Author/s:
Bui, DS;Cassim, R;Russell, MA;Doherty, A;Lowe, AJ;Agusti, A;Dharmage, SC;Lodge, CJ

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Lung Function Levels Influence the Association between Obesity and Risk of COVID-19

To the Editor:

Obesity is associated with immune suppression and may be associated with increased risk of coronavirus disease (COVID-19) (1). This association may be modified by factors such as lung function (2–4). We explored here the association between obesity and COVID-19 in relation to the underlying lung function strata. To our knowledge, this possible interaction has not been investigated to date.

We investigated the association between obesity and risk of a positive severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) test and how lung function levels influenced this association in 36,896 participants in the UK Biobank tested for SARS-CoV-2 (5). The UK Biobank study recruited 502,543 participants aged 40–69 years living close to one of 22 assessment centers across England, Scotland, and Wales, between March 2006 and July 2010; however, data on SARS-CoV-2 test results (for the period of March 16 to November 24, 2020) derives from the English subgroup alone. Body mass index (BMI) at recruitment (baseline) was used to define normal (BMI $<$ 25), overweight (25 $\leqslant$ BMI $<$ 30), and obese (BMI $\geqslant$ 30) groups. FEV_1, FVC, and their ratio at baseline were categorized using the median and quartiles (of their *z*-score values). Multivariable logistic regression models were generated to investigate the association of obesity with SARS-CoV-2 positivity adjusting for age, sex, smoking, socioeconomic status (Townsend index), diabetes, cardiovascular disease, physical activity, and ethnicity. Stratified analyses for lung function levels and formal interaction tests to investigate potential effect modification were conducted.

Of the 36,896 participants tested (mean age 69.3 $\pm$ 8.3 years), 5,757 were positive for SARS-CoV-2. Characteristics of those who tested positive and those who tested negative are shown in Table 1.

Table 1. Characteristics of Those Tested Positive and Those Tested Negative

	Negative Test Result (*n* = 31,139)	Positive Test Result (*n* = 5,757)
Age, mean (SD), yr		
At recruitment*	58.04 (8.01)	54.31 (8.84)
At SARS-CoV-2 test*	69.18 (8.03)	65.34 (8.82)
Sex*, n (%)		
F	16,549 (53)	2,871 (50)
M	14,590 (47)	2,886 (50)
Ethnicity*, *n* (%)		
White	29,102 (93)	5,247 (91)
Mixed	188 (1)	41 (1)
Asian	767 (2)	243 (4)
Black	579 (2)	137 (2)
Other ethnic background	428 (1)	81 (1)
Household income*, *n* (%)		
$<$18,000	6,888 (22)	1,279 (22)
18,000–30,999	6,610 (21)	1,147 (20)
31,000–51,999	6,335 (20)	1,332 (23)
52,000–100,000	4,774 (15)	944 (16)
$>$100,000	1,477 (5)	229 (4)
Education*, *n* (%)		
None of the following	302 (1)	74 (1)
College or university degree	9,038 (29)	1,339 (23)
A levels or AS levels or equivalent	3,164 (10)	527 (9)
O levels or GCSEs or equivalent	6,468 (21)	1,243 (21)
CSEs or equivalent	1,528 (5)	495 (9)
NVQ, HND, HNC, or equivalent	2,205 (7)	471 (8)
Other professional qualifications	1,800 (6)	277 (5)
Smoking history, *n* (%)		
Never	15,636 (50)	2,928 (51)
Past	11,732 (38)	2,148 (37)
Current	3,522 (11)	641 (11)
Smoking pack-years, median (IQR)	20.70 (10.88–34.38)	21.00 (11.45–34.00)
BMI, kg/m^2, mean (SD)*	27.99 (5.04)	28.41 (5.03)

Definition of abbreviations: A = advanced; AS = advanced subsidiary; BMI = body mass index; CSE = Certificate of Secondary Education; GCSE = General Certificate of Secondary Education; HNC = Higher National Certificate; HND = Higher National Diploma; IQR = interquartile range; NVQ = National Vocational Qualification; O = ordinary; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
*$P < 0.05$.

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The prevalence of overweight and obesity were 42.3% and 29.0%, respectively. Compared with normal weight, both overweight (odds ratio [OR], 1.20; 95% confidence interval [CI], 1.12–1.30) and obesity (OR, 1.31; 95% CI, 1.21–1.42) were associated with increased risk of testing positive for SARS-CoV-2, with the risk being greater in those who were obese than in those who were overweight ($P = 0.017$). The association between obesity and SARS-CoV-2 positivity was stronger in those with FEV_1 below the median (OR, 1.48; 95% CI, 1.29–1.71) than in those with FEV_1 above the median (OR, 1.22; 95% CI, 1.07–1.38; P for interaction = 0.02). The interaction was also stronger for FVC below the median (OR, 1.47; 95% CI, 1.28–1.69) compared with FVC above the median (OR, 1.28; 95% CI, 1.12–1.46; P for interaction = 0.002). Similar patterns were observed when stratifying the association between obesity and SARS-CoV-2 positivity by quartiles of lung function (both FEV_1 and FVC) (Table 2). We also observed significant interactions when FEV_1 and FVC were modeled as continuous variables (P-interaction = 0.01 and 0.008, respectively). For overweight, the association appeared to be weaker among the poor lung function group, but this difference was not significant (P-interaction = 0.7 and 0.14 for FEV_1 and FVC). Findings were similar when those with BMI <18.5 were excluded from the reference group (results not shown). When we investigated obesity class 1 ($30 \leq$ BMI $<$ 35) and obesity class 2+ (BMI $\geqslant$ 35) separately, the associations for risk of testing positive for SARS-CoV-2 were similar (OR, 1.31 [95% CI, 1.2–1.43] vs. 1.30 [95% CI, 1.15–1.44]). When underweight (BMI $<$ 18.5) was investigated as a separate group, it was associated with reduced risk of testing positive for SARS-CoV-2 (OR, 0.53; 95% CI, 0.30–0.95). We were unable to stratify the analysis for lung function owing to the small sample size.

An early analysis of a smaller sample ($n = 2{,}494$) of the UK Biobank study suggested associations between overweight and obesity and SARS-CoV-2 test positivity (2). Other analyses ($n = 4{,}855$ and 5,623) of the same cohort assessed the interaction between obesity and ethnicity (3, 4). We now confirm the association between obesity and SARS-CoV-2 test positivity in a much larger sample ($n = 36{,}896$).

In addition to this, we found that the association between obesity and SARS-CoV-2 was modified by lung function. Although both obesity and low lung function have been shown to increase risk of testing positive for SARS-CoV-2 independently, we observed that these two factors interact to multiplicatively increase risk of SARS-CoV-2 test positivity. Therefore, risk for SARS-CoV-2 test positivity was higher among individuals who were obese who also have low lung function compared with individuals who were obese with normal lung function.

Interestingly, we found that underweight was associated with reduced risk of testing positive for SARS-CoV-2. This association has not been previously reported. However, among those infected with SARS-CoV-2, underweight may be associated with more severe outcomes (6). This discrepancy regarding risk of testing positive and disease severity in relation to underweight needs to be further investigated. The underlying mechanism for the protective effect of being underweight in our study is not known, but an explanation could be underweight individuals are more likely to have chronic health conditions, diet heavily, and take extra precautions to reduce the risk of contracting the virus.

Table 2. Association between Obesity and Risk of a Positive Test for SARS-CoV-2 Stratified by Lung Function Levels

	Obesity Status	
Effect Modifiers	**Overweight (25 ⩽ BMI < 30), Compared with Normal (BMI < 25)**	**Obese (BMI ⩾ 30) Compared with Normal (BMI < 25)**
Strata of FEV_1		
Less than median	1.17 (1.04–1.32)*	1.48 (1.29–1.71)†
Greater than median	1.21 (1.07–1.37)*	1.22 (1.07–1.38)*
P-interaction = 0.02‡		
Strata of FVC		
Less than median	1.12 (1.00–1.26)§	1.47 (1.28–1.69)†
Greater than median	1.28 (1.13–1.45)†	1.28 (1.12–1.46)†
P-interaction = 0.002‖		
Strata of FEV_1/FVC		
Less than median	1.22 (1.07–1.39)*	1.41 (1.22–1.62)†
Greater than median	1.20 (1.07–1.35)*	1.29 (1.13–1.48)†
P-interaction = 0.65		
Strata of FEV_1		
Q1 (lowest)	1.09 (0.93–1.29)	1.53 (1.26–1.86)†
Q2	1.27 (1.07–1.51)*	1.46 (1.20–1.78)†
Q3	1.12 (0.95–1.33)	1.23 (1.03–1.48)§
Q4	1.33 (1.12–1.58)*	1.26 (1.05–1.51)§
P-interaction = 0.03		
Strata of FVC		
Q1	1.10 (0.95–1.29)	1.41 (1.15–1.72)*
Q2	1.16 (0.98–1.38)	1.56 (1.29–1.90)†
Q3	1.25 (1.05–1.49)§	1.29 (1.07–1.56)*
Q4	1.34 (1.12–1.61)*	1.29 (1.07–1.56)*
P-interaction = 0.01		
Strata of FEV_1/FVC		
Q1	1.16 (0.96–1.40)	1.44 (1.18–1.75)†
Q2	1.32 (1.10–1.58)*	1.43 (1.17–1.73)†
Q3	1.25 (1.06–1.47)*	1.27 (1.05–1.53)§
Q4	1.19 (1.02–1.39)§	1.37 (1.14–1.64)*
P-interaction = 0.67		

Definition of abbreviations: BMI = body mass index; CI = confidence interval; OR = odds ratio; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
Data are shown as OR (95% CI).
*$P < 0.01$.
†$P < 0.001$.
‡P value = 0.02 for an overall interaction obtained from the likelihood ratio test with specific P values for interaction terms for overweight and obese of 0.7 and 0.03, respectively.
§$P < 0.05$.
‖P value = 0.002 for an overall interaction obtained from the likelihood ratio test with specific P values for interaction terms for overweight and obese of 0.14 and 0.06, respectively.

Our study has some limitations. As this analysis was based on the tested subsample of UK Biobank, it may be prone to some degree of bias (7). In fact, those included in this analysis had a slightly higher prevalence of obesity compared with the whole cohort (29.0% vs. 24.4%), but we postulate that this issue is unlikely to explain the association found in this study, as we are investigating among obese groups whether lung function modifies risk of SARS-CoV-2 test positivity. Moreover, those included in this analysis and the whole cohort had similar demographic characteristics (Table 3).

In conclusion, our study found that obesity interacts with low lung function to increase risk of testing positive for SARS-CoV-2

Table 3. Characteristics of Those Included in This Analysis and the Original Cohort

	UK Biobank Whole Cohort (*N* = 502,505)	UK Biobank with SARS-CoV-2 Test Data (*n* = 36,896)
Age, mean (SD), yr		
At recruitment	56.3 (8.10)	57.46 (8.25)
At SARS-CoV-2 test	—	68.58 (8.28)
Sex, *n* (%)		
F	273,382 (54)	19,420 (53)
M	229,122 (46)	17,476 (47)
Ethnicity, *n* (%)		
White	472,695 (94)	34,349 (93)
Mixed	2,958 (1)	229 (1)
Asian	11,456 (2)	1,010 (3)
Black	8,061 (2)	716 (2)
Other ethnic background	6,436 (1)	509 (1)
Household income, *n* (%)		
<18,000	95,018 (19)	8,167 (22)
18,000–30,999	107,955 (21)	7,757 (21)
31,000–51,999	112,197 (22)	7,667 (21)
52,000–100,000	89,332 (18)	5,718 (15)
>100,000	24,642 (5)	1,706 (5)
Education, *n* (%)		
None of the following	4,448 (1)	376 (1)
College or university degree	162,715 (32)	10,377 (28)
A levels or AS levels or equivalent	54,986 (11)	3,691 (10)
O levels or GCSEs or equivalent	104,598 (21)	7,711 (21)
CSEs or equivalent	26,703 (5)	2,023 (5)
NVQ, HND, HNC, or equivalent	33,021 (7)	2,676 (7)
Other professional qualifications	25,971 (5)	2,077 (7)
Smoking history, *n* (%)		
Never	273,552 (54)	18,564 (50)
Past	173,056 (34)	13,880 (38)
Current	52,978 (10)	4,163 (11)
Smoking pack-years, median (IQR)	19.00 (10.00–32.00)	21.00 (11.00–34.13)
BMI, kg/m^2, mean (SD)	27.43 (4.80)	28.05 (5.04)

For definition of abbreviations, *see* Table 1.

infection. Our findings suggest that individuals with poor lung function, particularly individuals who are obese, should be encouraged to take extra precautions to reduce the risk of acquiring this disease. In the short term, this may include adhering strictly to mask and social distancing mandates and practicing good hand hygiene to mitigate risk as the pandemic continues. ■

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Dinh S. Bui, B.Pharm., M.P.H., Ph.D.*
Raisa Cassim, B.Sc., M.Sc., Ph.D.*
Melissa A. Russell, B.Phys., Ph.D.
Alice Doherty, B.Sc., M.Sc.
Adrian J. Lowe, B.B.Sc., M.P.H., Ph.D.
The University of Melbourne
Melbourne, Victoria, Australia

Alvar Agusti, M.D., Ph.D.
Centro de Investigación Biomédica en Red Enfermedades Respiratorias (CIBERES)
Madrid, Spain

Institut d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS)
Barcelona, Spain

Respiratory Institute
Barcelona, Spain
and
University of Barcelona
Barcelona, Spain

Shyamali C. Dharmage, M.D., Ph.D.‡
Caroline J. Lodge, M.B.B.S., Ph.D.‡§
The University of Melbourne
Melbourne, Victoria, Australia

ORCID IDs: 0000-0002-4388-784X (D.S.B.); 0000-0002-3422-3726 (M.A.R.); 0000-0002-4691-8162 (A.J.L.); 0000-0001-6063-1937 (S.C.D.); 0000-0002-2342-3888 (C.J.L.).

*Equal first authors.
‡Equal senior authors.
§Corresponding author (e-mail: clodge@unimelb.edu.au).

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