

Metabolic Healthy Obesity, Vitamin D Status, and Risk of COVID-19

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Supplementary Text.

Definitions of metabolic health using the cutoff points of specific metabolic syndrome components and waist circumference.

1. Under our definition of metabolic health using the cutoff points of specific metabolic syndrome components, participants having less than two of the four criteria were considered to be metabolic health¹, as follows: (1) normal triglyceride concentrations, defined as triglycerides <1.7 mmol/L (<150 mg/dL) and not on drug treatment for elevated triglyceride concentration at baseline; (2) normal high-density lipoprotein cholesterol (HDL-c) concentrations, defined as ≥ 1.05 mmol/L (40 mg/dL) for men and ≥ 1.25 mmol/L (50 mg/dL) for women; (3) normal blood pressure (BP), defined as a systolic BP <130 and a diastolic BP <85 mmHg, and not on antihypertensive drug treatment at baseline; (4) normal fasting glucose, defined as fasting blood glucose <5.6 mmol/L (100 mg/dL) and not on drug treatment at baseline.

2. Under our definition of metabolic health using the cutoff points of specific metabolic syndrome components plus waist circumference, participants having less than three of the five criteria were considered to be metabolic health, as follows: (1) normal triglyceride concentrations, defined as triglycerides <1.7 mmol/L (<150 mg/dL) and not on drug treatment for elevated triglyceride concentration at baseline; (2) normal high-density lipoprotein cholesterol (HDL-c) concentrations, defined as ≥ 1.05 mmol/L (40 mg/dL) for men and ≥ 1.25 mmol/L (50 mg/dL) for women; (3) normal blood pressure (BP), defined as a systolic BP <130 and a diastolic BP <85 mmHg, and not on antihypertensive drug treatment at baseline; (4) normal fasting glucose, defined as fasting blood glucose <5.6 mmol/L (100 mg/dL) and not on drug treatment at baseline; (5) waist circumference (WC), defined as WC <102 cm in men and <88 cm in women.

Reference

[1] Stefan N, Häring HU, Schulze MB. Metabolically healthy obesity: the low-hanging fruit in obesity treatment? *Lancet Diabetes Endocrinol.* 2018;6(3):249-258.

Supplementary Table 1. The associations of metabolic/obesity phenotypes with COVID-19 outcomes.

| Characteristics | Model 1 [†] | | Model 2 [‡] | |
|-------------------------------------|----------------------|---------|----------------------|---------|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| COVID-19 hospitalization | | | | |
| Metabolic/obesity phenotypes | | | | |
| MHNW | 1 (Ref.) | | 1 (Ref.) | |
| MHOW | 1.15 (1.03, 1.27) | 0.010 | 1.13 (1.01, 1.25) | 0.026 |
| MHO | 1.37 (1.21, 1.56) | <0.001 | 1.28 (1.13, 1.46) | <0.001 |
| MUHNW | 1.29 (1.11, 1.50) | 0.001 | 1.21 (1.04, 1.41) | 0.013 |
| MUHOW | 1.52 (1.36, 1.71) | <0.001 | 1.40 (1.25, 1.57) | <0.001 |
| MUHO | 2.24 (2.01, 2.50) | <0.001 | 1.96 (1.75, 2.19) | <0.001 |
| Confirmed COVID-19 | | | | |
| Metabolic/obesity phenotypes | | | | |
| MHNW | 1 (Ref.) | | 1 (Ref.) | |
| MHOW | 1.37 (1.14, 1.65) | 0.001 | 1.29 (1.08, 1.56) | 0.006 |
| MHO | 1.63 (1.31, 2.02) | <0.001 | 1.42 (1.14, 1.76) | 0.002 |
| MUHNW | 1.63 (1.24, 2.14) | <0.001 | 1.44 (1.10, 1.90) | 0.009 |
| MUHOW | 1.73 (1.41, 2.14) | <0.001 | 1.47 (1.18, 1.81) | <0.001 |
| MUHO | 2.32 (1.89, 2.84) | <0.001 | 1.83 (1.49, 2.25) | <0.001 |
| Severe COVID-19 | | | | |
| Metabolic/obesity phenotypes | | | | |
| MHNW | 1 (Ref.) | | 1 (Ref.) | |
| MHOW | 1.39 (1.10, 1.77) | 0.006 | 1.32 (1.04, 1.67) | 0.022 |
| MHO | 1.72 (1.31, 2.27) | <0.001 | 1.50 (1.14, 1.98) | 0.004 |
| MUHNW | 1.73 (1.24, 2.41) | 0.001 | 1.51 (1.08, 2.11) | 0.015 |
| MUHOW | 1.92 (1.48, 2.48) | <0.001 | 1.61 (1.24, 2.09) | <0.001 |
| MUHO | 2.48 (1.92, 3.19) | <0.001 | 1.94 (1.50, 2.50) | <0.001 |

[†]Adjusted for sex, age. [‡]Adjusted for sex, age, Townsend deprivation index, qualifications, employment, ethnicity, and smoking status. Abbreviations: COVID-19, Coronavirus Disease 2019; CI, confidence interval; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obesity; MHOW, metabolically healthy overweight; MUHNW, metabolically unhealthy normal weight; MUHO, metabolically unhealthy obesity; MUHOW, metabolically unhealthy overweight; OR, odds ratio.

Supplementary Table 2. The associations of vitamin D status with COVID-19 outcomes.

| Characteristics | Model 1 [†] | | Model 2 [‡] | |
|---------------------------------------|----------------------|---------|----------------------|---------|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| COVID-19 hospitalization | | | | |
| Vitamin D status | | | | |
| Vitamin D concentration (nmol/L) | 0.993 (0.991, 0.994) | <0.001 | 0.996 (0.994, 0.997) | <0.001 |
| Vitamin D deficiency (< 25 nmol/L) | 1.500 (1.370, 1.643) | <0.001 | 1.292 (1.175, 1.420) | <0.001 |
| Vitamin D insufficiency (< 50 nmol/L) | 1.337 (1.249, 1.431) | <0.001 | 1.214 (1.132, 1.303) | <0.001 |
| Confirmed COVID-19 | | | | |
| Vitamin D status | | | | |
| Vitamin D concentration (nmol/L) | 0.992 (0.990, 0.995) | <0.001 | 0.997 (0.994, 1.000) | 0.039 |
| Vitamin D deficiency (< 25 nmol/L) | 1.388 (1.180, 1.632) | <0.001 | 1.090 (0.919, 1.294) | 0.321 |
| Vitamin D insufficiency (< 50 nmol/L) | 1.381 (1.221, 1.562) | <0.001 | 1.204 (1.059, 1.368) | 0.005 |
| Severe COVID-19 | | | | |
| Vitamin D status | | | | |
| Vitamin D concentration (nmol/L) | 0.992 (0.988, 0.995) | <0.001 | 0.997 (0.993, 1.000) | 0.088 |
| Vitamin D deficiency (< 25 nmol/L) | 1.604 (1.322, 1.946) | <0.001 | 1.227 (1.000, 1.505) | 0.050 |
| Vitamin D insufficiency (< 50 nmol/L) | 1.413 (1.214, 1.644) | <0.001 | 1.206 (1.030, 1.412) | 0.020 |

[†]Adjusted for sex, age. [‡]Adjusted for sex, age, Townsend deprivation index, qualifications, employment, ethnicity, smoking status, and metabolic/obesity phenotypes. Abbreviations: COVID-19, Coronavirus Disease 2019; CI, confidence interval; OR, odds ratio.

Supplementary Table 3. Joint associations of metabolic/obesity phenotypes and vitamin D status with COVID-19 outcomes using the cutoff points of specific metabolic syndrome components as the definition of metabolic health.

| Characteristics | Vitamin D deficiency (< 25 nmol/L) | | | | | | Vitamin D insufficiency (< 50 nmol/L) | | | | | |
|---------------------------------|------------------------------------|--------|---------|--------------------------|--------|---------|---------------------------------------|--------|---------|--------------------------|--------|---------|
| | No | | | Yes | | | No | | | Yes | | |
| | OR (95% CI) [†] | 95% CI | P-value | OR (95% CI) [†] | 95% CI | P-value | OR (95% CI) [†] | 95% CI | P-value | OR (95% CI) [†] | 95% CI | P-value |
| COVID-19 hospitalization | | | | | | | | | | | | |
| | 1 (Ref.) | | | 1.25 (0.87, 1.79) | 0.233 | | 1 (Ref.) | | | 1.28 (1.00, 1.63) | 0.046 | |
| MHNW | 1.30 (1.08, 1.56) | 0.005 | | 1.50 (1.04, 2.14) | 0.028 | | 1.30 (1.01, 1.67) | 0.041 | | 1.60 (1.26, 2.03) | <0.001 | |
| MHOW | 1.22 (0.95, 1.57) | 0.122 | | 1.91 (1.27, 2.85) | 0.002 | | 1.10 (0.74, 1.64) | 0.648 | | 1.68 (1.27, 2.23) | <0.001 | |
| MHO | 0.93 (0.79, 1.09) | 0.383 | | 1.11 (0.85, 1.46) | 0.438 | | 0.96 (0.77, 1.19) | 0.688 | | 1.14 (0.92, 1.42) | 0.215 | |
| MUHNW | 1.05 (0.91, 1.22) | 0.507 | | 1.34 (1.09, 1.66) | 0.006 | | 1.10 (0.90, 1.34) | 0.348 | | 1.27 (1.05, 1.55) | 0.015 | |
| MUHOW | 1.44 (1.24, 1.68) | <0.001 | 1 | 1.98 (1.64, 2.39) | <0.001 | 1 | 1.45 (1.17, 1.79) | 0.001 | | 1.82 (1.50, 2.21) | <0.001 | 1 |
| Confirmed COVID-19 | | | | | | | | | | | | |
| | 1 (Ref.) | | | 0.79 (0.39, 1.57) | 0.495 | | 1 (Ref.) | | | 0.98 (0.64, 1.49) | 0.914 | |
| MHNW | 1.49 (1.10, 2.01) | 0.009 | | 1.25 (0.69, 2.26) | 0.465 | | 1.39 (0.92, 2.11) | 0.114 | | 1.55 (1.05, 2.28) | 0.028 | |
| MHOW | 1.31 (0.87, 1.96) | 0.202 | | 0.76 (0.30, 1.88) | 0.545 | | 0.88 (0.43, 1.80) | 0.725 | | 1.38 (0.86, 2.21) | 0.183 | |
| MHO | 0.95 (0.71, 1.26) | 0.704 | | 1.19 (0.75, 1.88) | 0.458 | | 0.89 (0.61, 1.30) | 0.550 | | 1.09 (0.75, 1.56) | 0.660 | |
| MUHNW | 1.08 (0.84, 1.40) | 0.545 | | 1.10 (0.75, 1.60) | 0.630 | | 1.04 (0.74, 1.46) | 0.826 | | 1.14 (0.82, 1.59) | 0.436 | |

| | | | | | | | | | |
|------------------------|-------------------|-------|-------------------|--------|-------------------|-------|-------------------|-------|--|
| MUHO | 1.33 (1.02, 1.74) | 0.035 | 1.80 (1.30, 2.51) | <0.001 | 1.11 (0.76, 1.62) | 0.580 | 1.60 (1.15, 2.22) | 0.005 | |
| Severe COVID-19 | | | | | | | | | |
| MHNL | 1 (Ref.) | | 0.60 (0.22, 1.68) | 0.335 | 1 (Ref.) | | 0.88 (0.50, 1.54) | 0.660 | |
| MHOW | 1.37 (0.92, 2.04) | 0.121 | 1.64 (0.82, 3.27) | 0.164 | 1.17 (0.68, 2.04) | 0.571 | 1.58 (0.96, 2.60) | 0.070 | |
| MHO | 1.20 (0.69, 2.08) | 0.513 | 0.79 (0.25, 2.57) | 0.701 | 0.47 (0.14, 1.57) | 0.221 | 1.43 (0.78, 2.61) | 0.244 | |
| MUHNW | 0.90 (0.63, 1.30) | 0.584 | 1.29 (0.74, 2.24) | 0.372 | 0.89 (0.55, 1.42) | 0.614 | 1.00 (0.63, 1.59) | 0.993 | |
| MUHOW | 1.08 (0.78, 1.51) | 0.631 | 1.15 (0.72, 1.83) | 0.564 | 1.01 (0.65, 1.56) | 0.961 | 1.14 (0.75, 1.73) | 0.551 | |
| MUHO | 1.33 (0.94, 1.87) | 0.105 | 2.03 (1.35, 3.04) | 0.001 | 1.16 (0.73, 1.85) | 0.537 | 1.59 (1.04, 2.41) | 0.031 | |

†Adjusted for sex, age, Townsend deprivation index, qualifications, employment, ethnicity, and smoking status. Abbreviations: COVID-19, Coronavirus Disease 2019; CI, confidence interval; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obesity; MHOW, metabolically healthy overweight; MUHNW, metabolically unhealthy normal weight; MUHO, metabolically unhealthy obesity; MUHOW, metabolically unhealthy overweight; OR, odds ratio.

Supplementary Table 4. Joint associations of metabolic/obesity phenotypes and vitamin D status with COVID-19 outcomes using the cutoff points of specific metabolic syndrome components plus waist circumference as the definition of metabolic health.

| Characteristics | Vitamin D deficiency (< 25 nmol/L) | | | | Vitamin D insufficiency (< 50 nmol/L) | | | |
|---------------------------------|------------------------------------|---------|-------------------|---------|---------------------------------------|---------|-------------------|---------|
| | No | | Yes | | No | | Yes | |
| | OR (95% CI)† | P-value | OR (95% CI)† | P-value | OR (95% CI)† | P-value | OR (95% CI)† | P-value |
| COVID-19 hospitalization | | | | | | | | |
| MHNL | 1 (Ref.) | | 1.23 (0.97, 1.57) | 0.084 | 1 (Ref.) | | 1.23 (1.05, 1.44) | 0.010 |
| MHOW | 1.19 (1.06, 1.34) | 0.004 | 1.34 (1.05, 1.70) | 0.017 | 1.18 (1.01, 1.39) | 0.042 | 1.42 (1.22, 1.65) | <0.001 |
| MHO | 1.26 (1.03, 1.53) | 0.025 | 1.83 (1.28, 2.62) | 0.001 | 1.32 (0.99, 1.77) | 0.060 | 1.54 (1.22, 1.93) | <0.001 |
| MUHNW | 1.00 (0.84, 1.19) | 0.997 | 1.15 (0.77, 1.71) | 0.494 | 0.98 (0.78, 1.25) | 0.887 | 1.22 (0.97, 1.52) | 0.087 |
| MUHOW | 1.12 (0.99, 1.27) | 0.061 | 1.52 (1.23, 1.88) | <0.001 | 1.15 (0.98, 1.36) | 0.089 | 1.35 (1.16, 1.57) | <0.001 |
| MUHO | 1.56 (1.39, 1.75) | <0.001 | 2.10 (1.79, 2.47) | <0.001 | 1.52 (1.28, 1.79) | <0.001 | 1.92 (1.68, 2.21) | <0.001 |
| Confirmed COVID-19 | | | | | | | | |
| MHNL | 1 (Ref.) | | 0.93 (0.60, 1.44) | 0.740 | 1 (Ref.) | | 1.01 (0.76, 1.34) | 0.942 |
| MHOW | 1.24 (1.01, 1.53) | 0.038 | 0.89 (0.57, 1.40) | 0.622 | 1.15 (0.87, 1.53) | 0.327 | 1.27 (0.97, 1.66) | 0.082 |
| MHO | 1.37 (0.99, 1.90) | 0.058 | 0.83 (0.39, 1.78) | 0.636 | 1.16 (0.69, 1.94) | 0.577 | 1.36 (0.93, 1.99) | 0.117 |
| MUHNW | 1.02 (0.73, 1.41) | 0.918 | 1.62 (0.90, 2.93) | 0.110 | 0.84 (0.53, 1.34) | 0.467 | 1.37 (0.93, 2.01) | 0.107 |
| MUHOW | 1.20 (0.97, 1.49) | 0.101 | 1.53 (1.06, 2.21) | 0.023 | 1.12 (0.83, 1.51) | 0.466 | 1.36 (1.04, 1.78) | 0.023 |
| MUHO | 1.44 (1.17, 1.77) | 0.001 | 1.88 (1.41, 2.52) | <0.001 | 1.18 (0.86, 1.61) | 0.307 | 1.72 (1.34, 2.19) | <0.001 |
| Severe COVID-19 | | | | | | | | |
| MHNL | 1 (Ref.) | | 0.91 (0.52, 1.59) | 0.738 | 1 (Ref.) | | 0.90 (0.63, 1.29) | 0.569 |
| MHOW | 1.20 (0.93, 1.56) | 0.162 | 1.10 (0.65, 1.85) | 0.727 | 1.02 (0.72, 1.45) | 0.922 | 1.26 (0.91, 1.75) | 0.172 |
| MHO | 1.27 (0.83, 1.94) | 0.267 | 0.81 (0.30, 2.21) | 0.674 | 0.82 (0.39, 1.71) | 0.598 | 1.32 (0.82, 2.08) | 0.255 |

| | | | | | | | | |
|-------|-------------------|-------|-------------------|--------|-------------------|-------|-------------------|-------|
| | 1.94) | | 2.20) | | 1.71) | | 2.14) | |
| MUHNW | 0.82 (0.54, 1.26) | 0.363 | 1.71 (0.86, 3.39) | 0.129 | 0.67 (0.37, 1.21) | 0.182 | 1.13 (0.70, 1.83) | 0.609 |
| MUHOW | 1.14 (0.87, 1.49) | 0.329 | 1.51 (0.97, 2.35) | 0.071 | 1.02 (0.71, 1.47) | 0.903 | 1.24 (0.89, 1.72) | 0.199 |
| MUHO | 1.39 (1.08, 1.80) | 0.012 | 2.07 (1.47, 2.93) | <0.001 | 1.16 (0.80, 1.69) | 0.424 | 1.61 (1.19, 2.17) | 0.002 |

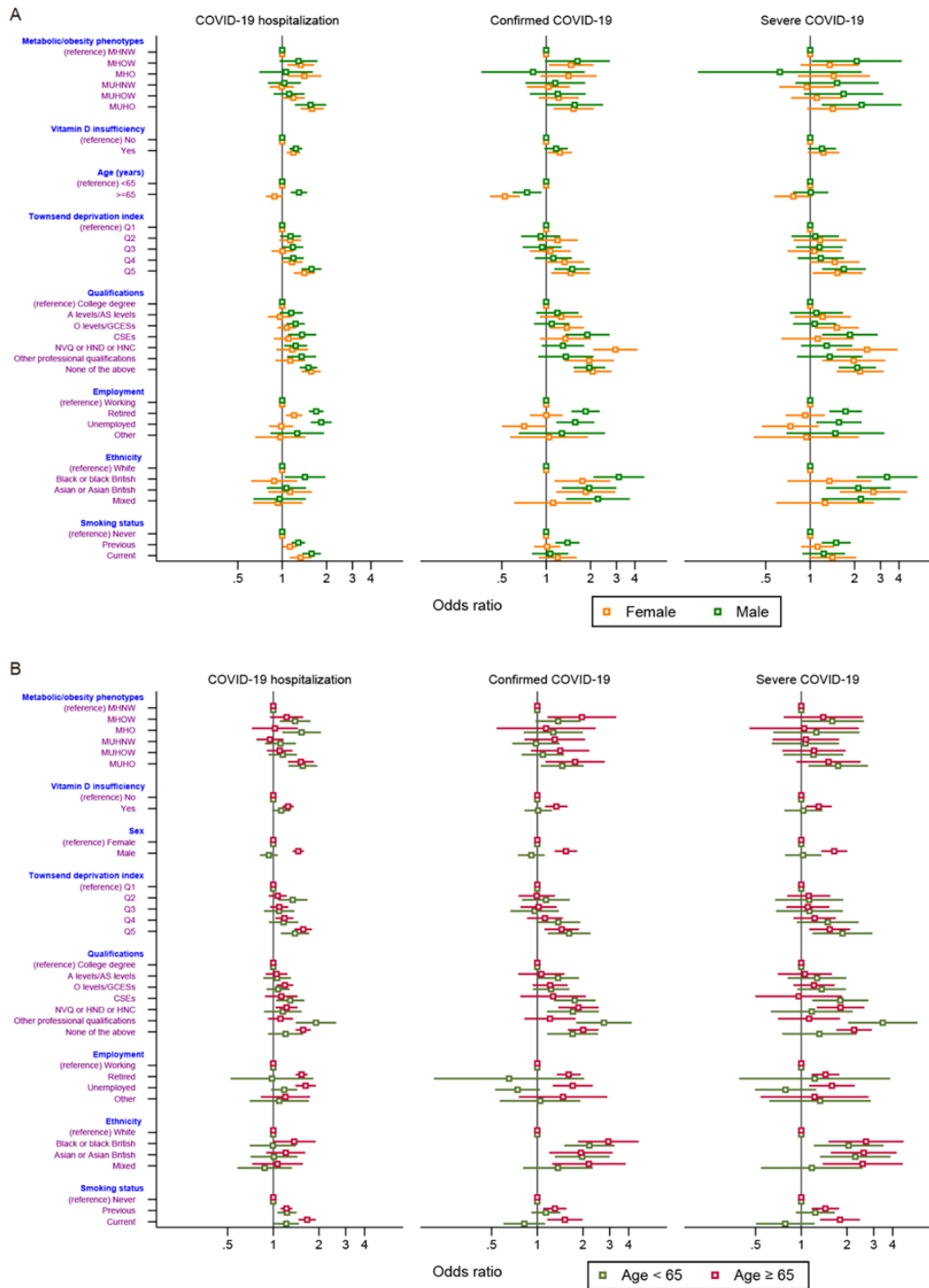
[†]Adjusted for sex, age, Townsend deprivation index, qualifications, employment, ethnicity, and smoking status. Abbreviations: COVID-19, Coronavirus Disease 2019; CI, confidence interval; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obesity; MHOW, metabolically healthy overweight; MUHNW, metabolically unhealthy normal weight; MUHO, metabolically unhealthy obesity; MUHOW, metabolically unhealthy overweight; OR, odds ratio.

Supplementary Table 5. The comparison of results regarding the difference between our data and the published paper in the role of vitamin D status in COVID-19.

| | Hastie <i>et al.</i> [†] | | Our data redefined [‡] | |
|---------------------------------------|-----------------------------------|---------|---------------------------------|---------|
| | OR (95% CI) | P-value | OR (95% CI) | P-value |
| Vitamin D concentration (nmol/L) | 1.00 (0.998, 1.01) | 0.208 | 0.997 (0.992, 1.002) | 0.240 |
| Vitamin D deficiency (< 25 nmol/L) | 0.92 (0.71, 1.21) | 0.564 | 1.080 (0.830, 1.407) | 0.566 |
| Vitamin D insufficiency (< 50 nmol/L) | 0.88 (0.72, 1.08) | 0.232 | 1.136 (0.927, 1.392) | 0.219 |

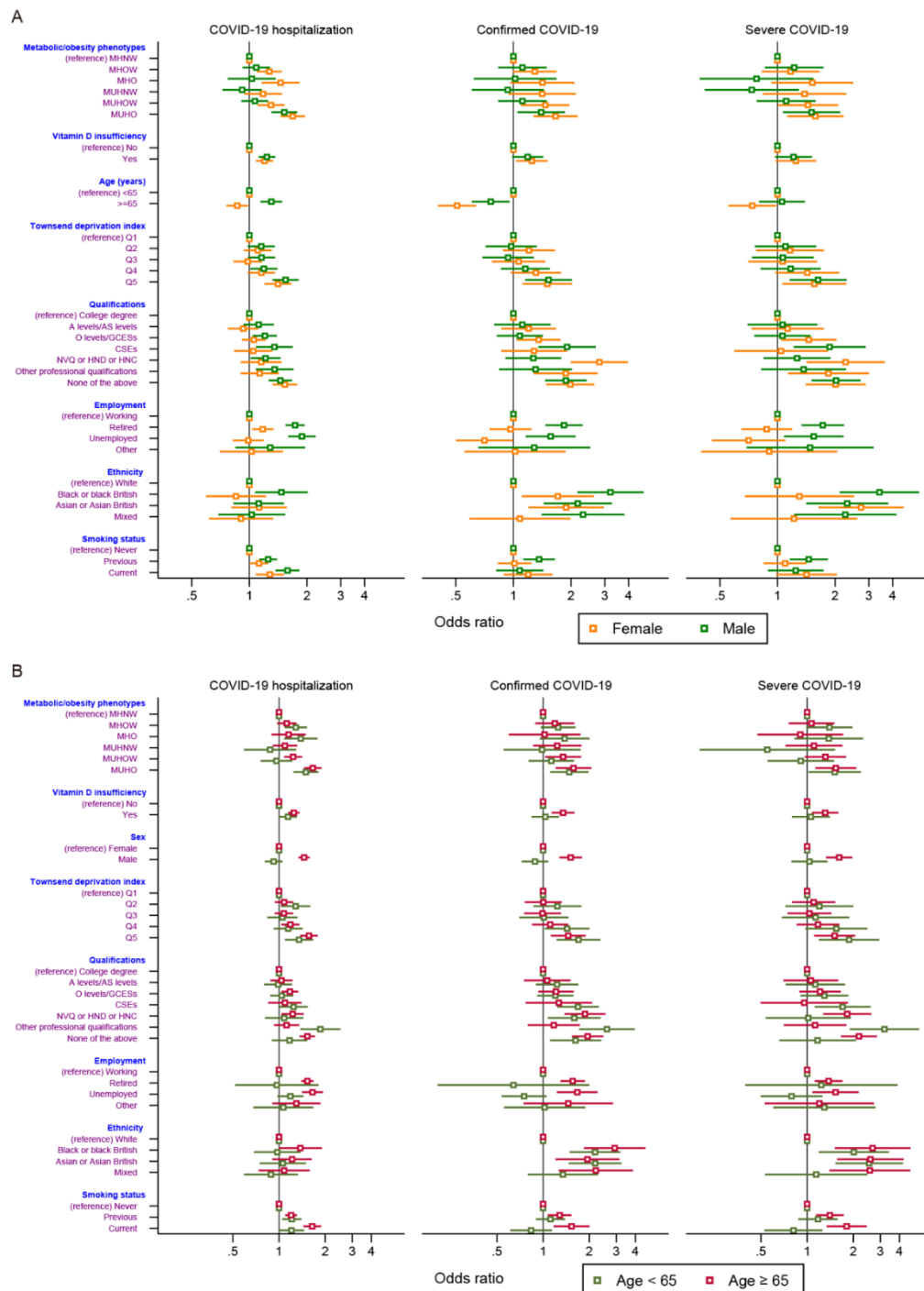
[†]Adjusted for ethnicity, sex, month of assessment, Townsend deprivation quintile, household income, self-reported health rating, smoking status, BMI category, age at assessment, diabetes, SBP, DBP, and long-standing illness, disability or infirmity. Acquired from the Table 2 of the previous paper published at *Diabetes Metab Syndr.* 2020 July-August; 14(4): 561–565.

[‡]Adjusted for sex, age, Townsend deprivation index, qualifications, employment, ethnicity, smoking status, and metabolic/obesity phenotypes. Our data redefined a total of 1481 individuals (versus 1474 individuals in Hastie *et al.*) with available SARS-CoV-2 test results by resetting the cutoff testing date.



Supplementary Figure 1. Associations of metabolic/obesity phenotypes and vitamin D status with COVID-19 outcomes using the cutoff points of specific metabolic syndrome components as the definition of metabolic health stratified by (A) sex and (B) age subgroups. The models adjusted for age, Townsend deprivation index, qualifications, employment, ethnicity, and smoking status. Abbreviations: COVID-19, Coronavirus Disease 2019; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obesity; MHOW, metabolically healthy overweight; MUHNW, metabolically unhealthy normal weight; MUHO, metabolically unhealthy obesity; MUHOW, metabolically unhealthy overweight.

SUPPLEMENTARY DATA



Supplementary Figure 2. Associations of metabolic/obesity phenotypes and vitamin D status with COVID-19 outcomes using the cutoff points of specific metabolic syndrome components plus waist circumference as the definition of metabolic health stratified by (A) sex and (B) age subgroups. The models adjusted for age, Townsend deprivation index, qualifications, employment, ethnicity, and smoking status. Abbreviations: COVID-19, Coronavirus Disease 2019; MHNW, metabolically healthy normal weight; MHO, metabolically healthy obesity; MHOW, metabolically healthy overweight; MUHNW, metabolically unhealthy normal weight; MUHO, metabolically unhealthy obesity; MUHOW, metabolically unhealthy overweight.