Adiposity by Differing Measures and the Risk of Cataract in the UK Biobank: The Importance of Diabetes

Xianwen Shang,[1,2] Zhuoting Zhu,[1,2] Xueli Zhang,[1] Yu Huang,[1,2] Zachary Tan,[3] Wei Wang,[4] Shulin Tang,[1] Zongyuan Ge,[5] Danli Shi,[4] Yu Jiang,[4] Xiaohong Yang,[1] and Mingguang He[1,3,4]

[1]Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, China
[2]Guangdong Cardiovascular Institute, Guangzhou, China
[3]Centre for Eye Research Australia, Victoria, Australia
[4]State Key Laboratory of Ophthalmology, Zhongshan Ophthalmic Center, Sun Yat-sen University, Guangzhou, China
[5]Monash e-Research Center, Faculty of Engineering, Airdoc Research, Nvidia AI Technology Research Center, Monash University, Melbourne, Victoria, Australia

Correspondence: Mingguang He, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou 510080, China; mingguang_he@yahoo.com.
Xiaohong Yang, Guangdong Eye Institute, Department of Ophthalmology, Guangdong Provincial People's Hospital, Guangdong Academy of Medical Sciences, Guangzhou, 510080 China; syyangxh@scut.edu.cn.

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Purpose. To examine the association between adiposity by differing measures and incident cataract and identify important factors contributing to the association.

Methods. Our analysis included 153,139 adults from the UK Biobank, aged 40 to 70 years at baseline (2006–2010). Cataract was ascertained using hospital inpatient, and self-reported data until the early of 2021. Anthropometric measures, body fat percentage, and glycosylated hemoglobin (HbA1c) were measured at baseline.

Results. During a median follow-up of 10.9 years, 15,255 cases of incident cataract were documented. HbA1c was an important contributor to the association between obesity and incident cataract. Obesity; defined by body mass index was associated with an increased risk of cataract (hazard ratio [HR], 1.21 95% confidence interval [CI], 1.16–1.26), and this association was attenuated but remained significant after additional adjustment for HbA1c (HR, 1.05; 95% CI, 1.00–1.10). Similar results were observed for obesity defined by waist circumference or waist-to-hip ratio. Obesity defined by fat percentage was associated with an increased risk of cataract before but not after adjustment for covariates. The association between obesity defined by body mass index and incident cataract was positively significant in individuals with normal HbA1c (HR, 1.07; 95% CI, 1.02–1.13), but inversely significant in those with prediabetes (HR, 0.80; 95% CI, 0.67–0.96) or diabetes (HR, 0.74; 95% CI, 0.61–0.89).

Conclusions. Anthropometric measurements are more predictive of cataract than bioelectrical impedance measures. Diabetes plays an important role in the association between obesity and incident cataract.

Keywords: obesity, cataract, anthropometric measures, body fat percentage, prediabetes, diabetes, glycosylated hemoglobin, moderation analysis

In 2020, cataract further accounted for 15.2 million cases of blindness and is the leading global cause of blindness in those aged 50 years and older.[1] Cataract is the second leading cause of moderate to severe vision impairment globally in 2020 (78.8 million cases), exceeded only by undercorrected refractive error (86.1 million cases).[1] Although the surgical removal of the lens may be used for the treatment of cataract, there may be serious adverse events after cataract surgery,[2,3] and patients may bear out-of-pocket expenses.[4] Therefore, the identification of modifiable risk factors for cataract is of great importance, so as to potentially decrease the increasing prevalence of cataract in the aging population.

Data from the UK Million Women Study of 1,312,051 postmenopausal women showed that diabetes, smoking, and obesity were the main risk factors for cataract surgery.[5] Adiposity assessed by anthropometric measures, including body mass index (BMI), waist circumference, and waist-to-hip ratio, has been linked to cataract in previous studies.[6–10] Previous studies have shown that body fat percentage is a better predictor of cardiovascular risk factors compared with BMI.[11,12] However, a possible association between body fat percentage measured at different body regions and the incidence of cataract has not yet been explored. In addition, some studies have shown that adjustment for diabetes may significantly change the association between BMI and incident cataract.[13] The impact of diabetes on the association between adiposity and incident cataract, and specifically adiposity as evaluated by differing types of measures, remains to be explored. There is also currently a lack of investigation into other factors that may affect the association between adiposity and incident cataract.

Using the UK Biobank, we sought to examine the association between adiposity, as evaluated using differing measures, and incident cataract; and to identify important factors that may contribute to this association. We then examined whether the association between obesity and incident cataract was moderated by the factors that were identified.

Methods

Study Population

The UK Biobank is a population-based cohort of more than 500,000 participants aged 40 to 73 years who attended 1 of 22 assessment centers throughout the United Kingdom between 2006 and 2010.[14] The UK Biobank study design and population have been detailed previously elsewhere.[14] Briefly, approximately 9.2 million people aged 40 to 73 years who were registered with the National Health Service were invited, and 502,505 individuals were assessed at baseline. Participants provided information on geographic factors, lifestyle, and other health-related aspects through comprehensive baseline questionnaires, interviews, and physical measurements.

The UK Biobank Study's ethical approval has been granted by the National Information Governance Board for Health and Social Care and the NHS North West Multicenter Research Ethics Committee. All participants provided informed consent through electronic signature at the baseline assessment. The study adhered to the tenets of the Declaration of Helsinki. The present study was conducted under application number 62443 of the UK Biobank resource.

Anthropometric Measurements

Weight was measured using the Tanita BC-418MA body composition analyzer (Tanita Corporation, Arlington Heights, IL). Height was measured in a barefoot standing position using the Saca 202 device. BMI was computed as weight in kilograms divided by height squared in meters. Waist and hip circumference were measured using the Wessex nonstretchable sprung tape. Overall obesity was defined as a BMI of 30 kg/m^2 or greater.[15] Central obesity was defined by a waist circumference of 88 cm or greater for females and 102 cm or greater for males.[16] The waist-to-hip ratio was calculated as the waist measurement divided by the hip measurement. Obesity was defined as a waist-to-hip ratio of 0.85 or greater for females and 1.0 or greater for males, whereas overweight was defined as waist-to-hip ratio between 0.80 and 0.85 for females and between 0.90 and 1.0 for males.[17]

Body Fat Percentage by Impedance

The Tanita BC-418MA body composition analyzer was used to assess bioelectrical impedance measures. Body composition measures were recorded for the whole body and limbs separately, including measures of fat mass and fat-free mass. Obesity was defined as a body fat percentage or more than 25% in men and more than 35% in women.[18,19]

Ascertainment of Cataract

Cataract cases in the UK Biobank Study were ascertained using hospital inpatient records, and self-reported data. For hospital admission data, the codes for *International Classification of Diseases* (ICD) were used to identify cataract (ICD10: H250, H251, H252, H258, H259, H261, H262, H263, H264, H268, H269, H280, H281, H282; ICD9: 366, 3661, 3662, 3663, 3664, 3665, 3668, 3669). Additional cataract cases were classified (field code: 1278) if participants selected the corresponding item from a predefined list of answers to the question "Has a doctor ever told you that you have any of the following problems with your eyes?" Self-reported cataract has been shown to be a good indicator of lens opacification.[20] Furthermore, we used surgical procedures (OPCS4) to identify cataract events (codes: C71.2 or C75.1).[21] Types of cataract including cortical and nuclear cataract were also analyzed. The earliest recorded code date was used as the onset date of cataract. Person-years were calculated from the date of baseline assessment to the date of onset cataract, date of death, or the end of follow-up (December 31, 2020, for England and Wales and January 18, 2021, for Scotland), whichever came first.

Covariates

Sociodemographic factors including age, sex, education, and income were self-reported. Participants completed a detailed questionnaire on a touch-screen computer about their lifestyle, including smoking status and frequency of alcohol consumption. Questions about physical activity, which were similar to those used in the short form of the International Physical Activity Questionnaire.[22] were used to estimate excess metabolic equivalent-hours/week of physical activity during work and leisure time. The intake of foods, including fresh fruits, dried fruits, cooked vegetables, and raw vegetables, in the last year was also self-reported. A healthy diet score was computed based on seven commonly eaten food groups (whole grains, refined grains, vegetable, fruit, fish, red meat, and processed meat) following recommendations on dietary priorities for cardiometabolic health.[23] The total score ranged from 0 to 7 with a higher score representing a healthier diet.

Systemic conditions at baseline were defined based on self-reported data, interviews, or hospital inpatient records. Participants were asked whether they had ever been told by a doctor that they had certain common medical conditions, including heart attack, angina, stroke, hypertension, and diabetes. Heart attack and angina were combined as heart disease. Depression was recorded during the interview with a research nurse. Additional cases were identified using hospital inpatient records (before the recruitment date). For example, diabetes at baseline and that occurred during follow-up (before the onset of cataract) was identified using hospital inpatient records (ICD-9: 250, ICD-10: E10-E14) and self-reported data (field code: 1223).

Cholesterol was measured by direct enzymatic methods (Konelab, Thermo Fisher Scientific, Waltham, MA). Glycosylated hemoglobin (HbA1c) was measured using high-performance liquid chromatography on a Bio-Rad Variant II Turbo. Diabetes was also defined as HbA1c $\geq$48 mmol/mol and prediabetes as 42 to 47 mM/M.[24]

Statistical Analysis

Data were expressed as frequency (percentage) and means $\pm$ standard deviations by BMI. ANOVA was used to test the difference in continuous variables across subgroups of BMI and χ^2 test in categorical variables.

Cox proportional hazard regression models were used to examine the association between obesity and incident cataract. We first adjusted models for geographic factors, namely, age and gender (model 1). Model 2 included adjustments for model 1 plus socioeconomic and lifestyle factors, namely, ethnicity, income, education, alcohol consumption, diet score, physical activity, sleep, and smoking (additional adjustment for height to waist circumference and waist-to-hip ratio, and weight for body fat percentage). Model 3 included adjustments for model 2 plus chronic conditions, namely, hypertension, heart disease, stroke, depression, age-related macular degeneration, and glaucoma. Model 3 and biomarkers were cholesterol and HbA1c and were entered into a full multivariable model (model 4). We would enter the covariates individually into models if the association between adiposity and incident cataract was substantially attenuated/strengthened after adjustment for the corresponding group of variables (≥5% of total variance). The Benjamin–Hochberg procedure was used to control the false discovery rate at a 5% level for multiple comparisons.[25] The association between obesity and cataract surgery, cortical cataract, and nuclear cataract was then tested.

The association between obesity and incident cataract stratified by diabetes (defined by self-reported data, interviews, or hospital inpatient records), HbA1c, and ethnicity was then analyzed.

A sensitivity analysis was conducted to examine the association between obesity and incident cataract by excluding individuals who developed cataract in the first five years of follow-up.

Data analyses were conducted using SAS 9.4 for Windows (SAS Institute Inc.) and all P values were two-sided with statistical significance set at less than 0.05.

Results

Population Selection and Baseline Characteristics

A total of 502,505 participants were assessed at baseline. After excluding individuals with missing data on cataract at baseline (n = 327,891) or body composition (n = 4716), or with prevalent cataract (n = 16,759), 153,139 adults (54.1% females) aged 40 to 70 years (mean ± standard deviation: 56.5 ± 8.1) were included in the final analysis (Fig. 1). Obese individuals were more likely to be older, men, non-Whites, and never smokers, and have lower physical activity, lower diet score, and long or short sleep duration compared with those with normal weight. Obesity was associated with

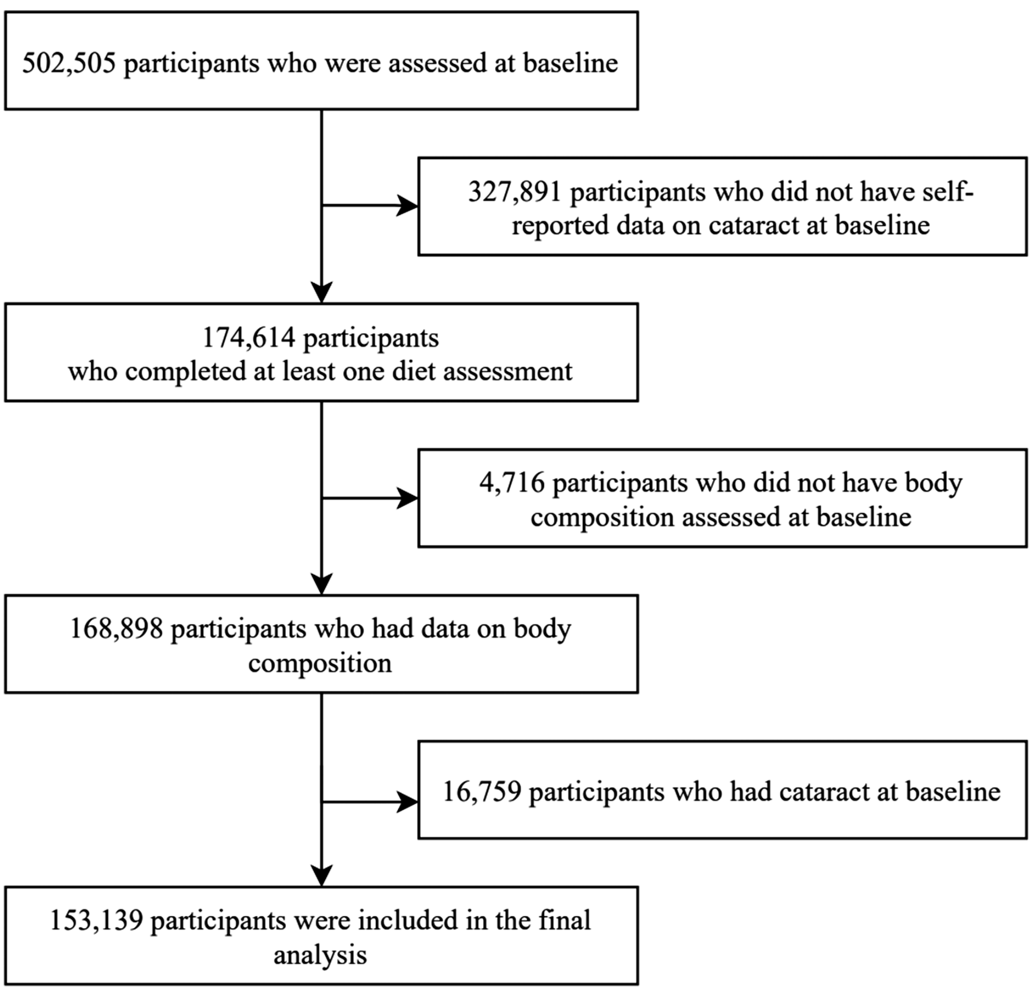

Figure 1. Flowchart of population selection from the UK Biobank.

Table. Baseline Characteristics of Participants According to BMI

	Normal Weight (n = 49,183)	Overweight (n = 64,858)	Obesity (n = 39,098)	P Value*
Age (years)	55.87 ± 8.19	57.06 ± 8.05	56.78 ± 7.88	<0.0001
Gender†				<0.0001
Women		36.6	24.8	
Men		49.1	26.4	
Ethnicity†				<0.0001
Whites		42.3	25.2	
Non-Whites		42.7	28.5	
Unknown		40.7	27.8	
Education†				<0.0001
0–5 years		41.2	19.6	
6–12 years		42.8	27.0	
≥13 years		43.3	33.0	
Missing		42.5	30.8	
Household income (pounds)†				<0.0001
<18,000		40.4	31.4	
18,000–30,999		43.3	25.7	
31,000–51,999		43.6	23.9	
52,000–100,000		42.9	21.5	
>100,000		42.4	16.4	
Unknown		38.9	30.0	
Not answered		42.1	26.5	
Physical activity (MET minutes/week)	2830 ± 2497	2685 ± 2455	2402 ± 2299	<0.0001
Diet score	4.10 ± 1.45	3.82 ± 1.42	3.66 ± 1.42	<0.0001
Alcohol consumption				<0.0001
Never		38.5	31.6	
Previous		38.5	32.8	
Current		42.7	24.9	
Missing		39.7	33.1	
Smoking				<0.0001
Never		41.5	24.0	
Former		44.0	28.5	
Current		41.5	23.6	
Missing		45.4	31.8	
Sleep duration (hours)				<0.0001
<7		41.3	29.6	
7–9		42.9	23.5	
>9		38.7	39.5	
Missing		35.5	37.7	
Cholesterol (mmol/L)	5.70 ± 1.04	5.72 ± 1.11	5.56 ± 1.16	<0.0001
HbA1c (mM/M)	34.84 ± 5.11	36.01 ± 6.45	38.87 ± 9.33	<0.0001
AMD	67 (0.1)	108 (0.2)	60 (0.2)	
Glaucoma	1623 (3.3)	2411 (3.7)	1540 (3.9)	
Diabetes	853 (1.7)	2642 (4.1)	4302 (11.0)	<0.0001
Heart disease	1083 (2.2)	2828 (4.4)	2817 (7.2)	<0.0001
Stroke	566 (1.2)	1039 (1.6)	979 (2.5)	<0.0001
Hypertension	7532 (15.3)	17750 (27.4)	16902 (43.2)	<0.0001
Depression	2451 (5.0)	3632 (5.6)	3244 (8.3)	<0.0001
Waist circumference (cm)	78.5 ± 8.3	91.1 ± 8.4	105.3 ± 112	<0.0001
Waist-to-hip ratio	0.82 ± 0.07	0.89 ± 0.08	0.93 ± 0.09	<0.0001
Weight (kg)	64.2 ± 8.7	78.4 ± 9.6	96.0 ± 14.6	<0.0001
% fat mass (whole body)	26.8 ± 7.1	31.2 ± 7.3	38.4 ± 7.8	<0.0001
% fat mass (trunk)	25.6 ± 6.9	31.6 ± 6.2	38.6 ± 6.3	<0.0001
% fat mass (arm)	24.1 ± 7.0	29.0 ± 8.5	38.2 ± 11.0	<0.0001
% fat mass (leg)	28.8 ± 9.6	30.9 ± 10.2	37.7 ± 10.6	<0.0001

Data are mean ± standard deviation, or number (%). AMD, age-related macular degeneration; MET, metabolic equivalent.
* ANOVA was used to test the difference of continuous variables between across subgroups of BMI and χ^2 for categorical variables.
† Data for these variables are prevalence of overweight or obesity.

higher a HbA1c and body fat percentage and a higher prevalence of diabetes, hypertension, depression, heart disease, and stroke at baseline (Table).

Incidence of Cataract

More than 1,662,769 person-years of follow-up (median length of follow-up, 10.9; interquartile range,

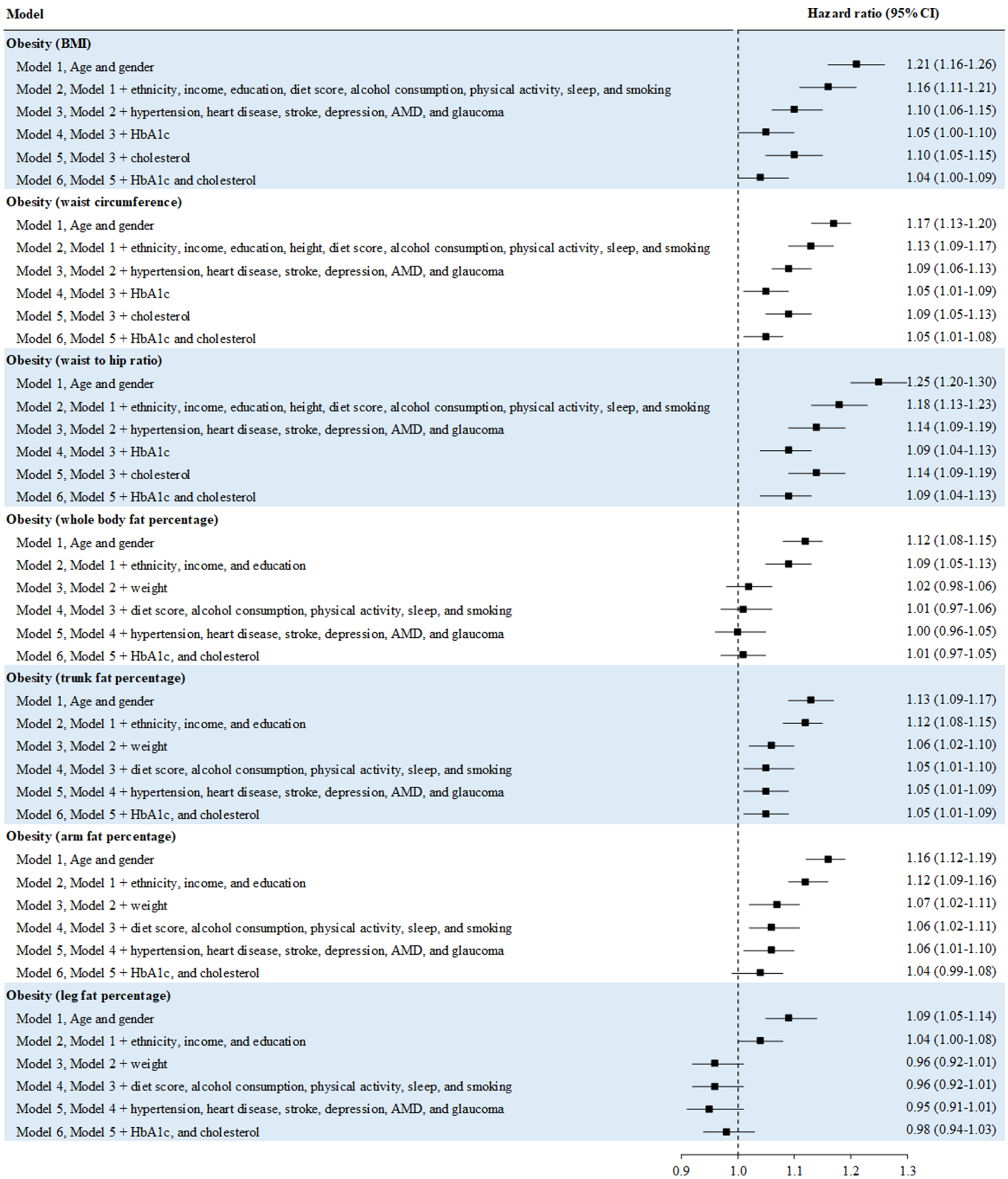

FIGURE 2. Adiposity by anthropometric measures and the incidence of cataract. The HR (95% CI) for incident cataract associated with obesity (obesity versus normal weight) was estimated using Cox regression models. **P* value for the association between obesity defined by trunk fat percentage and incident cataract = 0.0643.

10.6–11.3 years), 15,255 cases of incident cataract were documented. The incidence of cataract (cases per 1000 person-years) in individuals with normal weight, overweight, and obesity defined by BMI was 8.2, 9.2, and 10.4, respectively.

Obesity and Incident Cataract

The prevalence of obesity defined by BMI, waist circumference, and waist-to-hip ratio was 25.5%, 35.0%, and 26.6%, respectively. The prevalence of obesity defined by fat percentage of whole body, trunk, arms, and legs was 57.8%, 58.4%, 43.5%, and 56.7%, respectively.

Obesity defined by BMI was associated with a higher incidence rate of cataract after adjustment for age, gender, ethnicity, education, income, diet score, physical activity, smoking, alcohol consumption, sleep duration, hypertension, depression, heart disease, stroke, total cholesterol, AMD, and glaucoma (HR 1.10; 95% confidence interval, 1.05–1.15; model 5). This association remained significant

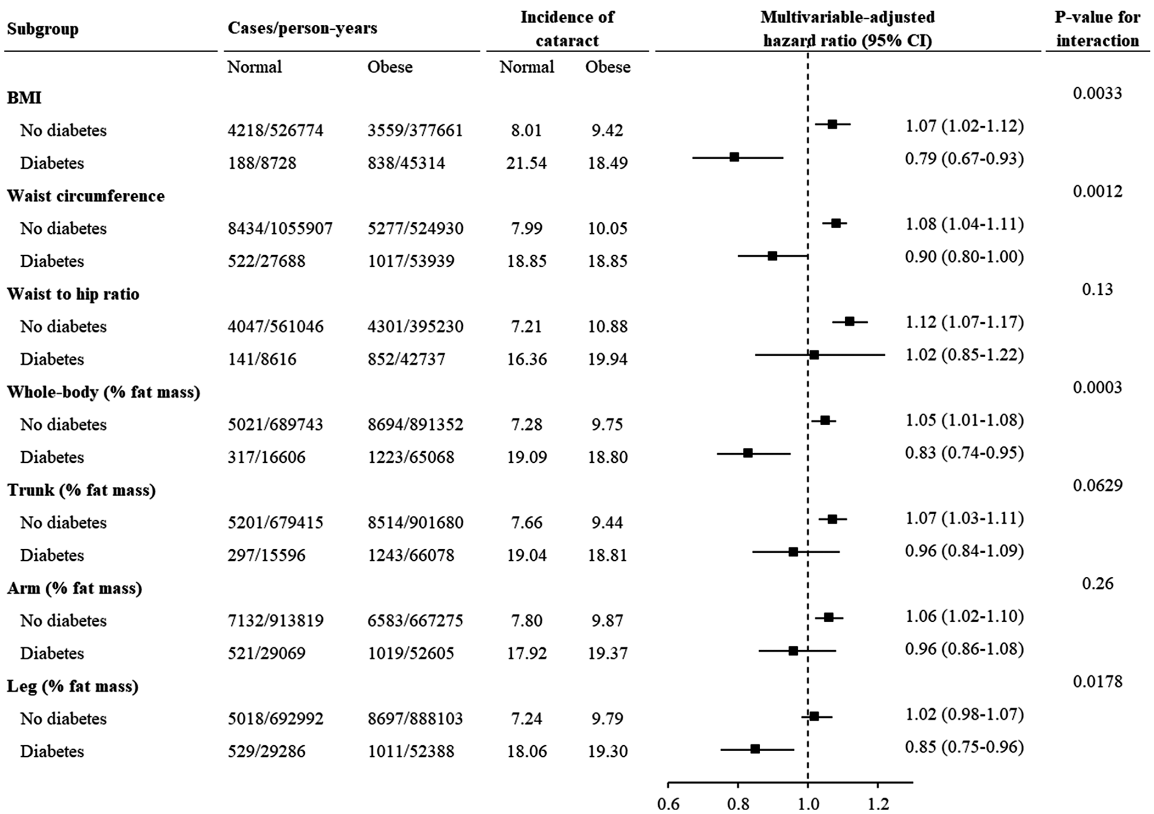

Figure 3. Potential moderation effects of diabetes on the association between adiposity and the incidence of cataract. Diabetes was defined based on self-reported data, interviews, or hospital inpatient records. The HR (95% CI) for incident cataract associated with obesity (obese versus normal individuals) was estimated using Cox regression models. For anthropometric measures, obesity was defined by a BMI of 30 kg/m^2 or greater, a waist circumference of 88 cm or greater for females and 102 cm or greater for males, and a waist-to-hip ratio of 0.85 or greater for females and 1.00 or greater for males. For body fat percentage, obesity was defined as a fat percentage or more than 25% in men and more than 35% in women. The Benjamin–Hochberg procedure was used to control the false discovery rate at a level of 5% for multiple comparisons with the *P* value cut-off point of significance (interaction) as 0.0286.

after additional adjustment for HbA1c (HR, 1.04; 95% CI, 1.00–1.10; model 6). Similarly, the association of obesity defined by waist circumference (HR, 1.05; 95% CI, 1.01–1.08) or waist-to-hip ratio (HR, 1.09; 95% CI, 1.04–1.13) with incident cataract was significant after adjustment for HbA1c and other covariates (model 6).

Obesity defined by whole body fat percentage was associated with a higher incidence rate of cataract before (HR, 1.12; 95% CI, 1.08–1.15; model 2) but not after adjustment for weight at baseline (HR, 1.02; 95% CI, 0.98–1.06; model 3). Obesity defined by trunk fat percentage was independently associated with a higher incidence rate of cataract (HR, 1.05; 95% CI, 1.01–1.09; model 6). Obesity defined by fat percentage of arms (HR, 1.16; 95% CI, 1.12–1.19), or legs (HR, 1.09; 95% CI, 1.05–1.14) was associated with a higher incidence of cataract before (model 1) but not after adjustment for covariates at baseline (model 6: HR, 1.04; 95% CI, 0.99–1.08 for arms and HR 0.98; 95% CI, 0.94–1.03 for legs) (Fig. 2).

Obesity and Incidence of Cataract Surgery and Types of Cataract

Individuals with obesity defined by BMI had a higher incidence rate of cataract surgery compared with those without obesity after adjustment for covariates (HR, 1.09; 95% CI, 1.02–1.16; model 4). Obesity defined by waist circumference (HR, 1.07; 95% CI, 1.01–1.12) and waist-to-hip ratio (HR, 1.09; 95% CI, 1.02–1.17) was associated with a higher incidence rate of cataract surgery independent of covariates (model 4). Obesity defined by fat percentage at arm (HR, 1.07; 95% CI, 1.00–1.14) and trunk (HR, 1.08; 95% CI, 1.00–1.14) was independently associated with an increased risk of cataract surgery. Whole-body (HR, 1.02; 95% CI, 0.96–1.08) or leg (HR, 1.01; 95% CI, 0.94–1.08) fat percentage was not significantly associated with incident cataract surgery after adjustment for covariates (model 4, Supplementary Table S1).

Obesity defined by waist circumference (HR, 1.06; 95% CI, 1.00–1.12) or and waist-to-hip ratio (1.09; 95% CI, 1.02–1.18) but not BMI (1.00; 95% CI, 0.93–1.08) was independently associated with a higher incidence rate of nuclear cataract (model 4). Obesity defined by fat percentage (HR, 0.99; 95% CI, 0.92–1.06) for the whole body (HR, 1.02; 95% CI, 0.95–1.09), for the trunk, 0.94; 95% CI, 0.87–1.02) and for the arms, 1.04; 95% CI, 0.97–1.12) for legs) was not independently associated with the incidence of nuclear cataract (model 4) (Supplementary Table S2). Obesity defined by BMI (HR, 1.18; 95% CI, 1.00–1.40) but not waist circumference (HR, 1.03; 95% CI, 0.90–1.17) or waist-to-hip ratio (1.12; 95% CI, 0.95–1.32) was associated with a higher incidence rate of cortical cataract (model 4). Obesity defined by trunk fat percentage (HR, 1.23; 95% CI, 1.05–1.44) was associated with a higher incidence of cortical cataract (model 4) (Supplementary Table S3).

Subgroup	Cases/person-years Normal	Cases/person-years Obese	Incidence of cataract Normal	Incidence of cataract Obese	Multivariable-adjusted hazard ratio (95% CI)	P-value for interaction
BMI						<0.0001
HbA1c (<42 mmol/mol)	3725/474825	2857/313451	7.84	9.11	1.07 (1.02-1.13)	
HbA1c (42-47 mmol/mol)	170/9434	448/32892	18.02	13.62	0.80 (0.67-0.96)	
HbA1c (≥48 mmol/mol)	144/6298	668/35626	22.86	18.75	0.74 (0.61-0.89)	
Waist circumference						<0.0001
HbA1c (<42 mmol/mol)	7399/946876	4282/440735	7.81	9.72	1.07 (1.03-1.11)	
HbA1c (42-47 mmol/mol)	410/27128	590/41307	15.11	14.28	0.89 (0.78-1.02)	
HbA1c (≥48 mmol/mol)	403/19831	831/42205	20.32	19.69	0.88 (0.77-0.99)	
Waist to hip ratio						0.0472
HbA1c (<42 mmol/mol)	3610/506189	3453/329490	7.13	10.48	1.10 (1.05-1.15)	
HbA1c (42-47 mmol/mol)	133/9475	489/32433	14.04	15.08	0.94 (0.77-1.14)	
HbA1c (≥48 mmol/mol)	111/6071	733/34510	18.28	21.24	0.95 (0.77-1.16)	
Whole-body (% fat mass)						0.0025
HbA1c (<42 mmol/mol)	4459/621965	7223/765835	7.17	9.43	1.03 (0.99-1.07)	
HbA1c (42-47 mmol/mol)	212/14893	790/53556	14.23	14.75	0.95 (0.81-1.11)	
HbA1c (≥48 mmol/mol)	229/11522	1006/50572	19.87	19.89	0.88 (0.76-1.02)	
Trunk (% fat mass)						0.1200
HbA1c (<42 mmol/mol)	4600/610530	7082/777270	7.53	9.11	1.05 (1.01-1.09)	
HbA1c (42-47 mmol/mol)	233/15331	769/53118	15.20	14.48	0.98 (0.84-1.15)	
HbA1c (≥48 mmol/mol)	221/11059	1014/51035	19.98	19.87	0.97 (0.83-1.12)	
Arm (% fat mass)						0.0161
HbA1c (<42 mmol/mol)	6253/819895	5429/567905	7.63	9.56	1.05 (1.01-1.09)	
HbA1c (42-47 mmol/mol)	357/25584	645/42865	13.95	15.05	0.99 (0.86-1.14)	
HbA1c (≥48 mmol/mol)	413/20837	822/41257	19.82	19.92	0.91 (0.80-1.03)	
Leg (% fat mass)						0.0003
HbA1c (<42 mmol/mol)	4387/621667	7295/766133	7.06	9.52	1.01 (0.96-1.06)	
HbA1c (42-47 mmol/mol)	274/20923	728/47526	13.10	15.32	0.98 (0.83-1.16)	
HbA1c (≥48 mmol/mol)	422/20831	813/41263	20.26	19.70	0.80 (0.69-0.92)	

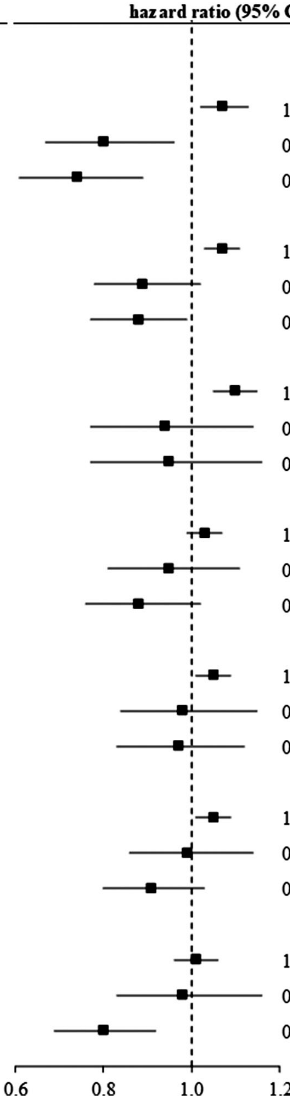

FIGURE 4. Potential moderation effects of HbA1c on the association between adiposity and incidence of cataract. The HR (95% CI) for incident cataract associated with obesity (obese vs. normal individuals) was estimated using Cox regression models. For anthropometric measures, obesity was defined by a BMI of 30 kg/m^2 or greater, a waist circumference of 88 cm or greater for females and 102 cm or greater for males, and a waist-to-hip ratio of 0.85 or greater for females and 1.00 or greater for males. For body fat percentage, obesity was defined as fat percentage of more than 25% in men and more than 35% in women. The Benjamin–Hochberg procedure was used to control the false discovery rate at a level of 5% for multiple comparisons with the *P* value cut-off point of significance (interaction) as 0.0357.

Obesity and Incident Cataract Stratified by Diabetes

A significant interaction between diabetes and obesity defined by BMI, waist circumference, and whole-body fat percentage for incident cataract was observed (all *P* values for interactions of <0.0178). For example, obesity defined by BMI was associated with a higher incidence rate of cataract in individuals without diabetes (HR, 1.07; 95% CI, 1.02–1.12) and with a lower incidence rate in those with diabetes (0.79; 95% CI, 0.67–0.93) (Fig. 3).

Obesity and Incident Cataract Stratified by HbA1c

There was a significant interaction between HbA1c and obesity defined by all markers besides trunk fat percentage for incident cataract (all *P* values for interactions <0.0472). The association between obesity defined by BMI and incident cataract was positively significant in individuals with normal HbA1c (HR, 1.07; 95% CI, 1.02–1.13), but inversely significant in those with prediabetes (HR, 0.80; 95% CI, 0.67–0.96) or diabetes (HR, 0.74; 95% CI,(.61–0.89). Similar results were found for obesity defined by other markers (Fig. 4).

Sensitivity Analysis

A sensitivity analysis among 149,693 participants who did not develop cataract in the first 5 years of follow-up showed that the association between obesity and cataract was consistent with the main findings (Supplementary Fig. S1).

Discussion

This large prospective cohort study with long-term follow-up for cataract investigated the association between adiposity by differing measures and cataract and the important role of diabetes in this association. Obesity defined by BMI, waist circumference, waist-to-hip ratio, and trunk fat percentage was associated with a higher incidence rate of cataract independent of HbA1c and other covariates. Moderation analysis showed that there was a positive association between obesity and incident cataract in individuals with normal HbA1c, and an inverse association in those with prediabetes or diabetes.

Previous studies have linked anthropometric measurements to cataract, but results have been inconsistent to date. A cross-sectional study of 466 women aged 53 to 73 years from the United States showed that obesity defined by both BMI and waist circumference was associated with a higher prevalence of cataract.[26] Data from the Physicians' Health Study of 17,150 men aged 40 to 84 years at baseline demonstrated that obesity defined by waist-to-hip ratio but not BMI was associated with an increased risk of cataract over 14 years of follow-up.[7] However, HbA1c was not adjusted for in the multivariable analyses carried out in these previous studies.[7,13,27] We found that obesity defined by BMI, waist circumference, and waist-to-hip ratio were all associated with a higher incidence rate of cataract after adjustment for HbA1c. More research is needed to warrant our findings.

No previous study has linked body fat percentage in different regions of the body to the incidence of cataract. Fat percentage at the trunk, but not other regions, seem to be predictive of cataract in our study. Research has shown that bioelectrical impedance analysis is relatively accurate in the estimation of body composition,[28] and android obesity is more predictive of metabolic health compared with gynoid obesity.[29] This finding might partly explain why trunk fat percentage is a stronger predictor of cataract in our study. However, the prevalence of obesity defined by body fat percentage was much higher than that by anthropometric measurements, suggesting that body fat percentage is more likely to misclassify individuals with a normal fat mass as having obesity. The present cut-offs of body fat percentage for obesity may not be ideal to predict the risk of cataract, as obesity defined by quintile 5 of fat percentage was independently associated with a higher incidence rate of cataract in our study (Supplementary Table S4).

Cataract is a multifactorial disease with well-known contributors, including age, education, socioeconomic factors, lifestyle, diabetes, and other cardiometabolic disorders. Our study has demonstrated that some adiposity markers are associated with cataract independent of these factors, but this association may also be due to confounding. Notably, chronic conditions, including hypertension, heart disease, stroke, and depression, may mediate the association between obesity and cataract such that the adjustment for these conditions may result in collider bias. However, our analysis showed that the adjustment for these conditions did not change the association substantially, suggesting a low risk of collider bias. We found simple anthropometric assessments are a similar or better measure for predicting cataract than bioelectrical impedance assessments are. Similar results were found for severe cataract (cataract surgery), as well as for types of cataract, including nuclear and cortical cataracts. Although we have linked multiple adiposity measures to cataract, whether fat distribution measured by computed tomography assessment or dual energy x-ray absorptiometry with a more accurate assessment of fat mass is more predictive of cataract than anthropometric assessments remains to be investigated.[30] Overall, simple anthropometric measures are useful in the prediction of cataract, regardless of the severity and type of cataract.

Several previous studies have highlighted the importance of diabetes in the association between obesity and cataract.[13,31–33] Our further analysis demonstrated that obesity was associated with a higher incidence rate of cataract in individuals without diabetes, but a lower incidence rate in those with diabetes. These findings were confirmed by the analysis stratified by subgroups of HbA1c. The mechanisms in which obesity has divergent associations with incident cataract in individuals with and without diabetes are unknown. Our results are consistent with the UK Million Women Study of 1,312,051 postmenopausal women showing that obesity defined by BMI was associated with an increased risk of cataract surgery in those without diabetes only at baseline.[5] A cross-sectional study of 420 Asian patients with type 2 diabetes reported that BMI was inversely associated with mild to moderate and severe diabetic retinopathy (odds ratio, 0.92 [0.85–0.99] per 1-unit increase).[34] A prospective cohort study of 2053 participants with poorly controlled type 2 diabetes showed that those with a BMI of less than 25 but not 28 kg/m^2 or greater was associated with an increased risk of mortality compared with those with a BMI between 25 and 27 kg/m^2.[35] In the Louisiana State University Hospital–Based Longitudinal Study of diabetic patients, the lowest mortality rate during a mean follow-up of 8.7 years was observed in those with obesity (BMI of 30–35 kg/m^2).[36] Another prospective cohort study of 3443 participants with type 2 diabetes reported that a higher BMI was associated with a decreased risk of mortality.[37] Although no previous study has reported the association between obesity and incident cataract stratified by diabetes and HbA1c, these studies on diabetic retinopathy and mortality provide indirect evidence for the potential benefits of obesity in patients with diabetes and potential detrimental effects of obesity in those without diabetes. It is possible that people with diabetes for a long duration who had their weight decreased to a normal level at baseline may have a higher risk cataract in our study, because a loss of more than 10% of body weight was shown to result in worse cardiovascular health.[38] The inverse association between obesity and cataract among diabetic participants may also be attributed to the fact that obese participants, after a diagnosis of diabetes, were more likely to modify their lifestyle behaviors, thus leading to a decreased risk of metabolic conditions (but not obesity) and cataract compared with those normal weight individuals.

This the largest prospective cohort study is the largest to examine comprehensively the association of obesity defined by differing measures with incident cataract. Our study also uniquely examined whether the association between obesity and incident cataract was modified by diabetes. The present study also has several potential limitations. First, some incident cataract cases might not be captured in the medical records (self-reported data for eye health during follow-up are only available in a small proportion of the participants), which might bias the association between obesity and cataract. Second, because of the observational design of our study, causal relationships cannot be established based on our findings. Third, the prevalence of cataract at baseline

(40–70 years of age) was 9.9% and the overall rate was 19.0% at the end of follow-up (50–84 years of age), which was lower than that of European adults.[39] This finding suggests that the study participants are healthier than the general population. Fourth, individuals with obesity are more likely to have more comorbidities and are more likely to seek help from physicians, thus resulting in better diagnosis of cataract, which might have biased the association between obesity and cataract. However, obesity is more likely to occur before these comorbidities, such that obesity is more likely to be causal risk factor of cataract. Fifth, some other confounders such as ultraviolet light exposure that might influence the association between obesity and incident cataract were not adjusted for in our analysis. Finally, our analysis was restricted to a subgroup of the UK Biobank cohort; thus, our findings may not be generalized to the whole population in the UK.

In conclusion, anthropometric measurements are even more predictive of cataract than bioelectrical impedance measures are. Diabetes plays an important role in the association between obesity and incident cataract. Future research needs to investigate the mechanisms for the inverse association between obesity and cataract in individuals with diabetes.

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