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CASE REPORT

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# Practicalities (and real-life experiences) of dementia in adults with Down syndrome

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## Abstract

Adults with down syndrome (DS) have a lifetime dementia risk in excess of 95%, with a median age of onset of 55 years, due to trisomy 21. Co-occurring Alzheimer's disease (AD) has increased morbidity and mortality, and it is now recommended to screen for AD in all adults with DS beginning at 40 years of age. In this manuscript, we present two clinical cases of adults with DS who developed AD summarizing their medical histories, presenting symptoms, path to diagnosis and psychosocial aspects of care collected from retrospective chart review with caregiver consent. These two cases were chosen due to their complexity and interwoven nature of the medical and psychosocial aspects, and highlight the complexity and nuance of caring for patients with DS and AD.

**KEYWORDS**
Alzheimer's disease, dementia, Down syndrome, trisomy 21

## 1 | CONTEXT

Over 200,000 people with Down syndrome (DS) live in the United States (de Graaf et al., 2017). For adults with DS, the lifetime dementia risk is in excess of 95%, with a median age of onset of 55 years (Startin et al., 2019). For the neurotypical population, dementia usually impacts individuals aged 65 and older (Centers for Disease Control and Prevention, 2023). Adults with DS experience increased morbidity and mortality from co-occurring Alzheimer's disease (AD), as they are at high risk for developing AD (Hithersay et al., 2017) largely due to the triplication of the *APP* gene (Antonarakis et al., 2020). Multiple screens for AD exist, including the Early Detection and Screen for Dementia (the NTG-EDSD), developed by The National Task Group on Intellectual Disabilities and Dementia Practices (NTG) (Silverman et al., 2021), the Adaptive Behavior Dementia Questionnaire (ABDQ) (Prasher et al., 2004), the Dementia Questionnaire for People with Learning Disabilities (DLD) (Evenhuis, 1990), and the American Association on Mental Deficiency Adaptive Behavior Scale, Part I (Suess et al., 1981). Though there have been large randomized, placebo-controlled trials studying treatments, for example, anti-amyloid treatment, for patients with pre-clinical and early clinical stage AD, adults with DS have not been included in these trials due to various challenges (Fortea et al., 2024; Rafii & Fortea, 2023). Only a small number of clinical trials for AD have included participants with DS (Rafii & Fortea, 2023). Here we present two clinical cases of adults with DS who developed AD to highlight the complexity and nuance of caring for these patients.

These two cases were chosen due to their complexity and the interwoven nature of the medical and psychosocial aspects. Consent was obtained from the caregivers of both patients, and retrospective chart reviews were conducted to gather all the specific information provided below.

  

## 2 | CASE 1

Proband 1 is a 47-year-old right-handed, English-speaking, white female with complete trisomy 21 and an estimated premorbid level of functioning with an intellectual disability. She received special education programming until 22 years of age and then was employed for ~20 years at a grocery store.

### 2.1 | Past medical history

Proband 1 established care in 2015 with the Massachusetts General Hospital (MGH) DS Clinic; after a gap in visits, care was re-established in 2019 to the present time. Proband 1's physical health was stable both prior to and after her gap in care.

Her early medical history was significant for congenital heart disease, atrial septal defect, high cholesterol treated with diet and exercise, gastroesophageal reflux disease, onycholysis, osteopenia, and anxiety. Her chronic medical diagnoses include celiac disease, lactose intolerance, eczema, osteoporosis, and elevated eye pressure, though these were well managed and being followed through primary care and subspecialists.

### 2.2 | Current complaints

At her most recent visit, she was in generally stable physical health, without dysphagia or urinary incontinence. A referral was placed to physical therapy to provide interventions to support mobility.

#### 2.2.1 | Mental health

In 2017, at the age of 41, proband 1 developed new anxiety, obsessive-compulsive disorder (OCD)-like behaviors and hoarding behaviors. Although not formally diagnosed with OCD, OCD behaviors increased with dementia, and family members had noted that this is still a problem in medical notes. She was referred to psychiatry, where she was assessed as meeting the criteria for hoarding disorder and displaying symptoms of an anxiety disorder. The hoarding and anxiety continued in 2019, and she was terminated from her job due to an escalation in these behaviors. In 2020, the family highlighted that facial tics (intermittent since childhood) had increased with stressful events. The anxiety continued, but her family reported her doing well at home. In 2021, after pandemic restrictions began to lift, anxiety increased with concerns about returning to a world outside home; compulsive behaviors were more severe and proband 1 began having auditory hallucinations (hearing voices).

#### 2.2.2 | Sleep

Daytime sleepiness had continued to be a chronic symptom for her, as reported by the family. Proband 1 seemed tired during the 2020 visit, and a sleep study was recommended. However, proband 1 had tried both in-hospital and in-home sleep studies over the years and did not tolerate wearing the required leads and pulse oximetry to assess vital signs during the sleep study. Fortunately, in December 2023, she was able to tolerate a Watch-PAT home sleep study that identified moderate obstructive sleep apnea (OSA) with an apnea–hypopnea index of 19.2 and an oxygen nadir of 86%.

#### 2.2.3 | Seizure

In 2024, proband 1 had her first convulsive seizure. She did not have a brain MRI post-seizure, but she did have a head CT scan during evaluation. This scan did not show any acute changes (stroke, hemorrhage, or other major abnormalities) to cause the seizure. Since then, she has been treated with anti-seizure medication and has remained seizure-free.

### 2.3 | Evaluation for AD and/or dementia and treatment planning

In 2017, proband 1 began having difficulty finding important items (i.e., keys, checks, and phone), but there were no changes in activities of daily living or daily functioning. She received a neuropsychological evaluation at age 44 (2021). Results from prior testing were not available for comparison. Findings from the evaluation indicated a limited ability in several cognitive domains, including verbal and nonverbal intellectual abilities, receptive and expressive vocabulary, reading and spelling, judgment, and verbal attention/memory.

A standardized parent report measure (SIB-R) did not reveal a decline in her adaptive skills or everyday activities of daily living. In addition, a dementia scale designed for individuals with intellectual disability (DLD) was completed by her mother, and the results were below the cut-off for dementia, although her mother described some areas of decline in the prior year. Given the modest cognitive decline from a previous estimated level of functioning, together with the preservation of adaptive or everyday activities of daily living, a DSM-5 diagnosis of mild neurocognitive disorder-probable AD with behavioral disturbance (e.g., obsessive-compulsive behavior and hoarding) was indicated.

In 2022, at age 46, proband 1 began to forget what she was doing in the middle of an activity and was more repetitive in certain language/phrases. Proband 1 also wanted to go to sleep right after dinner at 5:00 p.m. The family reached out to the MGH DSP due to "brain fog" and, in response, screening labs were obtained. The lipid panel and complete blood count were found to be abnormal: her cholesterol, calculated LDL, cardiac risk ratio, and non-HDL cholesterol were all high, while HDL was low. Thyroid function tests, hemoglobin A1C values, vitamin D level, and complete metabolic panel were normal.

In March 2023, at age 47, proband 1 was evaluated by a neurologist and diagnosed with moderate stage AD. Some signs and symptoms included nighttime confusion, constant repeating of the same

question, confusion with her schedule, support needed with eating and cutting up food, being unable to entertain herself, and more.

### 2.4 | Other psychosocial contributors

Prior to the 2022 visit, proband 1's father had been diagnosed with lung cancer with a poor prognosis. The team social worker offered resources and support for the family. Proband 1 had shown signs of being worried for her father in her March 2023 visit alongside possible AD symptoms—unfortunately, later that year, proband 1's father passed away.

### 2.5 | Treatment considerations

At this juncture in care, the team is considering the interplay of several factors including a death in the family, aging parents, diagnosed dementia, and how best to maximize family and environmental support. Her family opted not to meet with specialists (otolaryngology or sleep medicine) to proceed with options to treat moderate obstructive sleep apnea (OSA), given concern with tolerating interventions (such as surgery or wearing a continuous positive airway pressure (CPAP) mask).

At times, proband 1's behavior has become aggressive. In 2023, proband 1 was prescribed memantine by her neurologist due to severe agitation, with significant improvement in that symptom with decreased frequency and severity of aggression and agitation. Proband 1 tolerated memantine well without side effects. Treating the symptom of agitation has been helpful for quality of life as it allowed proband 1 to remain in her day program all day. New-onset seizure and its management increases the complexity of managing dementia in people with DS.

## 3 | CASE 2

Proband 2 is a 52-year-old, right-handed, English-speaking, white male with complete trisomy 21 syndrome and a premorbid level of functioning in the mild range of intellectual disability. He received special education programming until 22 years of age and then worked for several years independently.

### 3.1 | Past medical history

Proband 2's medical history is significant for ventricular septal defect status post-closure, borderline hypertension, OSA (treated with CPAP that he has been wearing well), overweight, constipation, vision issues (refractive error, cataracts, astigmatism), wears glasses, and mixed bilateral hearing loss treated with hearing aids.

In 2015, at age 44, his health was generally well managed and not impacting his quality of life.

In 2016, he was noted to have a mild postural tremor (right more than left) and intention tremor, which his physician felt to be likely benign. Although he had previously worn a CPAP mask for OSA well, in recent years, proband 2 has developed issues with nasal irritation from the mask and CPAP mask fit. He was seen by a sleep specialist and was prescribed a new mask with no leak. Since receiving the mask, he has been wearing the CPAP mask consistently.

### 3.2 | Current complaints

At their most recent visit in 2023, at age 52, the family had noticed subtle changes in his functioning and that he had "some days that are better than others". There were days when he completed tasks independently, but there were other days when he had trouble following his routine. This was a decline in comparison to his baseline skills in 2015, when he was independent with all his activities of daily living, including dressing independently and showering without assistance, making basic meals, reading and writing, and working independently in two settings. At baseline, he always had difficulty understanding time in the context of past, present, and future, and he always had communication issues, such as difficulty with expressive language; these had not changed.

His family described his memory as "up and down." This was also a decline compared to 2015, when he was felt to have good memory and recall, as now he would sometimes get "spacey" if presented with too much information.

He recently socialized well at a family barbeque and remembered all of the wrestlers' names at a wrestling event. In recent years, he started to return to his usual routines, going to the YMCA and participating in basketball, and seemed excited/animated/happy when he returned from visiting his sister.

His family reported that he was sometimes tired and took a daytime nap if busy that day; he was referred for repeating sleep studies and to otolaryngology to discuss treatment options.

### 3.3 | Evaluation for AD and/or dementia and treatment planning

Proband 2 began seeing a neurologist in 2018 at age 47; there were no cognitive changes at that point.

In 2019, proband 2 began to have episodes of "zoning out" for 15–20 min lasting for 6–7 months. He appeared "in a fog" and was less able to focus on family and others during these episodes. He was able to respond to his name and be brought out of the spells, and the spells were not thought to be due to being bored or disinterested. In 2020, he was diagnosed with mild cognitive impairment-DS (MCI) by a neurologist and was prescribed memantine and escitalopram. His mother described that they had not noticed any significant improvement in his mood or cognitive and adaptive functioning with either medication. After the height of isolation due to the COVID-19 pandemic (from 2021 onward) concern for his decline in cognition,

language, and decline were priorities at each medical visit. Over 2 years, he developed trouble with word finding and communication, and worsening mood. Behaviors and mood were impacted; he was sad, downcast or unhappy, tense, anxious or worried, preferred to do things on his own, and got upset or frustrated over small changes in routine. His parents wondered the extent to which the COVID pandemic had impacted him, and how his decreased socialization during this time period had impacted his overall well-being, including cognitive and functional decline.

Proband 2 received a neuropsychological evaluation in 2023 at 51 years of age. Relative to his initial evaluation in 2014, the findings from 2023 revealed a decline in a number of cognitive domains reassessed, including language, mental status (e.g., orientation), academic skills, irritability, mental status (e.g., orientation to time and place), activities of daily living, perceptual motor skills, and learning and memory.

In addition, a standardized parent report measure (SIB-R) revealed a significant decline in his adaptive skills or everyday activities of daily living from baseline 9 years ago.

Dementia rating scales designed for individuals with intellectual disabilities (DLD, DSDS) completed by his mother also revealed cognitive and adaptive skill concerns, such as increased problems with short- and long-term memory, a decline in self-care skills, and confused thinking.

Taken together, the most recent evaluation indicated the presence of an underlying early-onset dementia process. Given his decline in cognitive skills and everyday activities of daily living, he met the DSM-5 criteria for Major Neurocognitive Disorder-Probable AD without Behavioral Disturbance.

In 2022, he had signs of worsening cognitive decline including the loss of some functional skills though he remained independent in some of his activities of daily living.

In December 2023, proband 2 was seen by a neurologist in the memory unit who concurred that proband 2 likely had early clinical stages of AD; care included suggesting a referral to speech and language therapy for speech and augmentative communication evaluation (AAC), which was placed by MGH DSP, continued follow up with established psychiatrist, lifestyle approaches for brain health and consultation for family support, future planning, and resources with social work. Over time, he has developed more trouble with planning, following multi-step commands, and anger/frustration.

## 3.4 | Other psychosocial contributors

Proband 2's mother developed cancer in 2016 and wanted to start planning for his future. His father and brother-in-law were appointed co-guardianship.

In 2018, his mother was diagnosed with vascular dementia in her 80s; there is also a family history of a maternal aunt with dementia.

In December 2023, the neurologist discussed long-term care planning and the transition of guardianship. Guardianship and future medical care were difficult topics for his family due to various interpersonal dynamics. His sister and brother-in-law have offered to care for proband 2 when his parents no longer feel it is in his best interest due to their health and aging. As his sister would most likely be the one to take care of guardianship, it was recommended that she attend doctor's appointments in the future.

## 3.5 | Treatment considerations

At this juncture in care, the team is maximizing medical treatment for sleep apnea with a planned repeat sleep study and otolaryngology referral to discuss further treatment options. For proband 2, psychosocial care was a priority. The family has planned for a transition of care as his family currently continues to work on managing his behavioral symptoms and decline and navigating the dynamics of his care.

## 3.6 | Key takeaways

These two cases of adults with DS and dementia highlight the medical, cognitive, and psychosocial complexity of care for patients with DS and AD. Some of these concerns may be experienced by adults with dementia without DS, but many are unique to those with dementia and DS, particularly in the context of premorbid levels of intellectual disability. Adults with DS are at high risk for early-onset AD, largely due to overexpression of the *APP* gene on chromosome 21 producing amyloid precursor protein, a characteristic feature of AD. Nearly all adults with DS develop the neuropathology associated with AD by the age of 40. Consequently, adults with DS experience cognitive decline and dementia at a younger age than those with sporadic AD, with a median onset of 55 years, and sometimes beginning as early as their 40s (Hartley et al., 2015). The age of onset has significance: in addition to these underlying neuropathological changes, psychosocial factors are often present, including aging parents with their own corresponding health issues, changes in legal guardianship, long-term memories from a lifetime of interacting with the medical system, and a delayed grief response from the death of a family member.

### 3.6.1 | Medical

Although research is ongoing to identify treatments to prevent or modify the course of AD (Levey, 2021), as in the care of individuals with dementia in the general population, few medications have shown effectiveness in clinical trials (Alexander et al., 2021). The National Academy of Medicine has suggested that physical exercise, keeping an active mind, controlling other health issues (e.g., weight), and optimizing nutrition are supported by sufficient evidence to delay or possibly prevent dementia onset (Ingelfinger, 2020).

Despite the increasing life expectancy (Presson et al., 2013; Yang et al., 2002), adults with DS have a more than 90% risk of developing AD by the seventh decade of life (Iulita et al., 2022). It is now recommended to screen for AD beginning at age 40 for adults with DS

(Tsou et al., 2020). Practical considerations for giving a clinical diagnosis of AD include the low premorbid level of intellectual abilities, the demands on memory, attention, and language ability (Snyder et al., 2020). Comorbid medical conditions such as OSA, hearing loss, and abnormal thyroid function can potentially challenge the diagnosis of AD in DS; both of the individuals we describe had routine health maintenance, including monitoring of thyroid function tests and screening for conditions that co-occur with DS (Tsou et al., 2020). Consensus guidelines for the evaluation and management of DS have been proposed, relying on a personal historian who can accurately attest to an individual's premorbid level of functioning (Moran et al., 2013).

Nuance in the medical care of patients with dementia and DS exists. In discussing treatment options, both adults and families closely considered the possibility of side effects and behavioral impacts given the limited published efficacy. In Case 2, the family consulted with a neurologist to discuss this further. Similar to those with dementia without DS, there are few successful treatments to improve cognitive function or modify the course of the disease, but for adults with DS, the decision to start a medication may be more difficult as few clinical trials for AD have included adults with DS as research participants (Hendrix et al., 2021). Both families prioritized quality of life and overall wellbeing, given that there is currently no cure for AD.

### 3.6.2 | Psychosocial

Unique to DS and early-onset AD, the person experiences decline at a younger age when their parent and/or caregiver may still be relatively young. A published case report of three early-onset AD cases when parents are healthy and caring for sons or daughters with AD is informative (Franklin et al., 2022). However, our cases highlight the complexity of AD in DS when a parent is ill; in Case 1, the father had lung cancer, and in Case 2, the mother had cancer and vascular dementia. When parents are experiencing health issues at the time an adult with DS develops dementia, medical complexity regarding the logistics of medication administration, daily care needs, and managing medical appointments are doubled. In these cases, medical care may fall to another parent, siblings, or alternate caregiver, but this places substantial responsibility on that caregiver to oversee care of both. In Case 1, the parent with the chronic care needs developed memory concerns (vascular dementia) with implications on recall, memory, and planning, highlighting the need to consider the whole family when caring for adults with DS and dementia.

In Case 1, a family member with a worsening illness reported a delay in diagnosis, which brought feelings of distrust that carried over to their interactions with other specialists.

Emotional memories are long-lasting (durable) and likely to be retrieved (accessible), both positive and negative memories can be easier to retrieve, and more likely to influence behavior (Williams et al., 2022). Given the chronic medical concerns experienced by individuals with DS, patients and families have long-term relationships and develop memories within the medical community. Home-based therapies, such as early intervention in childhood, are standard of care and involve medical professionals entering the homes of individuals with DS and families (Bull et al., 2022). End-of-life care, including hospice, and in-home assessments may have a similar structure. In Case 1, a parent commented that the father's hospice and end-of-life care were a reminder of the early intervention services her daughter received as a young child and reflected feeling as though people were entering her home throughout her daughter's life. A lifetime of interactions with the medical system could be a positive support network but could also lead to reliance on, distrust of, or indifference to the medical system.

The presence of co-occurring intellectual disability with DS impacts the approach to diagnosis and dementia care. For example, the severity of an intellectual disability ranges from mild to profound, which can impact the degree of cognitive changes and approach to neuropsychological evaluation for an adult with DS. People with intellectual disabilities may not grieve in the same way given differences in communication skills, their concept of time, and their understanding of the developing process of dementia (Brickell & Munir, 2008). People with DS are described as having a "delayed grief" response with later presentation or appreciation of the grief; it may simply take people with DS longer to recognize and understand that a loss has occurred or that the loss is permanent (McGuire & Chicoine, 2006). Clinicians and family members may be uncertain how, when, and to what extent to describe the developing terminal medical condition. The grieving process for individuals with DS and dementia may be further complex given corresponding memory changes, and caregivers may wonder how best to navigate end-of-life for an ill parent when the person with DS has dementia.

Existing resources, such as the Alzheimer's Association, provide support to individuals with dementia. As a clinic, the MGH DSP offers resources to families, caregivers, and patients (Alzheimer's Association, 2024; National Down Syndrome Society, 2024; National Task Group on Intellectual Disabilities and Dementia Practices, 2024). Both families were provided "Alzheimer's Disease & Down syndrome: A Practice Guidebook for Caregivers," "End of Life and Down Syndrome, A Companion Guidebook to Aging and Down Syndrome: A Health and Well-Being Guidebook," and the "National Institute on Aging Home Safety Checklist for Alzheimer's Disease." Our social worker will discuss these resources as a standard of care with all patients with new dementia diagnoses, and these will continue to be offered in subsequent visits. Patients may also be referred to the Alzheimer's Association Care Consultation Program through the MA/NH chapter of the Alzheimer's Association; both proband 1 and 2 were referred. And, while these supports are useful, there may be unique needs of individuals with DS due to co-occurring psychiatric and behavioral phenotypes associated with DS. In our cases, both families felt frustrated and without sufficient resources available (lack of appropriate group homes or living situations, financial support, and respite care) to support their loved one with DS. In efforts to support such families, national DS organizations (including the National Down Syndrome Congress, the National Down Syndrome Society, and

LuMind IDSC) have dementia efforts and have pushed for research on dementia to include individuals with DS.

For example, most individuals with DS and their families confront future planning topics like guardianship, medical decision making, and estate planning when individuals turn 18. As such, caregivers have often been incorporated into decision making for decades before the diagnosis of AD is made for adults with DS. There may be existing family dynamics to navigate. In one of our cases, the family is currently navigating decsion-making between siblings and parents, and planning for a son and mother who both are experiencing dementia simulteanously. Meanwhile, some patients with DS and AD may have caregivers who are not related and the dynamics operate differently than listed in these two cases.

Further, although we would ideally like to include patients in their own care early on to have time to plan their desired treatment before their dementia advances (Ingelfinger, 2020), the range of function in adults with DS may not make this feasible for most. Still, it is important to support patients where they are and to support family and caregivers (Ingelfinger, 2020). Among caregivers of individuals with DS aged 40 and above, the top concern before a visit to a DS clinic was neurologic, including dementia (Cabrera et al., 2022). A survey of parents found that 92% would give a theoretical side-effect-free medication to prevent AD (Rogers et al., 2022).

## 4 | SUMMARY

The medical, cognitive, and psychosocial needs of adults with DS and co-occurring intellectual disability and AD are complex and can impact the entire family. Additional supports, resources, research, and time for nuanced medical care are needed to fully support families of individuals with DS and AD such as the two we highlight here. Our clinic is actively working to create a dementia protocol to ensure early dementia screening and assess alternate causes of cognitive decline; this will allow us to catch signs earlier and create a strong foundation for dementia care.

### AUTHOR CONTRIBUTIONS

**Stephanie L. Santoro**: Conceptualization; methodology; formal analysis; software; writing—original draft; writing—review and editing. **Clorinda Cottrell**: Conceptualization; clinical work; writing—review and editing. **Ayesha Harisinghani**: Writing; consent process with family; writing—review and editing; formatting. **Margaret Pulsifer**: Writing—reviewing and editing; focus on neuropsychology components of paper. **Karen Donelan**: Conceptualization; writing—reviewing and editing. **Alice D. Lam**: Writing—reviewing and editing.

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### CONFLICT OF INTEREST STATEMENT

SLS has received research funding from LuMind IDSC Down Syndrome Foundation to conduct clinical trials for people with DS within the past 2 years. She serves in a non-paid capacity on the Medical and Scientific Advisory Council and on the Board of Directors of the Massachusetts Down Syndrome Congress, the Board of Directors of the Down Syndrome Medical Interest Group (DSMIG-USA), and the Executive Committee of the American Academy of Pediatrics Council on Genetics. MBP received funding from the National Institutes of Health to conduct research with people with Down syndrome within the past 2 years. She serves in a non-paid capacity on the Board of Directors of the Massachusetts Down Syndrome Congress. The other authors do not have any conflicts to disclose.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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