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Risks and Benefits of Clinical Diagnosis Around the Time of Dementia Onset

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Abstract

Diagnostic delay in dementia is common in the U.S. Drivers of diagnostic delay are poorly understood, but appear related to misconceptions about dementia, stigma, concerns about autonomy, the nature of the diagnostic process, and provider-related factors. There is little quantitative evidence underlying cited risks and benefits of receiving a diagnosis around the time of dementia onset, including impacts on physical health, impacts on mental health, care partner interactions, costs of care, increased time for care planning, or earlier access to treatment. While various groups continue to push for reductions in diagnostic delay, realization of benefits and mitigation of harms will require new research on potential benefits and harms. Workforce and resource constraints, coupled with the expected growth in the number of persons living with dementia, may be a barrier to realization of potential benefits and mitigation of identified harms, which will require adequate access to providers, services, and supports.

Keywords

dementia, public health/public policy, caregiving and management, clinical geriatrics, literature review, cognitivie impairment

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What This Paper Adds

- We illustrate that there is little quantitative evidence available to support the numerous cited risks and benefits of reducing diagnostic delay or to demonstrate how to best address potential harms.

Application of Study Findings

- Research is needed to confirm benefits and identify potential negative consequences.
- Such research will be essential to appropriate resource allocation to promote associated benefits and address associated harms.
- Additional resources and changes to the workforce and care landscape will be needed to support persons living with dementia and their care partners as more persons are diagnosed with dementia in a timely fashion.

How Common Is Delayed Diagnosis of Dementia?

An estimated 6.5 million older Americans have Alzheimer's disease and related dementias, and the number of persons who have dementia in the U.S. is projected to more than double by 2060 (Rajan et al., 2021). However, many persons who have dementia have not received a dementia diagnosis from their healthcare providers. According to recent studies that evaluate all participants for the presence of dementia (Lang et al.,

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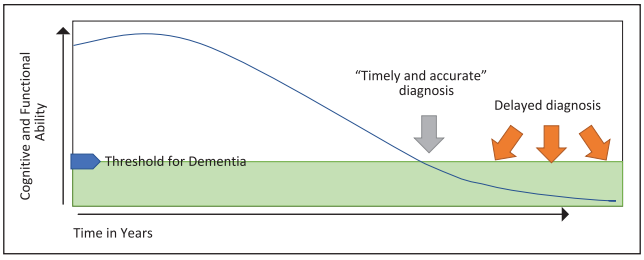

Figure 1. Illustration of diagnostic delay in dementia.

2017), 62% of persons who have dementia have not received a dementia diagnosis from their healthcare provider.

The onset of dementia is not an acute event; rather, dementia is a label applied when cognitive decline becomes severe enough to cause cognitive and functional impairment. Despite the inherent uncertainty around the timing of a person's transition to dementia, delays in receiving a clinical diagnosis past the time where a person meets criteria for diagnosis can be substantial (Figure 1). For example, while some studies report the mean duration between reported onset of symptoms consistent with dementia to clinical consultation or diagnosis at a specialty clinic to be as little as 1 year, others report a longer mean duration, with reports suggesting a mean duration of up to 4 years (Cattel et al., 2000; Helvik et al., 2018; van Vliet et al., 2013). Delays in the primary care setting, where most people receive an initial diagnosis (Cho et al., 2014; Wilkins et al., 2007), may be longer given primary care providers report substantial barriers to diagnosing dementia, including the desire to focus on more easily addressed health conditions, insufficient training on dementia diagnosis and management, and preference for referral to specialists to ensure accurate diagnosis (Bradford et al., 2009; de Levante Raphael, 2022).

What Contributes to Delayed Diagnosis of Dementia?

Dementia symptoms are often mistaken for normal signs of aging (Bradford et al., 2009). Care partners and persons living with dementia who do notice symptoms may not bring them to the attention of a clinician due to the stigma associated with dementia, including fear that a diagnosis will lead to restrictions on activities (Dubois et al., 2016). When cognitive concerns are brought to a clinician, clinicians may be hesitant diagnose dementia before symptoms become more severe to avoid the perceived negative consequences of diagnosis (Bradford et al., 2009). Thus, the degree of diagnostic delay likely varies based on provider beliefs about the benefits and risks of early diagnosis, which vary across providers (Iliffe et al., 2003).

As a clinical dementia diagnosis is based on assessment of symptoms, rather than a biomarker (Box 1), the nature of the diagnostic process may also contribute to diagnostic delay. To diagnose dementia, clinicians must establish the presence of cognitive and functional impairment and exclude other potential causes. This involves assessment of cognition and function, and, ideally, independent consultation with informants. However, no single cognitive assessment tool is universally recommended, and many screening tests fail to identify subtle cognitive symptoms (Robinson et al., 2015). Similarly, in the absence of severe cognitive impairment, assessment of functional impairment must be tailored to the individual and often requires informant consultation. This may explain why those with fewer functional impairments (Dubois et al., 2016) and cases of mild dementia (Bradford et al., 2009; Grodstein et al., 2022; Valcour et al., 2000) are more likely to be underdiagnosed. In addition, cognitive assessment, functional assessment, and patient/care partner counselling are relatively poorly reimbursed by U.S. payers, disincentivizing providers.

Patient characteristics also influence likelihood of diagnostic delay. Delayed diagnosis appears more common among those with lower education (Amjad et al., 2018; Borson et al., 2006; Savva & Arthur, 2015), low literacy (Borson et al., 2006), or who are non-English speaking (Borson et al., 2006); those who are older (Lang et al., 2017; Savva & Arthur, 2015; Valcour et al., 2000; Wilkins et al., 2007) or male (Lang et al., 2017;

Box 1. Alzheimer's Disease Biomarkers and Their Relation to Dementia Diagnosis.

Although neuroimaging can now be used to identify the presence of pathology associated with Alzheimer's disease (AD) in the brain (e.g. through amyloid-PET scans), diagnostic guidelines specify these biomarkers should not be the sole basis for a dementia diagnosis in a clinical setting.(McKhann et al., 2011) In part, this stems from the reality that many people with imaging evidence of AD pathology are cognitively normal and the presence of AD biomarkers does not guarantee progression to severe cognitive impairment or dementia within a person's lifetime.(Jansen et al., 2022; Price et al., 2009) Furthermore, AD is only one neurodegenerative disease that contributes to dementia, and substantial evidence exists that most persons with dementia—even those diagnosed as having "probable AD"—have more than one disease or condition contributing to their dementia. (Power et al., 2018; Schneider et al., 2009)

Savva & Arthur, 2015); and those who are not married (Savva & Arthur, 2015), live alone (Wilkins et al., 2007), or attend medical visits alone (Amjad et al., 2018). In the U.S., non-Hispanic Blacks may have nearly double the likelihood of underdiagnosis as non-Hispanic whites (Gianattasio et al., 2019). Additionally, likelihood of diagnostic delay may be related to a patient's health status. For example, underdiagnosis appears to be more common among cancer survivors and those with a history of hospitalization for myocardial infarction, but less common among persons with a history of depression treatment or stroke (Chodosh et al., 2004).

A handful of studies have considered correlates of time from symptom onset to provider diagnosis. In the U.S., persons from minoritized racial or ethnic groups are often diagnosed at a later stage (Chin et al., 2011; Cooper et al., 2010). Among memory clinic patients in the Netherlands, higher education and the presence of psychiatric symptoms were associated with shorter time from symptom onset to clinical identification (Helvik et al., 2018). A similar study in Italy suggests time to dementia diagnosis differs by age, sex, and cognitive performance, although the associations varied by physical function (Cattel et al., 2000). Finally, dementia type may differentially impact time to diagnosis (van Vliet et al., 2013), potentially due to differences in symptoms (Assal & Cummings, 2002; Kraybill et al., 2005; Rascovsky et al., 2002). Identifying risk factors for diagnostic delay and understanding how and why such factors contribute to delayed dementia diagnosis will be important for efforts to balance the risks and benefits of diagnosing dementia around the time of onset.

What Is Known and Unknown About Risk-Benefit Considerations Related to Diagnosis at Onset and Diagnostic Delay in Dementia?

Promotion of benefits and mitigation of harms requires understanding of the potential risks and benefits involved. While the proposed benefits and harms associated with receiving a dementia diagnosis around the time of onset (versus remaining undiagnosed and so unlabeled, particularly at mild disease stages) have face validity, there is little quantitative evidence characterizing the presence, likelihood, extent, and variability of these benefits and harms, particularly in the context of the U.S. healthcare system.

The most obvious benefit of diagnosing a disease at the time of onset is access to treatment. A small proportion of people living with cognitive dysfunction have potentially reversible causes of cognitive impairment (e.g. B12 vitamin deficiency, untreated sleep apnea, hyperglycemia, normal pressure hydrocephalus, side effects of medications) (Piccini et al., 1998); a delayed diagnosis is clearly harmful to this group. There are also some treatments for dementia attributable to other causes that can slow progression or help to address symptoms. For example, cardiovascular risk factor management may slow cognitive decline in persons with dementia caused by overt or subclinical cerebrovascular disease, that is, vascular dementia (Sun, 2018). Similarly, use of U.S. Food and Drug Administration (FDA)-approved medications in mild dementia attributable to Alzheimer's disease, including the recently approved anti-amyloid immunotherapies aducanumab and lecanemab, may help slow cognitive change (Patnode et al., 2020; van Dyck et al., 2022; Woloshin & Kesselheim, 2022). However, pharmaceutical treatments for non-reversible causes of dementia currently have only modest benefits and may have high cost or undesirable side effects. In particular, the recently U.S. FDA-approved monoclonal antibody treatments aducanumab and lecanemab are expensive and come with high risk of harmful side effects (Syrek Jensen et al., 2022; van Dyck et al., 2022; Woloshin & Kesselheim, 2022). Nonpharmacologic interventions may also have benefits, but again the demonstrated benefits are modest. For example, increased physical activity can decrease depression and reduce behavioral disturbances (Teri et al., 2003) and may slow cognitive decline (Baker et al., 2010), while behavioral therapy has been shown to significantly increase quality of life (Teri et al., 2005). Finally, while persons with a diagnosis close to the time of dementia onset are more likely to meet eligibility criteria for clinical trials of novel treatments, benefits of trial participation to the individual will depend on the efficacy of the treatment, treatment assignment, and costs of participation.

Whether or not a dementia diagnosis is received around the time of dementia onset may impact the mental health of the person living with dementia during the early stages of the disease and their care partners. Timely diagnosis may bring emotional relief and reduce mental distress. For example, a diagnosis may provide a reason for noticeable cognitive and behavioral changes, reducing anxiety by removing uncertainty. However, the effect may also be negative. Persons who are diagnosed with mild dementia often report feeling anxious about how others perceive them, leading them to hide their diagnosis or withdraw from friends and family, which subsequently negatively impacts quality of life (Riley et al., 2014). Self-stigma can also cause people living with dementia to feel embarrassed, frustrated, useless, or depressed (Riley et al., 2014). Many who receive a dementia diagnosis fear losing their independence and may also worry about the negative emotional consequences for their families (M. Boustani, 2013; M. Boustani et al., 2008; M. A. Boustani et al., 2011). Receipt of a diagnosis can also increase risk of suicide, although this outcome remains rare (Alothman et al., 2022). While the emotional impact of receiving a dementia diagnosis around the time of onset (rather than later in the disease course) likely varies across people

and may depend on personal resources and community context, we have little quantitative data on the variability in reactions and the experience of the majority, particularly in the U.S., or effective methods to mitigate negative impacts on mental health.

The timing of a provider diagnosis of dementia may also impact physical health. For example, persons who are prescribed statins often discontinue these medications after beginning dementia treatment (Picton et al., 2021), and those diagnosed with dementia appear less likely to receive anticoagulants and medication to lower blood pressure (Zupanic et al., 2020). While this may reflect appropriate discontinuation of preventative care or de-prescribing, it may also reflect inappropriate cessation of care or poor management of chronic disease. Overall, our understanding of the impact of timing of provider diagnosis on physical health is extremely limited. Research to understand this impact will be essential to efforts to mitigate potential harms of reducing diagnostic delay of dementia on physical health.

Care partner burden and care partner-care recipient interactions during the initial stages of dementia may differ depending on the timing of receipt of a clinical dementia diagnosis. If receipt of the diagnosis leads to increased understanding and more appropriate care partner support, health and well-being of the both the person living with dementia and their care partner may improve (de Vugt & Verhey, 2013). Family members are often the first to notice behavioral and cognitive changes, and increased understanding of the cause of such changes is believed to help care partners cope (Dubois et al., 2016). However, although those living with dementia typically remain largely independent in the earlier disease stages, a diagnosis at this time may make care partners feel that the person living with dementia is less capable or that they need to do more, increasing caregiver burden and potentially prematurely limiting care recipient autonomy. For example, there is some evidence that functional impairment leads to more restrictions on social activities when a person has a diagnosis of dementia than if they remained undiagnosed (Bass et al., 1994). As with physical and mental health, a better understanding of how common each potential outcome is, and what can be done to create positive change is needed.

Whether diagnosis around the time of dementia onset reduces or increases costs to the U.S. healthcare system remains unclear. In the U.S., increased hospitalization and emergency room (ER) visits increase medical costs for people living with dementia (Bynum et al., 2004; Zhao et al., 2008; Zhu et al., 2015). Proponents of diagnosis at the time of dementia onset hypothesize that this will reduce costs by reducing emergency room visits and preventable hospitalizations. For example, a dementia diagnosis may be accompanied by care partner education about how to appropriately manage agitation, altered mental status, or changes in functional status that increase accident risk, which can help reduce hospitalization. Similarly, a diagnosis may prompt better management of chronic conditions such as diabetes (e.g., through increased care partners support), limiting costly care or hospitalizations resulting from poor management. While existing studies have examined care utilization before and after receipt of a dementia diagnosis (Kosteniuk et al., 2022), it remains important to understand the impact of diagnostic *delay* on health care use and costs.

Home health aides and nursing home care are costly and commonly used by patients with dementia. It is plausible that diagnosis at the time of dementia onset may reduce use of home health or instituionalization at all stages of disease, through improving access to treatments addressing cognitive and behavioral symptoms (McLaren et al., 2013; Patnode et al., 2020) or by reducing care partner burden and burnout through earlier education and access to resources (Parker et al., 2008; Sorensen et al., 2006). On the other hand, care partners may feel less equipped to care for a person living with dementia if they have received a diagnosis, and may instead rely more on professional care. It is also possible that individuals without co-habiting care partners may be more likely to be moved to institutional settings if a diagnosis of dementia has been received. Research outside the U.S. has found that persons diagnosed in an early stage of dementia are more likely to be institutionalized (Pimouguet et al., 2016), while other researchers have found that diagnosis around the time of onset delays institutionalization (Littlewood et al., 2010); however, similar research in the U.S. is lacking.

Given diminished cognition defines dementia, the timing of diagnosis may also impact whether the person living with dementia is involved in or encouraged to participate in their own care planning. An earlier dementia diagnosis allows earlier planning for how care will be provided, addressing legal and financial needs, and advanced care planning for end-of-life care (Alzheimer's Association, 2022b). However, there is little data demonstrating whether persons who receive a diagnosis around the time of dementia onset take advantage of these opportunities to plan or what the ultimate impact of earlier planning may be on the person living with dementia or their care partner(s).

Finally, the medical system is a resource-constrained system. Providers must weigh potential advantages and disadvantages to the patient and their care partner(s), as well as concerns about the potential for overtreatment and diversion of resources or time (Bradford et al., 2009; Brunet et al., 2012; Dubois et al., 2016; Rimmer, 2016). How an individual or provider approaches the risk-benefit calculation around whether to pursue or prioritize a dementia diagnosis around the time of dementia onset, when symptoms are typically mild, will necessarily be personal. However, knowing the experience of others can help decision-making, but such data, particularly in the U.S. context, is lacking. Currently, in the context of the U.S., individuals who are offered follow-up

evaluation for dementia after a positive screening test frequently refuse it (M. Boustani et al., 2005; Fowler et al., 2014).

Can We Amplify the Benefits and Reduce the Harms?

At the individual level, whether receipt of a diagnosis at the time of dementia onset has net benefit or net harm likely varies. For example, personal reactions to a dementia diagnosis vary substantially. Studies recruiting from a variety of setting have shown short-term distress associated with receipt of a diagnosis, with care partner reports of continued long-term distress in a subset (Holroyd et al., 2002; Robinson et al., 2011). However, in a sample of persons who sought cognitive evaluation and felt they knew how to get more information and access services and resources, a diagnosis of dementia did not increase depression or anxiety (Carpenter et al., 2008). A better understanding of who experiences what benefit or harm, in what context, could inform interventions to promote benefits and reduce harms related to lessening diagnostic delay.

Currently, governments, non-governmental organizations, and advocacy groups have increasingly promoted diagnosis of Alzheimer's disease and related dementias around the time of onset. For example, in the U.S., the development of a strategy to ensure "timely and accurate diagnosis" is codified in the U.S. National Plan to Address Alzheimer's Disease.(Department of Health and Human Services, 2021) The Alzheimer's Association (2022b) and U.S. Centers for Disease Control have developed recommendations on how state and local agencies can accomplish this, and similar efforts are also promoted by other nations (Australian Government Department of Health, 2015; England Department of Health, 2009; Republic of Indonesia Ministry of Health, 2015; State of Qatar Ministry of Public Health, 2018) and recent World Health Organization (2017) recommendations.

While current efforts to reduce diagnostic delay are ongoing, regular screening for dementia is one approach that has not been widely adopted. Current opinion on the value of screening is mixed. In the U.S., the Indiana University Cognitive Health Outcomes Investigation of the Comparative Effectiveness of Dementia Screening (IU CHOICE) trial found no differences between those who were screened or not screened for dementia on measures of quality of life, anxiety or depression, healthcare utilization, or advance care planning over 1 year of follow-up (Fowler et al., 2014, 2020; Patnode et al., 2020), leading the U.S. Preventative Services Task Force to conclude that there is no empiric evidence that screening for dementia "improves patient, caregiver, family, or clinician decision making or other important outcomes nor causes harm"(Patnode et al., 2020). Given current lack of demonstrated net benefit or harm of an early dementia diagnosis, the U.S. Preventative Services Task Force (Patnode et al., 2020) and UK National Screening Committee (Solutions for Public Health, 2018) do not recommend for or against routine screening of all older adults for cognitive impairment. It is also notable that broad screening for cognitive impairment does not meet the World Health Organization Wilson-Jungner principles of screening criteria (Wilson & Junger, 1968). Nevertheless, in the U.S., routine assessment of cognitive function was recently added as a component of Medicare's annual wellness visit (Cordell et al., 2013).

Is the U.S. Healthcare System Prepared to Support Increased Diagnosis of Dementia Around the Time of Onset?

Many of the hypothesized benefits of a dementia diagnosis around the time of onset rely on the expectation of earlier and increased access to healthcare providers, who can link persons living with dementia and their care partners to services and resources. However, there is a shortage in clinicians and other workers who are uniquely likely to care for persons living with dementia (National Academies of Sciences, Engineering, and Medicine et al., 2021). Currently, the burden of caring for persons living with dementia lands primarily on family members or friends; in the U.S., these unpaid care partners provide an estimated 16 billion hours of unpaid care each year (Alzheimer's Association, 2022a). Reducing diagnostic delay in dementia may ease care partner burden by providing earlier access to providers, services, and resources, but only if they are sufficiently available.

Recent FDA approvals of new treatments for Alzheimer's disease and the existence of promising treatments in development suggest that disease-modifying treatments with substantial impact may be forthcoming. As many treatments are currently being tested in mild disease, reducing diagnostic delay will be necessary to maximizing access. However, this may not be the primary barrier to access. Current costs of these new drugs are substantial. Total costs associated with administration of lecanemab is estimated to be $82,500 per patient per year, based on a list price for lecanemab of $26,500 per patient per year and the costs of tests and clinic visits needed to establish eligibility, administer the medication, and monitor patients (Allen, 2023; Institute for Clinical and Economic Review, 2023).

Dementia is not a natural or inevitable part of normal aging, and our goal should be to make receipt of a timely and accurate diagnosis of dementia a net benefit to patients and their communities. To do so, we need to better understand the risks and benefits of receiving a dementia diagnosis around the time of dementia onset. This will allow us to develop policies and interventions to promote the benefits and mitigate the harms associated with receiving a timely and accurate diagnosis of dementia.

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Approvals

This paper is a review of the published literature. As such, it does not meet criteria for human subjects research and no IRB review was required.

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