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Adiposity and dementia among Chinese adults: longitudinal study in the China Health and Retirement Longitudinal Study (CHARLS)

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BACKGROUND: Evidence on the age-dependent association between adiposity and risk of dementia in the Chinese population is unclear. We aim to disentangle the association of mid- and late- life adiposity with subsequent dementia risk in Chinese adults and compare ageing trajectories of adiposity between those with/out dementia.

METHODS: Dementia was ascertained based on cognitive batteries and the Activity of Daily Living Scale in the China Health and Retirement Longitudinal Study (CHARLS). Adiposity was measured by body mass index (BMI), waist circumference (WC), and waist-to-height ratio (WtHR). We estimated hazard ratio (HR) of adiposity for incident dementia by age groups (i.e. 50–64, and ≥65). Age trajectories of adiposity measures were fitted using a mixed-effect model in a case-control design. The interaction terms of age and dementia were included to examine the difference between cases and controls.

RESULTS: Hazard ratios (HRs) for incident dementia in two age groups (50–64 and ≥65) were estimated in 13,355 participants. Raised mid-life BMI was associated with incident dementia (HR (95% CI): overweight 1.33 (1.03 to 1.73), obesity 1.63 (1.17 to 2.28)). Mid-life abdominal obesity was associated with incident dementia (WC 1.45 (1.15 to 1.84), WtHR 1.44 (1.08 to 1.94)), accounting for ≤24.2% of dementia cases. Among participants developing dementia, adiposity measures were higher in mid-life and declined faster with age, compared to those remaining dementia-free. Late-life adiposity was not associated with dementia risk.

CONCLUSION: Mid-life but not late-life adiposity was associated with dementia incidence in China. Accelerated weight loss in prodromal dementia is likely to explain the mixed evidence on adiposity and dementia risk in the Chinese population. Rapid decline in adiposity in later life may be an early sign. Reducing mid-life adiposity in the population may mitigate the future dementia burden.

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INTRODUCTION

The Chinese population continues to age rapidly, with a fast-rising number of dementia cases [1]. Evidence from high-income countries indicates that as many as 40% of cases can be prevented or delayed through targeting modifiable risk factors [2]. Mid-life obesity may be responsible for 16% of Chinese dementia cases, given its high and increasing prevalence in the population [3, 4].

Systematic reviews and meta-analysis based on research from high-income countries indicates that obesity but not being overweight was associated with late-life dementia [2, 5]. However, current evidence on the association between adiposity and risk of dementia in the Chinese population is inconsistent. Studies of adiposity in later life (65+ years), suggest underweight is a risk

factor for dementia (Supplementary Table 1). One cohort study with a baseline in mid-life (45+ years) concluded that higher general and abdominal adiposity is protective for cognitive decline [6]. Uncertainty remains whether the age-dependent association between adiposity and dementia in high-income countries [7, 8] can be generalized to China. Furthermore, to assess excess body fat and its associated disease risks, lower body mass index (BMI) and waist circumference (WC) have been suggested for Asians compared to Europeans [9]. The age-specific association between adiposity and dementia may vary by ethnicity, due to variations in genetics, living environments and wider socioeconomic contexts, and requires further study in diverse populations [10].

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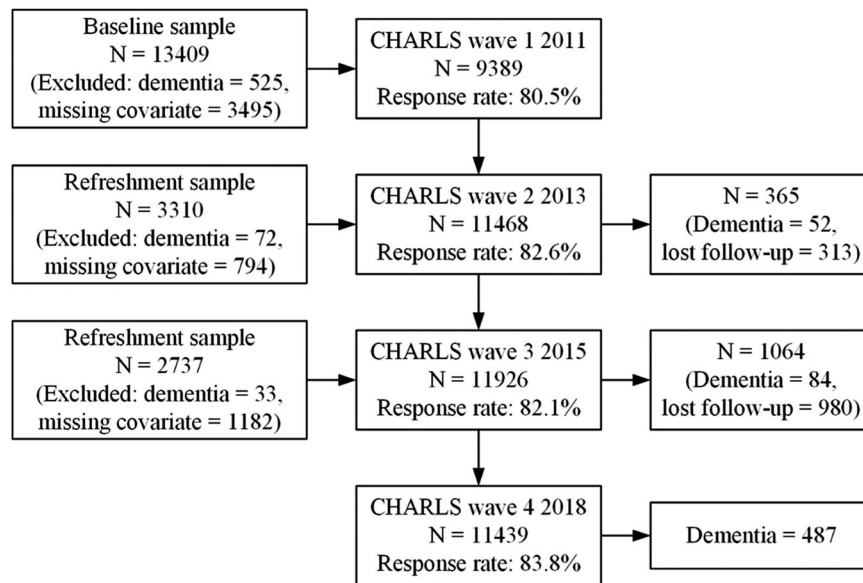


Fig. 1 Flow diagram of study participants.

Weight loss appears to be a feature of the long preclinical phase of dementia development [11–13]. Age-based trajectories of BMI and central adiposity measures by dementia status would illuminate our understanding of the age-dependent association in the Chinese context [14].

We hypothesize that (1) high BMI, WC, and waist-to-height ratio (WtHR) in mid-life, but not later life, are associated with raised subsequent dementia incidence; and (2) that age trajectories of BMI, WC and WtHR differ between those developing dementia and matched controls free of dementia over follow-up, reflecting increased weight loss with age of people in the preclinical phase of dementia. Further, we quantified the proportion of dementia cases that attribute to high BMI, WC, and WtHR by estimating the corresponding population attributable fraction (PAF) tailored to Chinese population.

SUBJECTS AND METHOD

Study design and participants

This study used nationally representative panel data from four waves (in 2011, 2013, 2015, and 2018) of the China Health and Retirement Longitudinal Study (CHARLS). CHARLS is a national survey of a representative sample of Chinese population aged 45 years and older. The response rates were over 80% for each wave. Data on sociodemographic, lifestyle, health status, and clinical measurements were collected with standardized questionnaire and physical examination. Details about the study design of the CHARLS have been previously reported [15].

We selected data from CHARLS participants aged ≥ 50 years, and used the first height, weight and WC measurements as baseline. Participants with dementia at baseline ($n = 525$) or were missing covariates ($n = 3495$) at 2011 were excluded. Refreshment samples at CHARLS wave 2 ($n = 866$) and wave 3 ($n = 1215$) were selected using the same criteria. The detailed selection process is shown in Fig. 1, rendering 13,355 for the analysis sample with 623 dementia cases.

Assessment of dementia

Dementia was defined as the coexistence of functional impairment and cognitive impairment, or self-reported, doctor-diagnosed dementia or memory-related diseases. The definition conforms to Diagnostic and Statistical Manual of Mental Disorders

(DSM)-5 and International Classification of Diseases 10th edition (ICD-10) for dementia, which has been validated against a nationwide population-based survey [16]. Doctor-diagnosed memory-related diseases were identified by the item “Have you been diagnosed with memory-related diseases?” [15]. This information was used to identify cases among participants without cognitive scores (32%) [17].

Functional impairment was assessed by the Katz-scale in CHARLS [18]. Participants who required caregiving for one or more basic activities of daily living (bathing, getting in or out of bed, changing clothes, using toilet, cutting food and eating, controlling urination and bowel movement) were defined as functional impairment. Participants who reported functional impairment once but fully recovered to perform these activities independently in all subsequent waves, were not identified as having functional impairment.

Cognitive impairment was assessed using the Telephone Interview for Cognitive Status questionnaire (TICS), administered via face-to-face interviews across all CHARLS waves [15]. The 9-item TICS is a modified version of Mini-Mental State Examination, examined cognitive domains (i.e. orientation to time, memory, visuo-construction and attention) with a summary score ranging from 0–31 [19]. We previously derived three latent cognitive factors, namely orientation, memory, executive function and language, via confirmatory factor analysis based on TICS data from CHARLS [16]. Participants with two or more domains of impairment were defined as cognitive impairment. Domain-specific impairment was quantified as corresponding cognitive factor score of 1.5 standard deviations below the population mean of same education level. Participants with improved cognition by more than 1 standard deviation in two or more domains at the subsequent wave, were not identified as having cognitive impairment.

Assessment of adiposity

Referring to the national criteria for adult weight set by the National Health and Family Planning Commission of the People’s Republic of China, BMI was categorized into four groups: underweight ($\text{BMI} < 18.5 \text{ kg/m}^2$), normal weight ($\text{BMI} = 18.5 \text{ kg/m}^2$ to 24 kg/m^2), overweight ($\text{BMI} = 24 \text{ kg/m}^2$ to 28 kg/m^2), and obesity ($\text{BMI} \geq 28 \text{ kg/m}^2$) [20]. To account for visceral excess fat distribution, WC and WtHR were also used to

determined abdominal obesity [21, 22]. According to the national criteria and previous studies, WC was divided into two group: non-abdominal obesity ($WC < 90$ cm for male or < 85 cm for female) and abdominal obesity ($WC \geq 90$ cm for male or ≥ 85 cm for female) [20]. WtHR was divided into two group: on-abdominal obesity ($WtHR < 0.5$) and abdominal obesity ($WtHR \geq 0.5$) [23]. Weight and height was measured in bare feet with the participant standing erect. WC was measured with the participants in standing position at the level of navel [15].

Covariates

Sociodemographic characteristics included baseline age, sex, and education level. Lifestyle included smoking frequency and drinking frequency. Education level was categorised as low education level (0 year), middle education level (1–6 years), and high education level (7 years or higher) [24]. Smoking frequency was measured by cigarettes / day. Drinking frequency was categorised into none, less than once per day, once per day, twice per day, and more than twice per day.

Statistical analysis

Following previous study and the National Bureau of Statistics [25, 26], A Cox proportional hazard model was used to separately test the age-specific (50–64 years and ≥ 65 years) association between each adiposity measure and subsequent dementia adjusting for sociodemographic characteristics, and lifestyle factors. To avoid over-adjustment, potential mediators in the etiological pathways such as cardiovascular disease and diabetes [27], were not adjusted in the model.

Mixed models were used to explore how the trajectory of adiposity measures with age differed between those with subsequent dementia and those without. To account for age, sex, education, and the period effect in the measures and dementia, as well as the effects of selection bias and loss to follow-up, one dementia case was matched with four controls using the MatchIt package [28], based on baseline age, sex, education, year of inclusion and follow-up duration. The trajectories were modelled as a function of spline age to allow nonlinear trend [29]. To examine the differences in aging effect between cases and controls, dementia and its interaction with spline age were included. For ease of interpretation of the model coefficients, baseline age was centred at 65 years so that the coefficient of dementia indicated the difference in these measurements in the early old ages and birth year was centred at 1945. Due to the small number of dementia incidence and short follow-up under 60 ($n = 169$, 27%), trajectories were fitted only for those aged over 60 at baseline to avoid overfitting. Model selection was based on Akaike information criterion (AIC), Bayesian information criterion (BIC) and Wald test.

To quantify the impact on population of adiposity, PAF was interpreted as the proportion of dementia risk that could be eliminated. PAF was calculated based on Miettinen's formula, where p_c is the prevalence of risk in the cases and HR_{adj} is the adjusted hazard ratio [30].

$$PAF = \frac{p_c(HR_{adj} - 1)}{HR_{adj}}$$

The prevalence was estimated using CHARLS and considering individual weight with household and individual non-response adjustment. To compare with Mukadam's report [3], the prevalence was calculated aiming the same age group.

Sensitivity analyses were conducted by excluding dementia events that occurred at the adjacent wave after baseline to reduce the impact of reverse causation of weight loss.

All statistical analysis was performed with R (version 4.2.3).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report, or in the decision to submit the paper for publication.

Ethics approval and consent to participate

The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline was followed [31]. All participants provided informed consent. CHARLS was approved by the Ethical Review Committee of Peking University (ethical approval number: IRB00001052-11015).

RESULTS

Table 1 summary the follow-up, baseline demographics, adiposity measures, smoking frequency, and drinking frequency in the total population ($N = 13,355$) and in cases ($N = 623$) and control groups ($N = 3115$). In the 50–64 years group, compared with the no dementia group, those developed dementia during follow-up were older (mean baseline age 58.6 vs. 57.5) and had higher adiposity measures, and drank less. However, measures of adiposity were not different between dementia and no dementia group in the other age group. All measures of obesity were lower in the mid-life matched control group, but not different in the late-life group.

(Table 1. Baseline characteristics of participants in CHARLS by dementia).

A total of 31.8% participants were overweight and 12.2% had obesity in mid-life. Overweight ($HR = 1.41$ (1.08 to 1.82)) and obesity ($HR = 1.76$ (1.26 to 2.46)) were associated with higher risk of dementia in mid-life but not in older-age (overweight: $HR = 1.07$ (0.82 to 1.40), obesity: $HR = 1.14$ (0.74 to 1.75)). The analyses were underpowered to examine the effect of underweight on dementia. Further adjustment for smoking and drinking did not attenuate the association (overweight: $HR = 1.41$ (1.09 to 1.83), obesity: $HR = 1.77$ (1.26 to 2.47)). The association between abdominal obesity in mid-life and dementia was similar to obesity (measured by WC: $HR = 1.56$ (1.23 to 1.98), measured by WtHR: $HR = 1.55$ (1.16 to 2.08)). All covariates were analysed in the study, and details were presented in the Supplementary Table 2–4. Sensitivity analysis based on follow-up did not alter the association significantly and was presented in Supplementary Table 5.

(Table 2. Association of BMI, WC, and WtHR in different age group with dementia).

The trajectory of BMI with age was different in the case group compared with the control group (Fig. 2A). Those with dementia had higher BMI at 60 years and accelerated decline in later life. The BMI declined more slowly with age for those without dementia and was higher than demented patients after 78 years. The trajectory of WC (Fig. 2B) with age was similar to that of WtHR (Fig. 2C), which increased in mid-life and declined in later life. The changes of trajectories between cases and controls were close to that of BMI. Those with dementia had higher WC and WtHR in mid-life but experienced accelerated decline with aging, which was lower than the control group at 76 years and 80 years. Details of all mixed effect models for the trajectories were in Supplementary Table 3.

Furthermore, we estimated that 10.5%, 5.1%, 17.2%, 24.2% of dementia would be due to overweight, obesity, abdominal obesity measured by WC and WtHR in the future. Details of PAF estimation were in Table 3.

(Table 3. PAF of overweight, obesity, and abdominal obesity for dementia).

Table 1. Baseline characteristics of participants in CHARLS by study samples and dementia.

	Total population sample		Case-control sample ^a	
	No dementia	Dementia	No dementia	Dementia
Middle-aged group^b N	8926	296	510	127
Follow-up, mean (SD)	5.8 (1.7)	5.7 (1.8)	5.6 (1.8)	5.6 (1.8)
BMI, mean (SD)	23.7 (3.5)	24.4 (3.6)	23.6 (3.6)	24.7 (3.5)
Waist circumference, mean (SD)	85.9 (9.9)	88.1 (10.1)	86.2 (10.2)	89.2 (10.3)
Waist-to-height ratio, mean (SD)	0.54 (0.06)	0.56 (0.07)	0.54 (0.06)	0.57 (0.07)
Sex, N (%) female	4565 (51.1)	155 (52.4)	261 (51.2)	65 (51.2)
Age, mean (SD)	57.5 (4.2)	58.6 (4.1)	62.6 (1.4)	62.5 (1.4)
Education, N (%)				
Low education level	1696 (19.0)	58 (19.6)	108 (21.2)	27 (21.3)
Middle education level	3953 (44.3)	135 (45.6)	276 (54.1)	68 (53.5)
High education level	3277 (36.7)	103 (34.8)	126 (24.7)	32 (25.2)
Smoking frequency ^c , mean (SD)	4.5 (9.6)	3.4 (8.8)	3.4 (8.6)	3.0 (7.9)
Drinking frequency, N (%)				
None	6029 (67.5)	229 (77.4)	369 (72.4)	102 (80.3)
Less than once per day	1699 (19.0)	34 (11.5)	79 (15.5)	13 (10.2)
Once per day	640 (7.2)	12 (4.1)	23 (4.5)	3 (2.4)
Twice per day	428 (4.8)	12 (4.1)	27 (5.3)	5 (3.9)
More than twice per day	130 (1.5)	9 (3.0)	12 (2.4)	4 (3.2)
Older-aged group^b N	3806	327	1306	327
Follow-up, mean (SD)	5.3 (1.8)	5.2 (1.9)	5.2 (1.9)	5.2 (1.9)
BMI, mean (SD)	22.7 (3.7)	22.4 (3.6)	22.6 (3.7)	22.4 (3.6)
Waist circumference, mean (SD)	85.5 (10.3)	85.4 (10.2)	85.4 (10.6)	85.4 (10.2)
Waist-to-height ratio, mean (SD)	0.55 (0.07)	0.55 (0.07)	0.55 (0.07)	0.55 (0.07)
Sex, N (%) female	1876 (49.3)	173 (52.9)	691 (52.9)	173 (52.9)
Age, mean (SD)	71.8 (5.4)	73.3 (6.0)	73.1 (5.7)	73.3 (6.0)
Education, N (%)				
Low education level	1090 (28.6)	72 (22.0)	288 (22.1)	72 (22.0)
Middle education level	1915 (50.3)	179 (54.7)	712 (54.5)	179 (54.7)
High education level	801 (21.1)	76 (23.2)	306 (23.4)	76 (23.2)
Smoking frequency ^c , mean (SD)	3.0 (7.8)	2.0 (6.2)	2.6 (7.5)	2.0 (6.2)
Drinking frequency, N (%)				
None	2834 (74.5)	249 (76.2)	1004 (76.9)	249 (76.1)
Less than once per day	526 (13.8)	43 (13.2)	166 (12.7)	43 (13.1)
Once per day	239 (6.3)	17 (5.2)	74 (5.7)	17 (5.2)
Twice per day	141 (3.7)	9 (2.8)	44 (3.4)	9 (2.8)
More than twice per day	66 (1.7)	9 (2.8)	18 (1.4)	9 (2.8)

CHARLS China health and retirement longitudinal study, BMI body mass index.

^aBaseline age, sex, education, year of inclusion and follow-up duration were matched. Participants aged <60 years were excluded because follow-up was short.

^bMiddle-aged group: adiposity measured at 50–64 years for total population and 60–64 years for participants case-control design. Older-aged group: adiposity measured at ≥65 years for total population and participants case-control design.

^cSmoking frequency, cigarettes/day.

DISCUSSION

Utilizing nationwide ageing cohort spanning over eight years, our study confirmed that mid- but not late-life adiposity was associated with increased risk of subsequent dementia in Chinese population, accounting for up to 24% of future dementia cases. Moreover, we revealed that those who developed dementia had higher adiposity measures in mid-life but declined faster with age than their cognitive healthy counterparts. To our best knowledge, we are the first study clarifying the age-dependent association of adiposity and dementia risk in the Chinese population, which has been mixed and largely overlooked previously [32–35].

Our finding on the positive associations between mid-life obesity, abdominal obesity and dementia incidence are in line with evidence in high-income countries [36–38]. Additionally, we found that mid-life overweight also increased risk of dementia, which was not found in American and European population [38]. This association may result from a high proportion of abdominal obesity among Chinese overweight, while about one-third in the westerners [39]. In our study, 75.9% of mid-life overweight participants were found to have abdominal obesity, and the relation between abdominal obesity and visceral adipose tissue has been widely reported [40]. Such that for a given BMI, higher

Table 2. Risk for dementia associated with mid- and late-life adiposity.

	<i>N</i> dementia/ <i>N</i>	Minimally adjusted model ^a		Fully adjusted model ^b	
		HR (95% CI)	<i>P</i>	HR (95% CI)	<i>P</i>
Adiposity measured at 50–64 years	296/9 222				
BMI					
Underweight	12/437	0.95 (0.52 to 1.72)	0.86	0.92 (0.51 to 1.67)	0.79
Normal weight	129/4729	Ref	-	Ref	-
Overweight	106/2933	1.41 (1.08 to 1.82)	0.01	1.41 (1.09 to 1.83)	0.01
Obesity	49/1123	1.76 (1.26 to 2.46)	<0.01	1.77 (1.26 to 2.47)	<0.01
Waist circumference					
No abdominal obesity	138/5111	Ref	-	Ref	-
Abdominal obesity	158/4111	1.54 (1.21 to 1.95)	<0.01	1.56 (1.23 to 1.98)	<0.01
Waist-to-height ratio					
No abdominal obesity	60/2521	Ref	-	Ref	-
Abdominal obesity	236/6701	1.55 (1.15 to 2.07)	<0.01	1.55 (1.16 to 2.08)	<0.01
Adiposity measured at ≥ 65 years	327/3806				
BMI					
Underweight	44/468	1.21 (0.87 to 1.69)	0.25	1.22 (0.88 to 1.70)	0.24
Normal weight	176/2278	Ref	-	Ref	-
Overweight	82/1046	1.07 (0.82 to 1.40)	0.60	1.07 (0.82 to 1.40)	0.62
Obesity	25/341	1.14 (0.74 to 1.75)	0.55	1.14 (0.74 to 1.74)	0.56
Waist circumference					
No abdominal obesity	178/2022	Ref	-	Ref	-
Abdominal obesity	149/1784	1.12 (0.89 to 1.41)	0.34	1.11 (0.88 to 1.40)	0.36
Waist-to-height ratio					
No abdominal obesity	88/775	Ref	-	Ref	-
Abdominal obesity	239/3031	0.97 (0.75 to 1.25)	0.82	0.97 (0.75 to 1.25)	0.80

BMI body mass index group.

Cox model was used to separately test the age-specific association between each adiposity measure and subsequent dementia. Adiposity was measured at baseline for each participant. The distribution of age at adiposity measurement and dementia onset is shown in Supplementary Fig. 1.

^aMinimally adjusted model: baseline age, sex, and education level were adjusted.

^bFully adjusted model: baseline age, sex, education level, smoking frequency, and drinking frequency were adjusted.

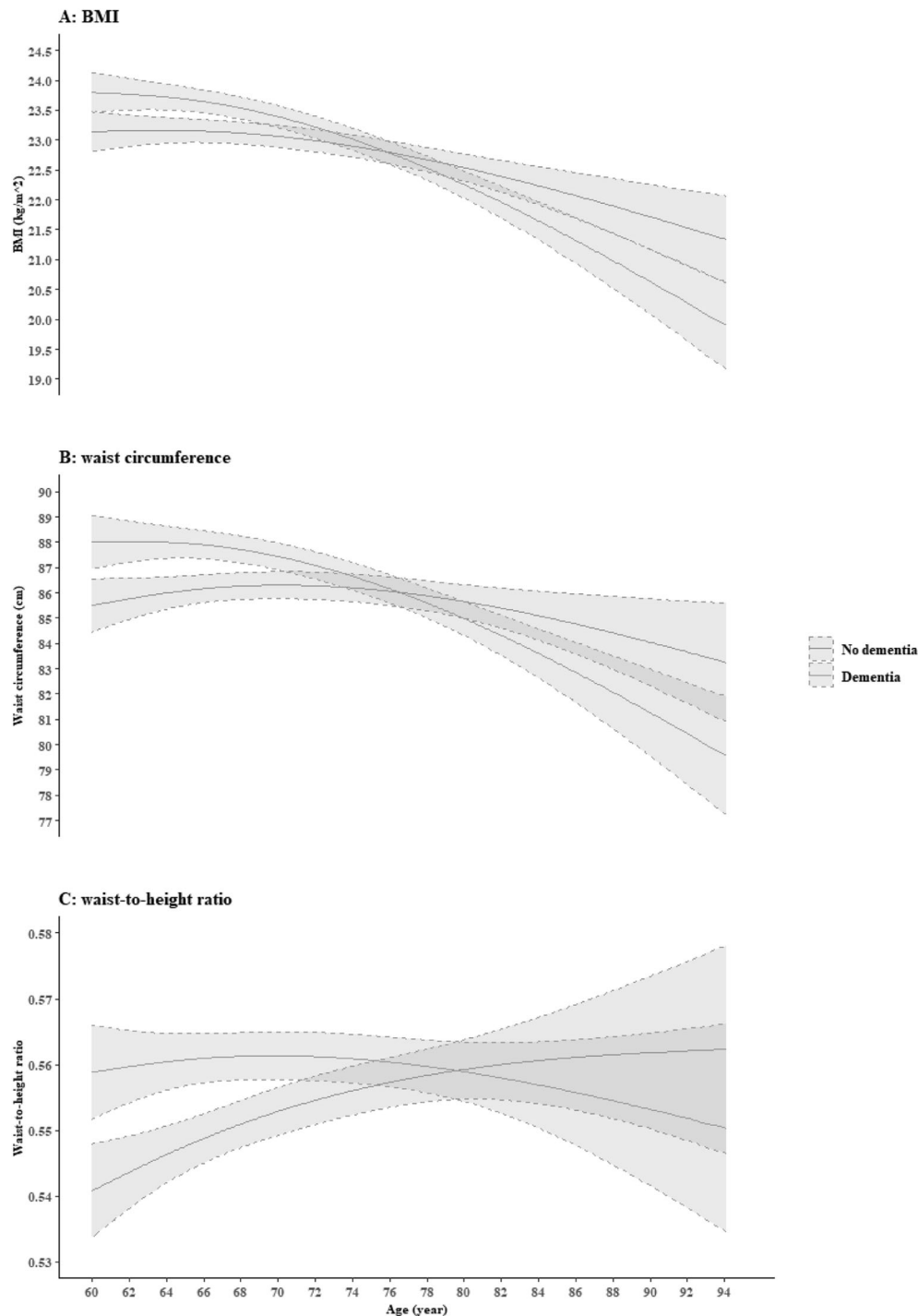
concentrations of visceral adipose tissue, which are associated with metabolic risks [41], are more commonly seen in Chinese population than their Western counterparts [42]. A recent study using structural equation modelling suggests that metabolic consequences of adiposity- such as diabetes, hypertension and cardiovascular disease- may mediate the relationship between adiposity and cognitive decline [27]. Accordingly, our analysis was adjusted only for baseline sociodemographic and lifestyle factors to avoid over-adjustment. Our finding is further supported by a latest Mendelian randomization study in Singapore, which verified a causal relationship between increased visceral adiposity and reduced cognition among 6099 Chinese mid-aged (mean age 51.9) adults [43].

Our updated PAFs of several adiposity measures further indicated the vital role of abdominal obesity. As such 17–24% new dementia cases may be avoided if abdominal obesity can be controlled, about 50% larger than prior estimates [3]. Our trajectories reveal that participants from later birth cohorts had higher average adiposity measures, corresponded to previous evidence [44]. The increasing trends in mid-life abdominal obesity across generations underscored the importance of early prevention and intervention in adiposity across Chinese population.

We did not find any statistically significant association of degree of adiposity, including underweight, in late-life with dementia incidence. This observation differs from prior findings that link late-life underweight with a high risk of dementia and cognitive

impairment, based on the Shanghai Ageing Study [34] and the Chinese Longitudinal Healthy Longevity Survey [45]. The proportion of participants aged 80+ in these two studies was at least twice as many as in CHARLS, which at present lacks power to detect possible increased dementia risk linked to low adiposity. Reverse causation, namely accelerated weight loss and declining abdominal obesity as a result of prodromal dementia, is likely to take place progressively from early old age and to continue into late old age [7]. Our analysis of the age-trajectory of adiposity between participants who develop dementia and those who remain dementia-free lends support to this proposition. The trajectories show that participants who developed dementia had higher adiposity measures in mid-life, which dropped faster as they aged, and around 80 years, their adiposity measures became lower than their cognitively healthy counterparts.

Moreover, the differences in age-related decline rate of BMI between dementia and non-dementia people in China were 1.5 times than those of their American and European counterparts [12, 13]. Besides ethnic variations of weight change, sociocultural factors may also contribute to this huge disparity [46, 47]. Awareness and knowledge about dementia is generally low among Chinese public [48] and health personnel [49], rendering large number of undiagnosed and untreated individuals hiding in community [50]. Once identified, those with dementia are more likely to be in later stages, experiencing faster and irreversible health deterioration such like weight loss. Thus, timely cognitive impairment screening should



Age at dementia incidence and last observation for matched controls

Ages	60-64	65-69	70-74	75-79	80-84	85-90	≥90	Total
Controls	51	397	483	445	259	139	42	1816
Cases	13	101	118	112	57	36	17	454

Fig. 2 Trajectory of adiposity measures with age and age at last observation. **A** Trajectory of BMI with age in the dementia group (cases) compared with the non-dementia group (controls). **B** Trajectory of waist circumference with age in the dementia group (cases) compared with the non-dementia group (controls). **C** Trajectory of waist-to-height ratio with age in the dementia group (cases) compared with the non-dementia group (controls). Trajectory of adiposity measures with age by dementia (cases) and non-dementia (controls) *Bands indicate 95% CI. BMI body mass index. **Baseline age, sex, education, year of inclusion, and follow-up duration were matched. ***Due to very few cases, trajectories were fitted only for those aged over 60 at baseline to avoid overfitting.

Table 3. Population attributable fraction of mid-life (45–64 years) adiposity for dementia.

Risk factor	Prevalence ^a	PAF with minimally adjusted HR	PAF with fully adjusted HR
Overweight, measure by BMI	42.0%	10.4%	10.5%
Obesity, measure by BMI	13.1%	5.1%	5.1%
Abdominal obesity, measure by waist circumference	55.2%	16.6%	17.2%
Abdominal obesity, measure by waist-to-height ratio	78.7%	24.1%	24.2%

BMI body mass index.

^aRisk factor prevalence in dementia cases was estimated in CHARLS wave 3 (2015); survey weights were applied.

be introduced to high-risk middle-aged adults with overweight and obesity, combined with continue monitoring on their weight and cognitive function change over years.

Using nationally representative aging cohort in China, our study disentangled the association of mid- and late-life adiposity with subsequent dementia risk in Chinese adults and compare aging trajectories of adiposity between those with/out dementia, which broaden the evidence to another ethnicity. Nevertheless, limitations should be noted. First, dementia was not diagnosed by neurologist. However, this algorithmic definition is standard practice in population-based cohorts with limited resources and has been validated against survey with clinical diagnosis [16]. Besides, the maximum follow-up in our study was seven years, which was relatively short compared to relevant studies (over 10 years). Limited by the follow-up time, we cannot fully assess the association between mid-life adiposity and later-life dementia at this stage because 83.1% of the dementia cases for the middle-aged group were identified at age 60 and above, with 56.9% of them occurring at age over 65 (Supplementary Fig. 1). Our trajectories of adiposity measures were anchored by age but not time to dementia. This may not be the best way to characterize weight loss in prodromal dementia [29]. Future studies with longer follow-up fitted these trajectories by year before dementia, would facilitate the understanding of the long-term association and the identification of when and how much weight is lost before dementia onset following the etiologic stage. Last, our PAFs rely on the assumption that the distribution of other dementia risk factors remains constant. The assumption may result in underestimation because adiposity also increases the risk of other dementia risk factors (e.g., cardiovascular diseases). However, this does not undermine the value of preventing mid-life abdominal obesity based on the relative importance of the three different adiposity measures.

In conclusion, our study disentangles the association of mid- and late-life adiposity with subsequent dementia risk in Chinese adults. Mid-life adiposity is associated with dementia in Chinese population, which may cause up to 24.2% dementia cases in the future. The adiposity measures with age in those develop dementia are significantly different for those cognitively intact. Our findings provide evidence for the importance of weight management and monitoring since in mid-life to meet the challenge of dementia in China.

DATA AVAILABILITY

The datasets analysed during the current study are available on <https://charls.pku.edu.cn/>.

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AUTHOR CONTRIBUTIONS

MRZ contributed to the analysis and interpretation of the data and drafted the manuscript. YTC contributed to the analysis and interpretation of the data, and reviewed and edited the manuscript. SLR contributed to the discussion, and reviewed and edited the manuscript. YYL contributed to the data analysis. AS contributed to the review. EJB and JL contributed to the study concept and design, and reviewed and edited the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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