

Review

A Narrative Review of Alzheimer's Disease Stigma

Eric R. Rosin^{a,1}, Drew Blasco^{b,1}, Alexander R. Pilozzi^a, Lawrence H. Yang^{b,c,2}
and Xudong Huang^{a,2,*}

^a*Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA, USA*

^b*Department of Social and Behavioral Sciences, School of Global Public Health, New York University, New York, NY, USA*

^c*Department of Epidemiology, Mailman School of Public Health, Columbia University, New York, NY, USA*

Accepted 8 September 2020

Abstract. As the most common form of senile dementia, Alzheimer's disease (AD) is accompanied by a great deal of uncertainty which can lead to fear and stigma for those identified with this devastating disease. As the AD definition evolves from a syndromal to a biological construct, and early diagnoses becomes more commonplace, more confusion and stigma may result. We conducted a narrative review of the literature on AD stigma to consolidate information on this body of research. From the perspective of several stigma theories, we identified relevant studies to inform our understanding of the way in which implementation of the new framework for a biological based AD diagnosis may have resulted in new and emerging stigma. Herein, we discuss the emergence of new AD stigma as our understanding of the definition of the disease changes. We further propose recommendations for future research to reduce the stigma associated with AD.

Keywords: Aging, Alzheimer's disease, dementia, mild cognitive impairment, stigma, subjective cognitive impairment

OVERVIEW OF ALZHEIMER'S DISEASE

How the definition of AD has changed to include biologically-based markers

Alzheimer's disease (AD) is a neurodegenerative disorder that progressively impairs memory, thinking, and the ability to use language, with the most common early symptom being trouble remembering

new information [1]. As the disease progresses into its later stages it severely impairs decision making and the ability to function independently, with eventual death [1]. AD is the most common underlying disease resulting in dementia, with 60–80% of cases worldwide accounted for, making AD dementia a significant cause of morbidity and mortality [1].

To date, AD has generally been diagnosed based on clinical symptoms; however, with more recent research indicating that AD may be present well before symptoms emerge [1], new AD research has focused on a framework for a biological-based diagnosis [2]. This new framework, proposed by the National Institute on Aging-Alzheimer's Association (NIA-AA), differentiates between individuals with

¹These authors contributed equally to this work.

²Co-senior authors.

*Correspondence to: Xudong Huang, PhD, Department of Psychiatry, Massachusetts General Hospital and Harvard Medical School, Charlestown, MA 02129, USA. Tel./Fax: +1 617 724 9778; E-mail: Huang.Xudong@mgh.harvard.edu.

underlying AD pathology and those with clinical symptoms of AD [2]. AD is split into three stages: the preclinical stage, the prodromal stage—sometimes referred to as mild cognitive impairment (MCI) due to AD, and fully developed dementia symptoms, or AD dementia [2]. The preclinical stage is marked by the presence of abnormal biomarkers and no, or subtle, cognitive impairment. In this framework, AD is diagnosed based on positive biomarkers such as amyloid- β (A β) deposition, neurofibrillary tangles (NFTs) of pathologic tau protein, and neurodegeneration [AT(N)] [2]. The prodromal stage is marked by the presence of abnormal biomarkers and episodic memory impairment. The dementia stage, the stage most associated with AD among the general public, is marked by the presence of abnormal biomarkers and clear cognitive functioning impairment [3].

New developments in the AD research field and purpose of this narrative review

Many illnesses are associated with significant stigma including mental illness, HIV, cancer, and others [4, 5]. Given the relative novelty of examining the stigma associated with AD, direct comparisons with other stigmatizing conditions are relatively rare. As an example, an earlier study examining differences in stigma (e.g., perceived stability of the condition) among 10 conditions including AD, AIDS, cancer, and other conditions reported that AD showed relatively high levels of stability (e.g., immutability) when compared with other stigmatizing conditions (e.g., child abuse) [6]. Among observers, AD also elicited relatively lower intent to help (e.g., make charitable donations) when compared to illnesses such as cancer [6]. Further emerging evidence has suggested that AD is a stigmatized condition that causes significant negative effects on individuals diagnosed with AD as well as their caregivers, such as low self-esteem, isolation, poor mental health, and decreased quality of life [7]. Stigma also contributes to the avoidance of help-seeking behaviors, thereby resulting in delayed diagnosis and under-utilization of health and social services [8–10]. An update in 2014 on the National Plan to Address Alzheimer's Disease reports “Stigmas and misconceptions associated with Alzheimer's disease are widespread and profoundly impact the care provided to and the isolation felt by people with Alzheimer's disease and their families” [8]. Therefore, research on AD stigma is an important research area that is underinvested currently. A previously-published systematic

review (2014) on empirical articles collected between 1990–2012 identified 48 studies, primarily focused on public and family stigma related to AD, many without a theoretical background and in which stigma was used colloquially [11]. A systematic review on dementia broadly and stigma also cited a lack of research on self-stigma compared to public stigma and the need for more research in the field generally [12]. Recently, a number of new areas in the AD research field have emerged which have direct implications regarding the stigma associated with the disease for both patients and caregivers. While not claiming this narrative review to be comprehensive, we focus upon the following areas, detailed below, which we believe are especially salient in regard to emerging AD research and their intersections with stigma.

Area 1: Persistent lack of a disease-modifying treatment or a cure for AD

Decades of research has not yet been translated into a cure for AD or even a disease-modifying treatment that can slow the progression of AD [13]. This persistent lack of a cure or a disease-modifying treatment has continued to greatly influence the perceptions of people suffering from AD within society, as an AD diagnosis remains a death sentence. Perceptions of those with terminal illnesses have been linked to stigma [14]. A study on the public's perception of terminal illness demonstrated that the lay public “clearly expressed a desire to avoid a person dying from a disease” [14]. Further, the public viewed the terminally ill with more negative attitudes than the ill or healthy, and viewed them as having lost social value [14]. Perceptions of those with terminal illnesses, including AD since it ends in the identified person's eventual death, have resulted in some key stereotypes and stigma including social constructions of the “living dead” that have persisted at least in part due to the lack of a disease-modifying treatment for AD [15].

The media and general public often ignores the complex reality of living with the disease, both in the dementia phase as well as the preclinical and prodromal phases (see “AD Stereotypes, Public Stigma, and Implications for Patients and Families”) [16]. Enduring negative stereotypes of AD patients as the “living dead” (further discussed in the following sections) persist and have influenced public perceptions of the disease, which impact diagnosed individuals and caregivers [15].

Area 2: Early detection and new ways of diagnosing AD

Over the last few decades, researchers have been developing accurate ways to predict both preclinical and prodromal AD thus shifting the definition from a purely clinical-pathological disease to a clinical-biological one [2, 17, 18]. MCI, for individuals with memory problems termed amnesic MCI, has been conceptualized as a prodromal diagnosis for AD; however, low AD conversion rates are associated with significant stigma concerns around this label [19]. Further, The National Council on Aging, Alzheimer's Association, and the International Working Group have submitted criteria supporting that preclinical/asymptomatic biomarkers may be used as accurate diagnostic tests; however, to date, this is primarily a research framework and more research must be done until these tests are commonplace in the clinical setting [3]. Currently, early detection remains problematic due to a lack of accuracy and ability to predict who will go on to develop AD [19]. A prodromal or preclinical diagnosis (based on biomarkers) may also create a period of waiting, resulting in uncertainty, in which individuals wait to develop symptoms that may never emerge within their lifetime [7, 20].

This narrative review aims to discuss the most relevant research conducted over the past few decades through the theoretical lens of several fundamental stigma theories and conceptualizations, as applied to the new and emerging field of AD stigma, which has only started to receive attention when compared with other stigmatized illnesses (i.e., mental illness, HIV/AIDS). We seek to review what is known about the effects of stigma on those identified with or at-risk for AD, primarily based on the identified areas of AD-related research above. We conclude with recommendations for future research.

DEFINING ALZHEIMER'S DISEASE STIGMA

Stigma conceptualizations relevant to emerging AD research

Stigma is a complex concept and may occur at the individual, interpersonal, family, societal, and institutional level. Erving Goffman, often considered the originator of the modern conceptualization of stigma, defined stigma as "the situation of the individual who is disqualified from full social acceptance" who is then "reduced in our minds from a whole and usual person to a tainted, discounted one" due

to a mark or attribute [21]. Conceptualizations of stigma have further evolved over time, with Link and Phelan more recently proposing a conceptual framework for understanding stigma as six interrelated concepts, whereby human differences are labeled (i.e., "Alzheimer's patient") and linked to stereotypes ("Alzheimer's is a death sentence"), thereby leading to cognitive separation into categories of "us" ("persons whose cognition is affected by age normally") and "them," ("AD patient"), emergence of emotional responses (i.e., "hopelessness" in being identified with AD), and status loss and discrimination, all which occur in the context of an unequal power situation [22]. Stigma, when fully enacted, then excludes individuals from participation in everyday life or "full personhood" [23]. Additional stigma concepts have focused on the impact on the individual (self-stigma), in which identified individuals internalize negative stereotypes and apply them to the self, often leading to worse psychosocial outcomes [24, 25]. Further, culturally-salient conceptualizations of stigma are also important for future consideration [23]. Among these myriad stigma conceptualizations, we briefly review several here that we believe are most applicable in the context of the emerging AD research.

First, stereotypes are beliefs, learned through growing up in a particular society, about the characteristics of a definable group of people, usually which are exaggerated or inaccurate [26, 27]. For example, stereotypes around AD include "a physical body left to be managed" or an "empty shell" [16]. Stereotypes contribute to public stigma, which occurs as a result of large proportions of the general public agreeing with negative stereotypes associated with a condition [26].

Second, and key to the era of new mechanisms of early AD identification, is the process by which an individual becomes "labeled" with a diagnosis of AD or as being at-risk for AD and the potential consequences that may result from this label [28]. In this model, individuals understand that negative stereotypes are associated with a disease (i.e., AD), and that these stereotypes become personally relevant when they are officially labeled, or diagnosed, with AD or as being at-risk for AD [28]. This may lead to labeled individuals then anticipating stigma from others (e.g., being aware that others may think of them as "the living dead") resulting in poor coping mechanisms by the diagnosed individual such as keeping one's diagnosis a secret and limiting social interactions [28]. These negative coping responses may lead to harmful social, psychological, or financial consequences [28].

Third, what is known as attribution theory is key to the conceptualization of how biological identification of AD, either through genetic or biomarker testing, may result in decreased stigma. This theory proposes that how individuals interpret the cause or “attribution” of an outcome impacts their perceptions and behaviors toward those who are identified as having that outcome [29, 30]. Previous literature on the intersection of attribution theory and mental illness has proposed that attribution of mental illness to a genetic cause would reduce blame toward individuals with mental illness, since our genetic makeup cannot be changed [30, 31]. However, any benefits in stigma via decreased ascribed responsibility may be counterbalanced by the effects of the geneticization of stigma whereby perceived permanence and severity of an illness is increased [31, 32]. In sum, genetic and biologically-based attributions may reduce blame and therefore causal responsibility for an illness; however, this may also increase the perceived permanence and seriousness of an illness [31]. Due to AD's posited gene-by-environment interaction, providing information to activate individuals at risk for AD (i.e., improving other health conditions such as vascular diseases or metabolic conditions, diet, exercise, social engagement, etc., in relation to the genetic risk) could also potentially counterbalance any negative stigma implications of a genetic risk explanation by empowering individuals to take health promoting actions [33, 34].

Finally, given the likely future increase in AD identification via biological means and early or at-risk diagnoses, structural discrimination is important to consider. Structural discrimination can be thought of as the ways in which institutional practices lead certain stigmatized groups to experience disadvantage (i.e., confidentiality of an early AD diagnosis that is marked in one's health records) [35, 36]. Structural discrimination may also impact individual engagement in participating in genetic and biomarker testing to confirm an at-risk diagnosis of AD, due to fears of future structural discrimination (e.g., via one's workplace or insurance coverage).

APPLYING STIGMA THEORY TO ALZHEIMER'S DISEASE

AD stereotypes, public stigma, and implications for patients and families

Aging is often associated with negative perceptions such as a lack of ability to care for oneself

or function independently, especially within Western society. In the United States where ideas of individuality, personal sovereignty, and productivity are central, it seems that AD has become symbolic of the fear of losing these prized characteristics. Under the biomedical model, conceptualizations of “normal” versus “non-normal” aging emerge, with those diagnosed with AD identified as part of “non-normal” aging, often resulting in the notion of an AD patient as a “non-person” [15]. Due to the significant brain dysfunction and the resulting memory impairment and loss of functioning that occurs, especially in the later stages of AD, the concept of “a body left to be managed” emerges as the brain, or what constitutes one's being, is destroyed [15]. A common social construction associated with AD includes the conception of the “living dead”, as there continues to be no cure or disease-modifying treatment for AD available [1, 15]. The “zombie” like social construction of AD patients has led to a significant stigma of AD and the dehumanization of those diagnosed [15]. Related to this notion is the perception that AD patients have little to no quality of life due to their disease, which may lead to a loss of independence and dignity [37]. Other common stereotypes of dementia more broadly include perceptions of: “incompetence”, “being burdensome” to one's family or the healthcare system, “an inability to contribute to society”, and “on a path to eventual death” [38].

Uncertainty about when and/or if an individual will develop symptoms of dementia due to AD may cause psychological distress [7, 39, 40]. Fear around the uncertainty surrounding the disease and the portrayal in both the media and medical field influence public perceptions and consequently the public stigma surrounding AD [16]. Advertisements in the media often depict people diagnosed with AD in the final stages of the disease and thus, the end stages of their lives. AD patients are typically shown looking lost, scared, or infantilized [41, 42]. Research shows that this portrayal increases donations but furthers stigma of the disease, with the general public discounting, infantilizing, and marginalizing AD patients [9, 16]. Alzheimer's advocacy groups seek to reduce AD stigma yet may potentially rely on a certain degree of cultural fear to increase fundraising [9]. Interestingly, the media portrayals of AD patients often run counter to the messages written in autobiographies of individuals with AD. One of the themes in autobiographies demonstrates that people displaying symptoms still desire to partake in the societal norm of productivity. However, AD dementia patients also discussed

the meaning they find in the disease, ambivalence, an urge to learn from it, and an understanding of death [16]. These aspects of living with the disease, from the patient perspective, are rarely discussed in popular culture [16], and could, if made more prominent, be used to combat prevalent public stereotypes of AD (see “Conclusion and Future Directions”).

Previous studies have indicated gaps in knowledge around AD with the public often understanding more general information but lacking knowledge about the specifics of AD [43], including a lack of medication to prevent AD or a disease-modifying treatment [44]. Public stigma, due to misunderstandings of AD, may have significant impacts on the daily lives of AD patients. Misinformation about AD may further perpetuate stereotypes and public stigma thereby leading to an environment where those with dementia may be isolated or hidden due to the stigma of AD and anticipated negative reactions from others [8]. Further, the persistent and widespread stereotypes and resulting public stigma often have significant consequences for individuals identified with AD. Even in countries where dementia is more known and accepted, there is still an unwillingness to give power to the patient, still a fear that the patient will be unpredictable, and uneasiness and a lack of understanding in how to interact with the patient [45].

Confusion with mental illness and potential misattributions for AD

Confusion between AD and mental illness and corresponding misattributions in the causes and symptomatology of AD [32], can also generate stigma. AD shares many characteristics with some mental illnesses, such as depression (which may lead to attributions of perceived responsibility) and schizophrenia (which may lead to perceptions of dangerousness) [9]. Research on mental illness has shown greater stigma when mental illness is attributed to one's own behavior (e.g., the cause of mental illness is their own fault) and is within their control to prevent [31]. Due to the overlap in symptoms with schizophrenia, such as delusions, that may occur in the later stages of AD when an individual has developed dementia, this may increase AD stigma due to perceptions of increased likelihood of unpredictability and violence [9]. Results of a survey of 2,000 English and American individuals demonstrated that “35% of respondents believed very strongly that Alzheimer's disease was a mental illness, and those who believed more strongly that

Alzheimer's disease was a mental illness rated symptoms more severely” (i.e., were more stigmatizing in their perception of symptoms) than those who did not strongly believe it was a mental illness [9].

Confusion over terminology and the impacts on labeling

There are many terms associated with AD (i.e., dementia, Alzheimer's disease related dementias (ADRD), subjective cognitive impairment (SCI), and MCI) with distinctions often not apparent for the public, those diagnosed, or family members, which may create uncertainty about the symptomatic progression of one's illness experience [19, 46]. ADRD refer to frontotemporal degeneration, Lewy body dementia, vascular dementia, and mixed etiology dementias [47]. ADRD are termed as such because they share many of the pathological and cognitive features with AD which can make them difficult to distinguish. AD patients often present with different mixtures of pathologies which makes treatment and diagnosing the disease difficult [47]. Confusion over the diagnosis, how and if a diagnosis will result in AD or ADRD, and a lack of cure or a disease-modifying treatment can negatively impact an individual's psychological well-being, life satisfaction, and induce a period of waiting due to uncertainty [7, 39, 46].

Further, misconceptions are common regarding the difference between “normal” and “non-normal” aging with regards to how dementia fits into that dichotomy [48]. While both the US Centers for Disease Control and Prevention (CDC) and the Alzheimer's Association make clear distinctions that the symptoms of dementia are not normal effects of aging [49, 50], the distinctions in the earlier phases of AD (preclinical and prodromal) are less clear. The medicalization of the earlier phases of AD, which may overlap with normal phases of aging, increases the amount of people diagnosed, thus increasing the amount of people “in waiting” who may or may not develop symptoms [51]. Medical models of dementia are obscure and can be impenetrable to the public thus creating more confusion around if and how symptoms will progress [39, 52]. As research progresses the field has sought to make better distinctions about the differences between preclinical and prodromal AD and normal aging using the NIA-AA framework [2].

However, a systematic review on the general public's knowledge of dementia and AD found that dementia was often misconstrued as a “normal” part of aging and there was a lack of knowledge

regarding when symptoms are no longer a “normal” part of aging but are actually “dementia” [48]. An additional study of individuals diagnosed with MCI reported that “most respondents identified their forgetfulness as a consequence of the normal aging process rather than a brain-based disorder” [46]. The confusion between normal aging and non-normal aging is especially high in minority populations in the United States [7, 53, 54]. Misunderstanding the symptoms and terminology related to the disease may prevent diagnosis and increase stigma. For example, believing that dementia is a normal age-related process may further a belief that the symptoms of AD are character faults and are not caused by neurodegenerative reasons, increasing perceived causal responsibility [27]. Misunderstandings of terminology may result in increased emotional consequences, less access to medical and social support, increased social isolation, and less knowledge about a patient’s rights [55].

Confusion over terminology related to AD may increase the stigma associated with related concepts. SCI, a term used to describe subjective memory related complaints without pathological results on neuropsychological tests, is another term that may generate confusion. SCI has indicated a “positive yet moderate association” with future AD or ADRD [56]. For this reason, the International Working Group for SCI has suggested that SCI may be a possible first symptomatic expression of AD [56]. However, since most people with SCI do not progress to MCI or dementia, and since SCI lacks common assessments and classifications, this term may contribute to additional confusion around AD [56, 57].

MCI has been proposed as a prodromal diagnosis for AD in some cases. The term MCI is widely used by medical professionals to describe patients showing cognitive decline without having dementia [46]. Confusion between MCI and AD may continue to perpetuate the stigma associated with AD and may lead to new intersections with labeling stigma, especially as the disease shifts to earlier diagnoses, before full dementia is present. This is the case in other “at-risk” diagnoses (e.g., for psychosis), where the at-risk designation can elicit stigma comparable to that of the full disorder [58]. Per “labeling” processes introduced above [28], individuals become socialized to become aware of stereotypes associated with a particular illness while growing up in a society (i.e., perceptions of AD patients as the “living dead”, or “unable to contribute to society”) [15, 28, 38]. When someone is officially labeled with MCI, the same

stereotypes that are associated with AD or dementia have the potential to become personally relevant, thus triggering anticipated stigma and potentially harmful coping mechanisms such as secrecy of the MCI label [28]. The term MCI is valuable for medical purposes, but when it becomes embedded in the public domain it may cause confusion [19]. This is largely because MCI does not always translate into AD or another form of dementia, therefore making it an unclear diagnosis [46]. Even though there are subgroup classifications of MCI, with amnesic MCI resulting in a higher likelihood of AD development, the rates vary drastically among studies with some research demonstrating as many cases of MCI reverting back to normal as converting to AD dementia [19]. Recent research has demonstrated that approximately 5–15% of MCI patients develop AD dementia per year while the remaining individuals diagnosed with MCI do not develop further cognitive decline [59]. While MCI has been proposed as a prodromal diagnosis for AD, and is useful in identifying those people who may go on to develop AD dementia, concerns arise around the potential negative impacts of labeling someone as at-risk to develop a disorder in which the current research suggests that most will never go on to develop AD. In sum, there is the possibility that the same stereotypes associated with AD dementia may be applied to those with MCI and result in similar negative consequences from being labeled [28].

The uncertainty around AD continues to expand as terminology related to prodromal or preclinical diagnoses and timely or early diagnoses have emerged. The fact that most SCI cases do not translate into MCI, and most MCI does not translate into AD dementia (or ADRD) [19, 56, 57] may create confusion for the population at large. Evidence suggests that an MCI diagnosis may cause more individuals to identify with the “dehumanizing” aspects that are associated with AD, potentially impacting their social and personal rights [19]. Among qualitative studies of individuals with MCI, accounts of the experiences of coping with an MCI diagnosis and a sense of uncertainty about the future were consistent themes [60]. Recent studies suggest that people with MCI can still suffer from the stigma of social isolation and internalized distress even with mild or no symptoms [19, 60]. This results in an increase in the number of people who perceive themselves to be “patients in waiting”, thus leading an MCI diagnosis to elicit the same labeling stigma associated with AD, even for patients without a full diagnosis of dementia due to AD [28, 59]. The goal of early detection is important, espe-

cially if prevention, a cure, or a disease-modifying treatment is realized in the future which will reduce the number of full cases of AD dementia; however, it remains imperative to understand the impact of the MCI designation on the population, including its potentially stigmatizing consequences [19] (see “Conclusion and Future Directions”).

Shifting AD definition from syndromal to a biological construct and its effects on stigma: New methods of labeling and the impact on patients

Redefining AD in living people from syndromal to a biological construct [2] may reduce some aspects of stigma, due to a reduction in causal responsibility for the disease, but may also have negative implications such as increased perceptions of permanence of the disease [31]. In addition, public understanding of pre-symptomatic AD testing needs to be further addressed [44]. While the link between presence of certain biomarkers and development of AD is still primarily a research framework and not routinely used in clinical practice, it has the possibility of being used in such a manner in the future [61]. Previous research in mental illness has demonstrated that the stigma associated with the “origin” of disease development may be reduced through genetic explanations, as the cause is not perceived as the fault of the individual. One study reported that when an AD diagnosis was understood to have biological causes it evoked “greater sympathy and less anger, judgments of less responsibility and lower personality contributions to behavior, and greater willingness to help” [62]. Additionally, framing the disease as biological instead of a mental illness generated more sympathy toward hygiene issues [7, 55]. Previous research has also shown that when AD is described as a mental or behavioral disease, rather than biological, it generates harsher judgements toward the patient and makes symptoms appear worse [7, 55]. However, linking biomarkers with the development of AD could also increase perceptions of the disease’s seriousness and permanence, potentially deepening existing AD stereotypes of “hopelessness” and AD patients being “on a path to eventual death” [31, 32, 38]. These potential negative consequences remain in need of future exploration.

As the disease switches to a clinical-biological model it may be possible to detect AD at a pre-clinical stage, before symptoms emerge. Even though a biological definition could help with understanding the disease and remove the stigma of “character

faults”, until a disease-modifying treatment or a cure is discovered, it may also increase the length of time that someone becomes defined by the disease and thus exposes them to stigma [59]. Further, under this biomarker framework, patients may never develop symptoms during their lifetime, although they may be “labeled” with AD. Unless the public stigma of AD shifts, patients might internalize the stigma associated with AD even when pre-symptomatic. The implications of labeling individuals with a disease in which they may never develop symptoms must also be considered for future research. Similar to a prodromal AD diagnosis of amnesic MCI, individuals diagnosed with AD or who are at-risk to develop AD based on their biomarker profiles (but who are currently asymptomatic), may internalize the same AD stereotypes, thereby leading to negative outcomes [28]. Additionally, as previously mentioned, biological labeling of an illness may have complex impacts on stigma, potentially resulting in both less blame but increased perceptions of permanence [30, 31]. Previous literature has begun to conceptualize the potential benefits and challenges of a “timely diagnosis”, or the time at which patients seek treatment due to concerns about symptoms (i.e., in cognition, functioning, or behavior), which could be applied to prodromal diagnoses as well [61]. Timely diagnosis, although more research concerning this is required especially in the prodromal stage before dementia sets in, may confer benefits such as accurate diagnoses and correct administration of treatment (i.e., avoidance of “medical nomadism”), the ability to prolong time prior to institutionalization, a reduction in “feelings of uncertainty and anxiety in people with memory complaints and their families”, and allow for time to plan for the future; however, this may also lead to feelings of uncertainty about the progression of the disease and may be linked to stigma at multiple levels (i.e., public, self, family/caregiver) [61]. Per Dubois and colleagues’ literature review, to date, the literature on this topic is relatively scarce and often based on expert opinion; therefore, there is little conclusive research on the cost/benefit of a timely diagnosis in the prodromal stage [61]. A “timely diagnosis” is different than an early diagnosis, which would be conferred to those identified without symptoms, but who may be identified via biological mechanisms (i.e., biomarker or genetic risk) [61]. These benefits and costs, including consequent relationships with stigma should be further explored for early diagnoses as well. Therefore, the implications of how stigma may change due to the reframing of the disease as a biological one, and the

potential for early diagnoses, instead of one purely based on symptoms requires further research, as the framing of disease continues to shift (see “Conclusion and Future Directions”).

In terms of personal impact upon identified individuals, the stigma surrounding AD could dissuade people from getting tested and learning about the disorder [9]. Surveys continue to demonstrate differences between individuals who would hypothetically want to know if they are predisposed to AD and individuals who actually participate in testing [63]. One study gave participants a preliminary dementia screening involving a survey and a professionally administered memory test (which was not a diagnostic test) and patients who screened positive were then referred for a full cognitive evaluation and diagnostic assessment; however, only 33% of those who screened positive agreed to further testing [64]. Some reasons associated with individuals who refused a follow-up exam were living alone and higher endorsement of stigma related to screening for dementia [64]. Given that no disease-modifying treatment or a cure for AD currently exists, it is assumed that knowing one's risk has no benefit and would only lead to psychological distress [59]. Learning one is at risk may create a period of uncertainty in which the patient waits to develop symptoms, all the while potentially facing stigma associated with the disease, resulting in isolation, depression, and insurance and/or workplace discrimination [7, 39].

Being labeled as at-risk for AD dementia may result in worse outcomes for patients. For example, people that tested positive for a genetic AD risk but had not yet displayed any symptoms of cognitive impairment performed worse on verbal memory tests and rated their memory as worse than those who did not test positive [7]. Shame and depression from receiving an AD diagnosis may prevent individuals from asking for help or getting medical attention, thus potentially worsening the condition [7]. Further, the more patients anticipate that they will be devalued and discriminated against, the more they may feel threatened by interacting with others, potentially resulting in poor coping mechanisms such as limiting social interactions, thereby increasing social isolation [7, 28].

The impact of early and biologically-based diagnosis on structural discrimination

Structural discrimination contributes to reluctance on the part of individuals in receiving early diagnostic

testing due to fears about impacts on their medical insurance and discrimination from employers [9, 55]. Results of a U.S.-based study [55] revealed that about half of adults worried that their health insurance would be impacted if their medical history indicated having or risk for developing AD. About 45% of people also feared that the results of a genetic or brain imaging test would result in higher insurance payments [55]. Other findings revealed that 55% of people expected a person with AD dementia to be removed from making medical decisions for themselves and that they would be discriminated against by employers (55%) [7].

Further, AD genetic risk factors such as polymorphic Apolipoprotein E allele 4 (APOE ϵ 4), and biomarkers, including the presence of A β amyloid deposition and NFTs of tau protein are the current best ways of early identification based on the underlying biology [17]. Both methods of early identification—i.e., genetic testing and biomarker identification—only indicate increased risk of AD development, but are not fully predictive of AD development nor are they completely accurate [19, 20]. For instance, APOE ϵ 4 is present in individuals with memory issues unrelated to AD [20]. Similarly, the biomarker A β may be present in elevated amounts in as many as 33.3% of adults over the age of 65 [7, 39]. The potential of a misdiagnosis based on these biomarkers may elicit fear that an individual will be stigmatized in the absence of disease. When multiple predictive factors are combined (such as elevated levels of A β and Tau, coupled with a positive APOE ϵ 4 polymorphism), the predictive nature of these tests increase accuracy, but still are not perfect.

While the Genetic Information Nondiscrimination Act protects individuals from discrimination based on genetic information, it does not protect against discrimination based on neuroimaging such as a positron emission tomography (PET) or MRI scan, which are the current means of biomarker identification for AD patients [55]. Moreover, the Genetic Information Nondiscrimination Act also does not guarantee long-term care insurance or confidentiality of a patient's potential dementia risk [7]. This fear that a preclinical diagnosis may result in structural discrimination, regardless of whether patients display clinical symptoms or not, may also dissuade individuals from being tested [55]. To eliminate these fears and reduce structural stigma, predictive accuracy for biologically based diagnoses needs to be improved and passing of laws protecting against discrimination should be prioritized.

Aspects of structural discrimination related to financial security may be particularly salient for those individuals who experience “early onset AD”, a diagnosis used to describe patients with a clinical onset of the disease under the age of 65 [65]. A recent study by the Blue Cross Blue Shield Health Index reported an increase in the number of insured individuals diagnosed with early onset AD between the ages of 30–64, with a 131% increase in diagnosis reported from 1.3 adults per 10,000 in 2013 to 3 adults per 10,000 in 2017 [66]. The Alzheimer’s Association reports unique psychosocial stigma challenges for early onset AD patients, noting “Because of young age, people may not believe you have the disease, may question your diagnosis or dismiss it,” [67]. The Alzheimer’s Association also notes financial insecurity as a major concern for these patients since they may still be of working age, might have young families and may not yet have saved adequately for retirement. This is supported by a study noting that early onset AD patients reported greater stigma accompanied by financial instability. Another study reported that patients with early onset AD suffered from greater psychosocial problems including retained insight while experiencing depression due to having to simultaneously deal with familial and financial anxieties [65].

Courtesy/family stigma and caregiver burden

Courtesy stigma occurs when stereotypes, prejudice, and discrimination are also attributed toward someone who is associated with the labeled group [21, 45]. In the case of AD, this courtesy stigma is often applied to family members or caregivers, given the necessity of caregivers especially in the later stages of the disease when full symptoms of dementia are realized [68]. For example, a study explained that family stigma initially occurs when “negative perceptions, attitudes, emotions, and avoidant behaviors” get activated by the public and directed toward the family of the AD patient [68]. A study reported that caregivers of AD patients often expend energy for “impression management” to minimize negative social reactions such as making excuses for the behavior of someone with AD. In part elicited by these attitudes, stigmatized families may experience emotional reactions such as fear, anxiety, and shame [69]. Initially the caregiver and the AD patient work together to manage information about the patient and to navigate problematic situations. The caregiver participates in “passing” [21] in which potentially harmful information to the person with AD is

withheld from other members of the public. Next, when the symptoms of the person with AD become too severe to cover up, the caregiver is required to manage situations including increasing social isolation for patients, and the caregiver distancing themselves from the patient and realigning with other family members. Increased courtesy stigma for the caregiver at this stage can increase caregiver burden [69].

Families and caregivers may experience social consequences from stigma such as increased burden and judgement [70]. This may lead to interpersonal consequences, such as avoiding social relationships or moving to a different location [69]. Consequently, caregivers may experience social and psychological impacts of stigma such as isolation and increased depression [7]. A study demonstrated that adult children’s perceptions of being stigmatized by the association with their parents with AD increased their negative caregiving experiences beyond the effects of the behavioral problems associated with AD [70]. Family and caregiver stigma largely impacts the quality of life of those individuals [7].

Caretakers may lose jobs due to caretaking for an AD patient, may lose social relationships, and may encounter harsh judgements, even from other family members [7]. For example, extended family may interact less frequently with the caregiver due to stigma which puts more stress on and may increase depression on the immediate caregiver [69]. One study demonstrated that stigma within a family may prevent caregivers from finding services to reduce caregiver burden [19]. Further consequences may include poor mental health. In 2019 the Alzheimer’s Association reported that 40% of primary caregivers suffered from depression [18]. This may arise due to many reasons, including various behavioral problems (e.g., the AD patient’s problems of incontinence) and consequent feelings of shame, which may prevent caregivers from leaving their homes with AD patients, thereby increasing social isolation and depression.

CONCLUSION AND FUTURE DIRECTIONS

To enhance prior stigma research in AD that was largely atheoretical [11], we have via this narrative review identified how distinct stigma theories may illuminate how stigma may manifest given new developments in AD research. From our review, we

highlight several areas for future exploration regarding AD stigma research; however, truly addressing the negative impacts of AD stigma will require multiple and intersecting interventions in order to reduce stigma at the individual, societal, and institutional level.

First, to combat the enduring negative stereotypes of AD due to a persistent lack of a disease-modifying treatment, a cure, or prevention, “interactive contact-based” approaches (which have shown to be effective in countering mental illness stigma) [71] with AD patients who moderately disconfirm AD stereotypes can be utilized. In order to more efficiently reach a larger target audience, these “contact-based approaches” could include delivery via a virtual platform (i.e., video), as opposed to face-to-face contact, which has also been shown to be an effective contact approach for mental illness [71, 72]. A targeted specific educational plan would be beneficial here as well but research shows that education alone does not reduce internalized or public stigma [45, 73]. For example, media portrayals of symptomatic AD patients who counter the stereotypes of having a “death sentence” (e.g., still wishing to be productive in society, finding meaning in the disease, etc.) could be tested in their efficacy in addressing public stigma. Further, *in vivo* contact-based approaches that could reduce AD stigma among community members could be promoted via programs such as *Poetry for Life*, which uses AD specific knowledge to allow AD patients, caregivers, and members of the community to interact in challenging and creative ways [74]. While a disease-modifying treatment may reduce important aspects of AD stigma, as with other stigmatized conditions that are now able to be managed via treatment (i.e., HIV/AIDS), social ramifications of receiving an AD diagnosis are likely to remain [75, 76]. However, the development of a disease-modifying treatment may aid in reducing stereotypes associated with AD such as AD patients having “an inability to contribute to society” which may have long-term benefits for autonomy and quality of life for which patients currently suffer from due to the fact that AD is a death sentence [38].

When it comes to caring for AD patients, the 2018 Alzheimer's Association recognized person-centered care as the core of quality care for dementia patients. Person-centered care, which takes the AD spectrum and individual needs into account, focuses on care based in individual and interpersonal relationships [77]. The elements of person-centered care include: “valuing people with dementia and those

who care for them, treating AD patients as individuals, looking at the world from their perspective and creating a positive social environment in which the AD patient can experience relative wellbeing” [78]. A review of nine long-term care facilities demonstrated that person-centered care had “significant effects on residents’ psychological well-being” as well as “significant effects on decreasing behavioral symptoms [aggression and agitation] and use of psychotic medications” [77]. Studies suggest that people with cognitive impairment want to be included in the decision-making about their health and care, which contributes to feelings of self-worth and quality of life [79]. Maintaining use of person-centered care, at all stages of disease, may lead to continued reductions in stigma and an increased sense of autonomy.

Second, potentially stigmatizing and emotionally stressful effects that could result from early-detection states for AD, such as MCI, should continue to be assessed. Raising concerns for MCI, other at-risk designations (e.g., for psychosis) can elicit similar levels of public stigma to that of the full disorder [58]. However, the addition of a short educational insert clarifying the nature of the “at-risk” state (i.e., “the person has not yet developed a full disorder” and that only a proportion of these individuals will go on to exhibit the full disorder) worked to reduce stigma among community respondents in one study of an “at-risk” designation [58]. Examining to what extent the MCI diagnosis elicits stereotypes that are the same as or different from AD, and then what educational interventions could be used to mitigate any resulting stigma, remains crucial.

Third, as the disease switches to a clinical-biological model that utilizes an array of biomarkers such as genetic risk markers (*APOE ε4*), PET or MRI neuroimaging for A β and NFTs of tau protein biomarkers to confirm either risk for or presence of AD at varying stages of the disease, potential stigma associated with each biomarker should be assessed. This is crucial given the extensive research showing both positive and negative effects of geneticization of stigma for disorders such as mental illness (described above). Additionally, development of AD dementia in some cases has been attributable to environmental factors (i.e., vascular diseases and metabolic conditions, diet, exercise, social engagement, etc.) which may be modifiable [33, 34]. Research has also posited that AD may have a gene by environment interaction [33]. As susceptibility genes (i.e., *APOE ε4*) only confer partial risk, those individuals identified as at genetic risk should be counseled on ways to

decrease the likelihood of AD development to activate individuals to make changes, thus potentially countering any negative stigmatizing effects of perceived causal responsibility. An analysis as part of the Risk Evaluation and Education for Alzheimer's disease (REVEAL) study, a randomized controlled trial which enrolled adult children who had a parent with an AD diagnosis, examined the impact on health behaviors following disclosure of genetic risk and future risk of AD development [80]. Those identified as *APOE* $\epsilon 4$ positive were significantly more likely than those who were negative for *APOE* $\epsilon 4$ to engage in behavioral changes related to AD development (i.e., changing medications or vitamins, diet, or exercise) even though they were informed that there were currently no established methods for preventing AD [80]. While evidence is newly emerging about the relationship between *APOE* $\epsilon 4$ status and various environmental factors, as evidence becomes available it will be important to educate patients about which behavioral factors may protect against or put them at risk for AD development in relation to genetic risk in order to activate individuals [33]. While biological explanations of AD may increase perceived severity and persistence of the disorder, providing information that may empower the person to make changes to their environment and/or behaviors may help counterbalance any negative ramifications of a biological explanation. Further, clarifying potential stigmatizing effects of biomarkers should be assessed in relation to stage of disease (i.e., at-risk state, or confirming presence of AD), as should the effects of having combinations of these biomarkers. Particularly important to examine are the potential effects of stigma upon those individuals with a biomarker designating them as at-risk for AD and are currently (or remain) asymptomatic.

Finally, future studies should examine how AD stigma intersects with often already marginalized minority populations. Given the rise in detection of AD among racial/ethnic minorities in the U.S., including African Americans and Hispanics, the additional influence of culture and race/ethnicity and its potential impact on stigma is an important target for research [81, 82]. Ethnic and racial minorities are greatly underrepresented in both research and early AD testing [83]. In one survey conducted on minority groups in the United States, the most reported reason for not participating was viewing dementia as a normal side-effect of aging; therefore, studies examining how AD stigma intersects with minority populations is of vital concern moving forward [64, 84].

The implications of these questions await future empirical testing. Nevertheless, framing these issues in the context of stigma theories can guide the formulation and evaluation of these questions, as stigma concepts have often not been explicitly incorporated into AD stigma research. By articulating how new developments in the identification of AD and its at-risk states could elicit identifiable forms of stigma along theoretical lines, our review presents a conceptual advance that may facilitate implementation of the new framework for a biological based AD diagnosis while mitigating any potential harms from stigma.

ACKNOWLEDGMENTS

This work is partially supported by a grant from NIH National Institute on Aging (R01AG056614 to XH).

Authors' disclosures available online (<https://www.j-alz.com/manuscript-disclosures/20-0932r1>).

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