The Cost of Untreated Agitation in Alzheimer's:

Direct, Indirect, Intangible and New Directions in Research

Global Council on Alzheimer's Disease™

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

June 2024

01US23EUC0445

Table of Contents

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Opening Letter

In 2021, the Global Council on Alzheimer's Disease (GCAD) published ***The Costs of Untreated Agitation: A Literature Review***. The report examined a critically important, yet widely overlooked aspect of Alzheimer's disease: agitation.

Agitation is estimated to affect between approximately **24 and 67 percent** of community-dwelling people with Alzheimer's.[1] People with lived experience say these symptoms are among the most distressing aspects of the disease, as a person may reject care, become easily irritated or angry, pace, have verbal outbursts, or even display physical aggression.[2] Agitation is associated with a range of negative outcomes, including faster cognitive decline, deterioration in quality of life, the move to long-term residential care , and mortality.[1,2]

Yet there are still many gaps in the research on agitation, its impacts, and its costs. GCAD's previous literature review found only eight publications that directly estimate the costs of agitation, and **just two** in the U.S.

We believe this disconnect slows action on agitation. If we cannot understand one of the most important factors and cost drivers in Alzheimer's, we will not be able to design strategies to address it and help the millions of families facing the disease.

On the other hand, understanding the costs of agitation provides an "on-ramp" to step up solutions. By quantifying the impact, we can build the case for targeted efforts, policies, and interventions that work best for people and families.

Direct medical and long-term care costs are the most straightforward to measure, and they provide a compelling call to action. Yet they still do not tell the full story. We must also consider the many hidden costs of agitation, such as lost income for care partners, or the intangible costs of lower quality of life.

GCAD is committed to advancing this conversation – with a particular emphasis on the voices of those living with Alzheimer's and care partners. Since our 2021 literature review, two

- Several new studies have directly examined the costs of agitation in the United States, with one study finding it more than doubles the average direct medical and care costs of Alzheimer's.[3]
- GCAD, in partnership with the Dementia Action Alliance, has conducted a range of in-depth interviews with people living with Alzheimer's disease and care partners. Their lived experience indicates important focus areas for future research on agitation and strategies to address it.

This report, Building the Case for Action on Agitation: Research & Lived Experience, aims to take the next step for increasing focus and understanding of agitation. GCAD hopes it will drive progress – underscoring the critical role of agitation, increasing the urgency for new research, and informing strategies to help people and their families.

Mary Michael
Chair, Global Council on Alzheimer's Disease
Vice President, Patient Advocacy and Stakeholder Management, Otsuka America Pharmaceutical, Inc.

**We use the term "long-term residential care" throughout this paper to avoid the negative connotations of "institutionalization."*

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

The Costs of Agitation:

A Central Aspect of the Alzheimer's Disease Burden

> *" The behaviors associated with agitation take an indelible emotional toll on those living with dementia and those who care for them."*
>
> *Meryl Comer*
>
> *Chair & Co-Founder, Global Alliance on Women's Brain Health; Author of "Slow Dancing With A Stranger: Lost and Found in the Age of Alzheimer's"*

Accurately estimating the total costs of agitation in Alzheimer's disease can be a starting point for greater action and new solutions – just as estimates of global dementia prevalence and costs have helped to elevate dementia on the global agenda.

The available research, as well as interviews with people with lived experience, indicate that agitation significantly increases costs across the course of the disease. It does this through direct medical and healthcare costs, such as greater rates of professional caregiving and long-term residential care; through indirect costs, such as lost income and impacts on a care partner's mental and physical health; and through intangible costs, such as lower quality of life. [2,3,4,5]

The high costs of agitation underscore the importance of using available interventions and strategies to manage agitation, as well as the need for new, more effective treatments.

Direct Costs of Agitation

2x Higher Direct Costs
($20,000 per year vs. $9,200)[3]

>2x
More Professional Caregiving[3]

>3x
Higher Rate of Residential Care[3]

1.6x
Greater Risk for Falls[2]

Costs across disease progression

Indirect & Intangible Costs

Work Impacts and Lost Income[5]

Impacts to Care Partner's Health[5,6]

Declines in Quality of Life[2]

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Direct Costs

> *" We found a perfect nursing home that claim[ed] to specialize in dementia. They went to the hospital to assess [my dad] and have refused to take him. Due to his dementia, he can become agitated and has tried to kick doors and shouted at staff. So, they said they can't take him due to his challenging behavior."*
>
> *Care Partner*

A study published in 2021 sheds new light on the direct costs of agitation in the U.S., including for both people living in the community and in long-term residential care.

The results are striking. On average, agitation **leads to more than double** the direct healthcare costs: **$20,000 each year**, compared to **$9,200** for people with Alzheimer's but no agitation.[3] Higher levels of agitation were also associated with higher healthcare utilization across the spectrum of care.[3]

Higher Levels of Healthcare Consultation & Professional Caregiving

On average, people with agitation had **more provider consultations (7 per year)** than people with no agitation (4 per year).[3] This higher utilization held for different types of providers, from primary care physicians to specialists like neurologists, psychiatrists, and geriatricians.

People with agitation also received **more professional caregiving**, an average of **27 hours per week**, compared to **11 hours per week** for people without agitation.[3]

Hours of Professional Caregiving Received Per Week

With Agitation

27 HOURS

VS.

Without Agitation

11 HOURS

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Higher Rate of Long-Term Residential Care

Long-term residential care represents one of the greatest costs in Alzheimer's. Consider that a private room in a nursing home can cost **more than $100,000 per year**.[4] Therefore, the earlier a person must move to residential care, the greater the cost of their care overall; and agitation can be a critical factor in this transition.

In one study, people with agitation were **more than three times more likely** to be in long-term residential care – **11.9 percent** compared to **3.2 percent** for those with no agitation.[3] Another recent study found people with agitation were **20 percent more likely** to be in residential care – but even this relatively lower figure was estimated to lead to **$4.3 billion** in additional incremental costs.[1]

Greater Risk of Falls, Fractures and Infections

Research with people in long-term residential care indicates the high costs of agitation continue in this setting. Those with agitation were **~1.6 times more likely** to have a fall, **~1.3 times more likely** to have a fracture, and **~1.2 times more likely** to have an infection.[2] These complications can lead to costly care and hospitalization.

Higher Rates of Medication & Polypharmacy

The lack of treatment options in Alzheimer's disease can often lead to one of two undesirable outcomes: people receive no treatment at all, or they are prescribed a range of off-label drugs in an effort to reduce symptomatic behavior.[3] Given the range of agitation symptoms, people with agitation tend to have higher incidences of polypharmacy, leaving them at risk of complications due to adverse drug reactions,[2] a danger which, coupled with low confidence in efficacy,[1] leaves many patients with few viable treatment options.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Indirect Costs

> *“ [My diagnosis] was like a punch in the gut. I did not know what my life was going to be like. How was I going to support my family? This was uncharted territory.”*
>
> *Person Living with Alzheimer’s Disease*

The indirect and intangible costs of Alzheimer’s disease are, by definition, more difficult to measure than direct costs. However, the research that is available indicates a range of impacts, which are likely more severe and costly for people with agitation.

Professional Impacts & Out-of-Pocket Costs

Alzheimer’s care partners report that their care responsibilities often lead to impacts at work, such as reducing hours, coming in late or leaving early, passing up promotion opportunities, taking a leave of absence, or exiting the workforce entirely.[5] Further, care partners for dementia report almost twice the out-of-pocket costs as other kinds of caregivers – **more than $12,000 per year**.[5]

While continued research is needed to understand agitation and these indirect costs, we know that the strain placed on family or informal care partners is often greater when agitation is present. Therefore, agitation is likely a significant contributor to indirect costs like missed income and out-of-pocket costs.

Impacts on Care Partners’ Physical and Mental Health

Agitation can take a heavy toll on the physical and mental health of care partners. Again, while there is little research specific to agitation, studies find that **30 to 40 percent** of Alzheimer’s care partners report symptoms of depression.[5] A survey conducted by Alzheimer’s Disease International found **more than half of care partners (54%)** said they felt stress either often or all of the time.[6] Further, **38 percent** of care partners for Alzheimer’s and other dementias say the physical stress of care is high or very high.[5]

These health impacts can generate indirect costs through the care partners’ medical care. These impacts and costs are likely significant in cases of agitation, as caring for these symptoms can be both physically and emotionally taxing.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Intangible Costs

> *“ We caregivers become so distraught, we try so hard, and things don’t get better, we feel guilty, we don’t sleep because we want to devote more of our time to helping our loved one. We don’t sleep as well because we aren’t getting out and doing things that are good for us, and then we become irrationally irritable and become unraveled.”*
>
> *Care Partner*

Impacts Quality of Life

In addition to indirect costs, there are also the intangible costs of a deterioration in quality of life for people with agitation and care partners. Behavioral symptoms, which may include self-harm and verbal and physical aggression, can have a profoundly detrimental impact.[2] Further, as the disease progresses, and the person’s ability to communicate and care for themselves diminishes, an ever-increasing burden is placed upon the care partner.[2]

In response, many care partners find themselves unable to provide adequate care.[2] This highlights the connections between intangible costs and direct and indirect costs, demonstrating the importance of bringing these issues to light.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

New Directions in Research:

Insights from the Alzheimer's Community

As we seek to fill these gaps, where should future research on agitation in Alzheimer's focus?

To answer this question, we must start with the voices of those living with and caring for Alzheimer's. GCAD's interviews with people in this community provide important insights into gaps, disparities, and challenges that are not adequately reflected in the current literature – and which represent important areas for future research.

In particular, further research might be conducted with a primary focus on examining racial and cultural disparities that can have a significant impact on these costs. There are many historically marginalized communities within the US who may face disproportionate costs, such as the Black community and the LGBTQ+ community.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Racial Disparities:

Understanding the Costs for Black Americans

> *" In communities of color, there is more of a sense of keeping people at home. There is a lack of trust and a lack of resources that might lead people to keeping their loved ones at home."*
>
> *Care Partner*

In the U.S., the Black community is disproportionally affected by the health, economic, and societal burdens of dementia. Black Americans hold around **one-third of total societal costs** for dementia, despite making up less than one-fifth of the U.S. population.[7]

Our interviews find a consistent distrust between Black Americans and the medical profession, which is based in a long history of discrimination, racism, and exploitation.[8] This distrust complicates the dynamics of care for agitation and resulting costs in the U.S.

With this disparity in mind, additional research should focus on the costs of agitation within the Black community. Such research could focus on indirect and intangible costs, in particular, and demonstrate how these costs, though often hidden from view, are as impactful as the more visible direct costs.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

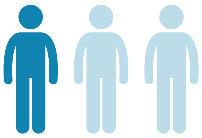
Cultural Disparities:

Understanding the Costs for the LGBTQ+ Community

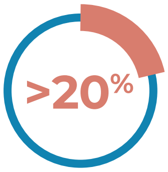
> *" My biggest concern right now is who's going to take care of me when I get to a point where I no longer can take care of myself."*
>
> *Person Living with Dementia*

The LGBTQ+ community faces unique challenges related to healthcare and Alzheimer's, including risk factors like social isolation and discrimination, barriers to healthcare access, and limited availability of and support for care partners. In a recent survey, **around 1 in 3** LGBTQ+ Americans faced difficulties accessing necessary medical care due to cost issues, including more than half of transgender Americans. Additionally, **over 20 percent** of LGBTQ+ Americans reported postponing or avoiding medical treatment due to discrimination, including nearly **1 in 3** transgender individuals.[9]

Around 1 in 3



LGBTQ+ Americans faced difficulties accessing necessary medical care due to cost issues



LGBTQ+ Americans reported postponing or avoiding medical treatment due to discrimination

In our conversations with members of the LGBTQ+ community, the question of who would take care of those living with dementia who don't have spouses or immediate family came up time and time again. It is estimated that by 2030, the number of lesbian, gay, bisexual and transgender older adults with dementia will **surpass 1 million.**[10]

We propose additional research focusing on the total costs of agitation within the LGBTQ+ community and how it differs from the overall average cost. Identifying areas of cost discrepancies could help provide guidance as to where additional support and resources are needed.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Geographic Gaps:

Understanding the Costs Within the U.S. Healthcare System

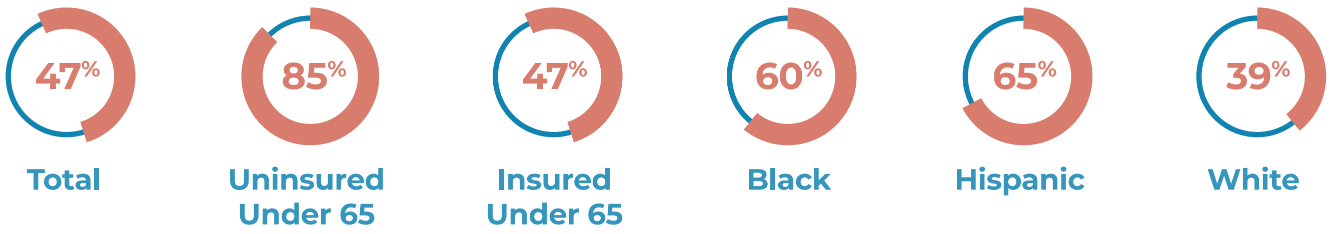
> *“ It took us four years to ultimately get a probable diagnosis and the geriatrician said, ‘you cannot drive, effective immediately. And your caregiver will experience financial stress, she will basically be burdened by you and, ultimately, you will go into long-term care and die.”*
>
> *Person Living with Dementia*

The lack of research on agitation is especially pronounced in the U.S. This is particularly troubling given the differences between the U.S. health system and European health systems, which have been the primary focus of research to-date.

Insurance and cost hurdles can present especially significant barriers to diagnosis and care in the U.S. As recently as 2020, **32 million Americans (9.7% of the population)** were uninsured.[11] Further, even among those who have insurance, many are still unable to afford treatment. **25% of Americans** report they have forgone treatment for a serious medical condition due to cost.[12]

Given these differences, additional studies focused specifically on the total costs of agitation in the United States would be enormously beneficial. In particular, research should examine the hidden costs that arise specifically as a result of barriers within the U.S. healthcare system. Such research could help spur strategies and solutions that are more closely tailored to the dynamics of the American healthcare system.

Share of Americans who say affording health care is somewhat or very difficult.[13]



© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Diagnostic Delays:

Understanding the Costs Earlier in Disease Progression

> *" It took me 8 years to finally get a diagnosis for the symptoms I was experiencing. I was relieved to finally find out what was going on with me."*
>
> *Person Living with Early Onset Alzheimer's*

Across our interviews, people report a long, challenging journey simply to receive an Alzheimer's diagnosis. Naturally, this limits the ability of researchers to measure the costs that occur before diagnosis, or in those cases where a diagnosis is simply never made.

Recent studies substantiate this concern. A 2019 survey showed that **nearly two-thirds** of respondents, which included people living with dementia, carers, healthcare practitioners, and the general public, believe memory loss is simply a normal part of the aging process.[14] Further, there has also been significant uncertainty about the definition and diagnosis of agitation.[1]

There is a need for research focusing on the time between a person's first consultation and their actual diagnosis, the symptoms exhibited in that time, and the costs and impacts of those early symptoms. Additionally, an accurate assessment of these preventable costs could prove useful in incentivizing improved diagnostic techniques, as well as demonstrating the need for new pharmacological and non-pharmacological interventions.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

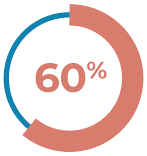
Lack of Healthcare Support:

Understanding the Costs of Inadequate Guidance After Diagnosis

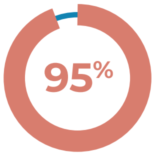
> *" What we didn't have was very good emotional support from the medical community and resources to deal with the issues, like agitation. That became a very front-and-center challenge."*
>
> *Care Partner*

In interviews, people with Alzheimer's and their care partners described an absence of practical advice on how to live with symptoms once they did receive a diagnosis. This includes symptoms of agitation that can be difficult to discuss, but which have some of the worst impacts on people and their families. As a result, people are left ill-equipped to manage symptoms, which could lead to higher costs.

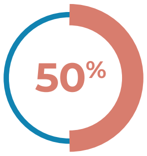
This is all the more tragic because there are interventions that have proven effective for managing symptoms of agitation.[15] However, if providers do not equip people with these strategies, symptoms and strain may worsen. Therefore, research on support levels from medical professionals for agitation – at diagnosis and ongoing after that point – could be particularly useful.



60% of Americans would NOT talk to their doctor right away about symptoms of mild cognitive impairment



More than 95% of physicians wait for patients or family members to raise symptoms or request a cognitive assessment



More than 50% of primary care physicians report a shortage of specialists in their area[5]

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Conclusion:

> *“ There are ways that my mom would express herself with agitations. Care partners need to be aware of these nuances. That’s how you see symptoms expressed and develop ways to manage them. One thing that calmed my mom down was listening to Elvis. She loved Elvis and drinking Coca-Cola.”*
>
> *Person Living with Early Onset Alzheimer’s*

Despite important recent progress to understand the true costs of Alzheimer’s disease, there is still a significant research gap for the costs of agitation. In response, GCAD aims to highlight needs in the current literature, put lived experience at the center of the conversation, and prompt new research that may uncover important insights. This research can provide the basis for strategies to address the unique challenges of agitation in Alzheimer’s – a central element of the disease burden.

GCAD looks forward to continued collaboration with researchers, advocates, policymakers, and other stakeholders as we work to accelerate solutions for the millions of people and families living with Alzheimer’s.

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Works Cited:

1. Cloutier, Martin, et al. “Institutionalization risk and costs associated with agitation in Alzheimer's disease.” Alzheimer's & Dementia: Translational Research & Clinical Interventions, 2019, **https://doi.org/10.1016/j.trci.2019.10.004**

2. Fillit, Howard, et al. "Impact of agitation in long-term care residents with dementia in the United States." International Journal of Geriatric Psychiatry, 2021, **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9291552/#gps5604-bib-0056**

3. Jones, Eddie, et al. "Agitation in dementia: real-world impact and burden on patients and the healthcare system." Journal of Alzheimer's Disease, 2021, **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8461728/#ref001**

4. Kaldy, Joanne, et al. “How to Pay for Nursing Home Costs.” U.S. News & World Report, 7 Feb. 2023, **https://health.usnews.com/best-nursing-homes/articles/how-to-pay-for-nursing-home-costs**

5. “2023 Alzheimer’s Disease Facts and Figures.” Alzheimer’s Association, 2023, **https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf**

6. Gauthier, Serge, et al. World Alzheimer Report 2022: Life after diagnosis: Navigating treatment, care and support. Alzheimer’s Disease International, 2022, **https://www.alzint.org/u/World-Alzheimer-Report-2022.pdf**

7. Gaskin, Darrell, et al. “The Costs of Alzheimer’s and Other Dementia for African Americans.” African American Network Against Alzheimer’s, Sep. 2013, **www.usagainstalzheimers.org/sites/default/files/USA2_AAN_CostsReport.pdf**

8. Michael, Mary, and Jackie Pinkowitz. “Calling All Voices: Stories From Black Community Members on Learning to Live Well with Dementia,” Global Council on Alzheimer’s Disease, Aug. 2022, **www.gcad.net/sites/g/files/qhldwo6026/files/2022-09/Calling%20All%20Voices%20-%20Stories%20from%20Black%20Community%20Members.pdf**

9. Medina, Caroline, and Lindsay Mahowald. “Discrimination and Barriers to Well-Being: The State of the LGBTQI+ Community in 2022.” Center for American Progress, 12 Jan. 2023, **https://www.americanprogress.org/article/discrimination-and-barriers-to-well-being-the-state-of-the-lgbtqi-community-in-2022/**

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.

Works Cited:

10. McGovern, Justine. “The forgotten: dementia and the aging LGBT community.” Journal of Gerontological Social Work, 24 Sep. 2014, **https://doi.org/10.1080/01634372.2014.900161**

11. Cha, Amy, and Robin Cohen. “Demographic variation in health insurance coverage: United States, 2020.” National Health Statistics Report, 11 Feb. 2022, **https://pubmed.ncbi.nlm.nih.gov/35166656/**

12. Saad, Lydia. “More Americans Delaying Medical Treatment Due to Cost.” Gallup, 9 Dec. 2019, **https://news.gallup.com/poll/269138/americans-delaying-medical-treatment-due-cost.aspx**

13. Montero, Alex, et al. “Americans’ Challenges with Health Care Costs.” Kaiser Family Foundation, 14 Jul. 2022, **https://www.kff.org/health-costs/issue-brief/americans-challenges-with-health-care-costs/**

14. “World’s Largest Dementia Study Reveals Two Thirds of People Think Dementia Is a Normal Part of Ageing, Rather than a Medical Condition.” Alzheimer’s Disease International, 20 Sep. 2019, **https://www.alzint.org/news-events/news/worlds-largest-dementia-study-reveals-two-thirds-of-people-still-incorrectly-think-dementia-is-a-normal-part-of-ageing-rather-than-a-medical-condition/**

15. Livingston Gill, et al. “A systematic review of the clinical effectiveness and cost-effectiveness of sensory, psychological and behavioral interventions for managing agitation in older adults with dementia.” Health Technology Assessment, Jun. 2014. **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4781145/**

© 2024 Otsuka Pharmaceutical Development & Commercialization, Inc. All Rights Reserved.