Different adiposity measures across sex, age, ethnicity, and COVID-19

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Abstract
We examined the link between several adiposity measures – BMI, fat mass, body fat
percentage, fat mass index, waist and waist to hip ratio) taken at baseline visits over a
decade ago to risk for COVID-19 positive tests that occurred in hospital in the UK biobank.
Overall, 793 participants tested positive in a hospital setting out of 380,976 participants.
Poisson models with penalised thin plate splines were run relating exposures of interest to
positive tests in hospital, adjusting for confounding factors. Each measure of adiposity was
associated strongly with positive in-hospital test, in a broadly linear fashion, despite the
model allowing for non-linear associations. There was a stronger gradient of risk across BMI
(P_interaction=0.09) and fat-mass index (P_interaction=0.048) in men compared with women.
Compared to a referent of 21 kg/m², men with BMI of 30 kg/m² (RR 2.08 95% CI 1.84-2.36)
and 35 kg/m² (RR 2.80, 95% CI 2.36-3.31) were at higher risk; corresponding RRs for women
were 1.36 (95% CI 1.49-1.63) and 1.86 (95% CI 1.59-2.17). The associations between BMI
and COVID-19 were largely consistent by age group and ethnicity. These data add further
support for linear links between excess body fat and more severe COVID-19 outcomes
across differing groups.

NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
We recently proposed multiple mechanisms by which obesity/ectopic fat might enhance risk for severe COVID-19.\(^1\) Our work was stimulated by observations in hospital intensive care units which showed that body mass indices (BMI) above 35 or 40 were associated with poorer prognosis.\(^2,3\) However, whether BMI is linearly related to risk in both sexes, in different ethnicities, ages, and different adiposity measures show similar patterns, is not well known. To address these issues, we used UK Biobank data to link different adiposity measures with confirmed SAR-CoV-2 infection in hospital; a measure of more severe COVID-19.

Over 500,000 participants (aged 50-81 on 16\(^{th}\) March 2020) from the UK general population were recruited between 2006-2010, with details described elsewhere. For this study, only participants from English assessment centres were included; we excluded all participants who had died prior to the SARS-CoV-2 pandemic (available up to January 2018). Participants with complete data for baseline anthropometric variables and covariates were included (n=381,320). Exposures of interest were BMI, waist circumference, waist-hip ratio, body fat mass, body fat proportion, and fat mass index from bioimpedance. Public Health England (PHE) provided the SARS-CoV-2 test data, including the specimen date, location, and result. Data were available for the period 16\(^{th}\) March 2020 to 18\(^{th}\) May 2020. Tests were conducted on 3,906 participants in the available cohort. Of these, 344 were excluded because the tests were conducted outside hospital suggesting less severe disease. Overall, 793 participants tested positive in a hospital setting out of 380,976 participants.

Robust Poisson models with penalised thin plate splines were run relating exposures of interest to positive tests in hospital. Model were adjusted for age, socioeconomic deprivation (Townsend Index), ethnicity, smoking (current, former, never), alcohol intake (unit/week), and baseline cardiovascular disease and diabetes. Interactions between adiposity measures and four moderators (sex, current age [<70 vs ≥70], and ethnicity [white vs non-white], were tested.

Each measure of adiposity was associated strongly with positive in-hospital test, in a broadly linear fashion (Figure 1 a-f), despite the model allowing for non-linear associations. There was a stronger gradient of risk across BMI (\(P_{\text{interaction}}=0.09\)) and fat-mass index (\(P_{\text{interaction}}=0.048\)) in men compared with women. Compared to a referent of 21 kg/m\(^2\), men with BMI of 30 kg/m\(^2\) (RR 2.08 95% CI 1.84-2.36) and 35 kg/m\(^2\) (RR 2.80, 95% CI 2.36-3.31) were at higher risk; corresponding RRs for women were 1.36 (95% CI 1.49-1.63) and 1.86 (95% CI 1.59-2.17).

The associations between BMI and COVID-19 were largely consistent by age group (Figure 1g) and ethnicity (Figure 1h). The associations of all other adiposity markers were also consistent between white and non-white ethnicity, but some age-associated interactions were evident with regional measures more strongly associated with risks in older people, and fat mass more strongly associated in younger individuals (data on request).

Our findings have some limitations. Only a small percentage of participants were tested but narrow confidence intervals provide reassurance that the associations are broadly linear. Those untested, as well as those tested negative, were grouped together in the analysis on the assumption that those tested in hospital were more likely to have severe disease.
Baseline anthropometric/adiposity measures were collected 10-12 years before COVID-19 positivity was gathered. As BMI levels generally track over time, these results are likely as valid as adiposity measures taken in the year prior to the pandemic. Whilst we adjusted for deprivation, individuals with higher weights may be more likely to be exposed to virus. However, as excess fat can impair lung function, impairs metabolic and inflammatory pathways, stresses cardiorenal systems, and thrombotic responses, our findings likely represent some causal elements. It is also possible that the link between adiposity and severer reactions to SARS-CoV-2. E.g. necessitating mechanical ventilation, may be stronger. More research is needed to explore this potential.

Currently the UK government advises people with BMI>40 to be more stringent at adhering to non-pharmaceutical interventions (i.e. physical distancing, hand hygiene etc). Our results suggest that there is no evidence of a threshold effect at BMI=40, and that women and men with the same BMI may have different levels of risk. If such findings can be replicated, sex-specific cut-offs (e.g. BMI>40 in women and BMI>30 in men) should be considered.

In the meantime, when taken into context with other emerging data, our results, support the need for public health campaigns to help and support men and women with overweight or obesity across different ethnic groups to lessen their chances of severe COVID-19 responses by losing weight. Whilst we lack trial evidence to prove weight loss lowers risks, there are many additional benefits of weight loss, including improved cardiorespiratory fitness and quality of life. We recognise that not all individuals are able to lose weight via lifestyle changes; some may require drug therapies, if even temporarily, to help lower risk.

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Figure 1. Associations of differing adiposity measures with COVID-19 confirmed in hospital by sex (panels a to f), and BMI associations by age (panel g) and by ethnicity (panel h).