BMI and risk of obesity-related outcomes in a large UK population-representative cohort: a CPRD/HES study

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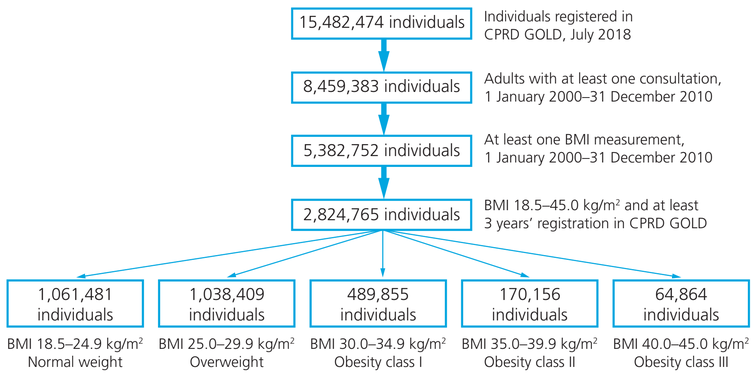
Introduction

- Several studies have indicated that individuals with higher body mass index (BMI) have higher risk for various diseases, including type 2 diabetes (T2D), gallbladder disease and osteoarthritis;[1] cardiovascular disease;[1,2] and sleep apnoea.[3]
- In this retrospective cohort study, we examined the association between BMI and the risk for 12 outcomes in a large, population-representative cohort from UK healthcare databases.

Methods

- The Clinical Practice Research Datalink (CPRD) GOLD is an ongoing database of anonymized primary care records from general practitioners in the UK, and is broadly representative of the UK population in terms of age, sex and ethnicity.[4]
- CPRD GOLD includes approximately 6.9% of the UK population.[4] For more than half of those included, primary care data are linked to other data sets, including information on secondary care.
- In this study, CPRD data were merged with Hospital Episode Statistics (HES) linkage information to capture diagnoses or events originating from hospital visits as well as those captured in CPRD GOLD.
- Individuals included in the study were 18 years or older, had a baseline BMI measurement of 18.5–45.0 kg/m^2 between the years 2000 and 2010, and had been registered in the database for at least 3 years before the index date (**Figure 1**).

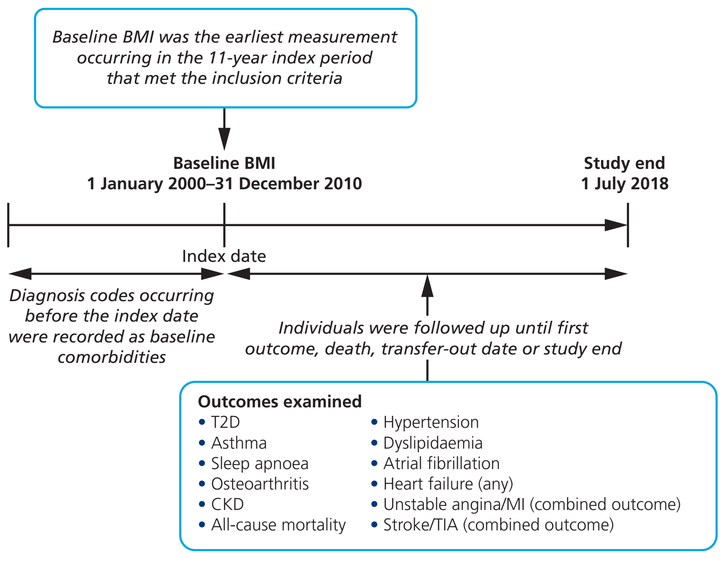
Figure 1 Study flow



BMI: body mass index; CPRD: Clinical Practice Research Datalink

- The population was stratified into groups according to baseline BMI. Individuals with a BMI of 18.5–24.9 kg/m^2 were considered normal weight and used as the reference group.
- Read codes in CPRD GOLD and International Classification of Diseases, 10th revision diagnosis codes in HES were used to identify the incidence of 12 outcomes (**Figure 2**).
- For all-cause mortality, the death date in CPRD GOLD was the outcome date. The prescription date of the first anti-hypertensive or lipid-lowering drug was the outcome date for hypertension and dyslipidaemia, respectively, if it occurred before diagnosis.
- Cox proportional hazard models with age as underlying time variable were used to estimate the association between BMI and occurrence of disease. All analyses were adjusted for sex and smoking status.
- Additional analyses to assess the impact of key baseline comorbidities and risk of disease across all BMI groups were carried out using models adjusted for history of T2D, hypertension, dyslipidaemia or any cardiovascular event.

Figure 2 Study design



BMI: body mass index; CKD: chronic kidney disease; MI: myocardial infarction; T2D: type 2 diabetes; TIA: transient ischaemic attack

Table 1 Baseline characteristics and comorbidities of individuals included in the study

	BMI group, kg/m^2				
	18.5–24.9 (reference group)	25.0–29.9	30.0–34.9	35.0–39.9	40.0–45.0
Number of individuals	1,061,481	1,038,409	489,855	170,156	64,864
Sex, % male	35.3	50.3	46.9	37.0	29.1
Smoking, % ever smoked	49.1	50.1	50.6	48.8	47.3
Median age, years (IQR)	47 (33–64)	54 (40–66)	52 (40–64)	49 (38–61)	47 (37–58)
Median follow-up, years (IQR)	10.6 (5.8–14.1)	11.2 (7.4–14.4)	11.2 (7.6–14.5)	11.2 (7.6–14.6)	11.0 (7.6–14.5)
Prevalence of comorbidities at baseline, % of individuals in each group					
Hypertension	15.5	24.9	30.4	32.0	34.3
Asthma	12.8	12.3	13.6	16.0	18.8
Osteoarthritis	7.4	11.0	12.9	13.0	13.9
Dyslipidaemia	6.3	11.4	13.4	12.8	13.4
Type 2 diabetes	2.7	5.7	8.6	10.6	14.5
Unstable angina/MI	2.6	4.0	3.9	3.1	2.3
TIA/stroke	2.4	2.7	2.6	2.0	1.8
Atrial fibrillation	2.0	2.2	2.1	1.8	1.9
Heart failure	1.3	1.5	1.7	1.7	1.9
Chronic kidney disease	1.1	1.4	1.5	1.4	1.6
Sleep apnoea	0.1	0.2	0.6	1.0	1.9

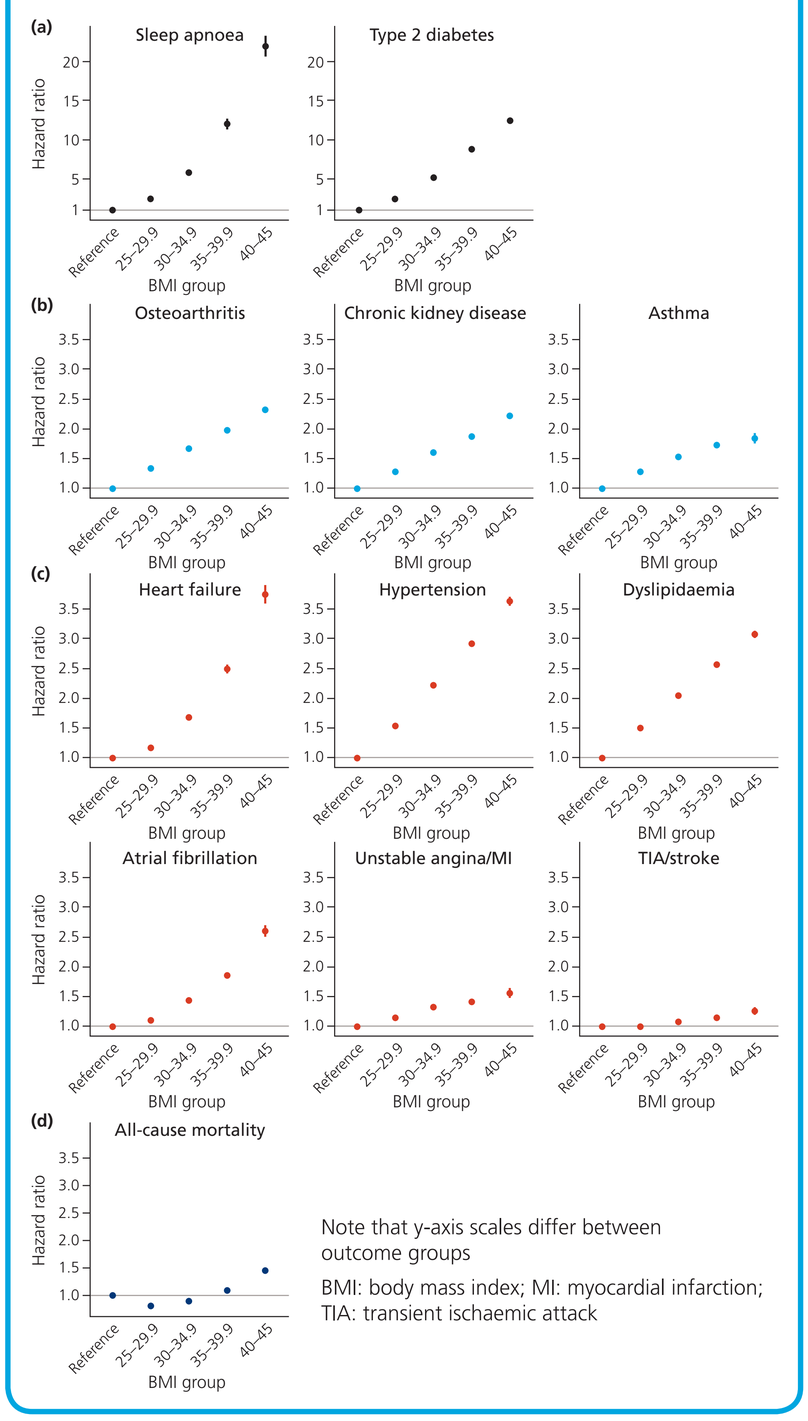
BMI: body mass index; IQR: interquartile range; MI: myocardial infarction; TIA: transient ischaemic attack

Results

- A total of 2,824,765 individuals were included in the study. Baseline characteristics for the BMI groups can be found in **Table 1**. Median age and BMI at baseline were 51 years and 26.5 kg/m^2, respectively, and 43% of the study population were male.
- Of the baseline comorbidities examined, the most common across all BMI groups were hypertension (22.8%), asthma (13.1%), osteoarthritis (10.2%), dyslipidaemia (9.7%) and T2D (5.2%). The prevalence of each outcome was greater in higher BMI classes than in groups with lower BMI.

Figure 3 Hazard ratios by BMI group for (**a & b**) non-cardiovascular outcomes, (**c**) cardiovascular outcomes and (**d**) all-cause mortality, in order of risk

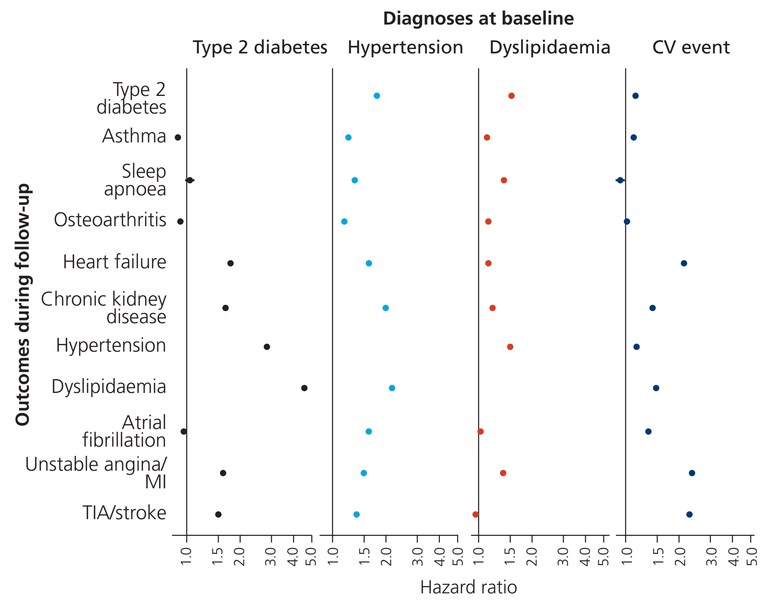
Key result



Note that y-axis scales differ between outcome groups

BMI: body mass index; MI: myocardial infarction; TIA: transient ischaemic attack

Figure 4 Hazard ratios for all outcomes by presence of baseline comorbidities (all BMI groups)



BMI: body mass index; CV: cardiovascular; MI: myocardial infarction; TIA: transient ischaemic attack

- During the follow-up period, individuals in all higher BMI groups had a higher risk for all outcomes investigated, except for transient ischaemic attack/stroke and mortality, compared with the reference group (**Figure 3**).
  - Individuals with a BMI of 40.0–45.0 kg/m^2 were at particularly high risk of sleep apnoea (hazard ratio [95% confidence interval]: 21.9 [20.6–23.3]) and T2D (hazard ratio [95% confidence interval]: 12.4 [12.1–12.7]), whereas hazard ratios for other outcomes were in the range 1.3–3.7 compared with the reference group.
- Smoking was a risk factor for all disease outcomes, and male sex was a risk factor for most disease outcomes.
- The contribution of baseline comorbidities to individuals' future risk varied across the outcomes assessed (**Figure 4**).

Strengths and limitations

- Using a large, UK-representative primary care database allowed us to examine a broad range of outcomes in the same study population. Therefore, our results can be considered highly generalizable to real-world populations.
- In future, death registry data providing information on individuals' cause of death, as well as more detailed information about their current smoking status, would allow more precise estimation of the outcome risks in such studies.

Conclusions

- Our results demonstrate that higher BMI is associated with higher risk of a range of serious health outcomes, including cardiovascular events.
- Of the outcomes examined, risks for sleep apnoea and T2D were the most strongly associated with increasing BMI.
- The associations between BMI and the occurrence of health outcomes are affected by individuals' sex and smoking status, and the presence of baseline comorbidities.

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References: (**1**) Must A et al. JAMA 1999; 282: 1523–29; (**2**) Khan SS et al. JAMA Cardiol 2018; 3: 280–87; (**3**) Li C et al. Prev Med 2010; 51: 18–23; (**4**) Herrett E et al. Int J Epidemiol 2015; 44: 827–36