

The Hidden Burden behind an Extra Chromosome: Alzheimer's Disease in Down Syndrome and the Expanding Role of Pharmacists

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ABSTRACT:

Individuals with Down syndrome (DS) are at higher risk of developing Alzheimer's disease (AD), primarily due to the triplication of chromosome 21. Modifiable risk factors such as metabolic syndrome, along with genetic predisposition accelerate the likelihood of developing AD. This narrative review was conducted to explore the relationship between DS and AD, highlighting the underlying pathophysiological process and key risks involved. It examines the evolving role of pharmacist as a primary health care profession, in supporting medication utilization and caregiver education. Enhancing pharmacists' dementia-related knowledge and communication skills may improve patient outcomes and quality of care for individuals with DS at risk or living with AD.

Keywords: Down Syndrome, Alzheimer's Disease, Dementia, Risk factors, Pharmacy education

Introduction:

The aging of the global population has accelerated the rise of Alzheimer's disease (AD) and related dementias, leading to increased care-related costs and substantial social and economic impacts (C. Wang et al., 2022). AD is the most common form of dementia accounting for 50–70% of all cases (Alzubaidi et al., 2020). While several studies focus on the management and drug utilization of dementia, many reviews continue to emphasize the urgent need to address its increasing incidence (Scerri, 2016). The number of people living with dementia is

projected to increase from 57 million in 2019 to 153 million by 2050 (Tampi & Jeste, 2022).

Individuals with Down syndrome (DS), also known as trisomy 21, are among the populations at highest risk of developing AD, with approximately 50–70% developing dementia by the age of 60 (Honig et al., 2005; Zigman & Lott, 2007) (Figure 1). DS is associated with overexpression of the amyloid precursor protein (APP) gene, resulting from the triplication of chromosome 21, leading to earlier cognitive decline compared with the general population (Hendrix et al., 2021).

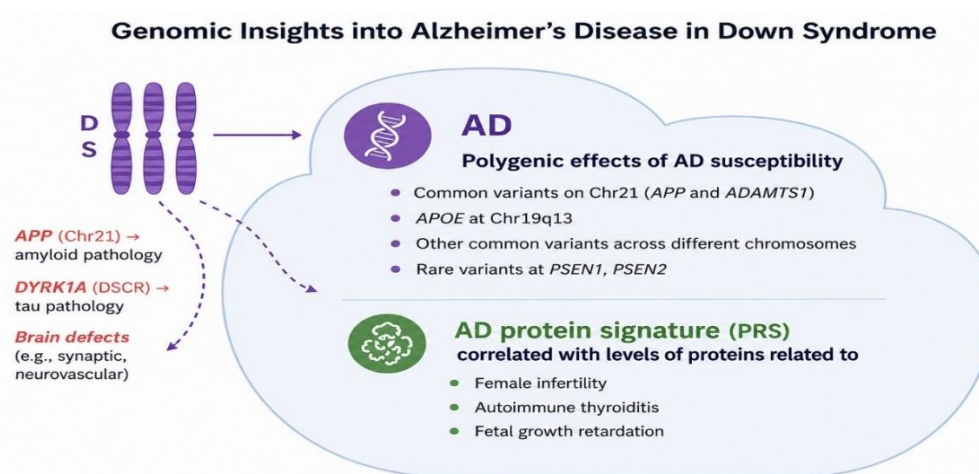


Figure 1: Mechanism linking trisomy 21 to Alzheimer's Disease. An extra copy of chromosome 21 causes APP gene overexpression, promoting amyloid- β accumulation and the development of Alzheimer's disease.

Unfortunately, the early diagnosis of dementia in DS remains challenging due to the limited availability of sensitive and reliable assessment tools capable of distinguishing dementia-related decline from pre-existing intellectual disabilities (Mann, 1988). This growing global burden has also raised concerns regarding whether healthcare professionals possess the necessary knowledge, skills, and resources to provide effective care for DS patients with dementia (Bender et al., 2022). Given their frontline role in caring for DS patients with dementia and supporting their caregivers, pharmacists must possess a high level of preparedness, highlighting the importance of ongoing educational initiatives and professional development to strengthen DS-dementia care competencies (Lavender et al., 2025). Therefore, this review aimed to explore

the association between DS and AD, with particular emphasis on risk factors, pathophysiological mechanisms, and the role of pharmacists in dementia care.

Methodology

A narrative review of the literature was conducted to explore the association between DS and AD, with a particular focus on pathophysiological mechanisms, risk factors, and the role of pharmacists in patient care. Relevant articles were identified through searches of PubMed, Scopus, and Google Scholar, alongside selected reports and clinical guidelines. Original research articles, review papers, and other relevant publications written in English were considered. The retrieved literature was reviewed to provide an overview of the current evidence

and to highlight the potential contributions of pharmacists in the management and support of individuals with DS and AD.

Clinical Characteristics and Risk Factors of Dementia:

Dementia is a syndrome characterized by a decline in memory and other cognitive functions caused by a wide range of conditions affecting the brain (Tampi & Jeste, 2022). Cognitive impairment is often considered a prodromal stage of dementia and may precede the development of neuropsychiatric symptoms or behavioral and psychological symptoms (García-Martín et al., 2022). These neuropsychiatric symptoms are highly prevalent in AD, affecting approximately 50–98% of patients, with anxiety, hallucinations, agitation, and irritability being among the most frequently reported manifestations (García-Martín et al., 2022; Lyketsos et al., 2002).

Clinical and longitudinal research has consistently shown that individuals with DS have a lifetime risk of developing dementia exceeding 90% (Fortea et al., 2021). Although dementia is uncommon before the age of 40, both its incidence and prevalence rise markedly with advancing age, affecting approximately 88–100% of individuals with DS who are older than 60 years (Zigman & Lott, 2007) (Figure 2). In addition to aging and trisomy 21, several mechanisms have been shown to increase protein deposit the brain leading to cognitive problems (Sun & Mok, 2025). These mechanisms include mitochondrial dysfunction, brain atrophy, amyloid pathology, and dysregulated nutrient-sensing pathways (Reddy et al., 2016; S. Wang et al., 2025).

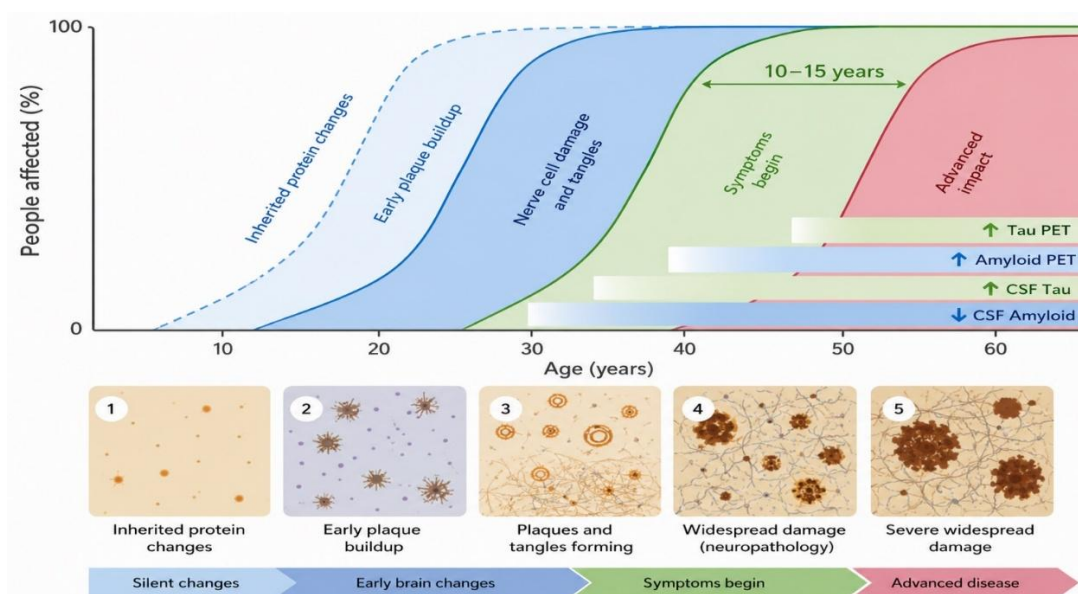


Figure 2: Direct causes of Alzheimer's Disease: Aging and Down syndrome

Furthermore, accumulating evidence suggests that modifiable risk factors contribute significantly to the development of AD (Edwards Iii et al., 2019). Smoking-related neurological changes may progress over time and have been linked to an increased risk of AD and dementia (T. Durazzo et al., 2014) due to the accumulation of APP, the fundamental precursor of AD pathogenesis (Ho et al., 2012). Individuals with DS who smoke have a 30–40% higher risk of developing AD compared with non-smokers (Ho

et al., 2012). Metabolic syndrome (Figure 3), which encompasses conditions such as diabetes mellitus, obesity, hypertension, and dyslipidemia, has been associated not only with an increased risk of cardiovascular diseases but also with a greater likelihood of developing AD-related manifestations (Rumble et al., 1989; Yue et al., 2025). Particular attention should be given to medication exposure, as long-term use of anticholinergics, benzodiazepines, opioids, and certain NSAIDs have been associated with an

increased risk of cognitive impairment and dementia (M. D. Ramos et al., 2026). Therefore, these medications should be prescribed and

monitored cautiously, especially in older adults and individuals at risk of cognitive decline (Alzubaidi et al., 2020).

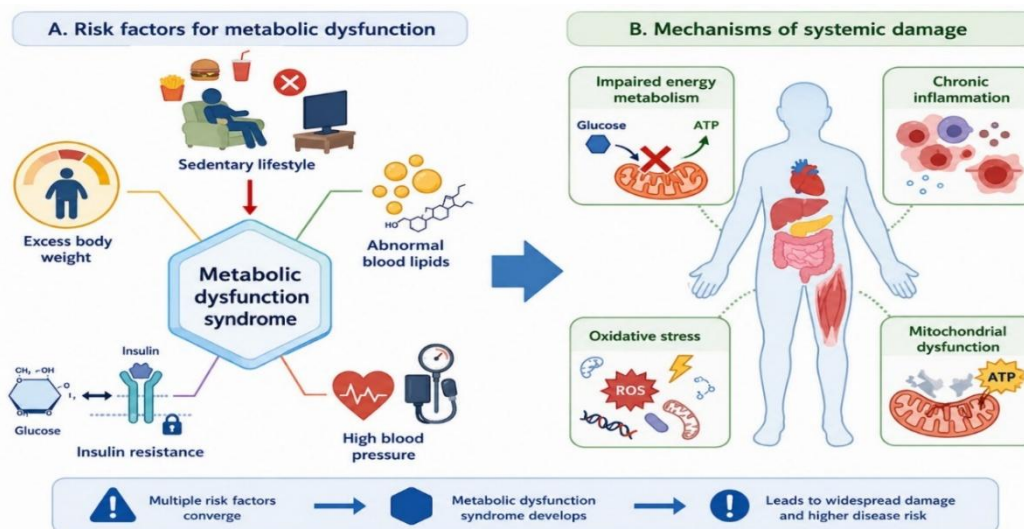


Figure 3: The Impact of Metabolic Syndrome on the Development of Alzheimer's Disease

Pharmacists' Role in Alzheimer's disease care:

Anti-dementia medications are used to manage symptoms but do not cure the disease. The primary pharmacological treatments include cholinesterase inhibitors and memantine (Muñoz-Contreras et al., 2022a; H. H. P. Staff, 2015; Wong, 2016). These medications are approved for the general population with AD; however, no pharmacological regimen has been specifically approved by the FDA for the treatment of AD in individuals with DS (Fortea et al., 2021; Mann, 1988). Numerous studies have demonstrated that medication adherence is associated with reduced mortality, improved clinical outcomes, and lower healthcare costs among patients with AD (Singh et al., 2024).

Although the number of approved medications for dementia-related symptoms remains limited, the role of the pharmacist in patient education remains essential (H. Ramos et al., 2021; Yang et al., 2025). Pharmacists are well positioned to support early identification of cognitive decline, contribute to ongoing disease management, and ensure continuity of care (Bender et al., 2022; Turk et al., 2024). Pharmaceutical care extends beyond medication dispensing to include empathy and an understanding of the impact of AD on individuals with DS and their caregivers.

This is particularly important given the higher prevalence of polypharmacy in this population, which increases the complexity of medication management (Singh et al., 2024; M. C. Staff, n.d.).

Caregivers represent a central component in the management of DS who develop AD, as most care is delivered in the home (Muñoz-Contreras et al., 2022a). The progressive cognitive and functional decline caused by dementia places a substantial physical, psychological, and financial burden on caregivers. In many cases, caregivers are responsible for administering medications and monitoring therapeutic effects, in addition to assisting with daily living activities (da Rocha et al., 2022). This burden could be alleviated through the active involvement of pharmacists when medication-related challenges are appropriately recognized and addressed (da Rocha et al., 2022; Figueroa & Darbra, 2025).

Pharmacists can provide essential support by offering medication counseling, simplifying therapeutic regimens, and educating caregivers about treatment plans. They may also enhance medication adherence through practical tools such as medication calendars, dosette boxes, reminder systems, and educational materials (George et al., 2025; Mittelman, 2000) (Figure 4). As integral members of the healthcare team,

pharmacists can contribute significantly to improved patient outcomes through effective interprofessional collaboration with physicians and other healthcare professionals (H. Ramos et al., 2021; Turk et al., 2024). Such collaboration can enhance both clinical outcomes and the quality of life of individuals with DS and AD, as

well as their caregivers. Pharmacists can work closely with prescribers to optimize pharmacotherapy by recommending simplified treatment regimens, including long-acting formulations when appropriate, to reduce dosing frequency and improve medication efficiency (H. Ramos et al., 2021; Turk et al., 2024).

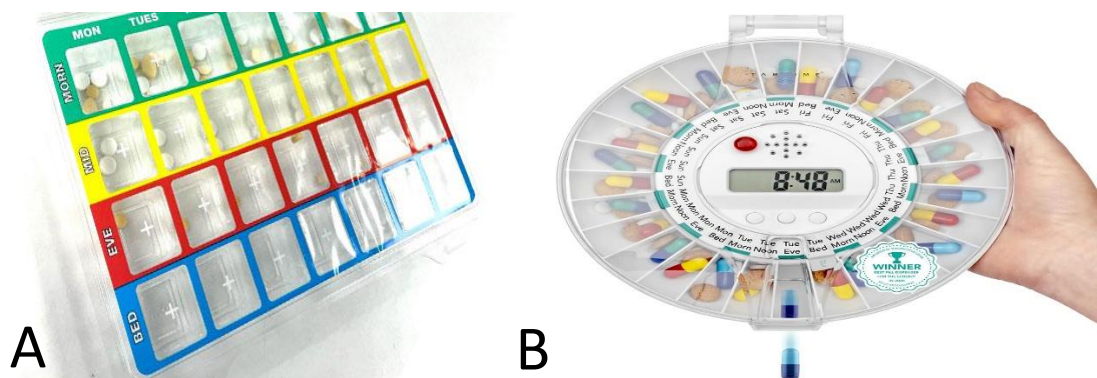


Figure 4: Counseling aids for patients with Alzheimer's disease: A: Dosette box B: Automated Dispenser

Pharmacist Communication Skills and Their Impact on Patient and Caregiver Outcomes

In community settings, pharmacists are frequently exposed to a wide range of pharmaceutical and clinical challenges (M. D. Ramos et al., 2026). One of the key barriers to achieving optimal patient outcomes is the level of professional preparedness among pharmacists. In addition, time constraints and increasing workload in community practice may further limit the depth of patient assessment (Bender et al., 2022). To manage such challenges effectively, pharmacists must demonstrate strong clinical competence, problem-solving abilities, and communication skills in order to establish trust and build a strong professional pharmacist–patient relationship.

A substantial body of literature emphasizes the importance of effective communication skills for improving patient treatment persistence and optimizing therapeutic outcomes (Bender et al., 2022; Rumble et al., 1989). However, effective communication is not limited to asking whether patients are taking their medications or experiencing side effects; rather, it is about how these questions are delivered and interpreted (Santana et al., 2020). The use of appropriate

tone, active listening, empathetic engagement, and structured questioning techniques plays a crucial role in improving the quality of patient interactions (Bender et al., 2022). Such approaches help pharmacists obtain more accurate and comprehensive clinical information regarding disease status, medication use, lifestyle factors, and potential barriers to adherence. Instead of asking a closed-ended question, such as, “Are you taking your medication as prescribed?”, healthcare professionals should use a more patient-centered and open-ended approach, such as, “How are you taking your medication?” or “How many times are you taking your medication?”. Open-ended questions encourage patients to share their experiences, concerns, and medication-taking behaviors more freely, allowing pharmacists to identify potential barriers to adherence and understanding (Bonnar et al., 2026; Figueroa & Darbra, 2025).

Effective communication begins with greeting the patient warmly, making him/her feel welcome, and establishing rapport, by demonstrating empathy, being assertive, giving solutions, reassuring, and showing respect. Asking simple questions such as, “How have you been feeling since starting this medication?” or “How is this medication working for you?” can

help create a comfortable environment in which patients feel valued and respected (Muñoz-Contreras et al., 2022a). Throughout the conversation, pharmacists should pay close attention not only to verbal responses but also to non-verbal cues, as these often provide important insights into the patient's feelings and level of understanding (Bonnar et al., 2026).

Non-verbal communication can reveal concerns that patients may be reluctant to express verbally. For example, signs such as crossed arms, lack of eye contact, furrowed eyebrows, repeated facial expressions of confusion, or difficulty maintaining focus may indicate anxiety, uncertainty, embarrassment, or misunderstanding (Bender et al., 2022; Bonnar et al., 2026). Individuals with DS may experience hearing problems or visual impairments, especially with advancing age (Botto et al., 2022; Rumble et al., 1989). Therefore, patients who repeatedly lean forward, ask for repetition, or appear to struggle with following the conversation may be experiencing hearing difficulties, visual impairment, or challenges in understanding the provided information (Muralidhar et al., 2025). Such communication barriers can often be overcome through the application of appropriate communication techniques and professional skills (Bender et al., 2022; Hendrix et al., 2021).

When medication regimens involve specific administration techniques or specialized dosage forms, pharmacists should complement verbal counseling with demonstrations. Examples include demonstrating the correct administration of inhalers, injectable medications, transdermal patches, eye drops, or other drug delivery systems. Such practical demonstrations can significantly improve patient comprehension and confidence in medication use (de Sousa & Souto, 2024). Furthermore, digital reminder systems, medication management applications, and pharmacist-led telehealth services may provide additional support for medication adherence and communication, particularly when used alongside verbal counseling and written instructions (Zigman & Lott, 2007).

By recognizing and responding appropriately to verbal and non-verbal cues, pharmacists can adapt their communication style, provide individualized clarification, and ensure that patients fully understand their treatment plans (Muñoz-Contreras et al., 2022b; Sharma et al., 2023). These communication strategies are particularly important when counseling individuals with DS who may experience cognitive decline, memory impairment, or reduced comprehension associated with the development of AD. In such situations, pharmacists may need to use simplified language, repetition, visual aids, and caregiver involvement to ensure effective communication and medication understanding.

Preparing Future Pharmacists for Dementia Care: Simulation-Based Education and Artificial Intelligence

Curricular progression is a fundamental factor in developing pharmacists' ability to achieve optimal patient health outcomes. Simulation-based training, combined with the strategic integration of therapeutics related to vulnerable and special patient populations, contributes to the development of competent and well-prepared future pharmacists (Meyer et al., 2022). Theoretical instruction on conditions such as DS, geriatric disorders, neurological diseases, and mental illnesses should be complemented by practical and experiential learning opportunities (Lavender et al., 2025). Such an approach enables students' to evaluate their own preparedness, identify areas requiring further development, reduce the likelihood of future errors and patient harm, and gain exposure to realistic clinical challenges (Muralidhar et al., 2025).

Incorporating individuals with DS and AD into the pharmacy curriculum through high-fidelity simulations, standardized patient encounters, role-playing exercises, and dementia-focused clinical scenarios can provide safe and structured environments in which students can practice communication, medication management, problem-solving, and interprofessional collaboration (Lavender et al., 2025; Rao, 2011). Furthermore, students should actively participate

in case-based discussions, reflective learning activities, and multidisciplinary team meetings that involve geriatric, psychiatric, neurological, and pharmaceutical perspectives (*SimulatED™*, n.d.).

The incorporation of artificial intelligence (AI) tools into pharmacy education may further enhance learning outcomes. AI-supported clinical decision-making systems, virtual patient simulations, predictive analytics, and personalized learning platforms can help students develop digital literacy and clinical reasoning skills while improving their ability to identify medication-related problems and optimize patient care (Meyer et al., 2022). The implementation of existing platforms and generative AI tools could enhance students' critical thinking and problem-solving approach. Examples of these platforms: Virtual dementia system, was used within geriatric center to minimize phone calls for consultations, medication recommendation, safety considerations (George et al., 2025). Safe-Medication simulation reviews integrated to help patients receive the correct therapy and dosing with hospitalized patients (Santana et al., 2020). Therefore, the integration of simulation-based education, interdisciplinary dementia training, experiential learning opportunities, and AI-assisted technologies may contribute significantly to the development of competent, confident, and future-ready pharmacists capable of delivering high-quality care to individuals living with dementia and other neurocognitive disorders.

Limitations:

Within the available literature, the role of

pharmacists in caring for individuals with DS and AD is still not well explored. Most studies on dementia focus on the general population and rarely include pharmacists' perspectives or assess pharmacy students' preparedness. In addition, little attention has been given to the specific clinical and cognitive needs of individuals with DS, despite their strong genetic risk for AD. This highlights the need for more pharmacist involvement, better targeted education, and more tailored approaches for this high-risk group. Overall, this review emphasizes the potential role of pharmacists in improving quality of life and strengthening the pharmacist–patient relationship, but stronger evidence from well-designed studies is still needed.

Conclusion:

This review highlights that AD in people with DS is an important condition that is still not well addressed in the literature. The role of pharmacists in this area remains limited, although they can provide valuable support to patients and caregivers through medication management and education. It also emphasizes that pharmacy curricula should place greater attention on this population, as real-world care requires well-trained pharmacists. Theoretical knowledge alone is not enough and should be complemented with experiential training, including face-to-face patient interaction, counseling, and communication with individuals with DS and their caregivers. Further research and focused training are needed to strengthen pharmacists' involvement and improve care for this population.

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Author Declaration

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