

# Sex and Gender Differences in Alzheimer's Disease

- Women are 2-3 times more likely to develop Alzheimer's disease (AD) than men. Increased risk of AD is likely due to estrogenic changes rather than longer survival.
- Clinical drug data stratified by sex is needed to elucidate differences in efficacy, dosing, and adverse effects as well as risk factors (i.e., blood, genetics, and neuroimaging biomarkers) in onset, progression, and treatment outcomes for women vs. men.
- Lifestyle behaviors (heart healthy diet, daily physical activity, social contact) may lessen cognitive decline in women more than men.
- Women are more likely to present with complaints of verbal memory loss and struggle with word recall rather than frustration with episodic memory. Neuropsychological testing is warranted in women who present with changes in cognitive function.
- Screening: Sex differences in women show more difficulty with language and confrontational naming tests. Women may also have greater difficulty with memory tests, particularly delayed recall of verbal information.
- Treatment: Differences in medication efficacy and adverse events by sex have not been fully evaluated. In one study, men showed 73% greater response to acetylcholinesterase inhibitor therapy than women. More research is needed.
- Prognosis: Sex differences can impact severity and prognosis of AD. Women have a faster rate of cognitive and functional decline and appear to face significantly greater cognitive impairment.
- Heritability is 60-80%. Strongest factor is Apolipoprotein E (ApoE). Each ApoE allele reduces the average age of symptom onset by a decade, except ApoE-e4 which increases risk in multiple pathways. Female carriers of ApoE-e4 are at greater risk than male carriers.
- Women have greater rates of autoimmune disease, which along with systemic inflammation, confers elevated risk for AD.
- Cardiorespiratory fitness is negatively associated with dementia mortality for both men and women, but women benefit less than men.
- Gender differences in spousal care are two-fold. Women tend to be the sole caregiver to their spouses and provide approximately twice the hours of care to that provided by men.

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