

## DEMENTIA

# Overweight or obesity during midlife is associated with late-life dementia

Being overweight or obese during midlife is associated with increased risk of dementia later in life, according to a Swedish twin study involving 8,534 individuals.

The findings relating to obesity, defined as BMI >30, have been shown in previous reports. However, “the effect of being overweight [BMI 25–30] during midlife on dementia is not well-established,” explains Weili Xu, who works at the Karolinska Institute in Stockholm and is the primary author of the study. “The life-course development of the adiposity–dementia association has been suggested, but the potential role of genetics and early life environments in the relationship had not been determined,” she adds.

Participants in the study were taken from the nationwide Swedish Twin Registry, and were ≥65 years (mean age 74.4 years). Their weight and height were documented 30 years previously as part of the registry, enabling their midlife

BMI to be calculated in the current study. An initial screening phase identified patients with cognitive dysfunction, who were then assessed by a nurse and a neurologist and diagnosed according to the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition* (DSM-IV). A total of 350 individuals (4.1%) were identified as having dementia, including 232 patients with Alzheimer disease (AD) and 74 patients with vascular dementia, which are the main dementia subtypes. An additional 114 participants were diagnosed with questionable dementia.

The researchers first performed an unmatched case–control analysis of all participants using statistical equations that are equivalent to logistic regression but also control for the clustering of twins within a given pair. They found that higher midlife BMI was associated with a significantly increased risk of all dementia, AD and vascular dementia. “This finding remained even after taking into account lifetime exposure to other vascular risk factors such as stroke and diabetes,” notes Rachel Whitmer, an epidemiologist at Kaiser Permanente, Oakland, California, USA, who was not involved in the study.

Being overweight during midlife was not as strongly associated with dementia as was obesity; nevertheless, the findings relating to being overweight could be of considerable importance given the increasing number of overweight adults worldwide. The results concerning vascular dementia should be interpreted with caution, however, owing to the small number of cases and consequently low statistical power of the BMI–vascular dementia analysis.

Next, Xu and colleagues performed a matched analysis of 137 dementia-discordant twin pairs (that is, excluding twin pairs in which neither or both twins had dementia). “Twins provide naturally matched pairs in which confounding effects of several potentially causal factors

are controlled for when comparisons are made,” explains Xu. “As such, twin studies involving a life-course approach can help to identify the role of genetic and environmental factors in the development of chronic disease.”

In contrast to the unmatched analysis, the twin-matched case–control analysis did not find a statistically significant association between a midlife BMI >25 and the risk of late-life dementia. That is, in a dementia-discordant twin pair—which controls for genetic and early life environmental factors—the BMI–dementia association was attenuated. These findings suggest that genetic and family environmental factors, such as childhood socioeconomic status, might affect the observed adiposity–dementia relationship.

“This is a well-done analysis of a large sample of twins,” comments Whitmer. “The study design allowed questions to be addressed regarding the association between adiposity and dementia risk over the long-term, taking into account the role of familial/genetic and environmental factors.”

“Our ongoing research is on the mechanisms linking these disorders,” says Xu. Candidate mechanisms include an altered inflammatory state accompanying a high BMI, which could contribute to impaired cognitive function and neurodegenerative processes. “Longer-term studies evaluating the role of risk factors over the life course on dementia are needed—particularly of risk factors that are modifiable, such as being overweight or obese,” says Whitmer. Such studies could inform the development of strategies to combat the growing health burden of dementia.

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**Original article** Xu, W. L. *et al.* Midlife overweight and obesity increase late-life dementia risk. *Neurology* 76, 1568–1574 (2011)

