# Adiposity and severe COVID-19, lower respiratory tract infections, and upper respiratory tract infections in the UK Biobank prospective study

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# Introduction

- Infectious Respiratory Diseases (IRDs) among leading causes of morbidity and mortality[1,2]
  - Lower Respiratory Tract Infections (**LRTI**): **2.5M deaths**, 100M DALYs in 2019
  - **COVID-19**: **14.9M excess deaths** in 2020/21
  - Upper Respiratory Tract Infections (**URTI**): 6.4M DALYs, **17.2B cases** in 2019

- Association between adiposity and severe IRD first studied more extensively during the COVID-19 pandemic
  - Previous studies have limitations:
    - Focus on **Body-mass index** as adiposity measure
    - **Confounding** due to lack of comprehensive data collection
    - Susceptible to **reverse causation bias**
    - Role of **comorbidities** unclear

[1]GBD 2019 Diseases and Injuries Collaborators. Lancet. 2020; 396 (10258): 1204-1222.
[2]Knutson V, et al. Estimating Global and Country-Specific Excess Mortality During the COVID-19 Pandemic. 2022

# Methods

- UK Biobank
  - 2006-2010: recruited 502,599 participants (40-69 years)
  - Exposure assessment: **anthropometrics** and **bioelectrical impedance**
  - Follow-up: linkage to **electronic hospital** or **death records**

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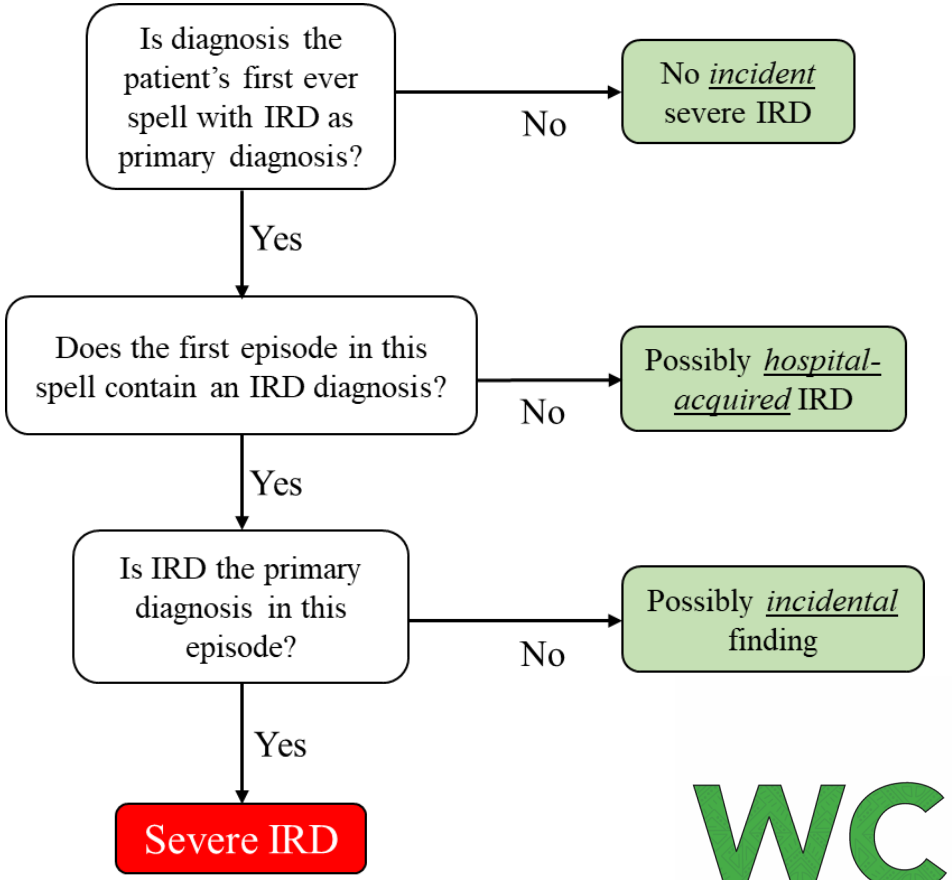
- IRD endpoint definition
  - **severe**
  - **incident**
  - **community-acquired**

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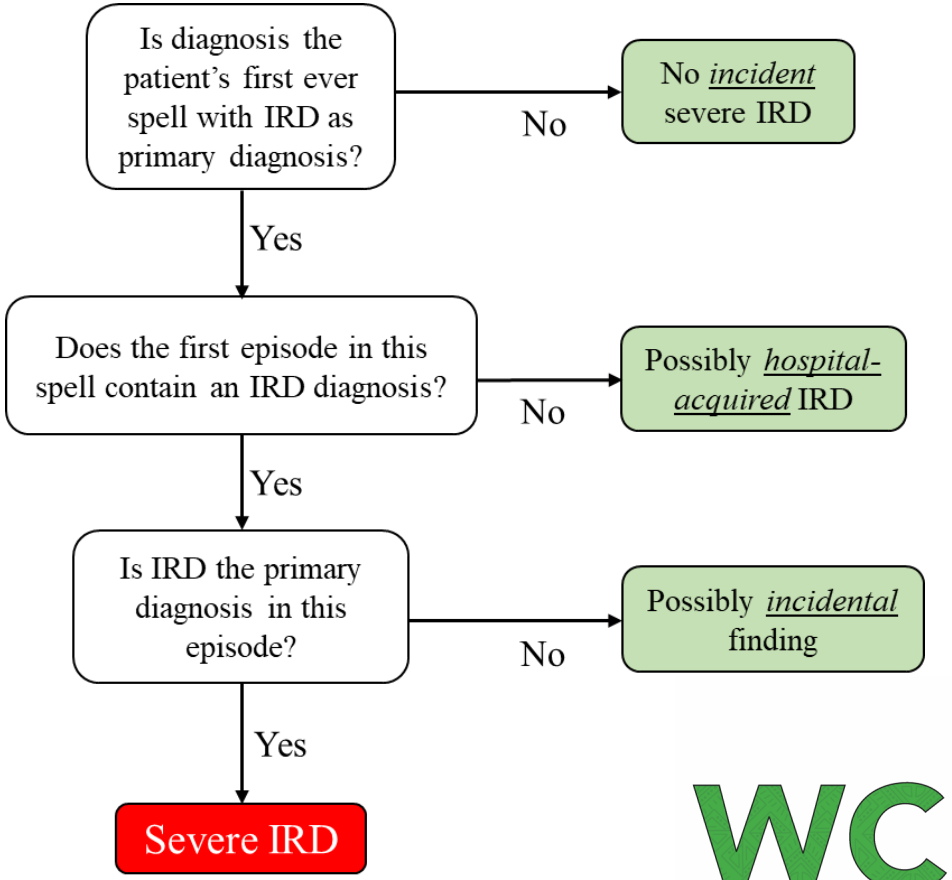
- 3 IRD subtypes
  - **LRTIs:** J09-J22
  - **COVID-19:** U07
  - **URTIs:** J00-J06

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    - By levels of adiposity
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    - Assessing effect modification by socio-demographic and lifestyle factors
  - Sensitivity analyses
    - Excluding early follow-up and ever smokers
    - Excluding prevalent (at baseline) or incident (acquired during follow-up) chronic disease

# Results

- 456,393 participants after exclusions
  - Median age 58 years
  - 55% women
  - 12 years mean follow-up
  - 94% of ‘White’ ethnicity
  - Healthy volunteer effect
    - higher education and income
    - 55% never smokers

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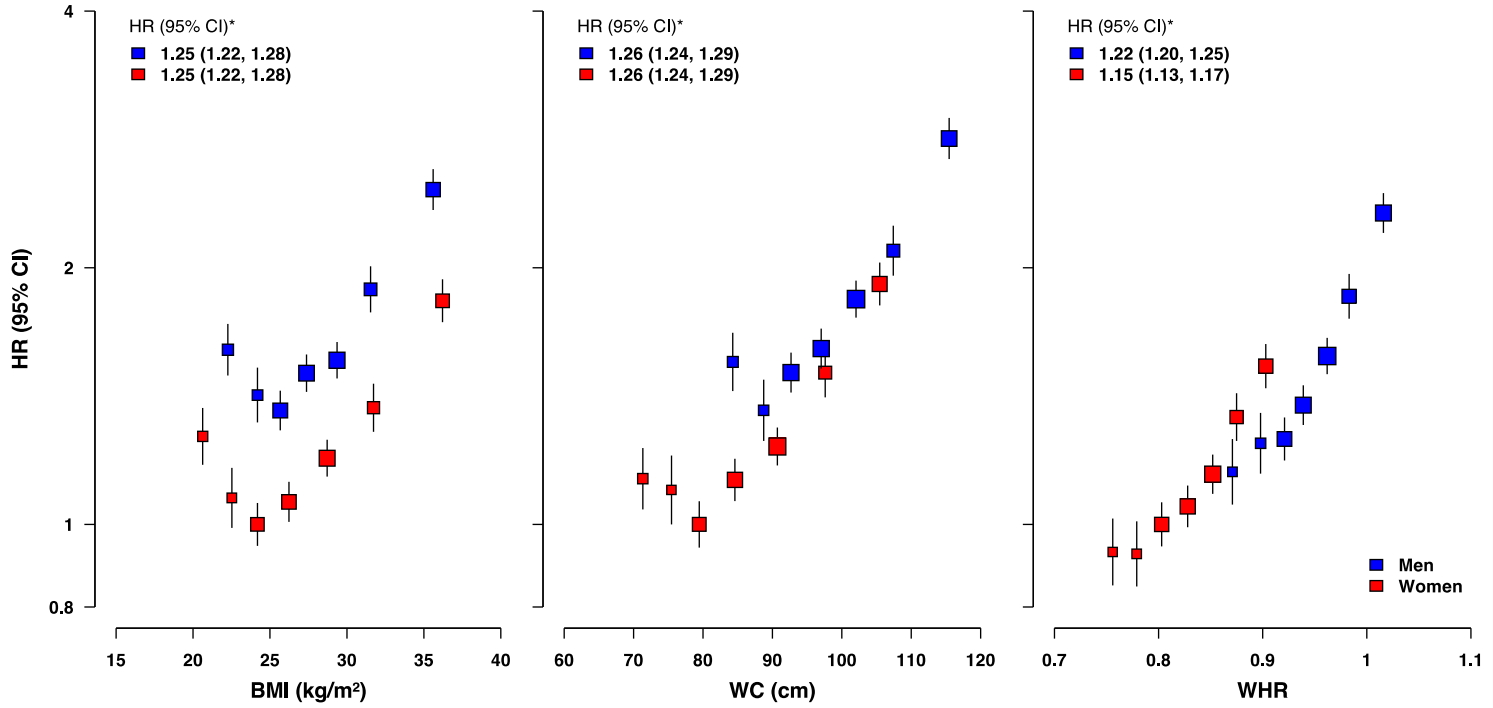
- 22,458 severe IRD events
  - 17,524 severe LRTIs
  - 3386 severe COVID-19
  - 1548 severe URTI

# Results

- **LRTI:** J-shape
  - log-linear in upper 80%




Stratified by 5-year age-at-risk group, and adjusted for standing height (except BMI), ethnicity, smoking status, education, UK region, socioeconomic deprivation, and alcohol consumption

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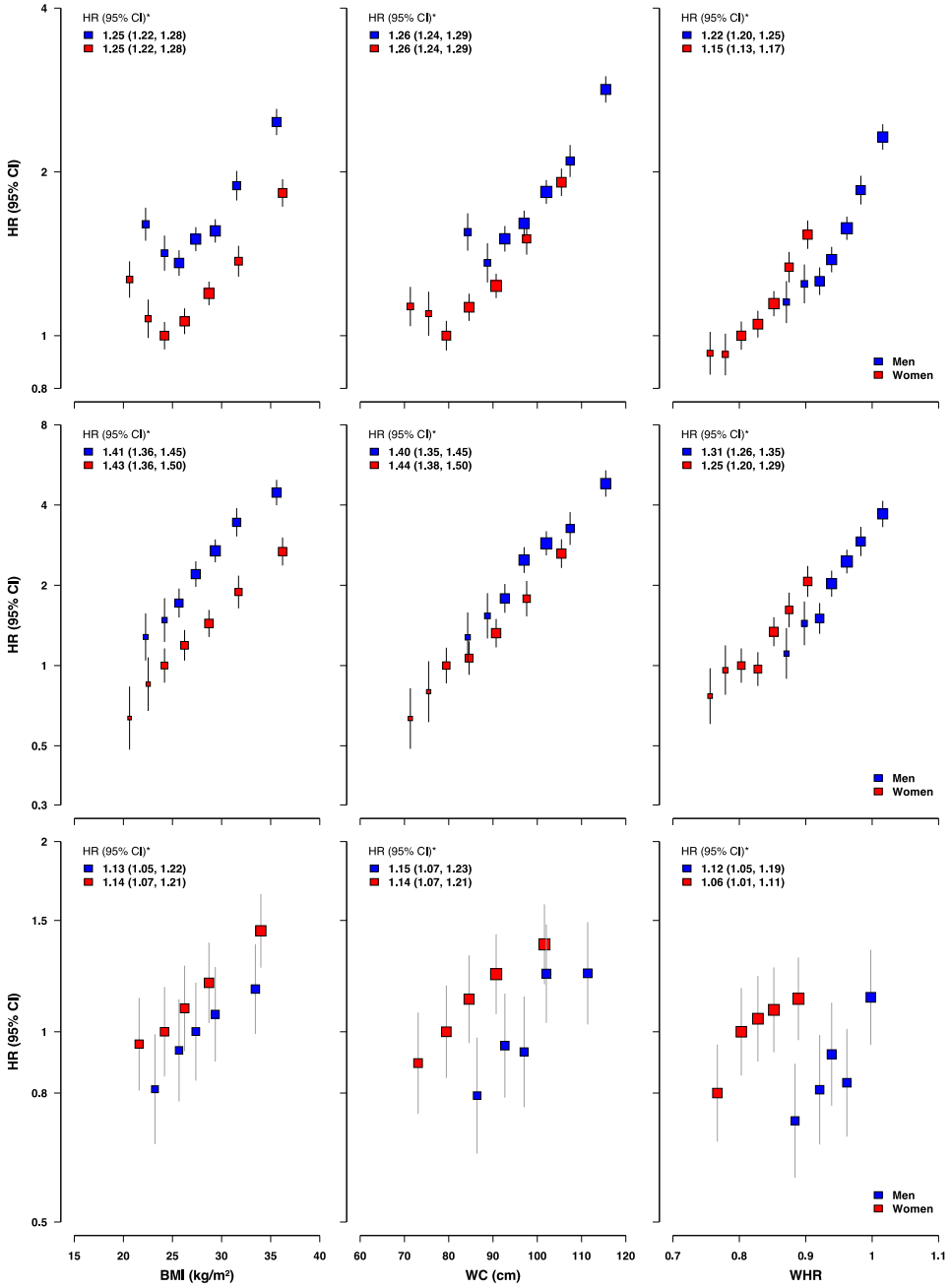


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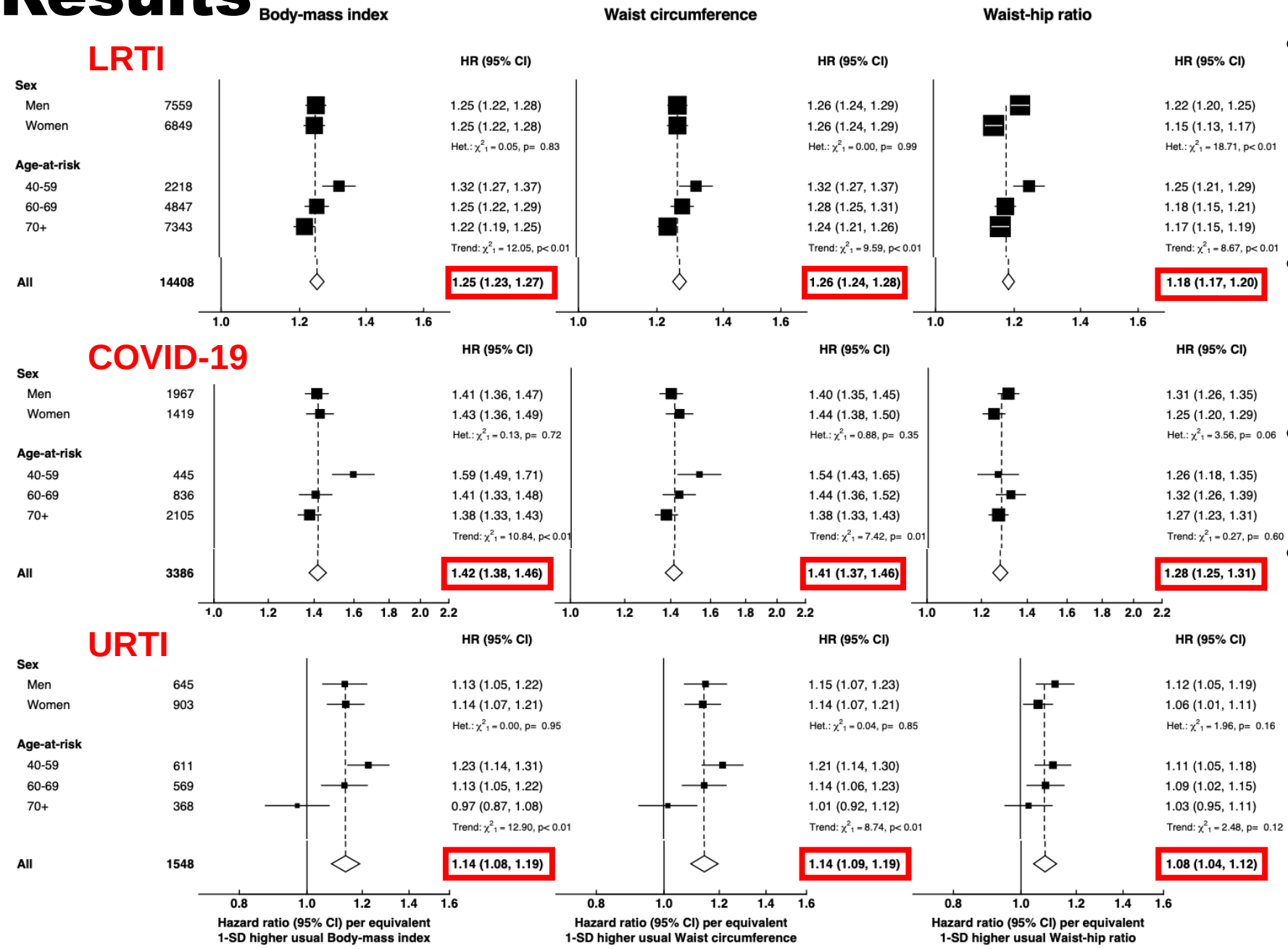


| | | Body-mass index | Waist circumference | Waist-hip ratio |
|---|---|---|---|---|
| **LRTI** | | | | |
| Sex | | | | |
| Men | 7559 | 1.25 (1.22, 1.28) | 1.26 (1.24, 1.29) | 1.22 (1.20, 1.25) |
| Women | 6849 | 1.25 (1.22, 1.28) | 1.26 (1.24, 1.29) | 1.15 (1.13, 1.17) |
| | | Het.: $\chi^2_1$ = 0.05, p= 0.83 | Het.: $\chi^2_1$ = 0.00, p= 0.99 | Het.: $\chi^2_1$ = 18.71, p< 0.01 |
| Age-at-risk | | | | |
| 40-59 | 2218 | 1.32 (1.27, 1.37) | 1.32 (1.27, 1.37) | 1.25 (1.21, 1.29) |
| 60-69 | 4847 | 1.25 (1.22, 1.29) | 1.28 (1.25, 1.31) | 1.18 (1.15, 1.21) |
| 70+ | 7343 | 1.22 (1.19, 1.25) | 1.24 (1.21, 1.26) | 1.17 (1.15, 1.19) |
| | | Trend: $\chi^2_1$ = 12.05, p< 0.01 | Trend: $\chi^2_1$ = 9.59, p< 0.01 | Trend: $\chi^2_1$ = 8.67, p< 0.01 |
| All | 14408 | **1.25 (1.23, 1.27)** | **1.26 (1.24, 1.28)** | **1.18 (1.17, 1.20)** |
| **COVID-19** | | | | |
| Sex | | | | |
| Men | 1967 | 1.41 (1.36, 1.47) | 1.40 (1.35, 1.45) | 1.31 (1.26, 1.35) |
| Women | 1419 | 1.43 (1.36, 1.49) | 1.44 (1.38, 1.50) | 1.25 (1.20, 1.29) |
| | | Het.: $\chi^2_1$ = 0.13, p= 0.72 | Het.: $\chi^2_1$ = 0.88, p= 0.35 | Het.: $\chi^2_1$ = 3.56, p= 0.06 |
| Age-at-risk | | | | |
| 40-59 | 445 | 1.59 (1.49, 1.71) | 1.54 (1.43, 1.65) | 1.26 (1.18, 1.35) |
| 60-69 | 836 | 1.41 (1.33, 1.48) | 1.44 (1.36, 1.52) | 1.32 (1.26, 1.39) |
| 70+ | 2105 | 1.38 (1.33, 1.43) | 1.38 (1.33, 1.43) | 1.27 (1.23, 1.31) |
| | | Trend: $\chi^2_1$ = 10.84, p< 0.01 | Trend: $\chi^2_1$ = 7.42, p= 0.01 | Trend: $\chi^2_1$ = 0.27, p= 0.60 |
| All | 3386 | **1.42 (1.38, 1.46)** | **1.41 (1.37, 1.46)** | **1.28 (1.25, 1.31)** |
| **URTI** | | | | |
| Sex | | | | |
| Men | 645 | 1.13 (1.05, 1.22) | 1.15 (1.07, 1.23) | 1.12 (1.05, 1.19) |
| Women | 903 | 1.14 (1.07, 1.21) | 1.14 (1.07, 1.21) | 1.06 (1.01, 1.11) |
| | | Het.: $\chi^2_1$ = 0.00, p= 0.95 | Het.: $\chi^2_1$ = 0.04, p= 0.85 | Het.: $\chi^2_1$ = 1.96, p= 0.16 |
| Age-at-risk | | | | |
| 40-59 | 611 | 1.23 (1.14, 1.31) | 1.21 (1.14, 1.30) | 1.11 (1.05, 1.18) |
| 60-69 | 569 | 1.13 (1.05, 1.22) | 1.14 (1.06, 1.23) | 1.09 (1.02, 1.15) |
| 70+ | 368 | 0.97 (0.87, 1.08) | 1.01 (0.92, 1.12) | 1.03 (0.95, 1.11) |
| | | Trend: $\chi^2_1$ = 12.90, p< 0.01 | Trend: $\chi^2_1$ = 8.74, p< 0.01 | Trend: $\chi^2_1$ = 2.48, p= 0.12 |
| All | 1548 | **1.14 (1.08, 1.19)** | **1.14 (1.09, 1.19)** | **1.08 (1.04, 1.12)** |

- LRTI: **~25%** excess risk per usual SD (in upper 80%)
- COVID-19: **~40%** excess risk
- URTI: **~10%** excess risk
- Effect modification by age, but not by sex, education, UK country, or deprivation

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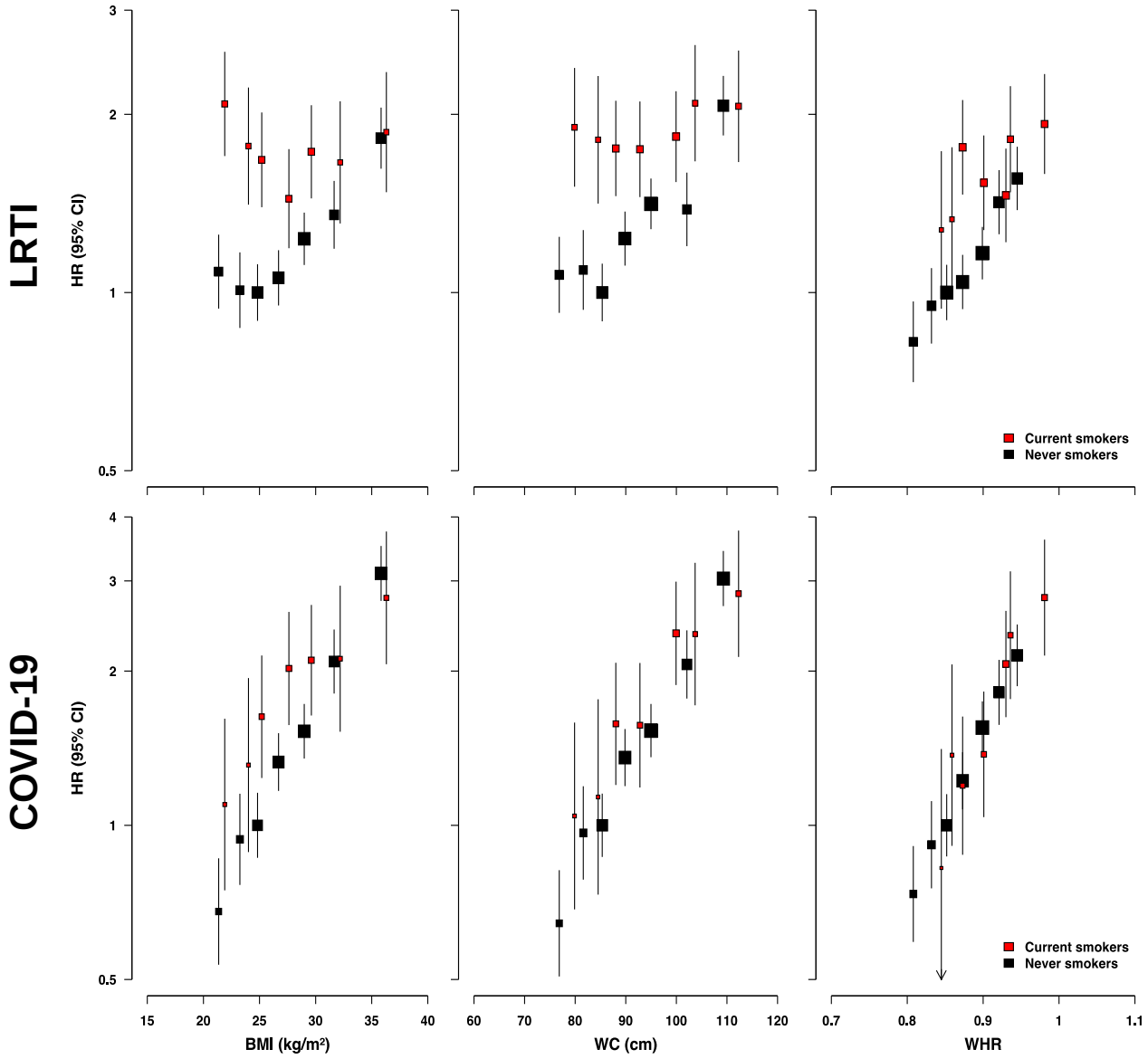
# Results

- Stronger associations in never smokers (LRTI, COVID-19)
- **Reverse causation:**
  - **LRTI:** attenuation of J-shape when excluding 10 years of follow-up and ever smokers
  - **COVID-19:** log-linear due to 10-14 years between baseline assessment and pandemic

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# Key findings

- Strong, log-linear associations of adiposity with risk of hospitalisation or death from severe LRTI (in upper 80%), COVID-19, and URTI
- Similar association strengths between COVID-19 and other LRTIs (~40% and ~25% excess risk per usual SD, respectively) might suggest shared biological mechanisms
- Associations with severe LRTI likely affected by reverse causation, but mostly robust to observational sensitivity analyses
- Associations predominantly accounted for by central adiposity (WC and trunk fat), despite similar strength of association
- Limitations:
  - Limited testing for LRTI and URTI causative agent → no further subdivision possible for different types of LRTI and URTI
  - UK Biobank has low ethnic variation → limited generalisability to other ethnicities

# Acknowledgments


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  - Sarah Lewington
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