

Review Article

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Dementia Disorders: A Narrative Review

Tiffany Field

University of Miami/Miller School of Medicine and Fielding Graduate University, USA

Corresponding author

Tiffany Field, University of Miami/Miller School of Medicine and Fielding Graduate University, USA.

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ABSTRACT

This narrative review of research includes summaries of 40 papers on dementia disorders that were published during 2023. The publications of this period are primarily randomized controlled trials and systematic reviews/ meta-analyses of randomized controlled trials. A few of these are focused on the prevalence of dementia which approximated one per cent of the world's population. Only a few studies focused on effects of dementia disorders including memory loss, discrimination, pain, depression and suicidality. Most of the studies addressed predictors of dementia disorders including neurotic personality, frequent tv/computer use and excessive exposure to metals. Loss of short-term memory and other negative experiences including negative life events, loneliness, stress and depression were also significant predictor variables in this recent literature. Physical conditions that were predictive of dementia included pain, hypertension, atrial fibrillation, multi-morbidities, inflammation, encephalitis and neuropathology. Potential underlying mechanisms included dysfunctional neurotransmitter systems (serotonergic, noradrenergic and dopaminergic) and gray matter loss in prefrontal, temporal and other regions associated with memory. Several research groups reported on effective interventions including a Mediterranean diet, plant-based diets, medicinal plants, psychedelics, second generation antidepressants, blood pressure medication, music therapy, aromatherapy and other alternative therapies. Methodological problems relate to the variability in the assessments of dementia disorders, the self-report measures and the cross-sectional data that are not definitive about directionality of predictors and effects of dementia disorders.

This narrative review involved entering the terms dementia disorders and the year 2023 into PubMed and PsycINFO. Although the search yielded 293 papers for the last year, exclusion criteria, including case studies, non-English papers and study protocols, reduced the number to 40 papers. This narrative review of research includes summaries of 40 papers on dementia disorders.

The publications of this period are primarily randomized controlled trials and systematic reviews/ meta-analyses of randomized controlled trials. A few of these are focused on the prevalence of dementia which approximated one per cent of the world's population. Surprisingly very few focused on effects of dementia disorders including memory loss, discrimination, pain, depression and suicidality. Most of the studies addressed predictors of dementia disorders including neurotic personality, frequent tv/computer use and excessive exposure to metals. Loss of short-term memory and other negative experiences including negative life events, loneliness, stress and depression were also significant predictor variables in this recent literature.

Physical conditions that were predictive of dementia included pain, hypertension, atrial fibrillation, multimorbidities, inflammation, encephalitis and neuropathology. Potential underlying mechanisms included dysfunctional neurotransmitter systems (serotonergic, noradrenergic and dopaminergic) and gray matter loss in prefrontal, temporal and other regions associated with memory. Several research groups reported on effective interventions including a Mediterranean diet, plantbased diets, medicinal plants, psychedelics, second generation antidepressants, blood pressure medication, music therapy, aromatherapy and other alternative therapies. Methodological problems relate to the variability in the assessments of dementia disorders, the self-report measures and the cross-sectional data that are not definitive about directionality of predictors and effects of dementia disorders.

This narrative review of the recent literature on dementia disorders is divided into several sections. These include the prevalence, the effects, the predictors, potential underlying mechanisms, interventions and methodological limitations of the literature.

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Different Dementia Disorders and Symptoms

Dementia is a group of conditions that are primarily characterized by memory loss [1]. These include Alzheimer's disease, vascular disease, Lewy body disease and other medical conditions. In addition to memory loss, the symptoms of dementia disorders can include difficulty concentrating, confusion and needing help with daily tasks, problems with language and understanding and changes in behavior. Some more specific symptoms are wandering and getting lost in a familiar place, trouble handling money and paying bills, repeating questions, using unusual words to refer to familiar objects, losing interest in normal daily activities, taking longer to complete tasks, being confused about time and place, losing balance, movement problems and mood changes.

The terms dementia and Alzheimer's are often used interchangeably. However, Alzheimer's is only one type of dementia, albeit the most common cause of dementia. Although the etiology of Alzheimer's is unknown, substances within the brain called amyloid and Tau can form structures called plaques and tangles, making it difficult for the brain to function. Ultimately the disease can cause decreased volume in areas of the brain as well as a loss of neurotransmitters that are needed for transmission of messages across the brain. Vascular dementia is the second most common type caused by reduced blood supply to parts of the brain. Other types of dementia include Lewy body disease which has been described as "clumps of protein that build up in the brain", Parkinson's disease dementia, frontotemporal dementia and mixed dementia.

Although 60 to 80% of those individuals with dementia have Alzheimer's disease, medical conditions can also lead to dementia including medication interactions or side effects, taking too many medications called polypharmacy, a respiratory infection including COVID-19, urinary tract infection, head injury, strokes, tumors, sleep problems, dehydration, normal pressure hydrocephalus, vitamin B12 deficiency and problems with the thyroid, kidneys or liver, among others.

Ten early warning signs of dementia published by AARP include Mild Cognitive Impairment, difficulty with everyday tasks, communication problems, repetition, getting lost, confusion about time and place, misplacing things, troubling behavior, personality changes, loss of interest or apathy and memory loss. Diagnostic testing includes cognitive and neurological evaluation, brain scans by computed tomography (CT) and/ or magnetic resonance imaging (MRI), psychiatric evaluation, genetic tests, cerebral spinal fluid tests and blood tests. Diagnosing the specific form of dementia is important for determining the appropriate treatment. Some forms of dementia are reversible and others respond to medications and rehabilitative therapies such as occupational, physical and cognitive stimulation therapy. Several "brain foods" have also been suggested including fatty fish, green leafy vegetables, berries, walnuts, tea and coffee.

Prevalence of Dementia Disorders

Different types of dementia disorders are discussed in a paper entitled "Dementia: dementia types" [1]. According to these authors, Alzheimer's is the leading cause of dementia and the prototypical form. It is characterized by insidious, progressive cognitive impairment across years. Vascular dementia is the second most common and often co-occurs with other cognitive disorders. Lewy body dementias encompass Parkinson's and Lewy body dementia which are differentiated by the order of the motor and cognitive symptom onset. Frontotemporal dementia occurs earlier and often has a genetic component as well as behavioral and psychological changes.

Table 1: Prevalence of	dementia disorders	(and first authors).

Prevalence First author
65 million people worldwide (<1% world population) DeLooze
55 million people worldwide Paraskevopoulos
25% for 85-year-old adults Wetterberg
22% for 88-year-old adults Wetterberg
37% for 90-year-old adults Wetterberg
80% for 100-year-old adults Wetterberg

Dementia disorders have been assessed in worldwide longitudinal studies on aging [2]. The assessments have included the Mini Mental State Examination, the Montreal, Cognitive Assessment, the Community Screening Instrument for Dementia, and the Telephone Interview for Cognitive Status. These authors have reported that 65 million people worldwide (less than 1 % of the world's population) have dementia and 40% of these are modifiable, suggesting significant potential for prevention. A lower prevalence of 55 million has been reported in a review on 17 aging studies [3]. These researchers forecasted that by 2050, 152 million individuals will experience dementia (almost 3 times the current prevalence).

Despite the forecast of increasing prevalence, a decreased prevalence has been reported for the period 1986 to 2015 from 30% to 25% for 85-year-old adults, from 42% to 22% for 88-year-olds and from 42% to 37% among 90-year-old individuals [4]. These figures were derived from the Gothenburg 470 Birth Cohort. Greater prevalence of dementia has been noted for those reaching 100 years of age (80%) [5]. These authors suggested that this high prevalence is related to little attention being paid to Mild Cognitive Impairment as a predictor of dementia, to aging of the vasculature and to many preventive therapies not being used.

Effects of Dementia Disorders

Surprisingly few papers in this recent literature have focused on the effects of dementia other than memory loss. These have included discrimination, pain, depression and suicidality. Discrimination was the focus of a paper entitled "Self-reported experiences of **discrimination** and dementia" [6]. In this study (N=6,509), 466 experienced dementia (7%). If there were more than two predictors of dementia, there was a greater risk for dementia.

Table 2:	Effects	of	dementia	(and	first authors)	
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Effect First author
Discrimination Bancks
Pain Liao
Apathy Connors
Depression Connors
Suicidality Maxfield

In a systematic review on 26 studies of people with dementia, 50% of the dementia patients experienced **pain** [7]. Given that most of the studies were cross-sectional, the directionality of dementia leading to pain or pain leading to dementia is unknown.

In a study entitled "Distinguishing **apathy** and **depression** in dementia", a three-year longitudinal study in Australia (N=779 adults with dementia), 52% experienced apathy, 50%, depression and 32% experienced both apathy and depression [8]. Apathy versus depression led to more severe dementia, poorer cognitive function, driving cessation and mortality. Both apathy and depression were associated with other psychological symptoms, and apathy increased over the three-year period, while depression remained stable.

In a paper entitled "Anticipated suicidal and death ideation in response to an imagined dementia diagnosis: a qualitative study", 50 adults 58-to-89-years-old who were attending a memory clinic for dementia were interviewed [9]. As many as 42 % of the sample anticipated that they would experience **suicidality or death ideation** if diagnosed with dementia. Three subthemes emerged from the data including becoming a burden, devaluation of life/loss of self and thwarting of personal control if given a diagnosis of dementia. Interestingly, these are very similar to the three problems that are given by suicidal individuals in the general population.

Predictors of Dementia Disorders

There is some ambiguity about whether memory loss is an effect of dementia or a predictor of dementia or both. And some would consider short-term memory loss as synonymous with dementia. The predictors of dementia disorders could be categorized as memory loss, negative psychological predictors, negative physical predictors and miscellaneous risk factors.

Table 3:	Predictors	of dementia
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Predictor First author
Memory loss Browning, Chu, Aberg
Negative psychological predictors
-Loneliness Wang
-Traumatic life events Severs
-Distress in later life Lu
-Depression Rababa, Yang, Collins
-Apathy and anxiety Collins
Negative physical predictors
-Multiple site pain Zhao
-Hypertension Soucek
-Atrial fibrillation Zhang
-Multimorbidities Veronese
-Inflammatory markers Zorkina
-Health-related conditions Shang
Miscellaneous risk factors
-Excessive tv-viewing and computer use Zhuang
-Exposure to metals Mateo
-Neuroticism Hunt
-Encephalitis Bastiaansen

Memory Loss

In a paper entitled "Prospective memory function predicts future cognitive decline and incident dementia", participants (N=121 older adults, age 72-91 years) were seen at baseline and at twoyear intervals over eight years [10]. **Decreased prospective memory** (i.e. remembering to do something in the future, e.g. to take medications) led to the frequency and severity of cognitive decline at 4 to 8 years. **Lower retrospective memory** (i.e. remembering information from the past, e.g. remembering the movie from the night before) was a particularly sensitive predictor of cognitive decline and incident dementia. Without a regression model analysis, it is difficult to know the relative variance in dementia severity that these two types of memory explained in this study.

In another paper entitled "Automated video analysis of audiovisual approaches to predict and detect cognitive impairment and dementia in older adults", both those with mild cognitive impairment (N= 41) and those with moderate dementia (N=54) were videotaped [11]. The videos were taken during the Short Portable Mental Status Questionnaire and were reported as having 76% accuracy of prediction. The accuracy rate increased to 93% when depression was excluded and 88% when anxiety was excluded. A moderate correlation between cognitive function and performance on the "cat versus dog task" occurred for females, but not for males. Comparisons between those with mild cognitive impairment versus those diagnosed with moderate dementia would have been informative.

In still another study entitled "Prediction of conversion to dementia disorders based on timed up and go dual-task test verbal and motor outcomes: a five-year prospective memory clinic-based study", both motor and verbal tasks were given [12]. In this study (N=186, mean age=78 years), the incidence of dementia was predicted over the five-year period by dual tasks including naming different animals and reciting months in reverse order. As many as 53% of the sample converted to dementia patients with subjective cognitive impairment and mild cognitive impairment. Words per time were the best predictor as well as step length during the timed up and go task. As the authors suggested, dementia is characterized by impairment of cognitive and motor skills with a gradual deterioration linked to cognition, mobility and gait that is explained by shared neuroanatomical structures and processes. Dual decline was associated with greater risk than memory or gait decline alone.

Negative Psychological Predictors

Several **negative psychological predictors** have been addressed in this recent literature on dementia disorders. These include loneliness, stress, and depression. In a meta-analysis on 32 studies, **loneliness** was a significant predictor of dementia disorders [13]. In contrast, social engagement and frequent social contact were significant buffers for dementia disorders.

Stress has been a significant predictor variable in a few studies in the 2023 literature on dementia disorders. In a meta-analysis on seven studies (N=276,570 participants), **traumatic life events** were associated with increased dementia risk [14]. Examples that were given included childhood trauma and participation in war. In a sample of 1522 middle-aged adults (mean age=57 years), greater perceived stress as well as less psychological

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resilience led to lower cognitive scores on attention, working memory and associative memory [15]. Perceived stress was also associated with dementia risk scores.

In a paper entitled "Psychological distress in later life and incident dementia", longitudinal data were presented on Japanese adults greater than 65 years (N=12,076) [16]. The adults were followed for six years. Paradoxically, greater dementia risk was noted for those who had higher cognitive scores at baseline but more serious psychological distress in later life.

Negative affect and **depression** have also been significant predictors of dementia disorders. In a sample of Jordanian adults with dementia (N=102), greater negative affect occurred in adults with dementia [17]. Negative affect was also associated with increased physical and verbal agitation.

In a paper entitled "Depression, depression treatments and risk of incident dementia", the UK Biobank Survey data were analyzed (N=354,313 adults between 50 and 70) [18]. The depressed sample (N =46,820) was divided into treated and non- treated groups. Treatment for those with chronically low symptoms led to a 32% decrease in the risk for dementia.

In a systematic review of the prevalence of depression, anxiety and apathy in adults with frontotemporal dementia (N =47 papers), depression was a significant predictor [19]. Apathy and anxiety also contributed to dementia in the reviewed studies. The combination of depression, anxiety and apathy has appeared in a few studies. The relative effects of these psychological states on the severity of dementia would help inform intervention protocols.

Negative Physical Predictors

Several physical conditions are also predictors of dementia disorders. They include pain, hypertension, atrial fibrillation, multimorbidities, inflammation, and neuropathology. In a study on elevated dementia risk, cognitive decline and hippocampal atrophy, multisite chronic pain versus single site pain was a significant predictor [20]. This finding noted in the UK Biobank Cohort (N=354,943) was not surprising as **multiple site pain** would be expected to be more predictive than single site pain especially since multiple site pain is often associated with chronic autoimmune conditions like fibromyalgia and arthritis.

In a study entitled "In the prevention of dementia, the focus should be on early and consistent treatment of hypertension", **hypertension** in middle-age adults led to a 61% increased risk of dementia [21]. These results were not surprising given that high blood pressure has significant effects on the vessel walls of the brain leading to atrophy of both gray and white matter. Blood pressure medication in this study reduced blood pressure to normal levels (130 systolic/80 diastolic) within three months in as many as 93% of the sample.

Atrial fibrillation is still another risk factor for dementia. Adults less than 65 who experienced atrial fibrillation in at least one sample had a greater risk for the onset of incident dementia [22].

In a paper entitled "Antibodies associated with autoimmune encephalitis dementia (N=920 patients with dementia), a small

but clinically relevant percent of patients with neurodegenerative dementia had neuronal antibodies indicative of autoimmune **encephalitis** [23]. These patients were thought to benefit from immunotherapy.

Multimorbidities have been significant predictors of dementia in a couple studies. In the Survey of Health, Ageing and Retirement in Europe (SHARE), multimorbidity increased the risk of dementia at a 15-year follow-up assessment [24]. In this sample (N=23,196), 36% of those experiencing multimorbidities (two or more conditions) at baseline had an increased risk of dementia. These conditions included high cholesterol, stroke, diabetes and osteoporosis.

In a paper entitled "Multimorbidity patterns and 18-year transitions from normal cognition to dementia", multimorbidity was a risk factor for dementia at age 75 in the National Study on Ageing and Care (N=3122 adults) [25]. Neuropsychiatric and cardiovascular patterns decreased life expectancy at age 75.

Inflammatory markers have also been implicated as predictors of dementia disorders. In a study entitled "Inflammatory biomarkers and lipid metabolism parameters in women with mild cognitive impairment and dementia", high density lipoprotein was low (N= 75 with dementia) [26]. Surprisingly, the inflammatory biomarkers IL–8 and TNF–alpha were extremely low in mild cognitive impairment but elevated in dementia. These results are difficult to interpret as inflammation might be expected to contribute to both mild cognitive impairment and dementia.

In a paper entitled "Study of neuropathological changes and dementia in 100 centenarians in the 90+ study", brain tissue was examined in 100 centenarians and 297 nonagenarians [27]. Fifty-nine per cent of the centenarians and 47% of the nonagenarians had at least four **neuropathological changes** that were associated with greater odds of dementia. For each neutopathological change, the Mini Mental State Exam score was two points lower.

In the UK Biobank study (N =5,117,381), 452 were noted to have young-onset dementia and 5476 to have late-onset dementia [28]. Health-related conditions explained 74% of the variance and was a stronger mediator for late-onset dementia. Lifestyle factors were a stronger mediator for early-onset dementia. Males had a greater risk for all-incident early and late onset dementia (early onset was considered less than 65-years-old). This gender effect is inconsistent with females being at greater risk in another sample [11]. This disparity of gender effects needs further research. The mediators for the relationship between sex and dementia were the multimorbidity risk score, creatinine, low density lipoprotein and lymphocyte percentile, but the relative variance each of these mediators explained was not reported in this study.

Miscellaneous Risk Factors

In a study entitled "Leisure–time television viewing and computer use, and family history of dementia", a large sample (N=415,048) was assessed over a 13 year period [29]. Of this sample, 5549 individuals were given a dementia diagnosis. More than three hours per day **TV viewing** was associated with a 42% greater

risk of dementia. Both low and high **computer use** was also associated with a greater dementia risk. The excessive television viewing and computer use are not surprising risk factors as they suggest sedentary behavior/inactivity which has been noted to lower neurotransmitter activity (serotonin and dopamine) which, in turn, could lead to dementia. The low computer use may be related to mild cognitive impairment which has been a precursor of dementia.

Excessive **exposure to various metals** has also been a risk factor. In a study entitled "Metals linked with the most prevalent primary neurodegenerative dementias in the elderly", continuous exposure to metals via dietary sources was a risk factor for dementia [30]. Excessive exposure in this study was thought to lead to dysbiosis (an imbalance in gut microbiota). Mild cognitive impairment was related to excessive exposure to iron and copper and Alzheimer's and frontotemporal dementia were associated with aluminum exposure.

In a study on personality traits (N= 1487 individuals with dementia and 1230 caregivers), **neuroticism** was negatively correlated with quality of life for both groups [31]. In this longitudinal study in which the sample was assessed at baseline, 12 and 24 months, extraversion, openness, agreeableness, and conscientiousness were positively correlated with quality of life. These relationships were not surprising given that self-reports of positive traits and quality of life are typically correlated, although positivity and self-report validity are likely negatively correlated with dementia severity.

Interventions for Dementia Disorders

Several different interventions have been researched as potential therapies for dementia. These include a Mediterranean diet, other plant-based diets, medicinal plants, psychedelics, second generation anti-depressants, blood pressure medication, music therapy, aromatherapy, acupuncture, and other alternative therapies

Table 4: Interventions for dementia

Intervention First author
Mediterranean diet Shannon
Plant-based diets Wu
Medicinal plants Acero
Psychedelics Winckelman
Second generation antidepressants Jellinger
Music therapy Paraskevopoulus, Lin
Aromatherapy, herbal medicine, acupuncture, mindfulness, tai chi

In the UK Biobank Prospective Cohort Study, adherence to a **Mediterranean diet** was associated with lower dementia risk independent of genetic predisposition [32]. In still another UK Biobank cohort study (N=180,532, including 1428 with dementia and 6781 with depression), healthful versus unhealthful **plant-based diets** reduced the risk of both dementia and depression [33]. Healthful foods included whole grains, fruits, vegetables, nuts, legumes, vegetable oils, tea and coffee. Non-healthful foods included juices, sweetened beverages, refined grains, potatoes, and sweets/desserts.

In another intervention study, **medicinal plants** (49 different species) were effective as therapy for dementia [33]. These were referred to as phytotherapeutic alternatives or nortropic supplements. As is usual for medicinal plants, they have very complex names like bacopa monnieri and huperzine A.

Classic (serotonergic), and non-classic **psychedelics** have been noted to slow or reverse brain atrophy [34]. These authors suggest that the neuroplasticity mechanism for this effect is the "modulation of glutamatergic neurotransmission and stimulation of synaptic and network remodeling".

Second generation antidepressants have also been prescribed for dementia at least for Lewy body dementia [35]. According to these authors, this type of dementia is related to dysfunctional neurotransmitter systems (decreasing serotonergic, noradrenergic and dopaminergic metabolism) that leads to gray matter loss in the prefrontal and temporal areas. They argue that tricyclic antidepressants have anticholinergic effects and therefore should not be used even though 35% of those with Lewy Body dementia are depressed, which is twice as high a rate as those with Alzheimer's dementia. The authors also suggested that for those who are medication resistant, ECT, TMS and deep brain stimulation should be prescribed.

In at least two reviews of literature on interventions for dementia disorders, **music** has been an effective therapy. In one review, 19 studies suggested positive effects of music on people with dementia [3]. In a second review, 15 of 21 trials on music therapy suggested greater cognitive improvement than non-music therapy trials [36].

In a review paper entitled "Complementary and integrative medicines for behavioral and psychological symptoms of dementia", 13 papers were reviewed [37]. Although **aromatherapy** was the most common of the alternative therapies, **herbal medicine, acupuncture, mindfulness, relaxation, and tai chi** were also effective.

Potential Underlying Mechanisms

Only a couple papers in this recent literature on dementia disorders could be classified as exploring potential underlying mechanisms for dementia disorders. In a paper entitled "Exploring shared neural substrates underlying cognition and gait variability in adults with dementia", gait variability and cognitive function were thought to share neural substrates and regions associated with memory and visual spatial navigation [38]. The authors suggested that these were mediated by **cortical thickness**.

Gray matter loss in the prefrontal and temporal areas has also been considered a mediating factor for the relationship between **dysfunctional neurotransmitter systems** and dementia disorders [36]. These neurotransmitter systems include serotonergic, noradrenergic and dopaminergic systems.

Surprisingly, given the severity and the debilitation of dementia disorders in general, this recent literature has been limited on potential underlying mechanisms. This may relate to the data suggesting reductions in the prevalence of dementia disorders despite the growth in the aging population worldwide and therefore the limited funding available for the more expensive mechanism studies.

Methodological Limitations of the Current Literature

Several methodological limitations of this recent literature on dementia disorders can be noted. These include study design limitations, sampling problems. confounding variables and limited exploration of interventions. Most of the studies derived from the UK Biobank Survey, which is a large sample and a rich source of variables, but data on the UK population may not generalize to other populations, especially to third world samples. Most of the studies from this sample and others were **crosssectional**, as opposed to being longitudinal, which has limited conclusions about directionality. **Arbitrarily selected variables** have been considered predictors or effects or both. For example, in a cross-sectional study design, the degree to which memory loss leads to a diagnosis of dementia versus decreased cortical thickness leading to memory loss is difficult to determine.

Although memory loss is typically the most prevalent symptom associated with dementia, the degree to which it contributes to a dementia diagnosis has not been determined. In addition, further studies are needed on the **different types of memory loss**. Typically, both **motor and verbal skills** are affected by dementia disorders, but many researchers have only measured motor or verbal skills. In research that included both skills, for example, words per time and steps in the time to go task, both skills were significant risk factors for dementia disorders

Several **confounding factors** have appeared in multiple studies, including gender as a predictor variable. As was noted, mixed data have been presented on males versus females being at greater risk as well as females being more at risk than males for dementia. Other confounding variables have appeared in this literature. For examples, loneliness was presented as a confounding variable in one study and traumatic life events in another study. However, in most studies, these were not entered as potential covariates or even measured. Further, depression, anxiety and apathy were confounding psychological variables in several studies, but they were rarely assessed in a regression model for the relative variance they contributed to dementia.

With respect to interventions, several **alternative therapies** have emerged as being effective. For example, music therapy and some plant-based food and medicine protocols as well as psychedelics have been effective. However, there has been limited focus on dietary interventions and virtually **no recent studies on medications** for reducing amyloid buildup and plaques that are thought to contribute to dementia disorders. These medications, for example, lecenemab and donanemab, are a new class of ground-breaking drugs that are extremely expensive and may have side effects, but they reputedly "strip amyloid beta from the brain" in at least Alzheimer's dementia. The drug companies are presumably conducting follow-up research, but less biased data might be expected from the academic community.

Despite these multiple methodological limitations, the studies in this recent literature are informative. They highlight the need not only for further studies on interventions for dementia but also on precursors for dementia disorders such as mild cognitive impairment. Although the prevalence of dementia disorders is low, some researchers have predicted increasing prevalence with the increased aging of the world population. This possibility highlights the need for further research on prevention as well as intervention protocols.

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