Supplementary Material

# Young adulthood adiposity in relation to all-cause and cause-specific mortality: a prospective study of 0.5 million Chinese adults

## Contents

## Table S1. Baseline characteristics of participant according to availability of young adulthood BMI ($BMI_{25}$)

| Characteristics | Self-reported $BMI_{25}$ | |
|---|---|---|
| | **Yes** (n = 430,373) | **No** (n = 82,349) |
| **Age and socioeconomic factors** | | |
| Age, years (SD) | 51.5 (10.3) | 54.7 (11.0) |
| Female, % | 57.1 | 69.2 |
| Urban, % | 48.3 | 21.9 |
| ≥6 years of education, % | 53.9 | 24.9 |
| Household income >20 000 yuan per year, % | 47.5 | 25.6 |
| **Lifestyle factors** | | |
| Male ever-regular smoker, % | 74.3 | 74.9 |
| Female ever-regular smoker, % | 3.1 | 4.0 |
| Male ever-regular alcohol drinker, % | 38.4 | 27.3 |
| Female ever-regular alcohol drinker, % | 2.6 | 2.0 |
| Physical activity, MET h/day (SD) | 21.1 (11.8) | 20.8 (10.6) |
| **Physical measurements, mean (SD)** | | |
| Baseline BMI, $kg/m^2$ | 23.8 (3.2) | 23.0 (3.2) |
| Systolic blood pressure, mmHg | 130.4 (19.1) | 134.4 (21.2) |
| Diastolic blood pressure, mmHg | 77.8 (10.7) | 77.7 (11.2) |
| Random blood glucose, mmol/L | 6.0 (2.2) | 6.2 (2.4) |
| FEV1/FVC ratio x 100 | 84.6 (7.3) | 84.1 (8.2) |
| **Medical history and health status, %** | | |
| Self-reported CVD* | 4.6 | 4.3 |
| Self-reported hypertension | 11.6 | 11.9 |
| Self-reported diabetes | 3.2 | 2.8 |
| Baseline prevalent diabetes** | 6.0 | 5.7 |
| Self-reported cancer | 0.5 | 0.4 |
| Baseline prevalent COPD† | 6.9 | 8.9 |
| Self-reported poor health status | 10.1 | 11.7 |

BMI: Body Mass Index; CVD: Cardiovascular disease; COPD: Chronic Obstructive Pulmonary Disease; FEV1: Forced Expiratory Volume in one second; FVC: Forced Vital Capacity; MET: Metabolic Equivalent of Tasks; SD: Standard deviation.

Values were standardized to age, sex and region structure of the study population.

* Defined as self-reported physician-diagnosed coronary heart disease, stroke or TIA.

** Including self-reported physician-diagnosed diabetes, fasting blood glucose level ≥7.0 mmol/l or non-fasting blood glucose level ≥11.1 mmol/l;

† Including self-reported physician-diagnosed COPD or those with FEV1/FVC <0.7.

## Table S2. Number of participants with missing young adulthood BMI ($BMI_{25}$) by baseline age group

| | No. of participants | | % of missing |
|---|---|---|---|
| | **No missing** | **Missing** | |
| **Baseline age group, years** | | | |
| < 50 | 230,546 | 29,723 | 12.9 |
| 50-59 | 157,593 | 24,015 | 15.2 |
| 60-69 | 91,710 | 19,247 | 21.0 |
| 70-79 | 32,873 | 9364 | 28.5 |
| **Education level** | | | |
| No formal education | 65,980 | 29,298 | 30.8 |
| Primary school | 132,615 | 32,571 | 19.7 |
| Middle school | 130,149 | 14,724 | 10.2 |
| High school | 72,698 | 4811 | 6.2 |
| College or higher | 28,931 | 1045 | 3.5 |
| **Sex** | | | |
| Men | 184,816 | 25,388 | 12.1 |
| Women | 245,557 | 56,961 | 18.8 |
| **Region** | | | |
| Rural | 222,227 | 64,304 | 22.4 |
| Urban | 208,146 | 18,045 | 8.0 |
| **Overall** | **430,373** | **82,349** | **16.1** |

## Table S3. Number of deaths by ICD-10 code

| Causes of deaths | ICD-10 code | No. of deaths |
|---|---|---|
| Cardiovascular disease (CVD) | I00–I99 | 13,620 |
| Ischaemic heart disease (IHD) | I20–I25 | 5119 |
| Ischaemic stroke | I63 | 1551 |
| Intracerebral haemorrhage (ICH) | I61 | 3712 |
| Cancer | C00–C97 | 13,394 |
| Lung cancer | C33–C34 | 3538 |
| Liver cancer | C22 | 1979 |
| Stomach cancer | C16 | 1673 |
| Esophageal cancer | C15 | 1338 |
| Colorectal cancer | C18–C20 | 962 |
| Breast cancer | C50 | 393 |
| Cervix, endometrial or ovarian cancer | C53, C54.1, C56 | 345 |
| Respiratory diseases | J00–J99 | 2929 |
| Transport accident | V01–V99 | 1137 |
| Other | | 5734 |
| All-cause | | 36,814 |

## Table S4. Association estimates of young adulthood BMI ($BMI_{25}$) with proteins

| Protein | Technology | Young adulthood BMI | | | | Baseline BMI | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | Estimate[a] | SE | Nominal p-value | Bonferroni[b] p-value | Estimate[a] | SE | Nominal p-value | Bonferroni[b] p-value |
| Cystatin M | SomaLogic | -0.130 | 0.022 | 4.93E-09 | 3.54E-05 | -0.150 | 0.022 | 1.50E-11 | 1.07E-07 |
| LILRB5 | Olink | 0.140 | 0.024 | 4.96E-09 | 3.56E-05 | 0.130 | 0.024 | 5.05E-08 | 3.63E-04 |
| **SEMA7A** | **Olink** | **0.137** | **0.023** | **4.97E-09** | **3.57E-05** | -0.095 | 0.023 | 5.10E-05 | 3.66E-01 |
| **CD163** | **Olink** | **0.132** | **0.023** | **1.72E-08** | **1.23E-04** | -0.049 | 0.023 | 3.52E-02 | 1.00E+00 |
| **GAS6** | **Olink** | **0.128** | **0.023** | **5.77E-08** | **4.14E-04** | -0.174 | 0.023 | 1.88E-13 | 1.35E-09 |
| **SIGLEC1** | **Olink** | **0.121** | **0.023** | **2.02E-07** | **1.45E-03** | -0.049 | 0.024 | 4.17E-02 | 1.00E+00 |
| **GAL** | **Olink** | **-0.119** | **0.023** | **2.08E-07** | **1.50E-03** | 0.110 | 0.024 | 3.54E-06 | 2.54E-02 |
| CO9A3 | SomaLogic | -0.115 | 0.022 | 2.77E-07 | 1.99E-03 | -0.296 | 0.021 | 7.64E-42 | 5.49E-38 |
| DSG4 | Olink | -0.120 | 0.023 | 3.65E-07 | 2.62E-03 | -0.142 | 0.023 | 1.33E-09 | 9.55E-06 |
| **CSF1R** | **SomaLogic** | **0.114** | **0.023** | **4.85E-07** | **3.48E-03** | 0.041 | 0.024 | 8.30E-02 | 1.00E+00 |
| **AXL** | **Olink** | **0.118** | **0.024** | **7.38E-07** | **5.30E-03** | -0.026 | 0.024 | 2.81E-01 | 1.00E+00 |
| **SEMA5A** | **SomaLogic** | **0.116** | **0.023** | **7.76E-07** | **5.57E-03** | -0.017 | 0.024 | 4.60E-01 | 1.00E+00 |
| **CD48** | **Olink** | **0.115** | **0.023** | **1.02E-06** | **7.32E-03** | -0.212 | 0.023 | 4.87E-20 | 3.50E-16 |
| **RBP** | **SomaLogic** | **-0.106** | **0.022** | **1.26E-06** | **9.05E-03** | 0.101 | 0.022 | 5.17E-06 | 3.71E-02 |
| **CRTAM** | **Olink** | **0.109** | **0.023** | **1.44E-06** | **1.04E-02** | -0.068 | 0.024 | 4.08E-03 | 1.00E+00 |
| **CD79B** | **Olink** | **0.109** | **0.023** | **1.98E-06** | **1.43E-02** | 0.025 | 0.023 | 2.82E-01 | 1.00E+00 |
| **LIFR** | Olink | **0.112** | **0.024** | **2.11E-06** | **1.52E-02** | -0.172 | 0.023 | 1.60E-13 | 1.15E-09 |
| **TIMD4** | **Olink** | **0.111** | **0.023** | **2.27E-06** | **1.63E-02** | -0.041 | 0.023 | 8.08E-02 | 1.00E+00 |
| C1QL3 | SomaLogic | -0.110 | 0.023 | 2.66E-06 | 1.91E-02 | -0.274 | 0.022 | 4.95E-33 | 3.56E-29 |
| **TYRO3** | **Olink** | **0.112** | **0.024** | **2.85E-06** | **2.05E-02** | -0.058 | 0.024 | 1.48E-02 | 1.00E+00 |
| IGLO5 | SomaLogic | -0.108 | 0.023 | 3.31E-06 | 2.38E-02 | -0.416 | 0.021 | 4.86E-79 | 3.49E-75 |
| SEM4D | SomaLogic | 0.109 | 0.024 | 4.32E-06 | 3.10E-02 | 0.163 | 0.024 | 7.39E-12 | 5.31E-08 |
| **VCAM1** | **Olink** | **0.108** | **0.023** | **4.36E-06** | **3.13E-02** | -0.105 | 0.023 | 6.50E-06 | 4.67E-02 |
| UNC5H4 | SomaLogic | -0.108 | 0.023 | 4.82E-06 | 3.46E-02 | -0.439 | 0.021 | 4.17E-86 | 3.00E-82 |
| NCAN | Olink | -0.104 | 0.023 | 5.40E-06 | 3.88E-02 | -0.380 | 0.021 | 1.66E-67 | 1.19E-63 |
| SLIK1 | SomaLogic | -0.106 | 0.023 | 6.70E-06 | 4.81E-02 | -0.399 | 0.021 | 1.47E-70 | 1.05E-66 |
| STX1a | SomaLogic | -0.103 | 0.023 | 6.74E-06 | 4.84E-02 | -0.301 | 0.022 | 1.18E-41 | 8.50E-38 |

Those protein names in bold were significantly associated with $BMI_{25}$ but not baseline BMI, or had significant but opposite associations with $BMI_{25}$ and baseline BMI.

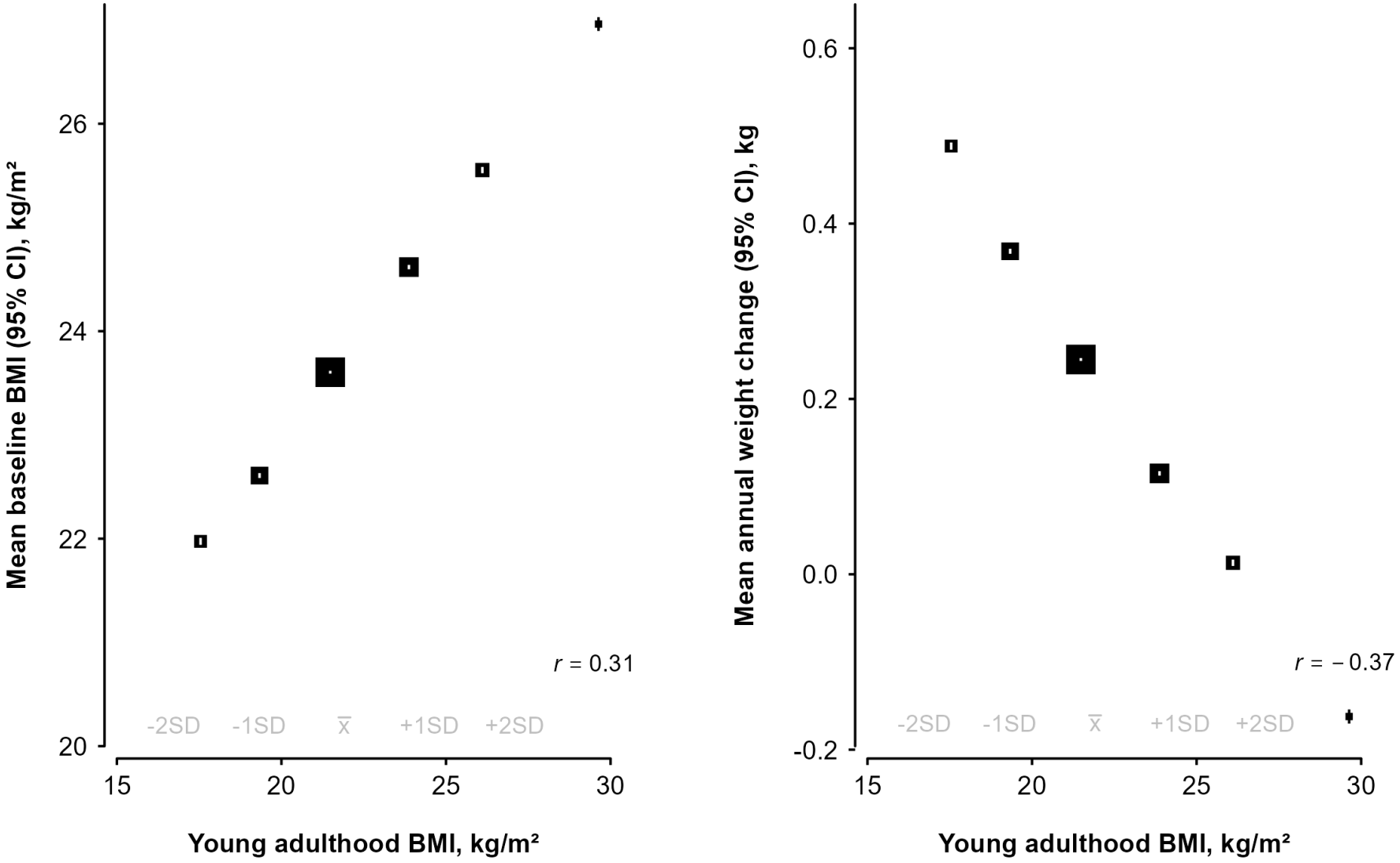
[a] Linear regression analyses were adjusted for age, age$^2$, sex, study area, fasting time, fasting time$^2$, outdoor temperature, outdoor temperature$^2$ and plate ID, where appropriate.

[b] Bonferroni correction was applied to associations across 7,164 unique proteins.

Proteins in bold are those significantly associated with $BMI_{25}$ but not baseline BMI, or demonstrating opposite-direction associations with BMI and $BMI_{25}$.

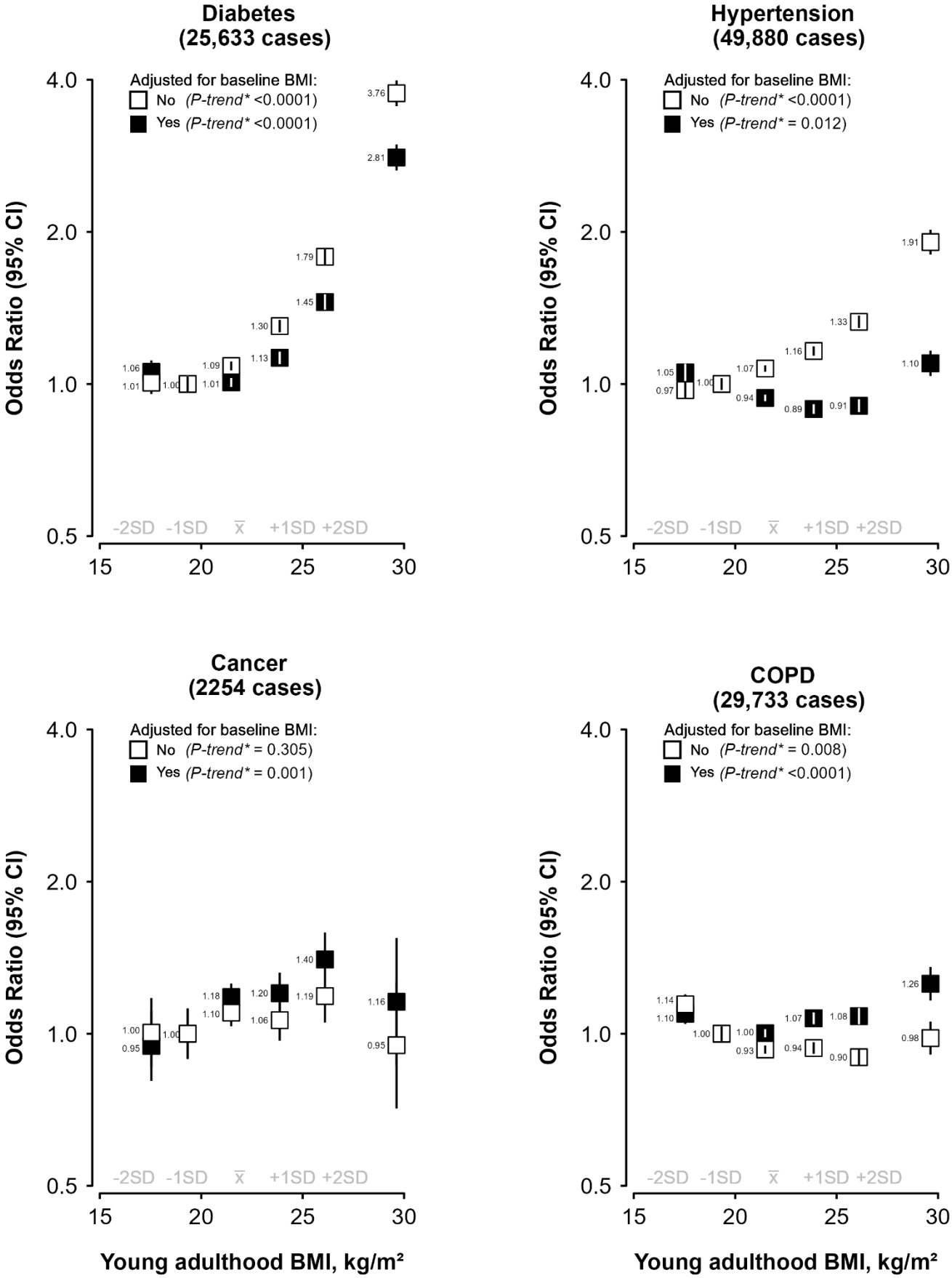
## Figure S1. Association of young adulthood BMI ($BMI_{25}$) with baseline BMI and annual weight change

Mean values adjusted for age (5-year groups), sex, study area, education, smoking and alcohol consumption, where appropriate. Each closed square represents the mean value. The vertical lines indicate 95% CIs. The length of y-axis represents ± 1 SD from the mean of baseline BMI and weight change. Abbreviations: BMI: body mass index, CI: confidence interval



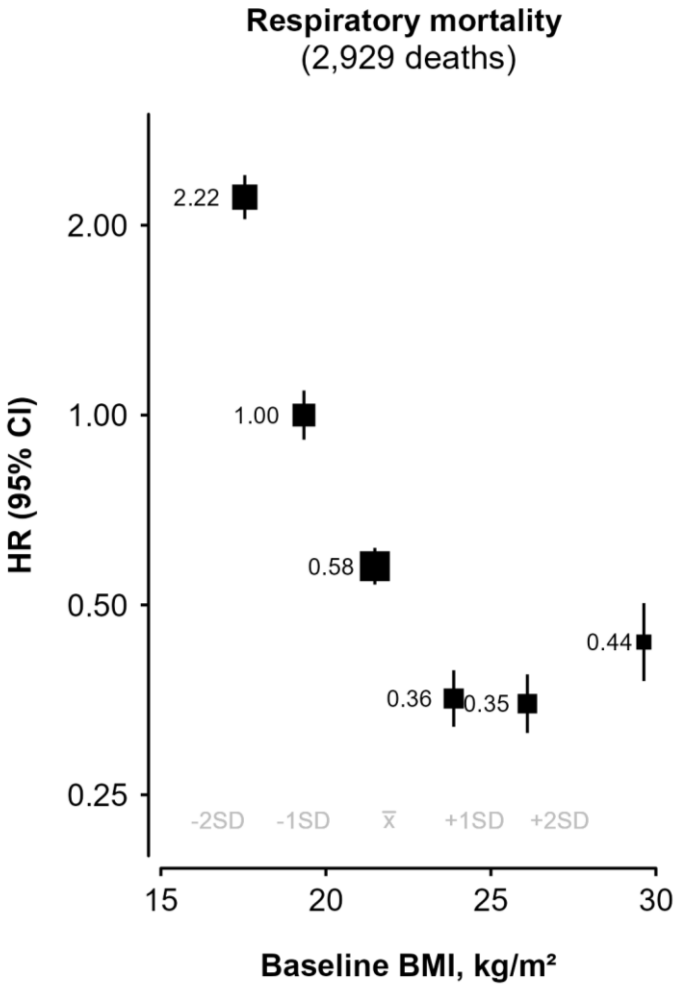
## Figure S2. Adjusted ORs for prior diseases by young adulthood BMI ($BMI_{25}$)

The adjusted ORs (95% CI) were adjusted for age (5-year groups), sex, study area, education, smoking, alcohol consumption and baseline BMI (deciles). Adjusted ORs are plotted against mean $BMI_{25}$ in each category. * P-trend reflects trend test at $BM_{I25}$ ≥20 kg/m$^2$. Abbreviations: BMI: body mass index, CI: confidence interval, COPD: chronic obstructive pulmonary disease, OR: odds ratio



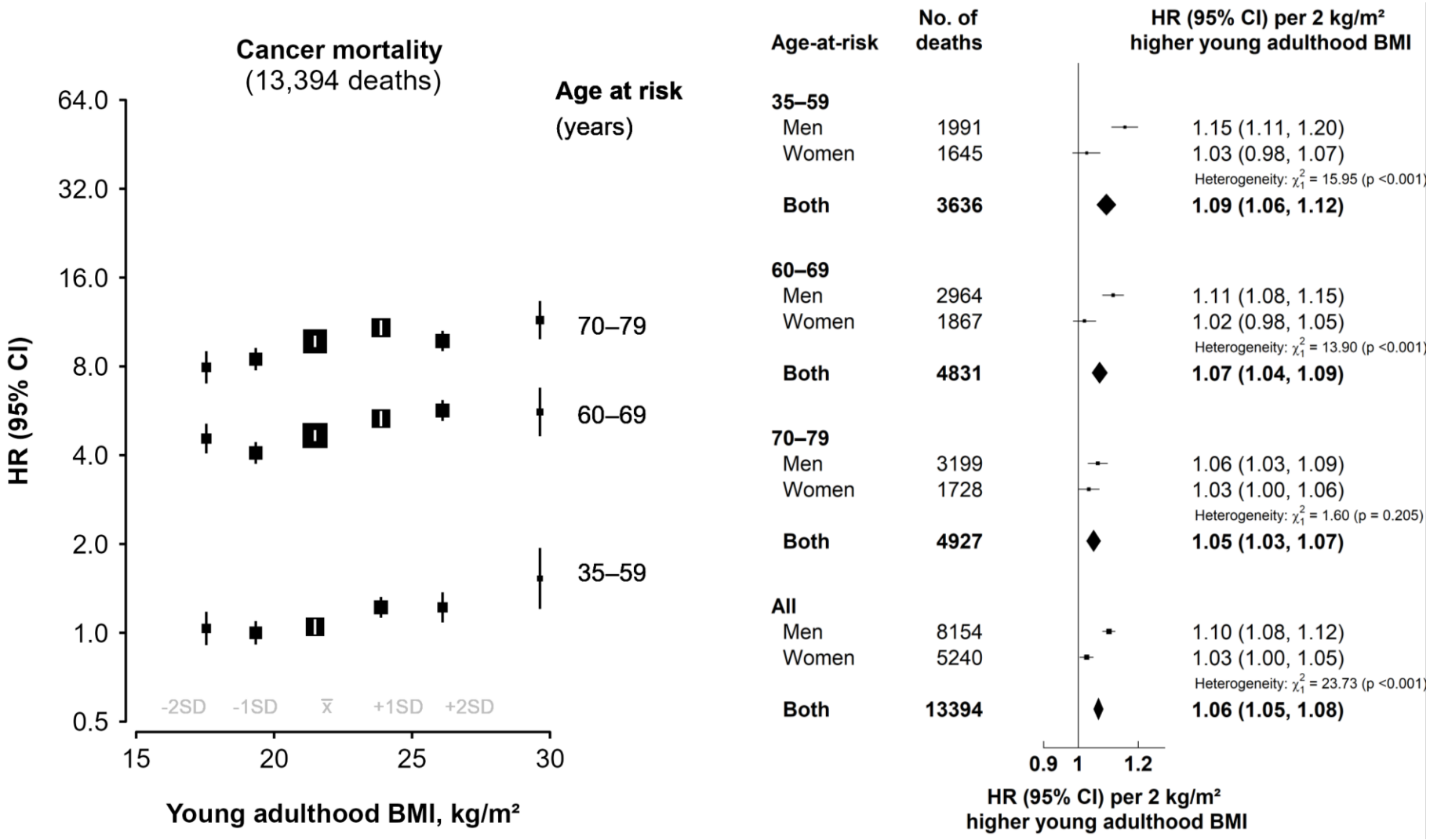
## Figure S3. Adjusted HRs for respiratory disease mortality by baseline BMI

The adjusted HRs (95% CI) were stratified by age-at-risk (5-year groups), and study area and are adjusted for education, smoking, and alcohol consumption. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate the 95%CIs. Adjusted HRs are plotted against baseline BMI in each category. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



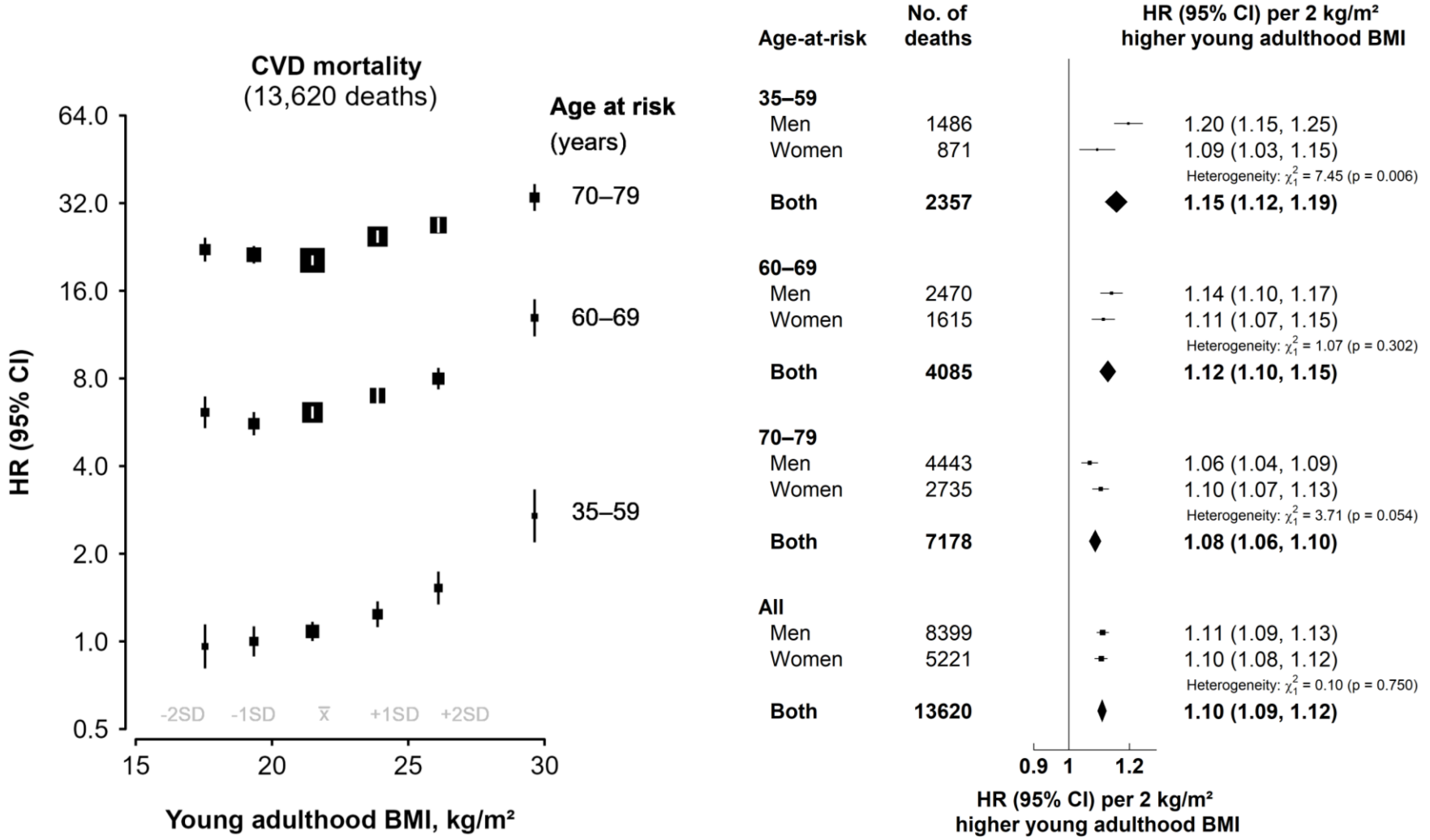
## Figure S4. Adjusted HRs for cancer mortality by young adulthood BMI ($BMI_{25}$), stratified by age at risk and sex

The left panel shows the adjusted HRs for cancer mortality by $BMI_{25}$, across different age-at-risk groups. Analysis was stratified by sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles). The group with age-at-risk being 35–59 years and $BMI_{25}$ of 18.5–20 kg/m$^2$ as reference. HRs are plotted against mean $BMI_{25}$ in each category. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate their 95%CIs. The right panel shows HRs for cancer mortality per 2 kg/m$^2$ higher $BMI_{25}$, by age-at-risk and sex. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate their 95%CIs. The diamonds indicate the overall values and its 95%CIs. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



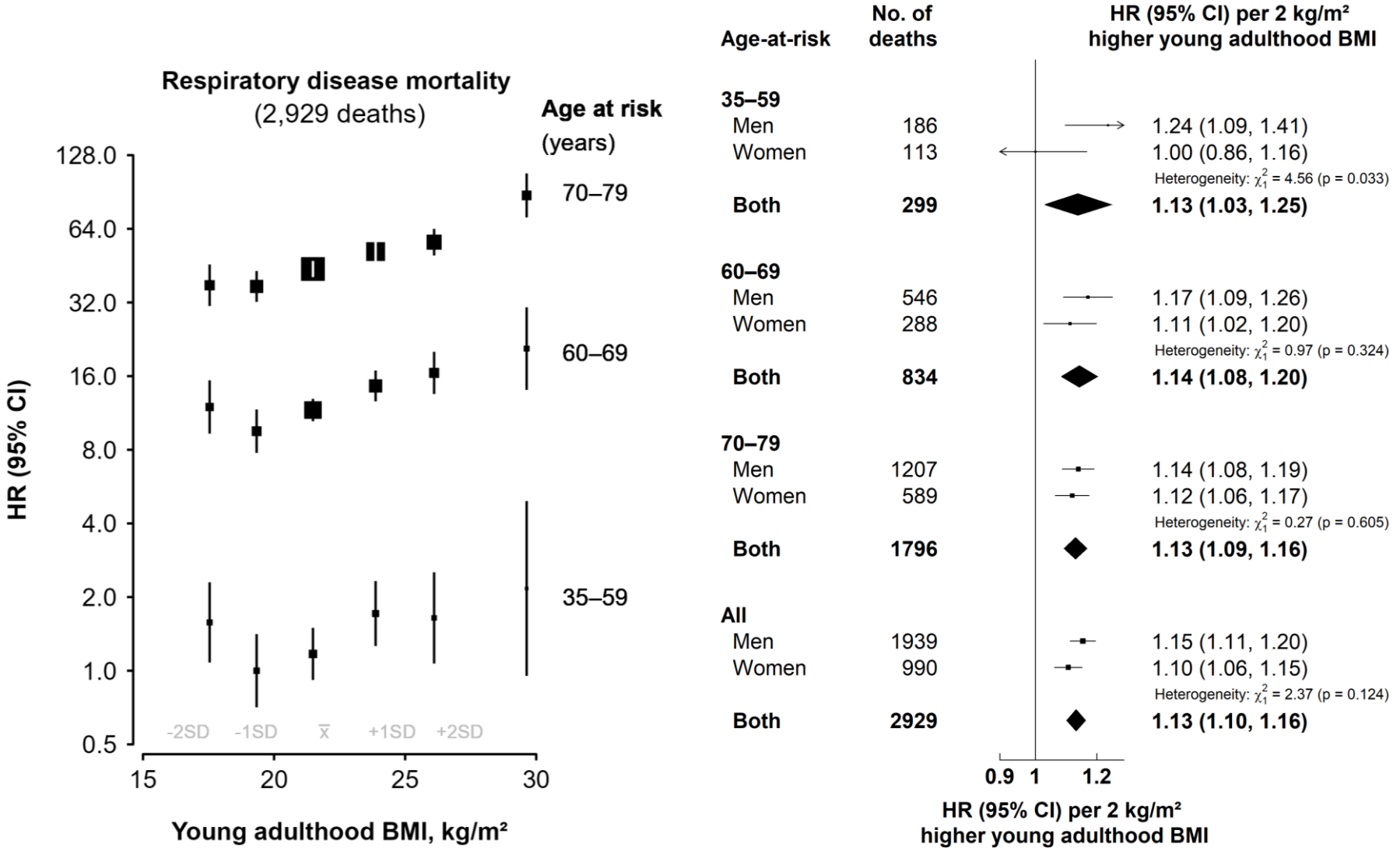
## Figure S5. Adjusted HRs for CVD mortality by young adulthood BMI ($BMI_{25}$), stratified by age at risk and sex

The left panel shows the adjusted HRs for CVD mortality by $BMI_{25}$, across different age-at-risk groups. Analysis was stratified by sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles). The group with age-at-risk being 35–59 years and $BMI_{25}$ of 18.5–20 kg/m$^2$ as reference. HRs are plotted against mean $BMI_{25}$ in each category. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate their 95%CIs. The right panel shows HRs for CVD mortality per 2 kg/m$^2$ higher $BMI_{25}$, by age-at-risk and sex. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate their 95%CIs. The diamonds indicate the overall values and its 95%CIs. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



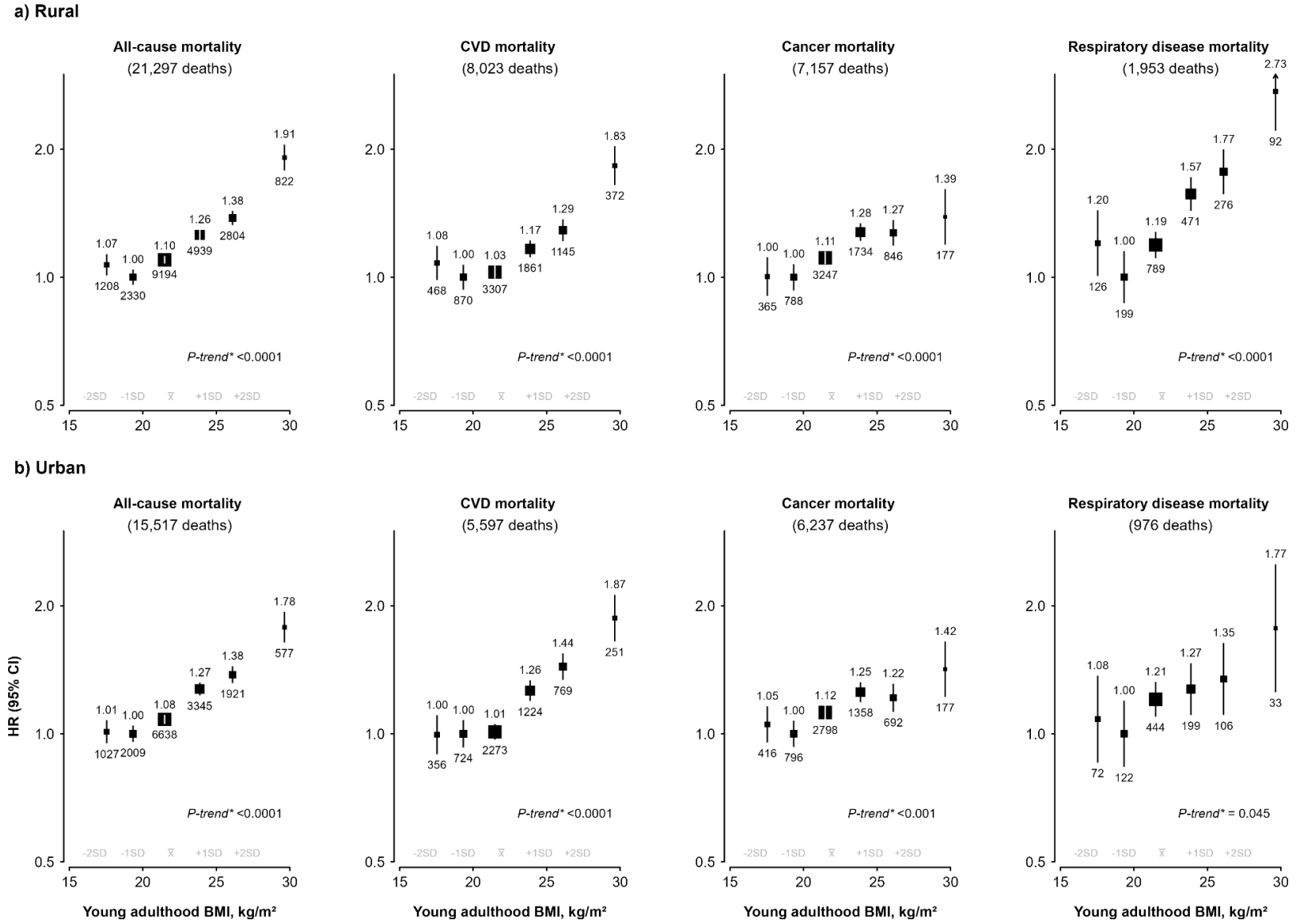
## Figure S6. Adjusted HRs for respiratory disease mortality by young adulthood BMI ($BMI_{25}$), stratified by age at risk and sex

The left panel shows the adjusted HRs for respiratory disease mortality by $BMI_{25}$, across different age-at-risk groups. Analysis was stratified by sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles). The group with age-at-risk being 35–59 years and $BMI_{25}$ of 18.5–20 kg/m$^2$ as reference. HRs are plotted against mean $BMI_{25}$ in each category. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate their 95%CIs. The right panel shows HRs for respiratory disease mortality per 2 kg/m$^2$ higher $BMI_{25}$, by age-at-risk and sex. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate their 95%CIs. The diamonds indicate the overall values and its 95%CIs. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



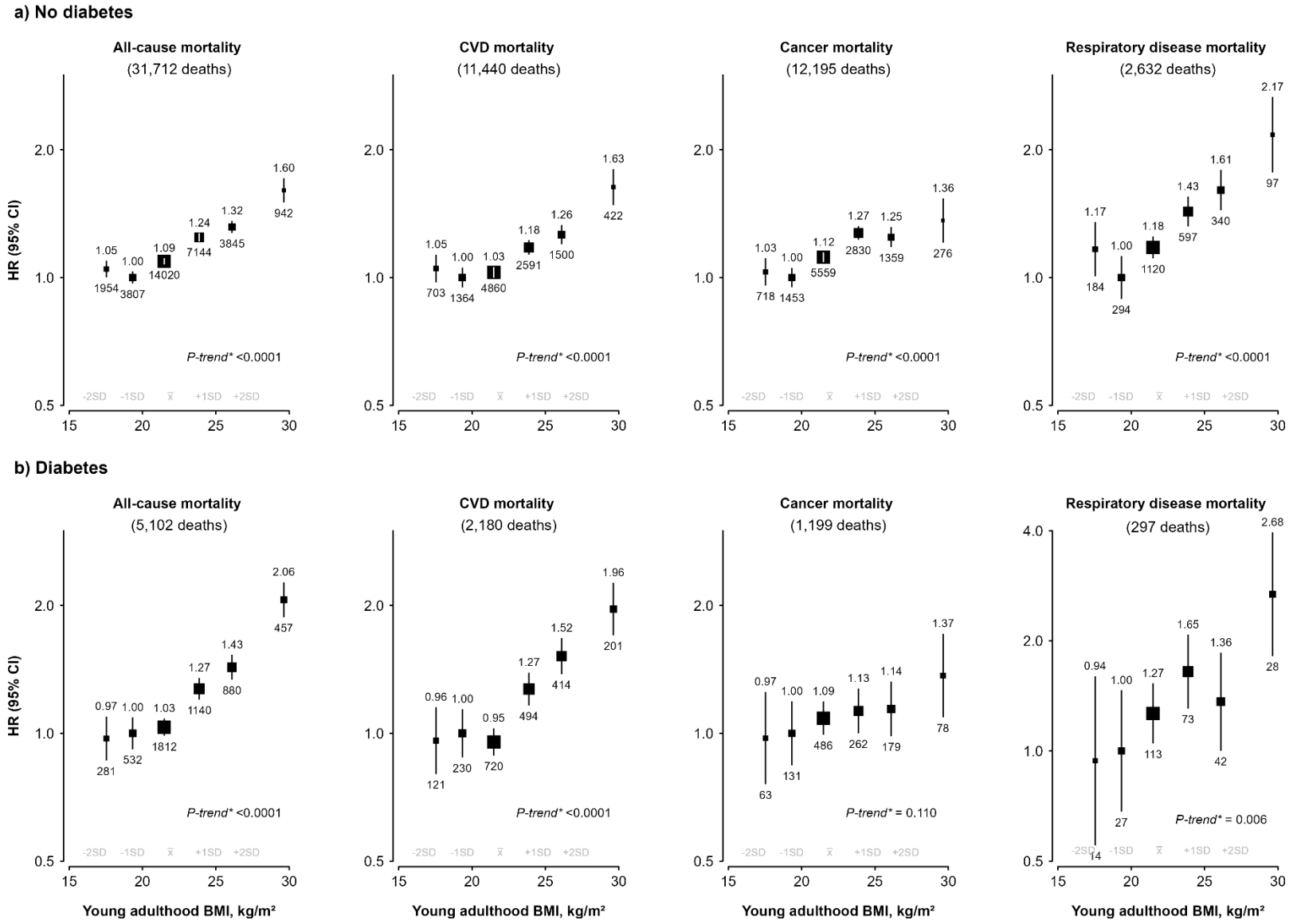
# Figure S7. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$), by region

The adjusted HRs (95%CIs) were stratified by age-at-risk (5-year groups), sex and study area, and are adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with those participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate the 95%CIs. HRs are plotted against region-specific mean $BMI_{25}$ in each category. * P-trend reflects trend test at $BMI_{25}$ ≥20 kg/m$^2$. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



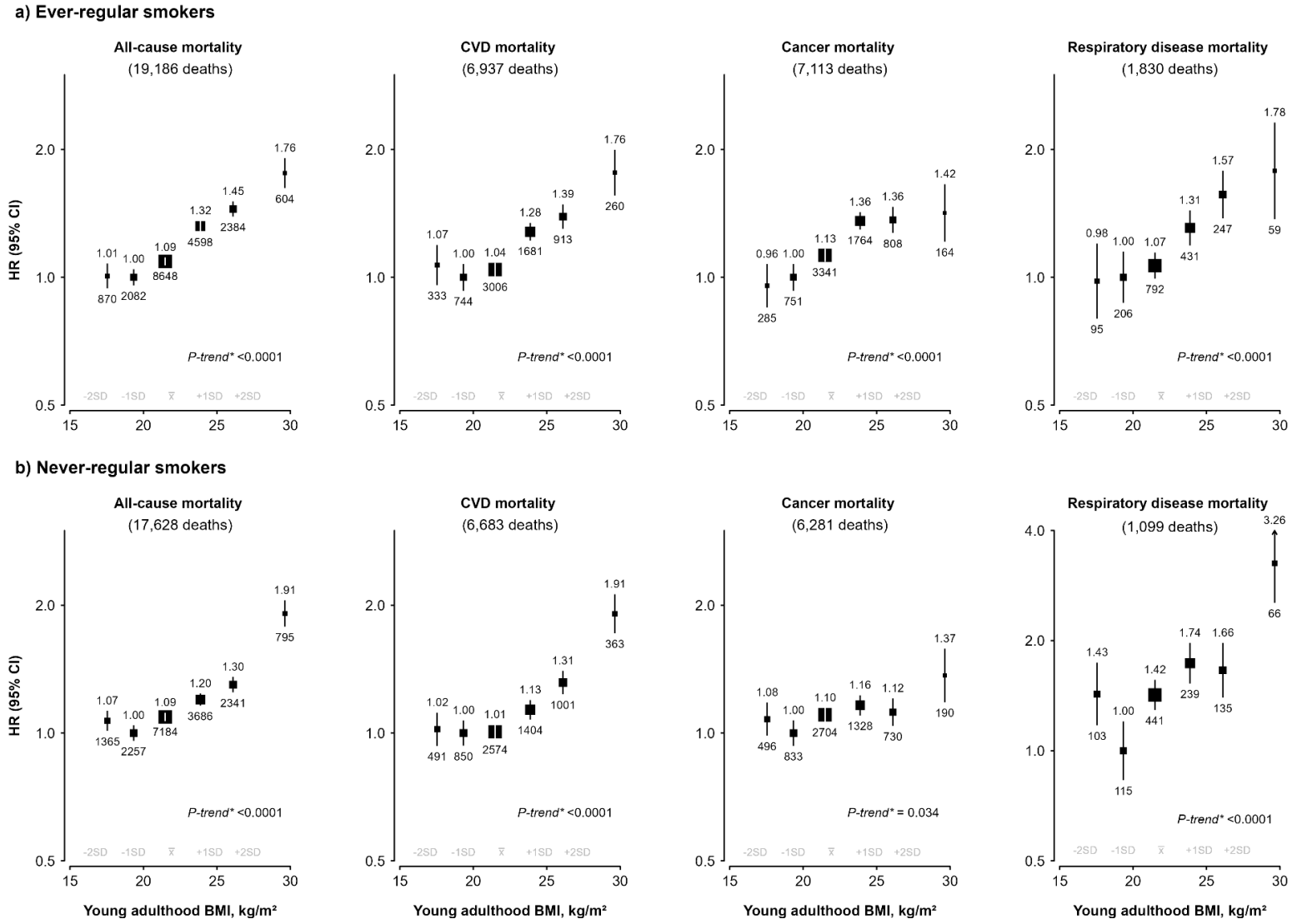
# Figure S8. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$), by prevalent diabetes

The adjusted HRs (95%CIs) were stratified by age-at-risk (5-year groups), sex and study area. and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with those participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate their 95%CIs. HRs are plotted against mean $BMI_{25}$ in each category. * P-trend reflects trend test at $BMI_{25}$ ≥20 kg/m$^2$. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



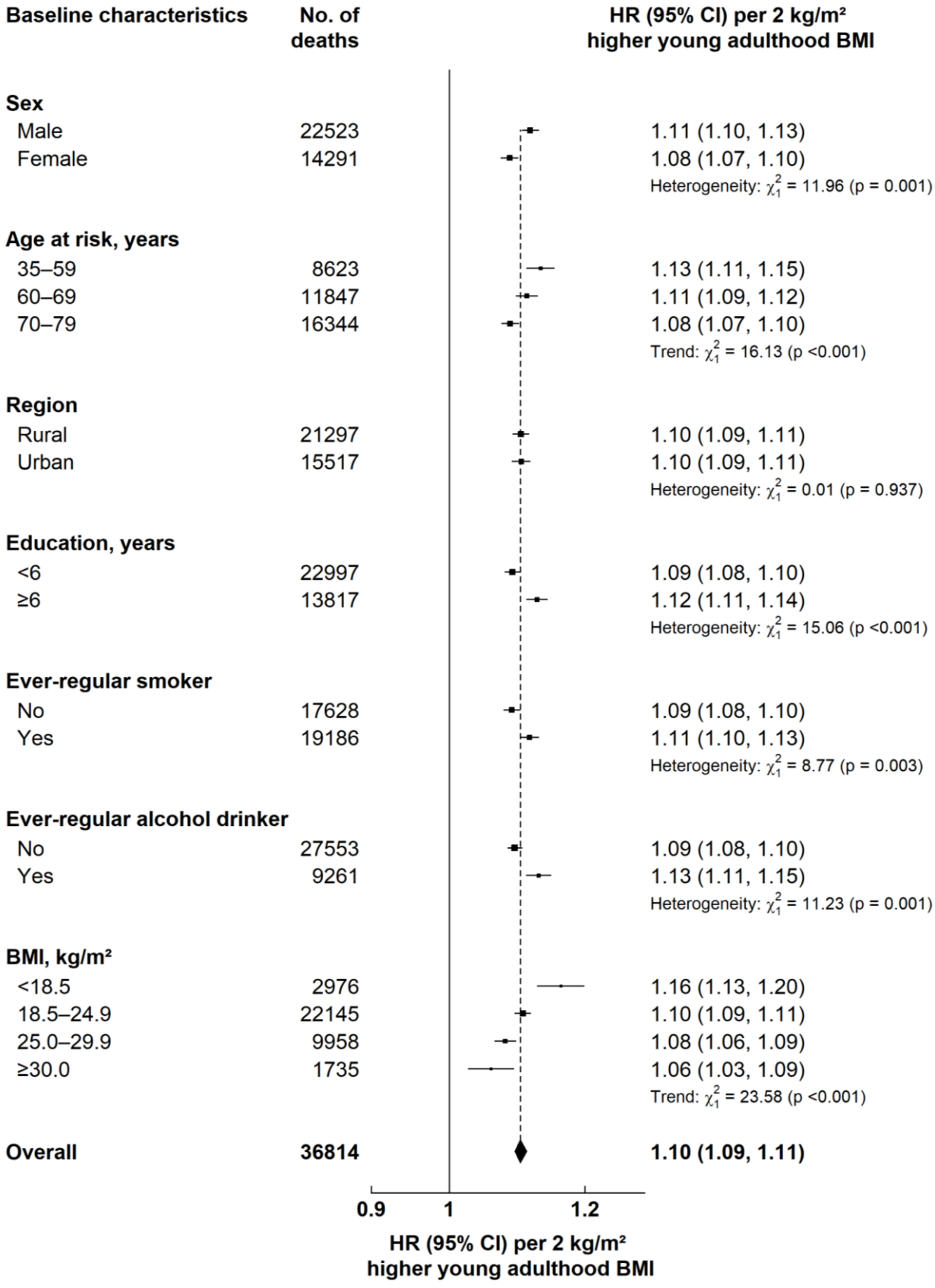
# Figure S9. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$), by smoking status

The adjusted HRs (95% CI) for all-cause, CVD, cancer and respiratory diseases mortality by young adulthood BMI are stratified by age-at-risk (5-year groups), sex and study area and are adjusted for education, smoking, alcohol consumption and baseline BMI (deciles). Squares represent the HR with area inversely proportional to the variance of the log HR, and error bars indicate the 95%CI. Adjusted HRs are plotted against smoking-status-specific mean young adulthood BMI in each category. * P-trend reflects trend test at young adulthood BMI ≥20 kg/m$^2$. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



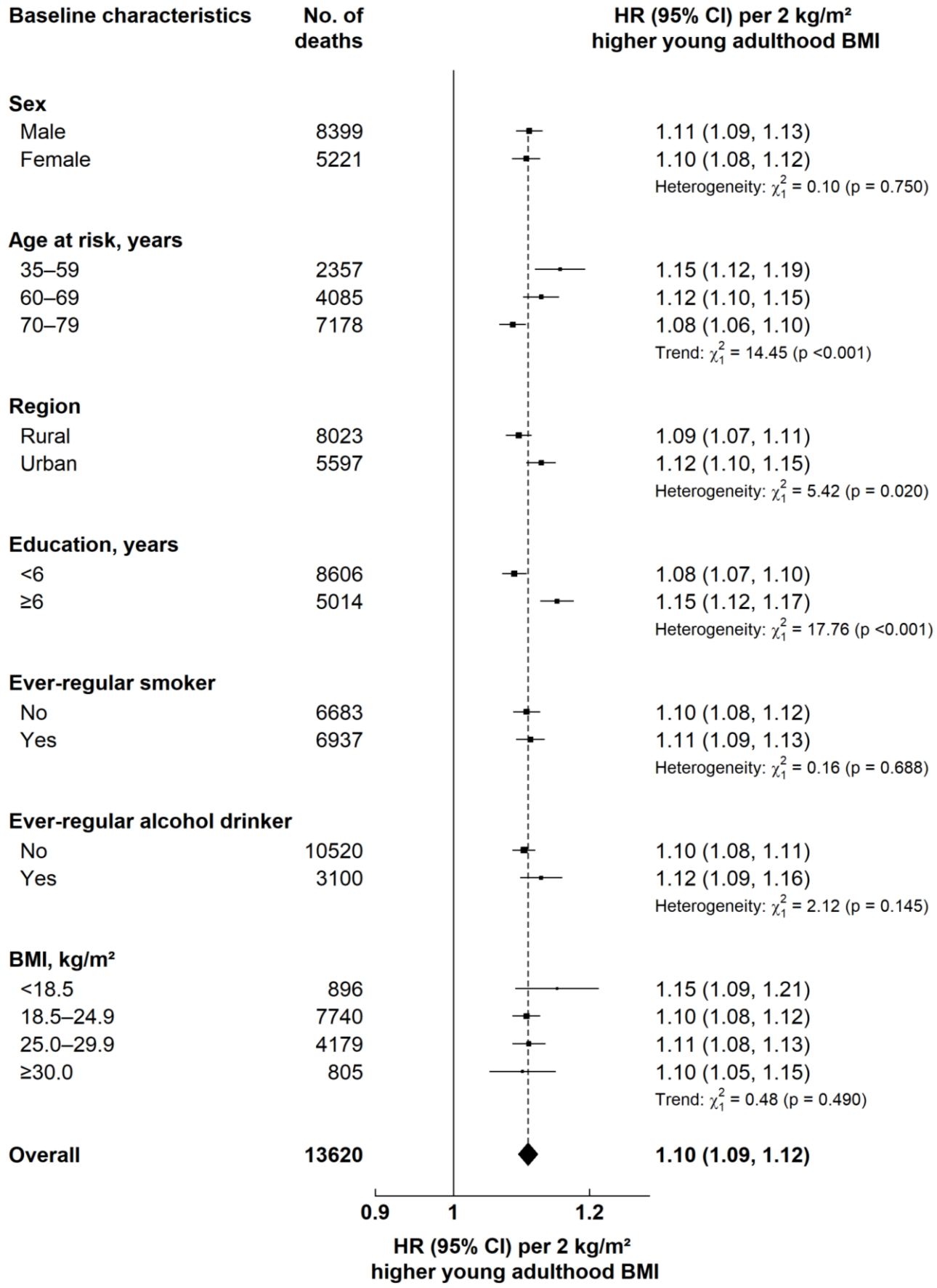
## Figure S10. Adjusted HRs for all-cause mortality per 2 kg/m² higher young adulthood BMI by baseline characteristics

Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate the 95%CIs. The dashed vertical line indicates the overall HR, and diamond indicates the overall value and its 95% CI. Analyses were stratified by age-at-risk, sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), where appropriate. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



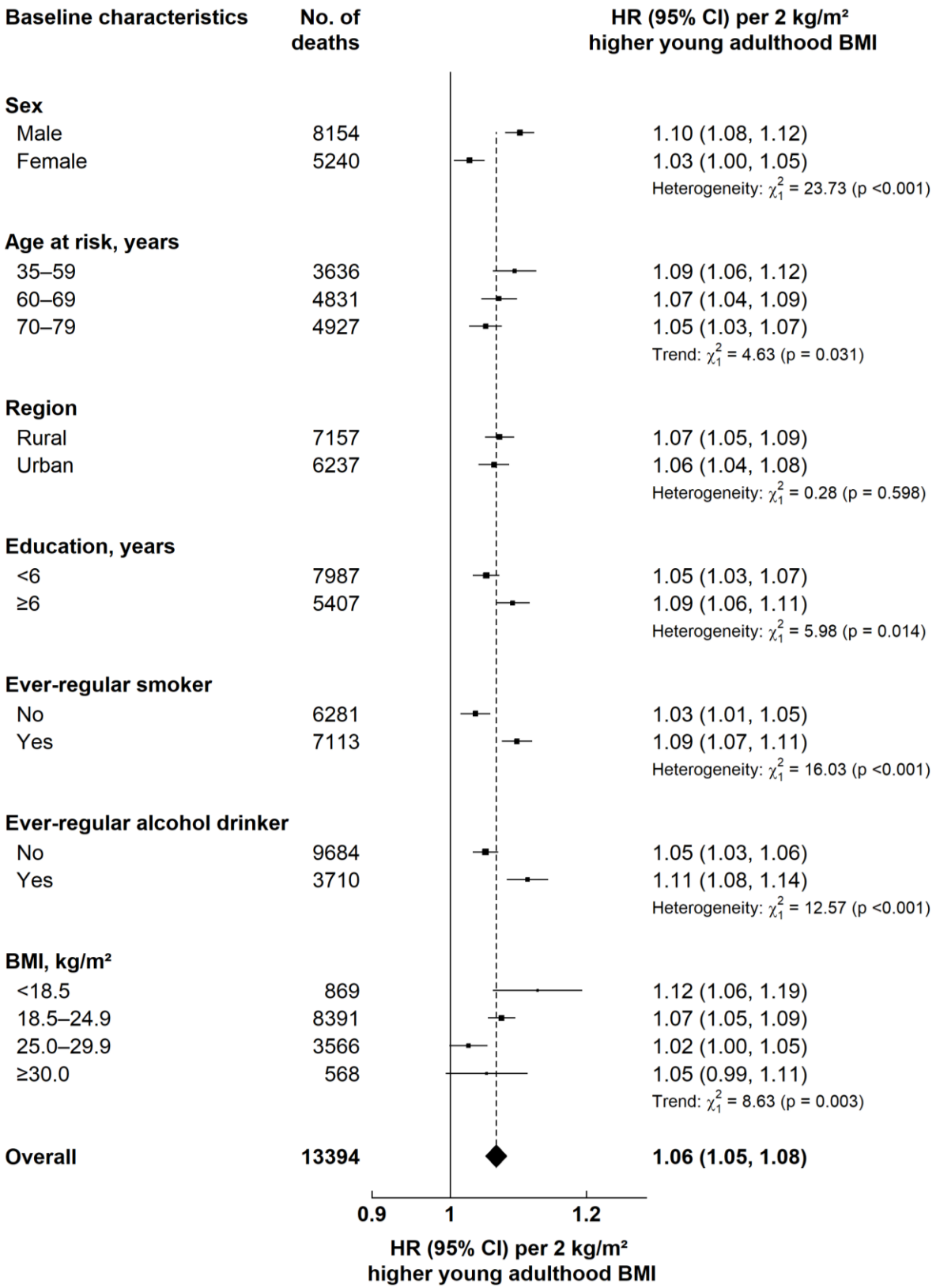
## Figure S11. Adjusted HRs for CVD mortality per 2 kg/m² higher young adulthood BMI by baseline characteristics

Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate the 95%CIs. The dashed vertical line indicates the overall HR, and diamond indicate the overall value and its 95% CI. Analyses were stratified by age-at-risk, sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), where appropriate. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



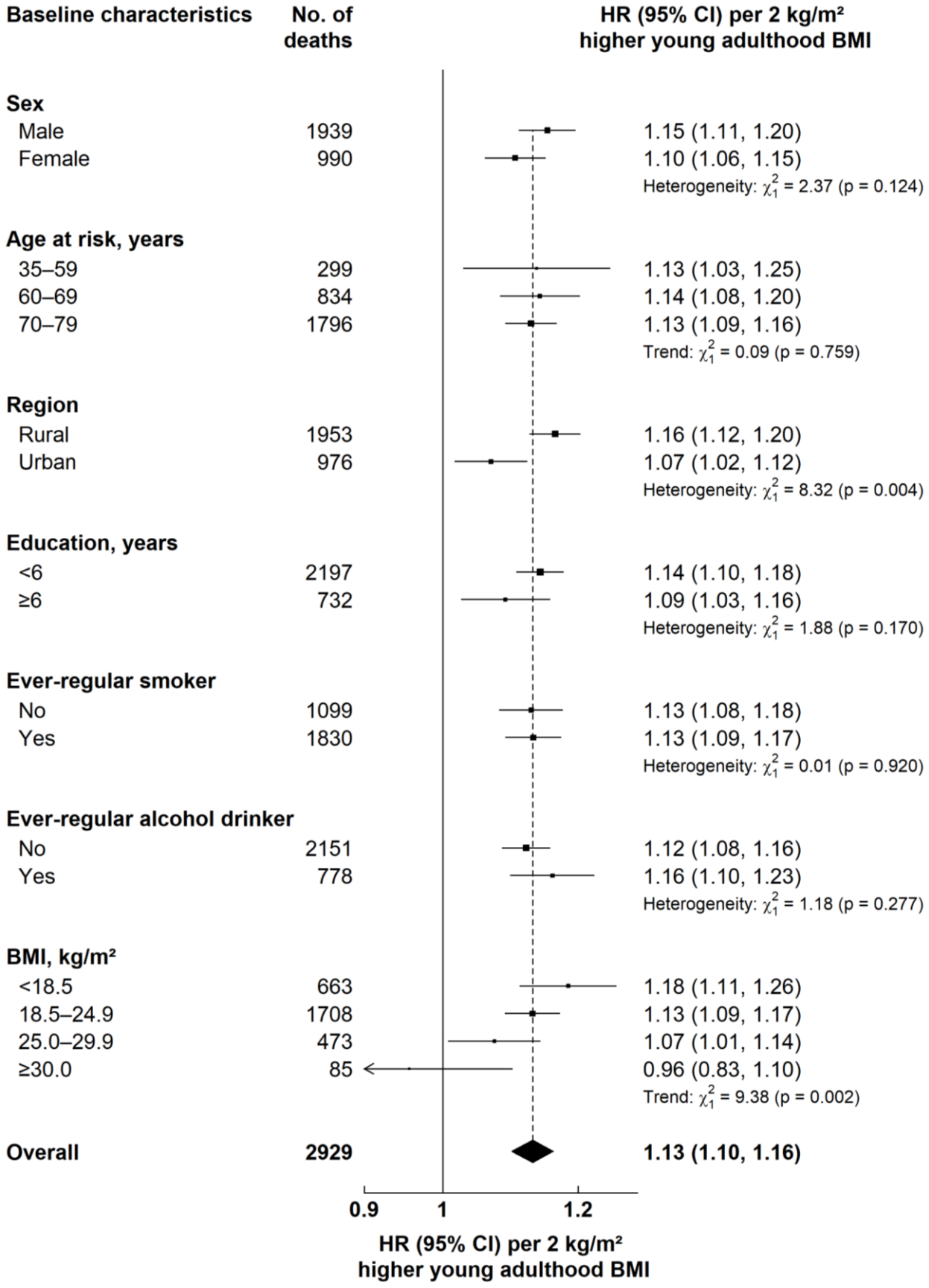
## Figure S12. Adjusted HRs for cancer mortality per 2 kg/m² higher young adulthood BMI by baseline characteristics

Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate the 95%CIs. The dashed vertical line indicates the overall HR, and diamond indicate the overall value and its 95% CI. Analyses were stratified by age-at-risk, sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), where appropriate. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



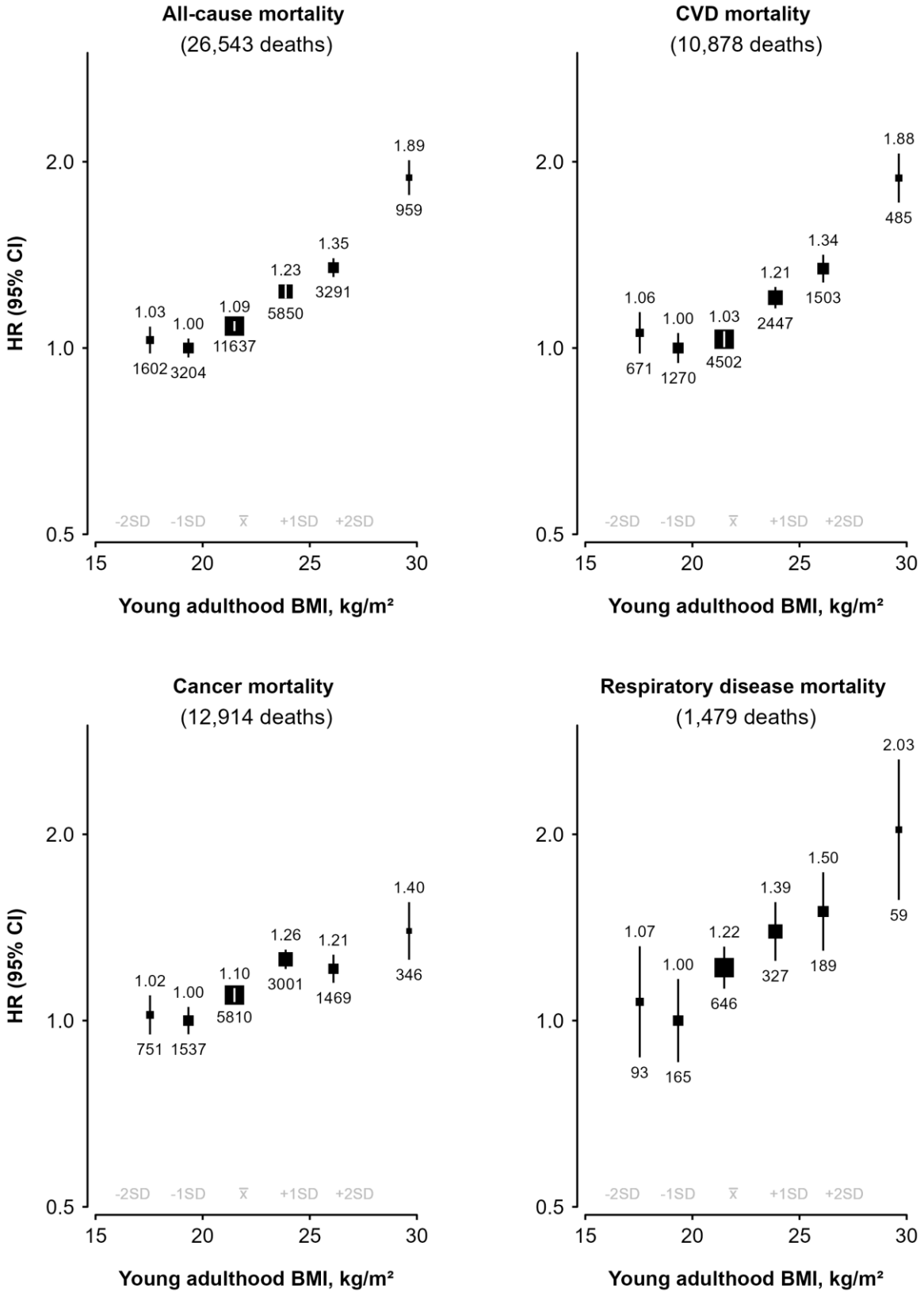
## Figure S13. Adjusted HRs for respiratory disease mortality per 2 kg/m2 higher young adulthood BMI by baseline characteristics

Squares represent the HRs with area inversely proportional to the variance of the log HRs, and horizontal lines indicate the 95%CIs. The dashed vertical line indicates the overall HR, and diamond indicate the overall value and its 95% CI. Analyses were stratified by age-at-risk, sex and study area, and adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), where appropriate. Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



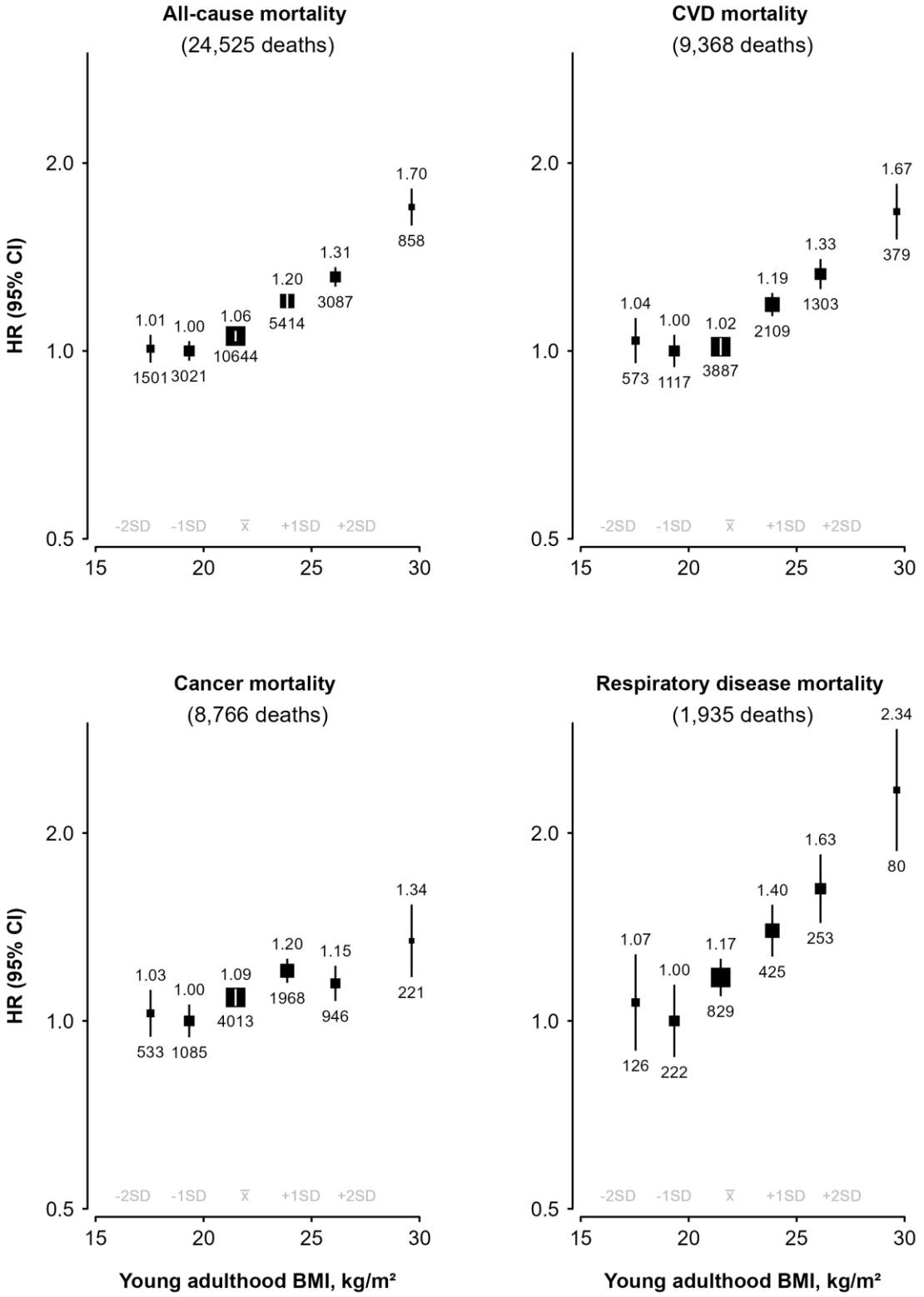
## Figure S14. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$) after excluding prior diseases

Participants with prior CVD, cancer, emphysema, bronchitis, or COPD were excluded from all-cause mortality analyses (n=49,351) and from the relevant specific outcome analyses (excluding 19,582 for CVD, 2,254 for cancer, and 29,733 for respiratory mortality ). Analyses were stratified by age-at-risk (5-year groups), sex and study area, and were adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate their 95%CIs. HRs are plotted against mean $BMI_{25}$ in each category. Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



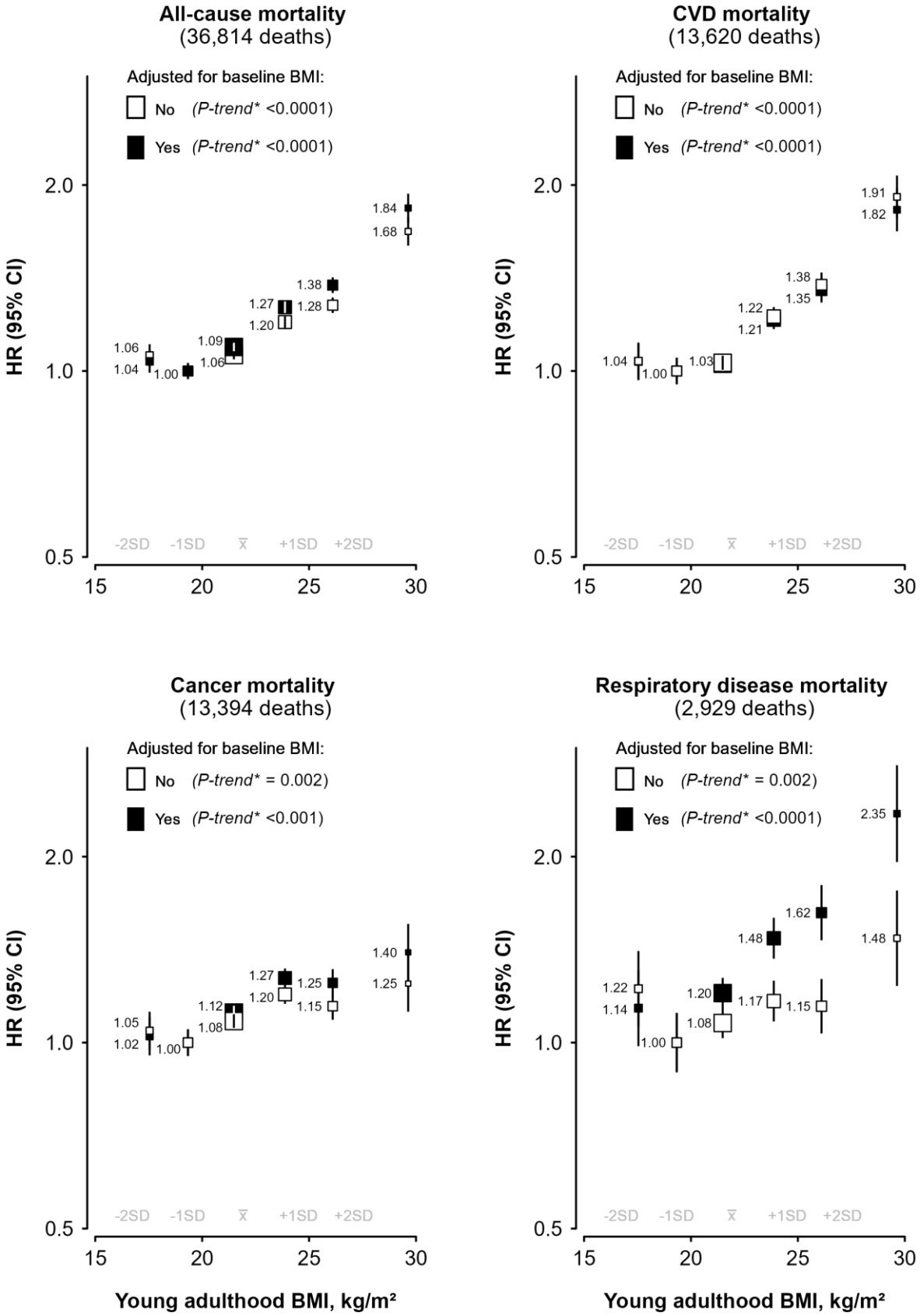
## Figure S15. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$) after excluding the first five years of follow-up

Analyse were stratified by age-at-risk (5-year groups), sex and study area and were adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with those participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of their log HRs, and error bars indicate the 95%CIs. HRs are plotted against mean $BMI_{25}$ in each category.
Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



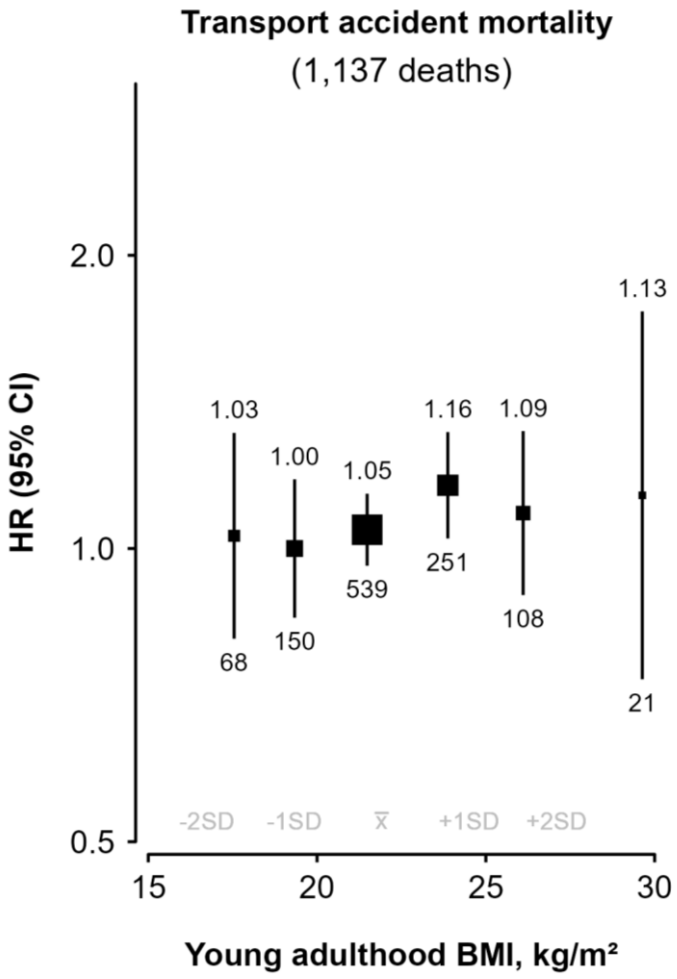
## Figure S16. Adjusted HRs for all-cause, CVD, cancer and respiratory disease mortality by young adulthood BMI ($BMI_{25}$) after additional adjustment for physical activity and consumption of fresh fruit and red meat at baseline

Analyse were stratified by age-at-risk (5-year groups), sex and study area and were adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with those participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of their log HRs, and error bars indicate the 95%CIs. HRs are plotted against mean $BMI_{25}$ in each category.
Abbreviations: BMI: body mass index, CI: confidence interval, CVD: cardiovascular disease, HR: hazard ratio



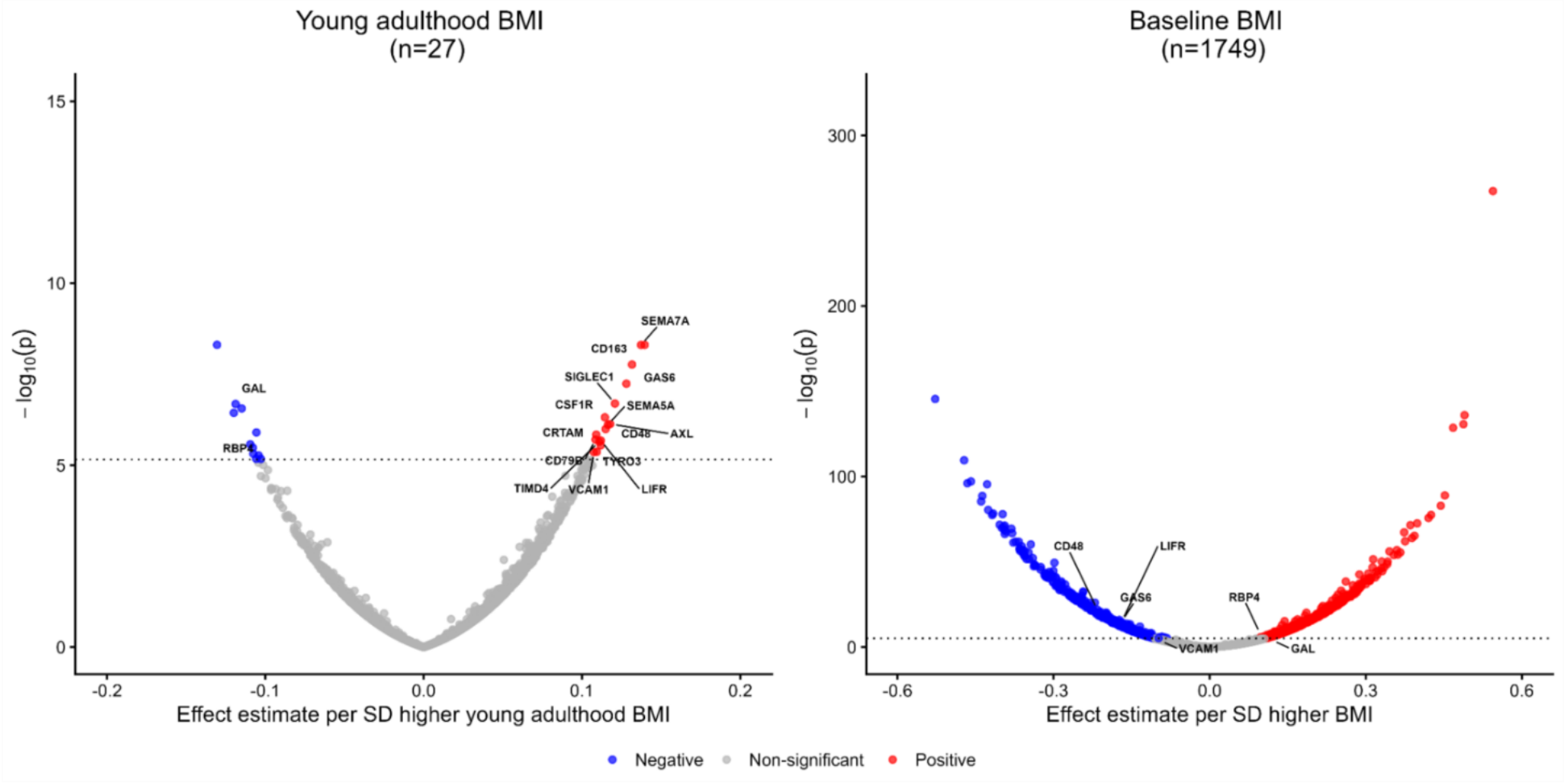
## Figure S17. Adjusted HRs for transport accident mortality by young adulthood BMI ($BMI_{25}$)

Analysis was stratified by age-at-risk (5-year groups), sex and study area and was adjusted for education, smoking, alcohol consumption and baseline BMI (deciles), with those participants having $BMI_{25}$ between 18.5–20 kg/m$^2$ as reference. Squares represent the HRs with area inversely proportional to the variance of the log HRs, and error bars indicate the 95%CIs. HRs are plotted against mean $BMI_{25}$ in each category.
Abbreviations: BMI: body mass index, CI: confidence interval, HR: hazard ratio



## Figure S18. Associations of young adulthood BMI ($BMI_{25}$) and baseline BMI with blood levels of proteins

Linear regression analyses were adjusted for age, age$^2$, sex, study area, fasting time, fasting time$^2$, ambient temperature, ambient temperature$^2$, and plate ID. The x-axis represents the effect size of the association between per SD increase in BMI with proteins, while the y-axis indicates the effect size of the association between per SD increase in baseline BMI with proteins. Bonferroni correction was applied to associations across 7,164 unique proteins. Numbers in brackets below the panel titles are the number of proteins significantly associated with $BMI_{25}$ or baseline BMI. In the left panel, only those 16 proteins which were only significantly associated with $BMI_{25}$ but not baseline BMI or demonstrate associations opposite in direction with baseline BMI were annotated. In the right panel, only those 6 proteins showing opposite-direction of association with $BMI_{25}$ were annotated. Abbreviations: BMI: body mass index



## Figure S19. Mean annual height reduction by age at baseline and by sex

The mean annual reduction in standing height was calculated as the difference in height between the baseline and the second resurvey, divided by the number of years between the two surveys.