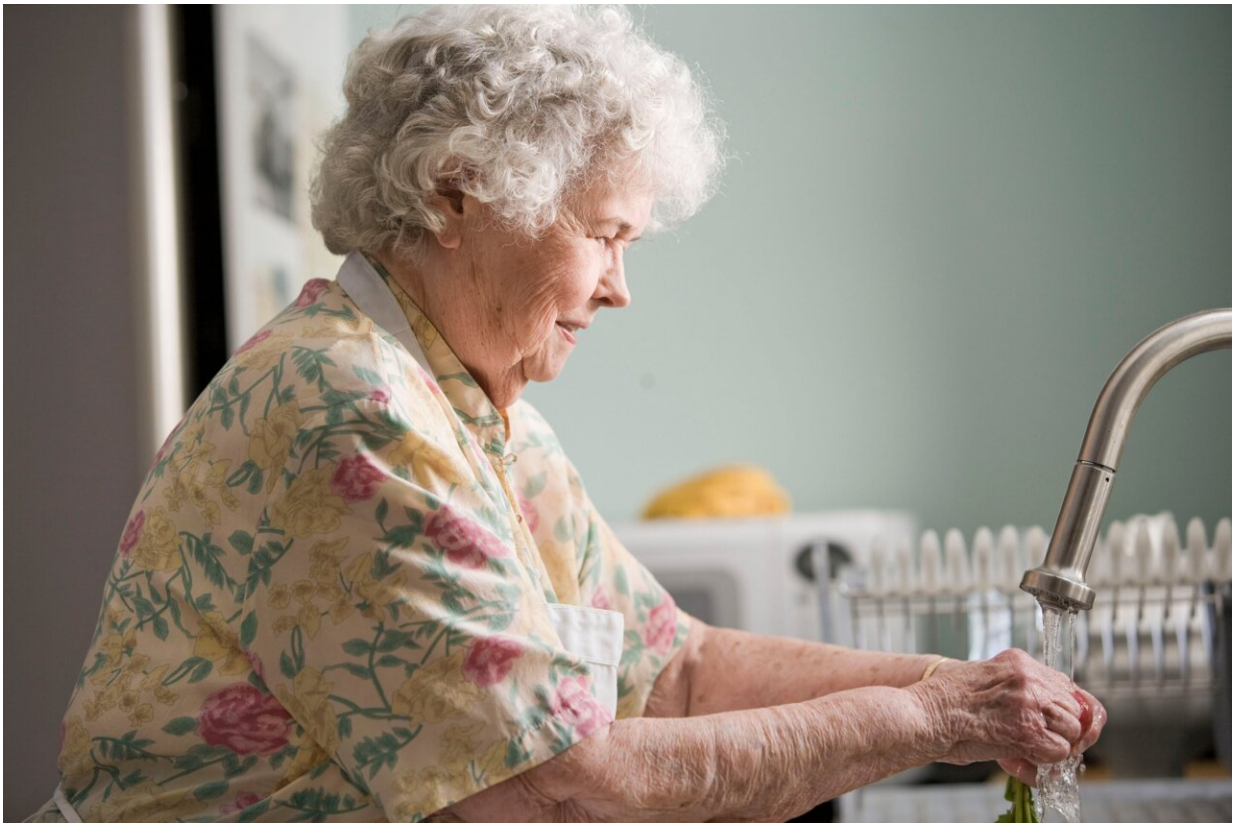


Experts show how resilience to Alzheimer's differs by sex and gender

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An international panel of experts led by the Barcelona Institute for Global Health (ISGlobal), under the umbrella of the Alzheimer's Association International Society to Advance Alzheimer's Research and

Treatment, has produced a consensus statement on sex and gender disparities in resilience to Alzheimer's disease and issued a call for incorporating these differences in future research.

The work has been [published](#) in *Alzheimer's & Dementia*.

Women make up the majority of people with Alzheimer's disease and have twice the [lifetime risk](#). The prevalence of protective and risk factors, as well as the burden of Alzheimer's disease pathologies and related conditions such as [cerebrovascular disease](#), differ by sex and gender because of biological factors (e.g., genetic risk) and socially constructed factors (e.g., education and lifestyle).

"Assessing how sex and gender interact is crucial to understanding the mechanisms that maintain cognitive function and reduce the accumulation of pathologies in aging and Alzheimer's disease, i.e., resilience and resistance factors," says Eider Arenaza-Urquijo, ISGlobal researcher, first author of the study and President of the Reserve, Resilience and Protective Factors Group of the Alzheimer's Association.

Resistance and resilience to Alzheimer's disease in men and women

Based on a review of a large body of literature, the team identified sex and gender differences in dementia risk and identified a gap in the understanding of specific risk and resilience pathways.

While women tend to have an initial cognitive advantage, they decline faster than men as the disease progresses. This may be due to differential development of pathologies, known as resistance to Alzheimer's disease, or different ability to maintain normal functioning over time and cope with pathology once this is present, known as cognitive resilience to

Alzheimer's disease.

In fact, women initially show greater resilience, coping better with [brain pathology](#) and atrophy and maintaining cognitive function. The greater initial resilience in women is supported by animal research showing a protective role of the X-Chromosome in Alzheimer's disease (females typically have two X chromosomes, while males have one).

However, this initial resilience fades away as they progress towards a clinical diagnosis of mild cognitive impairment and Alzheimer's disease, when they show greater vulnerability. Indeed, studies suggest that women are more likely to have an abnormal build-up of tau protein in the brain and show a higher burden of vascular pathologies, particularly after the menopause.

The authors propose various mechanisms explaining the difference in risk and resilience between women and men, including a higher prevalence of physical inactivity and affective disorders in women, but also [biological factors](#). In this regard, [genetic evidence](#) suggests that resilience might be associated with immune pathways in females and cardiovascular pathways in men.

Addressing modifiable factors

According to the research team, studies of resilience in Alzheimer's disease have mainly focused on individual behavior, without taking into account how social and cultural factors, such as gender, influence behavior and therefore risk and resilience.

Importantly, differences in cognitive function between men and women may be decreasing as gender inequalities also decrease due to more opportunities for women in education, workforce participation, and improvements in their economic status and living conditions.

"Protective factors, such as education, may have different effects in men and women. We need to understand the complexity of interactions between biological and [social factors](#) to understand resilience to Alzheimer's disease," argues Arenaza-Urquijo.

For this reason, the authors call for a sex- and gender-sensitive approach to resilience to better understand the complex interplay of biological and social determinants. "Focusing more on the differential effects of modifiable factors will help to determine whether a particular factor has a greater impact on cognitive or brain resilience in men or [women](#)," remarks Arenaza-Urquijo.

Recommendations for future research

To improve our understanding of how sex and gender affect cognitive resilience to aging and Alzheimer's disease, the researchers recommend several directions for future studies. First, they stress the need to explore how sex and gender factors interact across cultures, taking into account the demographic, genetic, social and clinical differences that influence dementia risk.

They point out that sex/gender differences in brain characteristics, such as brain connectivity, remain understudied as [resilience](#) factors for Alzheimer's disease that may minimize the impact of pathologies on cognition.

The authors also argue that publishing negative results is crucial to avoid bias and that all studies should include sex-disaggregated results. Finally, they point out the importance of considering sex and gender in a non-binary way, and of including LGTBIQ+ populations, who are often underrepresented and face a higher burden of chronic disease.

More information: Eider M. Arenaza-Urquijo et al, Sex and gender

differences in cognitive resilience to aging and Alzheimer's disease, *Alzheimer's & Dementia* (2024). [DOI: 10.1002/alz.13844](https://doi.org/10.1002/alz.13844)

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