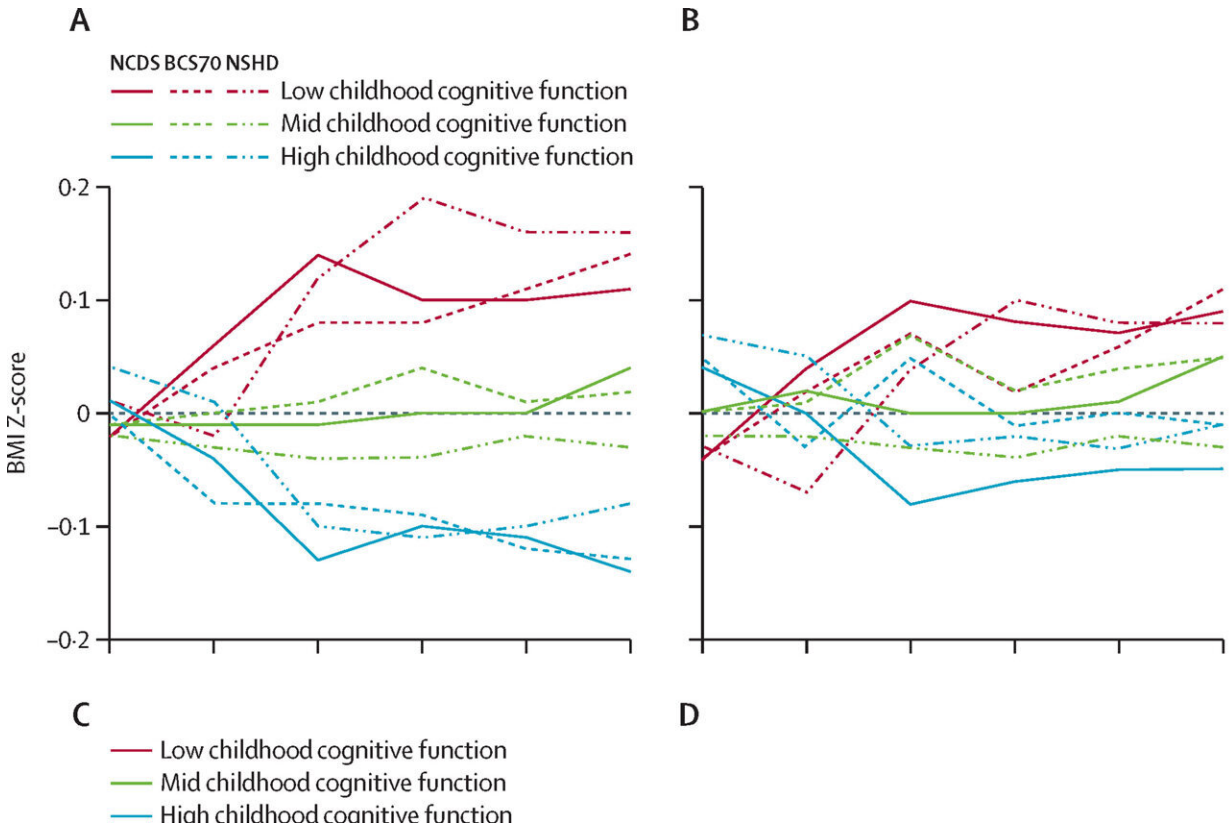
Does obesity really increase your risk of dementia?

April 30 2024, by Scott Chiesa



Early-life BMI trajectories categorized by tertiles of childhood cognitive function Simple line graphs connecting mean predicted values of BMI z-score at various ages across early life based on tertile of childhood cognitive function at age 10 years. Highest tertile of childhood cognitive function is indicated by blue lines, intermediate tertile is indicated by green lines, and lowest tertile is indicated by red lines. (A) NSHD, NCDS, and BCS70 adjusted for sex only. (B) NSHD, NCDS, and BCS70 adjusted for parents' BMI, child's birthweight, childhood socioeconomic status, and childhood household overcrowding. (C)

Pooled data from all three cohorts adjusted for sex. (D) Pooled data from all three cohorts adjusted for sex, parents' BMI, child's birthweight, childhood socioeconomic status, and childhood household overcrowding. Credit: *The Lancet Healthy Longevity* (2024). DOI: 10.1016/S2666-7568(24)00005-9

Many dementia charities advise people to maintain a healthy weight to reduce their risk of dementia. But some studies have suggested that obesity might actually protect against dementia. What does the science say?

The evidence linking obesity to dementia does at first appear to be convincing. For example, we know that being obese in middle age is associated with an increased risk of developing dementia in later life.

We also know that obesity damages the tiny vessels supplying blood to the brain, and is a major cause of high blood pressure, diabetes and chronic inflammation, all of which have been repeatedly linked to dementia risk.

However, the picture is not that clear. For example, if obesity really does cause dementia, why have dementia rates been falling in the west in recent decades at the same time as the number of obese people has been increasing? And why have several studies reported evidence of something termed an "obesity paradox," where being obese appears to be associated with a reduced risk of dementia?

Putting aside the longstanding problem of defining what we mean when we refer to obesity and dementia (both of which are relatively broad terms for conditions that can be defined in different ways), much of the difficulty in establishing whether one causes the other arises from limitations in the type of data available to scientists trying to answer this

question.

In an ideal world, we would look to test the question by designing a randomized trial. In this trial, thousands of people would be randomly assigned to an intervention that would result in half of them being obese for an extended period, while the other half are not.

If the obese people were then found to be more likely to have dementia in later life, we could be fairly confident that this must be the cause. These types of trials are rarely possible to conduct, however, as not only are they extremely time-consuming and expensive, they are unethical, too. (Imagine the outcry if you randomly assigned a group of people to purposefully be obese for an extended period of time.)

Most studies therefore rely on data from observational studies. This involves following a large group of people for a long time so that the long-term associations between obesity and dementia can be studied.

Although observational studies are a valuable resource for scientists, these studies can be plagued with biases that can often make it difficult to interpret the results.

One such bias relevant to dementia research is "reverse causation," particularly if the people being studied are old and the follow-up time is short. In this situation, it is possible that people already in the early stages of developing dementia when the study begins may lose weight over time as a result of the disease, rather than the other way around. This is what is suspected to underlie the obesity paradox.

Another common issue is "confounding bias." This is where the apparent link between obesity and dementia is caused by a different measure that is related to both. One such example is childhood intelligence, a factor that is rarely measured in observational studies, but, when available, has

been shown to potentially explain associations that could otherwise be blamed on obesity in later life.

For example, recent work from my lab published in *The Lancet Healthy Longevity*, using data from three separate groups, each followed for 50 years from birth, has shown that lower childhood intelligence probably explains why middle-aged people with obesity are often found to already have slightly worse cognitive skills than those with normal weight.

We found that although there was a clear association between higher levels of obesity and lower cognitive skills in midlife, this probably wasn't because one was causing the other.

Instead, it was likely because a third factor (childhood intelligence) was associated with both. That is, individuals with low intelligence in childhood not only had a higher risk of becoming obese as they grew up, but were also more likely to continue to be of lower intelligence (and therefore consistently have slightly worse cognitive skills).

Without knowing the intelligence levels of children in childhood, we may have interpreted this association between midlife obesity and cognitive skills as being one of cause and effect. In reality though, both are probably just a result of this third factor from earlier in the lifespan.

Nature's randomized trial

So how can we try to tackle these bias issues? One recent clever technique is to conduct something called a Mendelian randomization study—sometimes referred to as "nature's randomized trial."

In this type of study, scientists separate a large population into two groups based solely on whether or not they have a gene (or genes) that cause obesity. As these genes are randomly inherited from both parents,

this results in a "natural randomization" of the population into two groups who are collectively balanced for every factor except for their obesity status.

Although not without its own potential biases, any differences in dementia risk are therefore interpreted to be directly caused by this obesity.

At least ten studies have used this technique to test if obesity might cause Alzheimer's disease—the most common form of dementia. Only one has suggested a link between the two.

So, returning to the question: does obesity really increase your risk of dementia? As scientists like to say, an absence of evidence is not the same as evidence of absence. Or put another way, just because we don't yet have enough data yet to say that it does, it doesn't mean that it doesn't.

Science is an incremental process. In time, a clearer answer to this question will emerge as more data is collected and better techniques are developed.

Until then, my advice would be to follow the suggestion of dementia charities and try to maintain a healthy weight, anyway. At the very least, it will reduce your risk for a wide range of other major health problems, and it may even reduce your risk of dementia.

More information: Scott T Chiesa et al, Early-life cumulative exposure to excess bodyweight and midlife cognitive function: longitudinal analysis in three British birth cohorts, *The Lancet Healthy Longevity* (2024). DOI: 10.1016/S2666-7568(24)00005-9

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