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32 Changes in body mass and cognitive decline – disentangling a seeming paradox

- On average, women with a higher BMI perform cognitively worse than women with a lower BMI, but this is not true of men. However, the relation is non-monotonous: cognitive performance is highest for women at the lower end and men at the upper end of the normal weight range
- Individual changes in BMI over time are positively related to changes in cognitive performance. This association is driven by weight loss
- We find no evidence of a link between weight changes unrelated to illness and cognitive performance
- Our findings suggest that the obesity paradox in cognition results from disregarding (partially unobservable) factors that affect both BMI and cognition. Hence, any naïve interpretation of the obesity paradox ('a modest weight gain is beneficial') should be dispelled

32.1 The obesity paradox in cognition

According to the World Health Organization, the prevalence of obesity in later life has increased dramatically throughout the world, a trend that poses serious challenges to public health and healthcare systems. At the same time, obesity is a well-known risk factor for poorer health in later life. Obesity is related to several diseases, including diabetes mellitus, hypertension, cardiovascular diseases and mortality (Peeters et al., 2003). However, evidence also suggests that being overweight might actually be a protective factor against cardiovascular and all-cause mortality (Uretsky et al., 2007). This phenomenon is discussed in the literature as the obesity paradox or 'jolly fat'. First discussed against the background of cardiovascular diseases, the obesity paradox is now present in the literature with respect to different causes of mortality and with respect to cognitive decline.

Cross-sectional studies conclusively show that, for children and adults, obesity is positively associated with poorer cognitive performance; however, the relationship between obesity and cognition is less clear and more complex in the older population. In such populations, a higher body mass seems to

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preserve health, and extra weight appears to benefit cognition (Smith et al., 2011). Based on longitudinal data, Memel and colleagues (2016) find that, although an elevated initial BMI is detrimental to cognitive performance, *changes* in weight and cognitive performance are positively correlated. However, they do not account for diseases that might affect both weight loss and cognitive function. This issue raises the question of whether a higher BMI is truly protective against cognitive decline in old age or whether the obesity paradox in cognition is a mere artefact when taking into account relevant confounding variables. In other words: is being overweight in old age truly healthier or must the common naïve interpretation of the obesity paradox in cognition – that a (modest) weight gain is beneficial – be dispelled?

32.2 Possible explanations

The current literature measures obesity almost exclusively by BMI. Part of the obesity paradox could be the result of the fact that BMI is not informative about body composition. This lack of information is particularly important when observing the elderly because aging is accompanied by changes in body composition (sarcopenia), including an increase in fat mass and, at the same time, a decline in skeletal muscle mass (Ades and Savage, 2010). Thus, BMI might underestimate adiposity. To account for differences and changes in body composition, other measures might be better indicators, such as waist circumference or grip strength, as a measure of skeletal functioning muscle mass (Iliodromiti et al., 2018). Furthermore, weight loss and cognitive impairment may co-occur with other morbidities, particularly in older age. Thus, confounding health conditions might induce a spurious correlation between obesity and cognition. Moreover, the existing literature mostly lacks information on recent weight changes and whether weight changes were intentional or the result of chronic diseases.

Data from the Survey of Health, Ageing and Retirement in Europe (SHARE) can help mitigate these issues by providing a rich set of relevant longitudinal variables, including repeated measurements of isometric hand-grip strength. To that end, the obesity paradox in cognition could be disentangled and might disappear when the aforementioned problems are considered. Against this background, this chapter revisits the obesity paradox in cognition. After replicating the findings that people of higher BMI perform cognitively worse on average but BMI change is positively related to cognitive performance, we show that the latter is driven by weight loss and not by weight gain. We do not expect

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weight change to directly influence cognition. In fact, we suggest that the association between BMI and cognition is driven by unobserved confounding variables, such as severe diseases, leading to weight loss or a change in body composition and cognitive impairment. In line with this hypothesis, we find that a significant part of the association can be explained by controlling for severe diseases and that BMI change that is not the result of illness is unrelated to cognitive performance.

32.3 Data and method

The following analyses use longitudinal data from SHARE Waves 1, 2, 4, 5 and 6. Restricting the sample to respondents with non-missing information on all relevant measures leaves us with 195,046 observations. The data offer the possibility to both assess whether and how people with different levels of BMI differ in terms of cognitive performance (between-comparison) and study intra-individual change (within-comparison). We use fixed-effects and first-difference methods to assess whether a person experiencing a *change* in BMI also experiences a *change* in cognitive performance. These methods use each individual as his/her own control, alleviating the problem of unobserved individual characteristics related to the outcome, which would otherwise lead to biased results.

To measure respondents' cognitive performance, we created an index by adding the scores for immediate as well as delayed word recall and verbal fluency (see Memel et al., 2016). BMI is calculated as $\text{BMI} = \frac{\text{weight(kg)}}{\text{height(m)}^2}$ using self-reported weight and height after carefully correcting for obvious errors by utilizing the available information from all waves. To capture the difference between weight loss attributable to a reduction in body fat or muscle mass, we used respondents' grip strength as a proxy for unobserved conditions associated with a detrimental reduction in lean body mass. As possible confounders, that is, factors that might lead to (unintentional) weight loss *and* cognitive decline, we identified certain observed health conditions, namely, Parkinson's Disease, stroke, some types of (severe) cancer and dementia. We account for the possible enduring or cumulative effects of these conditions by adding the elapsed time since its first reporting. In our last model, we examine only respondents with self-reported weight loss who were asked for underlying reasons. Answers were collapsed into two categories that distinguish between reasons related to versus unrelated to illness. Finally, we include a quadratic function of age in our models to account for the fact that cognitive decline might accelerate with age. All models are calculated separately for women and men.

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32.4 Results

On average, a higher BMI in our sample is significantly associated with lower cognitive performance for women, but no such significant association exists for men. This relationship can be split in a within- and between-effect and is largely driven by the between-variation in the data. The latter is described in Figure 32.1, which illustrates the predicted cognition score over the BMI range using a piecewise linear specification (‘splines‘), taking into account that the relationship might be non-linear. The used cut-off points correspond to the WHO cut-offs for the BMI categories ‘underweight‘ (BMI<18.5), ‘normal weight‘ (18.5–24.9), ‘overweight‘ (25–29.9), ‘obesity class I‘ (30–34.9), ‘obesity class II‘ (35–39.9) and ‘obesity class III‘ (≥40).

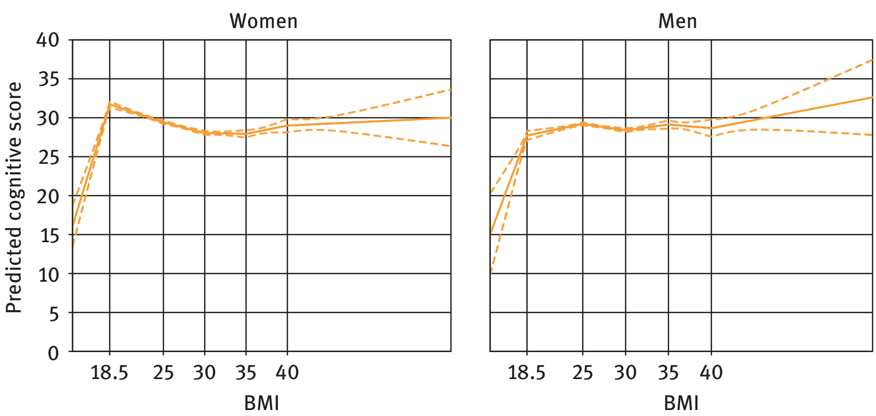

Figure 32.1: Cognition profiles over the BMI range (between-comparison).
Source: SHARE Wave 1– 6 release 6.0.0.

Figure 32.1 shows how the relationship between cognitive function and BMI score varies over BMI categories. For both sexes, the average (linear) association is driven by the BMI categories ‘normal‘ and ‘overweight’ because the majority of the respondents (approximately 80% of both women and men) belongs to these categories. Similar to the aforementioned average coefficients, the association is negative for normal weight and overweight women but is inversely U-shaped for men within this BMI range. In the ‘underweight‘ category, the association is in the opposite direction for both sexes: we observe lower cognitive function scores with lower BMI scores. Although only a few respondents were underweight, the association is strong and significant. For higher BMI categories (obesity classes

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I–III), although based on a larger number of respondents, no significant association can be found.

The picture looks different when investigating the within-effect of BMI changes (Figure 32.2). Here, an increase in BMI is associated with an overall increase in cognitive function for men and women. The relation is not linear but still fairly monotonous. No conclusion can be drawn for the highest obesity class III (i.e., BMI > 40) because estimates for the relating spline are rather imprecise.

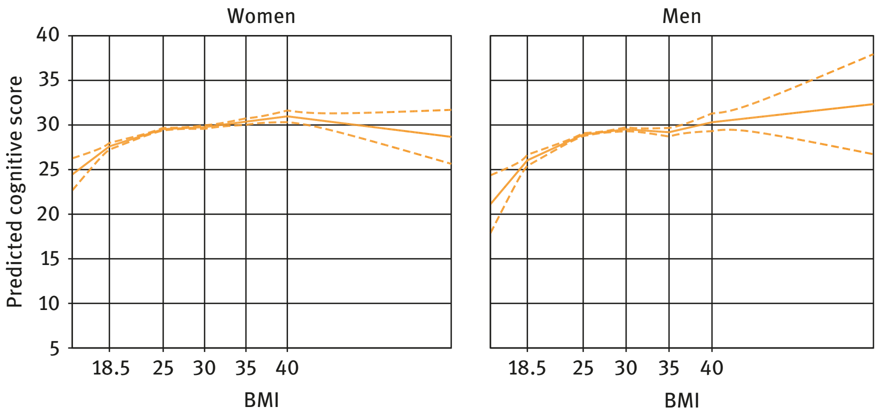

Figure 32.2: Cognition profiles over the BMI range (within-comparison).
Source: SHARE Wave 1–6 release 6.0.0.

As a shortcoming, the model forces the estimated function to be symmetric: an increase in BMI is assumed to promote cognitive performance by the same amount as a decrease reduces it. Because we hypothesize that this association (leading to the observed obesity paradox) is primarily driven by weight loss, we distinguish by the direction of the weight change between two consecutive waves ('first differences') in Figure 32.3. The first bar of each graph shows the regression coefficient for the BMI-score estimated in a model without further controls. Here, weight gain is not significantly correlated with changes in the cognition score, whereas weight loss is associated with cognitive decline. However, this association can be significantly reduced by adding possible confounders, such as age (second bar), grip strength (third bar) and the diseases previously described (fourth bar). The observed pattern holds for both genders but is stronger for men.

Although accounting for observed conditions significantly reduces the BMI-cognition association, it cannot completely explain this association. The

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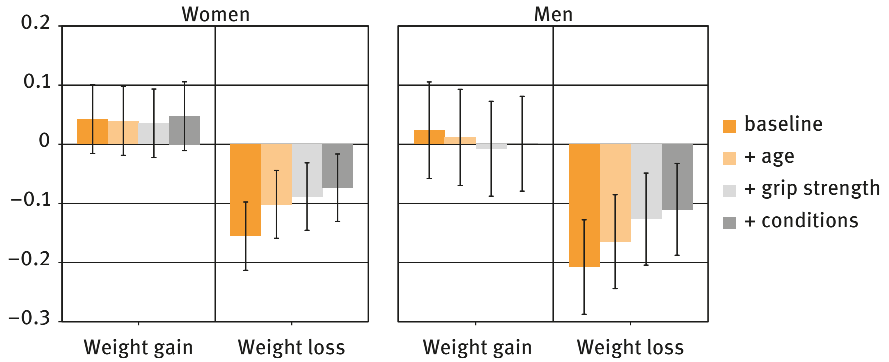

Figure 32.3: Effects of BMI gain vs. loss on change in cognition.
Source: SHARE Wave 1–6 release 6.0.0.

remaining correlation might, however, persist because the included confounders cannot be precisely measured. Other (undiagnosed or unreported) diseases might lead to weight loss and cognitive decline. Furthermore, the duration and severity of the included diseases may not be measured satisfactorily: even if we know when a disease was reported for the first time, we know neither when the diagnosis occurred nor when the actual onset of the disease took place. To address this concern, we include the self-reported reason for weight loss (Figure 32.4). Although not available for all cases, this information offers a straightforward approach to identifying (unintentional) weight loss attributable to illnesses as opposed to other reasons (e.g., physical activity or

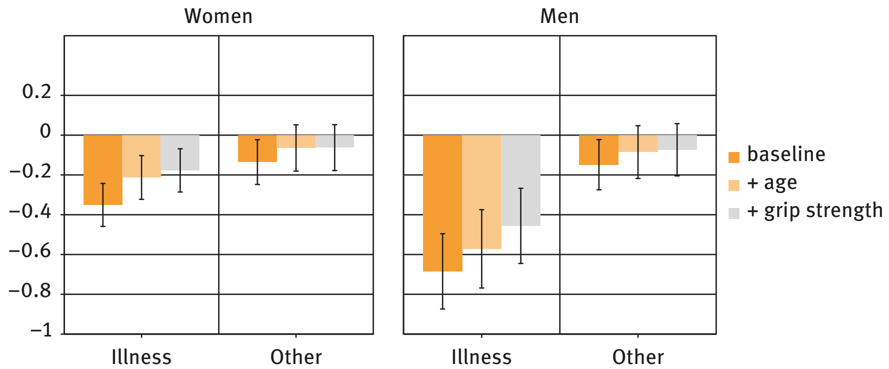

Figure 32.4: Effects of BMI decrease on change in cognition by reason for weight loss.
Source: SHARE Wave 1–6 release 6.0.0.

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diet). Again, we first ran a baseline model containing only the amount of weight loss and successively added age and grip strength.

In case of reasons for weight loss other than illness (right part of each box), the negative effect on cognition vanishes when controlling for age and grip strength. In contrast, the association between weight loss and cognitive decline is much stronger for respondents reporting an illness as a reason for losing weight and remains significant under all model specifications (left part of each box). Again, the pattern is stronger for men than for women.

32.5 Conclusion

Our results question previous findings that suggest that higher body mass becomes protective in older age and, hence, preserves health and cognition. Whereas recent studies also assume that BMI decrease is an indicator of cognitive decline in old age, we find no evidence for an adverse effect of weight loss unrelated to illness. Rather, the obesity paradox in cognition can be traced back to a spurious association attributable to partially unobserved health conditions affecting both body weight and cognitive performance.

Although the within-estimators used in our analyses do not suffer from attrition of respondents with certain (time-constant) cognitive predispositions, selective drop out given omitted time-varying variables could potentially distort our findings. However, additional tests (not shown) do not reveal a substantial bias in our estimates for BMI decrease resulting from selective attrition and, thus, do not challenge our general findings.

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