaches to communication with patients receiving information on Alzheimer's disease (AD) risk or diagnosis during the pre-symptomatic or minimally symptomatic stages. This article explores the ethical implications of psychological responses known as self-fulfilling prophecies that may impact cognitive decline among individuals diagnosed with or at risk for AD. We describe questions these potential effects raise about the ways clinicians communicate with patients, as well as how caregivers may interact with patients. Recent advancements in biomarkers and treatment for AD underscore the urgency of understanding these phenomena and developing appropriate responses.

Keywords

Alzheimer's disease, communication, dementia care, ethics, psychological response

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The US Food and Drug Administration (FDA) approved the drug lecanemab for patients with Alzheimer's disease (AD) in 2023, followed by donanemab in 2024. Medicare now covers 80% of the cost of these drugs, making them accessible to a growing pool of patients. These developments mean that there is now growing hope for effective interventions in individuals having positive AD biomarkers with the earliest clinical manifestations, and ongoing trials are currently evaluating these treatments in those with pre-symptomatic AD (i.e., those who have positive AD biomarkers but remain cognitively unimpaired). Thus, patients and clinicians alike will be incentivized to seek earlier testing for the disease, when cognition is only mildly impaired and the disability that comes with more advanced dementia may be years away. Rapid advances in plasma-based assays also promise less expensive, widely available options for diagnostic testing.¹ In addition, we have made progress in AD genetics, enabling better delineation of personalized risk profiles, regardless of cognitive complaints. Together, these innovations are likely to push clinicians toward ever-earlier diagnostic evaluation of cognitive concerns along with the challenging conversations that follow.

Recently, revised consensus guidelines introduced the biomarker-based diagnosis of AD, including in those with mild or even absent cognitive symptoms.² While agreeing with the value of etiologic diagnosis, a competing international workgroup subsequently questioned the wisdom

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of labeling cognitively normal individuals with positive biomarkers as having AD, since many may never actually progress to manifest cognitive symptoms.³ This debate highlights the importance of how we communicate with our patients and the public, as well as the challenges of integrating information about genetic risk, diagnostic biomarkers, and cognitive testing into patient care. Our objective here is neither to resolve nor take sides on this debate, but rather to highlight that additional study is needed to understand the potential impact of disclosure, including the words and labels we use. The phenomena we discuss are likely most important in the earliest stages of disease, potentially impacting those with positive AD biomarkers (with or without clinical manifestations) as well as those identified as having elevated genetic or similar risk factors but with negative disease biomarkers. Each of these categories present unique challenges for disclosure, compounding the inter-individual variation in reactions to receiving information on AD risk and/or diagnosis.

Research has been reassuring that most patients who seek out assessment and subsequently learn they are at increased risk of AD, for example due to genetic risk variants, generally do well psychologically with that information, showing rates of anxiety and depression similar to those who are not at increased risk^{4,5} and improvement of health behaviors in some patients.⁶ Even so, a growing body of literature demonstrates that individuals' psychological responses to new information and interactions with others can be varied and nuanced, with functional as well as affective consequences. Researchers have found that patients given an early diagnosis of mild cognitive impairment respond to that information in diverse ways⁷ and that getting such information can be threatening to a patient's personal identity and narrative.⁸ In addition, there are limited data supporting the hypothesis that validation therapy can help improve mood and cognitive performance in patients with dementia.⁹ One particularly intriguing possibility is that learning information about one's risk for developing dementia could create a type of self-fulfilling prophecy, i.e., a phenomenon in which a person's beliefs about the future, modified by interactions with healthcare professionals and caregivers, impact their behavior and thereby make the prediction come true.

The placebo effect is the classic example of how an individual's beliefs and expectations can have small but measurable effects on their perception and even performance,^{10,11} but a number of other psychological phenomena with similar consequences have been described. Higher levels of worry – dementia worry in particular¹² – have been correlated with lower performance on executive function assessments.¹³ More specifically, age-based stereotype threat—an individual's concern that they will confirm a negative stereotype about the elderly—has been shown to impair both cognitive and physical performance.¹⁴ With respect to AD in particular, one study¹⁵ found that

individuals who were aware that they carried the apolipoprotein E (*APOE*) ϵ 4 risk allele for AD performed worse on memory tests than those who were not aware; moreover, those who were aware they did *not* carry the *APOE* ϵ 4 risk allele performed better on the same tests as compared to those who were not aware. While these data are limited and have been critiqued,¹⁶ our understanding of how psychological factors impact decisions and behaviors more generally is growing.

A slightly different type of self-fulfilling prophecy has been described in which the expectations others have of an individual affect their performance. This phenomenon – called the Rosenthal effect when the impact is positive – has been best documented in the context of education, with studies showing that students perform better when their teachers have higher expectations of them.^{17,18} The converse, called the Golem effect, has also been demonstrated. In one study, participants were more likely to score poorly on a second physical fitness test when they were given an unfavorable interpretation of their scores on an initial fitness test.¹⁹ Similar “socially transmitted placebo effects” have been observed in a healthcare setting, with patients' reported pain levels varying according to clinicians' expectations.²⁰ While these studies were not conducted in the setting of AD, they support the hypothesis that clinicians' and caregivers' expectations, as well as the way they communicate with patients, may have similar self-fulfilling effects, necessitating further study.

These possible effects are particularly relevant in the setting of disclosing an AD diagnosis in individuals with minimal or absent clinical manifestations. It is possible that AD pathophysiology makes patients more susceptible to self-fulfilling prophecies. Indeed, mood and anxiety disorders are common comorbidities in those with AD biomarkers but absent or mild cognitive impairment,^{4,21–23} potentially increasing vulnerability to the psychological impact of disclosures. Commonly held beliefs about genetic determinism, in which patients view a significant genetic finding as definitive, might also exacerbate potential effects for those found to have genes associated with AD, even in the absence of biomarkers or symptoms.

If the way clinicians communicate with patients about their risk and diagnosis can affect cognitive performance – and therefore overall well-being – there is an ethical imperative to carefully consider how to best approach these disclosures and conversations. Similarly, if patient outcomes can be influenced by the expectations set by caregivers and others around them, ethical questions are raised about how to coach those individuals to interact with patients.

It is worth noting that the effects of self-fulfilling prophecies can be either positive or negative and, therefore, that clinicians and caregivers have the potential to affect patient outcomes for better or for worse. This observation raises the question of how it might be possible to leverage the potential benefits and prevent the potential harms

associated with self-fulfilling prophecies. Respect for patient autonomy would prohibit outright deception of patients about their cognitive status and prognosis, at least in the absence of compelling data that doing so offers substantial benefits that are unobtainable any other way. However, nuances in the way information is framed can shape patients' responses and outcomes.²⁴ The development of communication strategies incorporating insights about self-fulfilling prophecies may help clinicians and caregivers optimize patients' well-being.

Empirical data about the effects of various communication approaches used by clinicians and caregivers remains limited at present in the setting of AD, including disclosures of AD risk and/or provision of AD diagnoses in those with no or minimal symptoms. However, it is possible to hypothesize about the types of interventions that might benefit patients based on results of studies in other contexts. Clinicians who provide more optimistic interpretations and emphasize patients' capabilities rather than their deficits may raise patients' expectations of their own performance and therefore potentially delay their cognitive decline. For example, intentional efforts to subtly undermine stereotypes about aging have been discussed as a way to combat age-based stereotype threat²⁴; similar efforts might be appropriate within the domain of AD. It also seems plausible that the timing of testing or disclosure relative to the onset of symptoms has the potential to impact patient performance. If sufficient data were to demonstrate that such interventions can produce substantial benefit for patients at risk for AD and/or those with early AD pathophysiology, clinicians' duties of beneficence would require them to take that potential benefit into account. In such cases, this possible benefit would need to be considered alongside obligations to respect patient autonomy, as well as the anticipated benefits and risks of newly available drugs, to develop an appropriate care plan.

Additional layers of complexity are added when families and caregivers are considered. One might speculate that patients would maintain higher functioning if family members refrained from calling out situations in which cognitive impairment becomes evident, thereby avoiding reinforcing a stereotype or worry about dementia. It also seems possible that if caregivers reassure patients about their performance and maintain high expectations by encouraging autonomy and agency, cognitive performance in individuals with AD pathophysiology or elevated AD risk could be preserved. However, if such approaches were to be supported by empirical research, there could be good reasons to develop an educational program outlining best practices for those who will be interacting with patients, with the hope of slowing their decline.


Another approach that has been proposed to minimize the effects of cognitive biases such as self-fulfilling prophecies is to make patients aware of their potential existence.²⁵ Educating those who might be unconsciously affected by such biases about the influence they may have on their


functioning may reduce (but not eliminate) their impact. This might include addressing assumptions about genetic determinism and the limitations of risk prediction. Similarly, it will be important to validate communication strategies that clearly explain to those with positive AD biomarkers but absent symptoms the uncertainty for developing cognitive impairment.

In light of recent advances in biomarker-based diagnosis and treatment of AD, there will likely be a shift toward earlier diagnosis. Importantly, in the absence of effective interventions, there is currently broad consensus against the routine use of biomarker assays for the diagnosis of AD among individuals without cognitive complaints (i.e., pre-symptomatic AD). Nevertheless, clinicians and caregivers need to be aware of the additional complexity self-fulfilling prophecies might introduce in this context. This complexity is further compounded by the diverse risk profiles of patients, which include varying symptoms (e.g., with or without neuropsychiatric symptoms, amnesic versus non-amnesic predominant symptoms), biomarkers (e.g., amyloid⁺tau⁺ versus amyloid⁺tau⁻),²⁶ and genetic predispositions (e.g., high penetrance Mendelian AD alleles versus *APOE*). There are important differences between these categories that affect patient care, but because this paper's focus on psychological responses to risk information is common among them, we consider them together. Empirical research is needed to better document whether self-fulfilling prophecies exist and how the potential impact varies in different subgroups.


Careful consideration about what information clinicians should give patients and how that information can be best communicated is required. Caregivers, as well, need to be aware of the effect their own interactions with a patient may have. The paucity of evidence about the effects of various approaches to communication and interaction with patients receiving information on AD risk or disease biomarkers suggest there is a need to study these phenomena empirically to understand the role that self-fulfilling prophecies may play in this setting.


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Statements and declarations

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