Table 3. Continued

Variables		Model 1 OR (95% CI)[a]	Model 1 *P*-value	Model 2 OR (95% CI)[b]	Model 2 *P*-value	Model 3 OR (95% CI)[c]	Model 3 *P*-value
Frequency of intake of sweet foods	Almost every day					1.00 (referent)	
	1–4 times/week					1.28 (1.16–1.41)	$P < 0.001$
	≤1–2 times/month					1.45 (1.31–1.61)	$P < 0.001$
Smoking status	Current					1.00 (referent)	
	Past					1.42 (1.26–1.60)	$P < 0.001$
	Never					2.40 (2.12–2.72)	$P < 0.001$
History of diabetes	Yes					1.00 (referent)	
	No					1.16 (1.04–1.28)	0.006
Self-rated health	Poor					1.00 (referent)	
	Fair					1.16 (1.06–1.27)	0.002
	Good					1.37 (1.24–1.51)	$P < 0.001$

[a]Adjust for all neighborhood social capital variables simultaneously.
[b]Adjust for sex, age, all neighborhood social capital, educational level, individual social networks and social support and educational attainment variables simultaneously.
[c]Adjust for sex, age, and all explanatory variables simultaneously.

Individual- and community-level social support variables did not show any significant associations. The result of the intercept-only multilevel model showed significant neighborhood level variance ($\sigma^2_{\mu 0}$ (standard error) = 0.075 (0.012), $P < 0.001$). This means that dentate status significantly differed between neighborhoods. Since the neighborhood social capital variables explained the neighborhood level variance, neighborhood level variance in model 1 was decreased ($\sigma^2_{\mu 0}$ (SD) = 0.044 (0.009), $P < 0.001$). The neighborhood level variance in the model 2 was 0.023 (SD = 0.008, $P = 0.004$). The neighborhood level variance in the model 3 was 0.012 (SD = 0.007, $P = 0.093$).

Discussion

To our knowledge, this large-scale cross-sectional study is the first to have simultaneously examined the association between neighborhood social capital, individual social networks, and individual social support and oral health. After adjustment for individual- and neighborhood-level covariables, one aspect of neighborhood-level high social capital was found to be significantly associated with having 20 or more teeth. This result suggests that one aspect of neighborhood social capital has a contextual effect on the self-reported dentate status of elderly people. In addition, neither individual nor neighborhood social support variables showed any significant association. It was suggested that the network aspect of social capital has a more important effect on dentate status than the social support aspect of social capital. Only the friendship network neighborhoods had a statistically significant but small OR (1.17). However, because neighborhood social capital has an influence on all the residents in each area, this result was meaningful.

There were several plausible pathways linking social capital to health outcomes. At first, social capital may affect individual health by influencing health-related behavior through promotion of more rapid diffusion of health information and by exerting social control over deviant health-related behavior (27). For example, cigarette smoking by peers is among the best predictors of smoking in adolescents (28). Second, social capital may affect health by influencing access to local service and amenities (27). Access to service such as transportation, dental clinics and community health centers could affect dental health. Third, there are associations between social capital and psychological distress (29). Psychological distress is a risk indicator of periodontal disease (30, 31). In addition, psychological distress can lead to an increase in smoking and/or consumption of 'comfort foods' such as confectionary (12). These behaviors may increase the risk of periodontal disease and dental caries respectively. In addition, neighborhoods with higher social capital are less violent (32) with fewer dental injuries (8). In our results, only friendship-network-based social capital showed a significant beneficial association, while other kinds of network variables did not. This may suggest that access to dental clinics as well as dental health behavior and stress are influenced mainly by close friends.

A multilevel approach enables demonstration of whether social capital has an independent 'contextual' effect on individual health outcomes, regardless of individual characteristics, including individual-level social networks and social support (6). Our results emphasize the importance of community actions or governmental investment to establish amenities that promote the building of social capital, especially that based on friendship networks. In addition, our results showed a significant neighborhood level variation of dentate status. Approaches for influencing not only individual risk factors but also the underlying social determinants of oral health through upstream public health interventions, such as water fluoridation or a tobacco tax policy, are needed to reduce neighborhood level variation on dentate status by improving the dental health of the population (7).

Broadly speaking, there are two ways of measuring neighborhood variables: (i) aggregating individual level data and (ii) directly measuring the properties of groups (22). However, it is difficult to separate collective explanation about the neighborhood effect from the contextual explanation (33). Aggregating collective measurements have been generally used to estimate the neighborhood contextual effect (6). We determined the association between neighborhood level collective variables and health outcome with adjustment for individual level variables (22).

Our study had some limitations. First, although it demonstrated an association between one aspect of social capital and dentate health, a cross-sectional study showed no causal inference, and therefore prospective follow-up studies are required. Second, it could be argued that the questionnaire used in this study did not provide a full picture of social capital. There is still debate about the definition and measurement of social capital (6). Various types of social capital such as bonding, bridging and linking should be measured. Third, it could be argued that the questionnaire used in this study did not provide a full picture of the differences in quantity and quality of dental health behavior and dentate status. Because of our measure of remaining teeth was discrete variable, it could not describe the full picture of dental health status. In addition, we could not consider occlusal pairs of the teeth of respondents. Although we used many covariables pertaining to dental health behavior, more detailed variables, such as use of fluoride toothpaste, are needed. Additionally, variation of dental health behavior and dentate status were needed. Although previous studies in other countries have shown that the general population can provide accurate self-reported estimates of the number of remaining teeth (34), validation among Japanese elderly was needed. This study could not include other measurements of neighborhood and individual social capital or dental health variables. Therefore, there may be residual bias. Our study had some strength. Because dental health has an important influence on personal appearance and speaking ability, people with a poor dentate health status might have a less well developed social network. Our multilevel study showed that regardless of individual social networks, dental health behavior and self-rated health, neighborhood friendship networks were significantly associated with individual dentate status. This result was reliable because our study had a large number of participants and a sufficient response rate.

The present study has demonstrated a significant association between one aspect of neighborhood social capital and individual dentate status in the elderly population. In addition, only the network aspect of social capital, and not the social support aspect, was found to have a significant association with dentate status.

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Original Article: Clinical Investigation

Risk factors for overactive bladder in the elderly population: A community-based study with face-to-face interview

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Objectives: The aim of this study was to measure the prevalence of and risk factors for overactive bladder (OAB) in the elderly.

Methods: A cross-sectional study of elderly subjects was conducted by analyzing data from a community-based Comprehensive Geriatric Assessment on people aged 70 years or older. Trained interviewers performed face-to-face interviews for the assessment of urological symptoms. OAB definition was based on urgency and eight or more episodes of urination per day. The subjects completed a self-administered questionnaire including lifestyle evaluation, Geriatric Depression Scale, Mini-Mental Status Examination and medical history. Brachial-ankle pulse wave velocity was recorded to assess atherosclerotic disease. The analysis included 833 subjects, after the exclusion of 115 subjects who provided insufficient information.

Results: Based on the definition of OAB, 153 subjects (18.4%) were identified as having OAB. Univariate analysis showed a significant association between OAB and depressive symptoms. Multivariate analysis showed that the risk of having OAB was significantly higher in subjects with depressive symptoms, current drinkers, and overweight subjects with odds ratios of 2.37 (1.60–3.52, 95% confidence interval), 1.65 (1.04–2.62), and 1.51 (1.02–2.24), respectively.

Conclusions: This is the first report to show an association between OAB and depressive symptoms and alcohol intake in an epidemiological study of elderly people. The reasons for these correlations remain unclear, but should be the foci of future OAB studies.

Key words: depression, elderly, face-to-face interview, overactive bladder, risk factors.

Introduction

In 2002, overactive bladder (OAB) was defined by the International Continence Society (ICS) as the symptom of urgency, which is an indispensable condition, with or without urge incontinence, usually with increased frequency and nocturia.[1] Many epidemiological and clinical studies of these symptoms have been reported.[2–5] OAB occurs in a wide range of patients from the comparatively young to the elderly. By contrast, the number of OAB patients increases in proportion to the subjects' age. The reason for this association is not clear. Thus, it might be possible to elucidate the origin of OAB by investigating the risk factors for OAB in elderly people through epidemiological studies.

We conducted a cross-sectional study on subjects aged 70 years or older in an urban community to measure the prevalence of overactive bladder (OAB) in the elderly, and assessed the risk factors of the condition.

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Methods

Study participants

In July and August 2003, a community-based comprehensive geriatric assessment in elderly people was performed in the Tsurugaya district of Sendai City, one of the largest cities in northern Japan.[6–10] At this time, 2925 people aged ≥70 years lived in Tsurugaya. We invited all of them to participate in the assessment of their medical status, physical function, cognitive function and dental status. Of those invited, 948 (32.4%) of them particiapated, after providing informed consent for analysis of the data. All assessments were carried out in a non-clinical public facility. The protocol of this study was approved by the institutional review board of the Tohoku University Graduate School of Medicine.

We excluded subjects who did not respond to the questions related to our analysis ($n = 107$). We further excluded

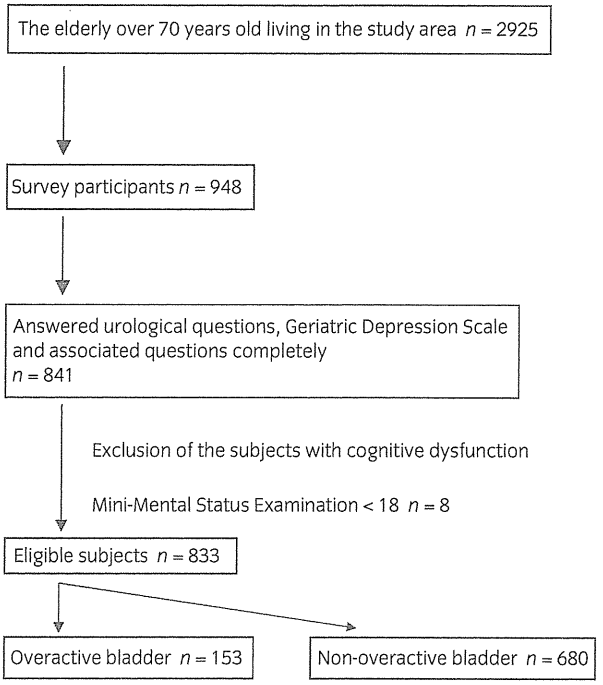

Fig. 1 The study flow.

participants who had scores of less than 18 points in the Mini-Mental Status Examination (MMSE), based on the possibility of incorrect answers due to dysgnosia ($n = 8$).[11] Therefore, a total of 833 subjects were included in the final analysis (Fig. 1).

Urological measurement

In the current study, we performed a survey of the symptoms of the lower urinary tract, including determination of the frequency of urination per day and the International Prostate Symptom Score (IPSS).[10,12] All urological interviews were performed by interviewers who were trained to identify that the urgency is the complaint of a sudden compelling desire to pass urine. OAB has been defined as urgency with urination eight times or more per day. Based on the survey results, the subjects were divided into OAB and non-OAB groups.

Anthropometric measures, lifestyle and medical history

Anthropometric measures (height, bodyweight) were recorded using a standardized protocol. The subjects completed a self-administered questionnaire that included their lifestyle and medical history.

Geriatric Depression Scale

The Geriatric Depression Scale (GDS) was used to evaluate depressive symptoms in the elderly people. Depressive symptoms were measured based on the Japanese version of the 30-item Geriatric Depression Scale (GDS 30), with a cut-off of 11.[8,9,13] We selected the cut-off of 11 because Schreiner *et al.* reported that the GDS cut-off score identified among Japanese participants was the same as that reported for Western participants using the 15-item GDS short form.[14] Each item was assessed by a yes/no question in one sentence. If the answering style tended to be depressive, we scored one point each, and summed up the 30 items. The maximum score was 30 points. The participants were further tested for cognitive ability based on the MMSE. Higher scores indicated higher cognitive function, and the maximum score was 30 points. The cognitive tests were conducted by trained personnel.

Pulse Wave Velocity measurement

Bilateral brachial-ankle pulse wave velocity (baPWV) was measured in all subjects, as an indicator of atherosclerosis, using the ankle-brachial pressure index (ABI)/pulse wave velocity (PWV) Form (Nihon Colin, Komaki, Japan), which incorporates an automatic oscillometer.[15] The ABI/PWV Form is a device with four cuffs that can simultaneously measure BP levels and pulse waves in both arms and both legs, and automatically calculates the ABI and baPWV. This device is useful for mass medical examinations and population-based studies because it enables measurement of PWV in a short time, and, more importantly, the measurement is non-invasive and is not affected by the operator's technique.[15] The validity, reproducibility and clinical significance of baPWV measurements have been reported previously.[16]

Statistical analyses

Based on the interview data, analyses of the distribution of OAB and the association of OAB with other factors were performed. The subjects were categorized into groups based on 26 factors, and significant differences in OAB prevalence were examined for each factor using logistic regression analysis; these factors included age, sex, depressive symptoms (GDS: 11 points or higher), history of comorbidities (stroke, hypertension, myocardial infarction, diabetes, cancer, kidney disease), smoking status, alcohol intake, body mass index (BMI), and baPWV. Regarding smoking, the subjects were divided into three groups: the never-smoking group (no history of smoking), the ex-smoking group and the current smoking group. In the same manner, they were also divided into three alcohol intake categories of never-drinker, ex-drinker and current drinker. For BMI, the subjects were divided into four groups: lean, <18.5; normal weight, ≥18.5 and <25; overweight, ≥25 and <30; and obese ≥30.

Table 1 General characteristics of the 833 subjects interviewed

Characteristics, *n* (%)	Men (*n* = 414)	Women (*n* = 419)	Total (*n* = 833)
OAB	73 (17.6)	80 (19.1)	153 (18.4)
Age (years)			
70–79	352 (42.3)	330 (39.6)	682 (81.9)
80–	62 (7.4)	89 (10.7)	151 (18.1)
GDS			
<11	338 (40.6)	282 (33.8)	620 (74.4)
≥11	76 (9.1)	137 (16.5)	213 (25.6)
Alcohol intake			
Never	71 (8.5)	292 (35.1)	363 (43.6)
Ex-drinker	62 (7.4)	37 (4.4)	99 (11.9)
Current drinker	281 (33.7)	90 (10.8)	371 (44.5)
Smoking status			
Never	85 (10.2)	382 (45.9)	467 (56.1)
Ex-smoker	252 (30.2)	27 (3.2)	279 (33.5)
Current smoker	77 (9.2)	10 (1.2)	87 (10.4)
BMI			
<18.5	22 (2.6)	24 (2.9)	46 (5.5)
≥18.5 and <25	244 (29.3)	227 (27.3)	517 (56.6)
≥25 and <30	134 (16.1)	145 (17.4)	279 (33.5)
>30	14 (1.7)	23 (2.8)	37 (4.4)
ABI			
≤0.9	29 (3.5)	19 (1.4)	41 (4.9)
>0.9	385 (46.2)	407 (48.8)	792 (95.1)
baPWV (m/s)			
<1.7	98 (11.8)	81 (9.7)	179 (21.5)
≥1.7 and <1.9	93 (11.1)	89 (10.7)	182 (21.8)
≥1.9 and <2.2	118 (14.2)	106 (12.7)	224 (26.9)
≥2.2	105 (12.6)	143 (17.2)	248 (29.8)
History/comorbidities			
Stroke	27 (3.2)	8 (1.0)	35 (4.2)
Hypertension	183 (22.0)	168 (20.2)	351 (42.1)
Myocardial infarction	58 (7.0)	33 (4.0)	91 (10.1)
Diabetes	72 (8.6)	51 (6.1)	123 (14.8)
Cancer	51 (6.1)	36 (4.3)	87 (10.4)
Kidney disease	23 (2.8)	33 (4.0)	56 (6.7)

ABI, ankle-brachial pressure index; baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; GDS, Geriatric Depression Scale; OAB, overactive bladder.

The potential correlations between each of these factors and OAB were examined using univariate and multivariate logistic regression analysis. SAS software (version 9.0) was used for all statistical analyses.

Results

The baseline characteristics are shown in Table 1. Of the 833 subjects in the analysis, 414 (49.7%) were male. The mean age was 75.4 ± 4.5 years. A total of 153 people (18.4%) were diagnosed with OAB, including 73 men (17.6%) and 80 women (19.1%). Subjects with a GDS score of 11 or higher were included in the group with depressive symptoms; this group comprised 213 subjects (25.6%), including 76 men (18.4%) and 137 women (32.7%).

Univariate analysis showed that the prevalence of OAB was higher in participants with depressive symptoms than in those without, but no apparent correlations were observed between other factors and OAB (Table 2). Multiple adjusted logistic regression analysis was performed to examine the association between OAB and individual factors. The multiple adjusted odds ratio (OR) for having OAB was higher in

Table 2 Factors associated with OAB and non-OAB

	OAB, *n* (%)	Non-OAB, *n* (%)	Univariate analysis OR (95%CI)	*P*-value	Multivariate analysis OR (95%CI)	*P*-value
Sex				0.59		0.91
Male	73 (17.6)	341 (82.4)	1.10 (0.78–1.57)		1.03 (0.60–1.78)	
Female	80 (19.1)	339 (80.9)	1		1	
Age (years)				0.77		0.94
70–79	124 (18.2)	558 (81.8)	1		1	
80≤	29 (19.2)	122 (80.8)	1.08 (0.68–1.68)		1.02 (0.63–1.70)	
GDS				0.0001		<0.0001
<11	95 (15.3)	525 (84.7)	1		1	
≥11	58 (27.2)	155 (72.8)	2.07 (1.43–3.00)		2.37 (1.60–3.52)	
Alcohol intake				0.34		0.064
Never	62 (17.1)	301 (82.9)	1		1	
Ex-drinker	15 (15.2)	84 (84.8)	0.87 (0.45–1.60)		0.98 (0.50–1.91)	
Current drinker	76 (20.5)	295 (79.5)	1.25 (0.86–1.81)		1.65 (1.04–2.62)	
Smoking status				0.12		0.1
Never	90 (19.3)	377 (80.7)	1		1	
Ex-smoker	42 (15.1)	237 (84.9)	0.74 (0.50–1.11)		0.68 (0.39–1.19)	
Current smoker	21 (24.1)	66 (75.9)	1.33 (0.78–2.29)		1.27 (0.65–2.48)	
BMI				0.39		0.17
<18.5	9 (19.6)	37 (80.4)	1.25 (0.58–2.68)		1.23 (0.55–2.74)	
≥18.5 and <25	77 (16.3)	394 (83.7)	1		1	
≥25 and <30	59 (21.1)	220 (78.9)	1.37 (0.94–2.00)		1.51 (1.02–2.24)	
>30	8 (21.7)	29 (78.3)	1.41 (0.62–3.21)		1.74 (0.74–4.13)	
ABI				0.54		0.5
≤0.9	9 (22.0)	32 (78.0)	1.27 (0.59–2.71)		1.32 (0.59–2.99)	
>0.9	144 (18.2)	648 (81.8)	1		1	
baPWV (m/s)				0.77		0.7
<1.7	35 (19.6)	144 (80.4)	1		1	
≥1.7 and <1.9	34 (18.7)	148 (81.3)	0.95 (0.56–1.60)		0.91 (0.53–1.56)	
≥1.9 and <2.2	36 (16.1)	188 (83.9)	0.79 (0.47–1.32)		0.73 (0.43–1.26)	
≥2.2	48 (19.4)	200 (80.6)	0.99 (0.61–1.60)		0.92 (0.55–1.56)	
History/comorbidities						
Stroke				0.29		0.23
Yes	4 (11.4)	31 (88.6)	0.56 (0.20–1.62)		0.51 (0.17–1.55)	
No	149 (18.7)	649 (81.3)	1		1	
Hypertension				0.78		0.9
Yes	66 (18.8)	285 (81.2)	1.05 (0.74–1.50)		0.98 (0.66–1.44)	
No	87 (18.0)	395 (82.0)	1		1	
Myocardial infarction				0.13		0.16
Yes	22 (24.2)	69 (75.8)	1.49 (0.89–2.49)		1.48 (0.86–2.54)	
No	131 (17.7)	611 (82.3)	1		1	
Diabetes				0.54		0.61
Yes	25 (20.3)	98 (79.7)	1.16 (0.72–1.87)		1.14 (0.69–1.89)	
No	128 (18.0)	582 (82.0)	1		1	
Cancer				0.38		0.39
Yes	13 (14.9)	74 (85.1)	0.76 (0.41–1.41)		0.76 (0.40–1.43)	
No	140 (18.8)	606 (81.2)	1		1	
Kidney disease				0.8		0.92
Yes	11 (19.6)	45 (80.4)	1.09 (0.55–2.17)		1.04 (0.51–2.10)	
No	142 (18.3)	635 (81.7)	1		1	

ABI, ankle-brachial pressure index; baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; CI, confidence interval; GDS, Geriatric Depression Scale; OAB, overactive bladder; OR, odds ratio.

participants with depressive symptoms (OR = 2.37; 1.60–3.52, 95% confidence interval [CI]). Similarly, the risk of OAB was significantly higher in current drinkers (OR = 1.65; 1.04–2.62, 95%CI) and overweight participants (OR = 1.51; 1.02–2.24, 95%CI) (Table 2). While it did not reach statistical significance, obese participants also exhibited a higher OR for OAB (OR = 1.74; 0.74–4.12, 95%CI)

Discussion

In 2002, OAB was defined by the ICS as a syndrome of urgency and frequency of urination.[1] The ICS definition arose from a practical view of OAB, and the diagnostic standards of OAB were established based on subjective symptoms. These changes have allowed for more straightforward clinical judgment, diagnosis and evaluation of treatment effects. Since the ICS definition of OAB, epidemiological surveys have been performed in Europe, the USA, and in Asian countries.[2–5]These surveys have suggested a greater number of OAB patients than was anticipated from earlier studies.

Two large-scale studies on OAB prevalence have been reported. One was conducted in Europe,[2] and the other in the USA.[3] The former study was performed on 16 776 adults aged ≥40 years. The overall prevalence of OAB was 16.6%, with an increase to 22.1–41.9% in the elderly, aged 70 years or more. The other study in the USA reported that the overall prevalence was 16.0% in men, 16.9% in women, and more than 25% in the elderly ≥65 years. Regarding Japanese epidemiological investigations of OAB, there was one random sample study using a mail-in questionnaire in 2003.[5] In this study, participants were selected randomly in proportion to the numbers of households in Japan. The responses from 4570 subjects were collected and analyzed (collection rate, 45%). The overall prevalence of OAB was 12.4%, but it increased to 22.6% and 36.8%, in the elderly people, aged 70–79 years and over 80 years, respectively.

In our study, in which the participants were aged 70 years or older, the prevalence of OAB was 18.4%. One reason for the differences in the prevalence of OAB between the previous studies and ours may be in the environment and specific characteristics of the study population. There are several possible reasons for such differences. The first possibility is the difference in the subjects of the research. As our community-based study was a part of a health promotion program for the elderly, it may be that these participants tended more towards health-seeking behaviors compared with the general population. Those with health-seeking behaviors have a tendency to avoid risk factors for their own health, and may have a low prevalence of various disorders. Moreover, as all our subjects were asked to come to the public facility where we carried out the comprehensive assessment, it might be possible that those with severe disorders did not join in our research. For example, only 34 persons (4.2%) in the present study had previously suffered from stroke, and this selection bias could affect the result of analysis with OAB and the associated factors in this study.

The second is the difference in survey methods. Tikkinen *et al.* reported that the prevalence of OAB was 17.6% in men aged 70–79 years in the population-based study in Finland,[17] and this prevalence was similar to our outcome. They suggest that the prevalence of OAB has been overestimated in earlier studies by vague criteria. Both earlier studies were performed mainly by telephone interviews or postal questionnaires for a random sample of participants. Phone and postal surveys are less costly, and can collect information from a larger population than a face-to-face interview. However, phone interviews that are generally performed by multiple staff members may have problems in uniformity and reproducibility, in addition to deviations as a consequence of the relative responsiveness of the subjects. Postal surveys also have limitations similar to phone interviews, and generally achieve lower response rates, especially in the elderly population.[18] In contrast, the face-to-face interview used in our survey avoided these problems and can define strict criteria of urgency. Furthermore, several reports have described the differences between questionnaire and face-to-face interviews, all of which showed that the prevalence of disease based on face-to-face interview is lower than that obtained using a questionnaire.[18,19] To our knowledge, the present report is the first epidemiological study of definite OAB based on face-to-face interview data.

To date, there have been few surveys on OAB that included as large a sample size of older people as our study. In the National Overactive Bladder Evaluation study, among 5204 participants, 898 people (17.3%) were older than 65 years old.[3] However, this survey was performed by telephone interviews. Milsom *et al.* reported an international survey of OAB syndrome in Europe, but included few coexistence factors in the questionnaires.[2] In our survey, we performed a comprehensive geriatric assessment using many questionnaires and examinations of various types, and data obtained from 833 subjects aged 70 years old or older was analyzed in this report. To our knowledge, this study was the largest population survey of OAB in subjects aged 70 years or over, to date.

Comorbidities associated with OAB have been reported in some epidemiological studies, including age, sex, depression, menopause, parity, constipation, higher BMI, current smoker, diabetes, occupation, type of toilet, and place of residence.[3,20–23] We performed multivariate analysis on factors related to OAB, and found that OAB was significantly higher in participants with depressive symptoms, current drinkers and overweight subjects.

Some studies have reported that depressive symptoms often coexisted with urinary incontinence.[24] Increased frequency and urgency incontinence are frequently observed in

patients with psychological instability, and it is generally considered that the mental condition is the cause of the urgency incontinence, although there are different opinions on this issue.[25] A correlation between depression and nocturia has also been reported.[26] Stewart *et al.* first suggested an association between OAB and depression in the ICS definition of OAB,[3] but the cause of the correlation in the elderly population is not clear. One report describes that frontal cerebral blood flow is decreased in depressive disorder patients in late life using single photon emission computed tomography.[27] Furthermore, one of the bladder sensation centers in the cerebral cortex is found in the frontal lobe.[28] These findings suggest that some degree of idiopathic OAB and depression might have a common cause in elderly people.

We observed a positive correlation between OAB and current drinkers. With regard to the association between lower urinary tract symptoms (LUTS) and alcohol intake, inconsistent results have been reported in previous studies. Several studies found no significant association between drinking and LUTS.[29,30]Meanwhile, one study reported a significant negative association.[31] Because these previous studies did not include many elderly people, the association between drinking and LUTS might not be overt.

Many studies have shown that obesity or a higher BMI is one of the risk factors for stress urinary incontinence. Some reports have also revealed a positive correlation between obesity and OAB. However, the mechanism underlying this correlation has not been elucidated. Zhang *et al.* hypothesized that excess bodyweight might increase bladder pressure and urethral mobility, leading to OAB.[20] Dalloso *et al.* reported that while obesity was a risk factor for OAB onset in women, there was little evidence to indicate this in men.[31]

Recently, it has been assumed that pelvic arterial insufficiency and chronic ischemia of the bladder are associated with detrusor dysfunction. In experimental studies, Azadzoi *et al.* reported that moderate bladder ischemia was associated with detrusor overactivity in the rabbit bladder models.[32] Lower ABI suggest atherosclerosis in lower limbs or pelvic organs. In fact, bifurcation of the iliac arteries is often affected by atherosclerotic change. Although PWV is an indicator of arterial stiffness, we could not show significant associations between OAB and ABI, or PWV in the present study.

There are several limitations to the present study. First, there may be some selection bias, such as health-seeking behaviors and the relatively smaller participation rate in our community-based study. Second, our study design was a cross-sectional one. The inherent limitation of a cross-sectional study is that sampling takes place at only one time-point, so it can be difficult or impossible to infer cause and effect. Further studies are warranted to elucidate the cause of OAB.

Using a face-to-face interview method, we conducted a cross-sectional study on subjects aged 70 years or older in an urban community and assessed the prevalence of and risk factors for OAB in Japan. OAB was significantly associated with depressive symptoms, current drinkers, and BMI. These findings may help to prevent older people from developing OAB symptoms and to promote their health-related quality of life.

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ORIGINAL ARTICLE

Association between Body-Mass Index and Risk of Death in More Than 1 Million Asians

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ABSTRACT

BACKGROUND

Most studies that have evaluated the association between the body-mass index (BMI) and the risks of death from any cause and from specific causes have been conducted in populations of European origin.

METHODS

We performed pooled analyses to evaluate the association between BMI and the risk of death among more than 1.1 million persons recruited in 19 cohorts in Asia. The analyses included approximately 120,700 deaths that occurred during a mean follow-up period of 9.2 years. Cox regression models were used to adjust for confounding factors.

RESULTS

In the cohorts of East Asians, including Chinese, Japanese, and Koreans, the lowest risk of death was seen among persons with a BMI (the weight in kilograms divided by the square of the height in meters) in the range of 22.6 to 27.5. The risk was elevated among persons with BMI levels either higher or lower than that range — by a factor of up to 1.5 among those with a BMI of more than 35.0 and by a factor of 2.8 among those with a BMI of 15.0 or less. A similar U-shaped association was seen between BMI and the risks of death from cancer, from cardiovascular diseases, and from other causes. In the cohorts comprising Indians and Bangladeshis, the risks of death from any cause and from causes other than cancer or cardiovascular disease were increased among persons with a BMI of 20.0 or less, as compared with those with a BMI of 22.6 to 25.0, whereas there was no excess risk of either death from any cause or cause-specific death associated with a high BMI.

CONCLUSIONS

Underweight was associated with a substantially increased risk of death in all Asian populations. The excess risk of death associated with a high BMI, however, was seen among East Asians but not among Indians and Bangladeshis.

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Over the past few decades, there has been a dramatic increase in the prevalence of obesity in many countries. The World Health Organization (WHO) estimates that more than 1 billion adults worldwide are overweight; of these, at least 300 million are obese.[1] A large number of epidemiologic studies have evaluated the associations between body weight and, more often, the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) and a wide range of health outcomes. Obesity is associated with multiple chronic diseases, including type 2 diabetes, hypertension, coronary heart disease, stroke, and several cancers.[2] Since most of the studies have been conducted in populations of European origin, however, the dose–response relationship between BMI and the overall risk of death among Asians, who account for more than 60% of the world population, remains unclear.

The definitions of overweight (BMI ≥25.0) and obesity (BMI ≥30.0) are based essentially on criteria derived from studies that involved populations of European origin. The validity of these criteria in Asian populations has yet to be determined. It has been suggested that the associations of BMI with body composition and health outcomes may differ between Asian and European populations.[3] Studies have shown that for a given BMI, Asians generally have a higher percentage of body fat than do Europeans.[3] Asian populations have also been shown to have an elevated risk of type 2 diabetes, hypertension, and hyperlipidemia at a relatively low level of BMI.[3] On the basis of these observations, it has been proposed that the BMI cutoff points for overweight and obesity should be lower for Asian populations than they are for European populations (suggested cutoff points for Asians, ≥23.0 for overweight and ≥27.5 for obesity).[3] However, a 2004 consensus statement from the WHO concluded that the available data were not sufficient to support Asian-specific cutoff points to define overweight and obesity.[3] The optimal weight range associated with a minimal risk of death in Asian populations remains controversial.

To address these unresolved issues, we evaluated the relationship between BMI and the risk of death using data from 19 cohorts, involving more than 1 million participants. Conducted as part of the Asia Cohort Consortium, this pooling project, with its large sample, provides the opportunity not only to address carefully the methodologic challenges that cannot be handled adequately in any single study but also to evaluate the associations according to major Asian ethnic groups.

METHODS

STUDY POPULATION

We identified cohorts that would be potentially eligible for inclusion in the Asia Cohort Consortium BMI Project through a systematic search of the literature in early 2008, followed by a survey that was sent to the investigators associated with each cohort to further determine eligibility for the study. A total of 19 cohorts were included in the pooling project. With the exception of the Taiwan Cardiovascular Disease Risk Factors Two-Township Study (CVDFACTS) cohort, all the cohorts had accrued at least 5 years of follow-up data and included a minimum of 10,000 participants with baseline data on BMI. All the participating cohorts were required to have available baseline data on BMI, age, sex, and cigarette-smoking status and follow-up data on deaths from any cause. Additional data were collected on selected baseline illnesses and cause-specific deaths. Individual data from participating cohorts were collected and harmonized for the statistical analysis. This study was approved by the ethics committee overseeing each of the participating studies and by the ethics committee at the Fred Hutchinson Cancer Research Center. Written or oral consent was obtained from all the subjects who participated in the study.

A total of 1,155,676 subjects were included in the 19 participating cohorts. We excluded from the analysis subjects with missing data on age (2 subjects), BMI (13,780), and vital status (7). In addition, we excluded subjects who were younger than 18 years of age (14 subjects), those who had a BMI of more than 50 (174), and those for whom data on survival were invalid or missing (105). After these exclusions, 1,141,609 subjects remained (535,199 men and 606,410 women).

STATISTICAL ANALYSIS

The association between BMI and the risk of death was analyzed with the use of Cox proportional-hazards regression models, with a categorical representation of BMI as the predictor variable. To define BMI groups for the analysis, we used the BMI cutoff points of more than 25.0 for overweight and more than 30.0 for obesity.

We then established 10 BMI levels that included the lowest BMI group (≤15.0) and the highest (>35.0) and 8 levels in between, each comprising 2.5 BMI units (i.e., ≤15.0, 15.1 to 17.5, 17.6 to 20.0 . . . 32.6 to 35.0, and >35.0). Using the BMI range of 22.6 to 25.0 as the reference, we estimated hazard ratios and 95% confidence intervals for the other BMI ranges, after adjusting for potential confounders, including baseline age, sex, educational level, urban or rural residence, and marital status. We performed additional analyses in which we also adjusted for the variables of cigarette-smoking status (former or current smoker vs. lifetime nonsmoker) and status with respect to known baseline conditions (cancer, coronary heart disease, stroke, diabetes, and hypertension). Analyses were performed separately on data from the Indian and Bangladeshi population and the East Asian population (Chinese, Japanese, and Koreans), since there is considerable heterogeneity between these two populations. Prespecified stratified analyses were performed according to smoking status and sex to evaluate the consistency of the associations. Some analyses were performed among lifetime nonsmokers to eliminate the potential confounding effect of cigarette smoking on the association between BMI and the risk of death. To minimize the influence of possible "reverse causation" (illnesses causing low BMI) owing to the presence of terminal diseases at baseline in some subjects, we excluded the first 3 years of follow-up and restricted some analyses to subjects who did not have a history of cardiovascular disease, stroke, or cancer at baseline and other analyses to lifetime nonsmokers without these conditions at baseline. The ages of the subjects when they entered and exited the cohort were used to define the time variable in the Cox models. The age at exit from the cohort was defined as the age at death or the age at the end of the follow-up period, whichever was earlier.

In the models, the effect of BMI on the risk of death was assumed to be cohort-specific. For each cohort, we assumed that the log hazard ratio for BMI had a fixed-effect component that was common to all cohorts within each of the two major Asian populations (one comprising East Asians and the other compromising Indians and Bangladeshis) and a random effect that was cohort-specific. The random effects for the log hazard ratios were assumed to be normally distributed, with mean zero; that is, we assumed that $\hat{\beta}_{ij}$, the estimated log hazard ratio for the BMI level in a cohort, where j is the BMI level and i is the cohort, has the distribution $\hat{\beta}_{ij} \sim N(\beta_j, \hat{\sigma}_{ij}^2 + \hat{\tau}_j^2)$, where $\hat{\sigma}_{ij}^2$ is the within-study variance of $\hat{\beta}_{ij}$ and $\hat{\tau}_j^2$ is the between-cohort variance of $\hat{\beta}_{ij}$, as estimated from the Cox regression model.[4,5] The β_j parameters and their 95% confidence intervals were estimated in the meta-analysis. Cox model estimation for each cohort was performed with the use of the PHREG procedure in SAS, version 9.2. The meta-analysis estimation was performed with the use of the PROC MIXED procedure in SAS.

RESULTS

STUDY POPULATION

More than 1.14 million participants from 19 cohorts were included in the analysis (Table 1). Overall, the mean (±SD) BMI for the study population was 22.9±3.6 (range, 19.8 to 23.7). Nearly 34% of the study subjects were current or former smokers. Over a mean follow-up period of 9.2 years, approximately 120,700 cohort members died. Approximately two thirds of the deaths were due to cardiovascular diseases (35.7%) or cancer (29.9%), and the other third to other causes (34.3%). Considerable variation, however, existed across the cohorts.

ASSOCIATION BETWEEN BMI AND RISK OF DEATH FROM ANY CAUSE

In both Asian populations, the adjusted hazard ratios for death from any cause were elevated among groups with BMIs lower than the reference range of 22.6 to 25.0 (Table 2). Subjects in the lowest BMI group (≤15.0) had a risk that was increased by a factor of approximately 2.0 to 2.8. Among groups with BMIs higher than the reference range, the hazard ratios for death from any cause were elevated in the East Asian population but not in the Indian and Bangladeshi population. In general, the magnitude of the association was similar between subjects who were current or former smokers and those who were lifetime nonsmokers. The results for men and women were similar to the results of combined analyses of data from men and women (Tables 1 and 2 in the Supplementary Appendix, available with the full text of this article at NEJM.org).

To evaluate the possible influence of reverse causation, we performed analyses that excluded subjects with a baseline diagnosis of coronary

Table 1. Characteristics of the Participating Cohorts.*

Cohort	No of Subjects	Dates of Enrollment	Mean Follow-up Period	Mean Age at Entry	BMI†	Female Sex	Current or Former Smoker	Deaths	Cause of Death‡		
									Cancer	CVD	Other
			yr			%		no.	%		
India											
Mumbai Cohort Study§	146,820	1991–1997	5.2	50.8	22.3±4.2¶	40.4	18.9	13,001	8.7	43.8	47.5
TOCS	129,097	1995–2002	7.5	49.5	21.8±4.1¶	61.6	23.5	10,680	11.8	37.4	50.8
Bangladesh: Health Effects of Arsenic Longitudinal Study	11,452	2000–2002	6.6	37.1	19.8±3.2¶	57.0	35.6	392	15.6	43.7	40.7
Mainland China											
CHEFS	154,737	1990–1992	7.2	55.4	22.6±3.7¶	51.1	37.9	17,687	22.5	46.4	31.0
SCS§	18,100	1986–1989	16.3	55.3	22.2±3.0	0.0	57.3	4,983	39.6	33.8	26.6
SMHS	61,379	2001–2006	3.1	54.9	23.7±3.1¶	0.0	69.6	946	45.2	31.1	23.7
SWHS	74,873	1996–2000	8.6	52.1	24.0±3.4¶	100.0	2.8	2,895	46.4	27.6	26.0
Taiwan											
CBCSP	23,763	1991–1992	15.2	47.3	24.0±3.4¶	49.7	28.9	2,758	36.6	20.1	43.3
CVDFACTS	5,129	1990–1993	14.9	47.0	23.7±3.5¶	55.9	24.8	829	26.7	26.3	47.0
Singapore: SCHS	63,242	1993–1999	11.5	56.5	23.1±3.2	55.8	30.6	10,689	36.4	34.7	28.9
Japan											
3 Pref Aichi§	32,210	1985	11.6	56.2	22.1±3.0	52.6	50.7	5,764	32.9	34.8	32.4
Ibaraki Prefectural Health Study	97,578	1993–1994	11.5	58.8	23.5±3.2¶	65.8	30.3	10,980	NA	NA	NA
JACC	86,671	1988–1990	12.7	57.6	22.8±3.0	58.2	38.6	12,888	36.8	31.0	32.2
JPHC1	42,771	1990–1992	14.4	49.6	23.6±3.0	52.2	40.3	3,394	43.6	26.1	30.3
JPHC2	55,712	1992–1995	11.5	54.2	23.5±3.1	52.6	40.1	5,357	44.5	24.9	30.7
3 Pref Miyagi	29,525	1984	11.6	56.9	23.2±3.3	55.0	43.1	5,880	30.2	40.5	29.3
Miyagi Cohort Study	44,867	1990	12.8	52.0	23.6±3.0	52.1	49.5	3,441	54.9	27.1	18.0
Ohsaki National Health Insurance Cohort Study	47,670	1995	9.9	60.1	23.5±3.1	51.8	48.6	6,892	35.9	32.9	31.2
Korea: KMCC§	16,013	1993–2004	6.5	55.6	23.7±3.3¶	60.3	36.4	1,302	29.6	25.4	45.0
Total	1,141,609	1984–2006	9.2	53.9	22.9±3.6	53.1	33.5	120,758	29.9	35.7	34.3

* Plus–minus values are means ±SD. CBCSP denotes Community-based Cancer Screening Project, CHEFS China National Hypertension Survey Epidemiology Follow-up Study, CVD cardiovascular disease, CVDFACTS Cardiovascular Disease Risk Factor Two-Township Study, JACC Japan Collaborative Cohort Study, JPHC Japan Public Health Center–based Prospective Study, KMCC Korea Multi-center Cancer Cohort, NA not available, SCHS Singapore Chinese Health Study, SCS Shanghai Cohort Study, SMHS Shanghai Men's Health Study, SWHS Shanghai Women's Health Study, 3 Pref Three Prefecture Cohort Study, and TOCS Trivandrum Oral Cancer Screening Trial.

† The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

‡ Deaths from unknown causes are not included.

§ Data on status with respect to diagnosed coronary heart disease at baseline were unavailable for these cohorts. Data for cohorts with and those without baseline data on coronary heart disease are available in Table 8 in the Supplementary Appendix.

¶ The BMI was calculated with the use of weight and height measured at enrollment. For the other studies, weight and height were self-reported.

Table 2. Association between Body-Mass Index and Risk of Death from Any Cause in Two Asian Populations, According to Smoking Status.*

Population	BMI at Baseline									
	≤15.0	15.1–17.5	17.6–20.0	20.1–22.5	22.6–25.0	25.1–27.5	27.6–30.0	30.1–32.5	32.6–35.0	35.1–50.0
All subjects										
East Asians										
No. of deaths	456	3795	13,547	21,200	21,391	11,009	4679	1623	484	283
Hazard ratio (95% CI)	2.76 (1.88–4.07)	1.84 (1.65–2.05)	1.35 (1.25–1.45)	1.09 (1.05–1.14)	Reference	0.98 (0.95–1.01)	1.07 (1.02–1.12)	1.20 (1.10–1.32)	1.50 (1.31–1.71)	1.49 (1.31–1.69)
Indians and Bangladeshis										
No. of deaths	755	2412	3340	3196	2349	1269	537	233	64	57
Hazard ratio (95% CI)	2.14 (1.78–2.57)	1.59 (1.40–1.81)	1.26 (1.12–1.41)	1.09 (0.97–1.23)	Reference	0.98 (0.84–1.13)	0.94 (0.77–1.16)	1.03 (0.77–1.39)	0.86 (0.50–1.49)	1.27 (0.71–2.26)
Current or former smokers										
East Asians										
No. of deaths	191	1990	7590	11,737	10,450	4733	1722	531	127	82
Hazard ratio (95% CI)	2.66 (1.62–4.37)	1.81 (1.61–2.04)	1.38 (1.28–1.49)	1.14 (1.09–1.18)	Reference	0.97 (0.93–1.00)	1.01 (0.95–1.07)	1.18 (1.07–1.30)	1.44 (1.13–1.84)	1.60 (1.26–2.03)
Indians and Bangladeshis										
No. of deaths	267	1055	1277	1067	678	318	116	41	9	5
Hazard ratio (95% CI)	1.97 (1.43–2.72)	1.59 (1.28–1.98)	1.24 (1.01–1.53)	1.13 (0.92–1.40)	Reference	0.99 (0.74–1.33)	0.99 (0.64–1.53)	1.16 (0.58–2.32)	NA	NA
Lifetime nonsmokers										
East Asians										
No. of deaths	247	1618	5280	8366	9925	5704	2713	1017	325	179
Hazard ratio (95% CI)	2.43 (2.06–2.87)	1.72 (1.52–1.94)	1.23 (1.12–1.35)	1.02 (0.97–1.07)	Reference	1.00 (0.95–1.06)	1.11 (1.04–1.20)	1.27 (1.12–1.43)	1.51 (1.30–1.76)	1.56 (1.31–1.86)
Indians and Bangladeshis										
No. of deaths	488	1357	2063	2128	1671	951	421	192	55	52
Hazard ratio (95% CI)	2.15 (1.71–2.69)	1.54 (1.31–1.81)	1.24 (1.07–1.43)	1.07 (0.93–1.23)	Reference	0.97 (0.82–1.16)	0.94 (0.74–1.19)	1.01 (0.73–1.41)	0.86 (0.48–1.55)	1.34 (0.73–2.46)

* Included in the analysis were all East Asian subjects (779,537) and Indian and Bangladeshi subjects (265,036), current and former smokers in the two populations (270,045 and 55,435 subjects, respectively), and lifetime nonsmokers in the two populations (479,492 and 209,596 subjects, respectively). The analyses for the calculation of hazard ratios were adjusted for age, sex, educational level, urban or rural residence, marital status, and status with respect to baseline illnesses; data from subjects with less than 3 years of follow-up were excluded. NA denotes not available.

heart disease, stroke, or cancer (Table 3). Excluding these subjects had only a minimal effect on the point estimate of hazard ratios for the association between BMI and the risk of death from any cause. Excluding 2 additional years of follow-up (i.e., excluding the first 5 years instead of the first 3 years) slightly attenuated the positive association of the risk of death with low BMI but had no effect on the results for high-BMI groups. In an analysis in which current or former smokers were excluded, the elevated risk associated with a lower BMI was attenuated, whereas the positive association with a higher BMI among East Asians was slightly strengthened. No positive association between death from any cause and a high BMI was seen in the Indian and Bangladeshi population in any of the analyses, regardless of the types of exclusions. These results indicate that any possible reverse causation was adequately addressed in the analyses that were performed on data from lifetime nonsmokers, after the exclusion of deaths that occurred within the first 3 years of follow-up — an approach that was used in all the main analyses in this study.

ASSOCIATION BETWEEN BMI AND RISK OF DEATH FROM SPECIFIC CAUSES

As with the findings for death from any cause, a U-shaped association was seen between BMI and the risk of death from cardiovascular disease, cancer, or other causes among East Asians but not among Indians and Bangladeshis (Fig. 1). In fact, no elevated risk of death from any of these three causes was seen in the high-BMI groups of Indians and Bangladeshis. The positive association between a low BMI and the risk of death was strongest for death from causes other than cardiovascular disease or cancer. The results of analyses stratified according to smoking status were, in general, consistent with the pattern shown in Figure 1, although point estimates for some BMI categories were not significant, owing to the small sample (Tables 3 and 4 in the Supplementary Appendix).

The strikingly positive association between low BMI and death from causes other than cardiovascular disease or cancer was primarily the result of deaths due to respiratory diseases (Fig. 2). After exclusion of deaths from respiratory diseases, the positive association with low BMI was substantially reduced. The association between BMI and death from respiratory diseases was similar in smokers and nonsmokers (Fig. 1 in the Supplementary Appendix). It is possible that the strong association observed between low BMI and death from respiratory diseases could be explained, in part, by reverse causation, since respiratory disease can lead to weight loss long before the clinical diagnosis is made.

DISCUSSION

In the pooled analysis of approximately 850,000 East Asians, both a low BMI and a high BMI were associated with an increased risk of death from any cause and of cause-specific death, resulting in an overall U-shaped association. Analyses of data from more than 287,000 Indians and Bangladeshis, however, showed an elevated risk of death only among those with a low BMI. This large pooled analysis not only provides reliable estimates of the overall effect of BMI on the risk of death from any cause and of cause-specific death among Asians, but also offers opportunities for a careful evaluation of the association between low BMI and the risk of death that could not be adequately investigated in most previous studies, which were conducted in populations of European origin.

A U-shaped association between BMI and the risk of death was also seen in a recent pooled analysis of data from the Prospective Studies Collaboration (PSC), involving 900,000 participants in 57 prospective studies, mostly in Western Europe and North America.[6] Only 8% of the PSC populations were Asians (Japanese). In our analysis of data from Indians and Bangladeshis, however, a virtually inverse association between BMI and death from any cause was seen. Even among East Asians, the shape of the curve for the association in our analysis was quite different from that in the PSC, as were the hazard ratios (which were higher at the low-BMI range among Asians than in the European population and higher at the high-BMI range in the European population than among Asians). Over the past 10 years, several large cohort studies have also evaluated the association between BMI and the risk of death, again mostly in populations of European origin.[6-10] Although the BMI groupings that were used varied among the studies, these studies, in general, have shown that the lowest risk of death is associated with a BMI in

Table 3. **Association between Body-Mass Index and Risk of Death from Any Cause in Subgroup Analyses Designed to Address Reverse Causation.***

Subgroup Analysis	All Subjects				Lifetime Nonsmokers			
	Low BMI		High BMI		Low BMI		High BMI	
	no. of deaths	*hazard ratio (95% CI)*	*no. of deaths*	*hazard ratio (95% CI)*	*no. of deaths*	*hazard ratio (95% CI)*	*no. of deaths*	*hazard ratio (95% CI)*
East Asians								
All subjects	74,226	1.18 (1.14–1.22)	47,512	1.06 (1.04–1.08)	31,543	1.13 (1.09–1.18)	24,010	1.08 (1.05–1.10)
Excluding first 3 yr of follow-up	59,933	1.18 (1.14–1.22)	39,469	1.06 (1.04–1.08)	25,189	1.13 (1.09–1.18)	19,863	1.08 (1.05–1.10)
Including all subjects with baseline data on CHD†	49,807	1.18 (1.14–1.23)	34,666	1.05 (1.03–1.08)	21,895	1.14 (1.09–1.19)	17,999	1.08 (1.05–1.10)
Excluding subjects with CHD at baseline†	46,706	1.18 (1.14–1.23)	31,832	1.06 (1.03–1.08)	20,597	1.14 (1.09–1.19)	16,531	1.08 (1.05–1.11)
Excluding subjects with CHD, cancer, or stroke at baseline‡	44,115	1.18 (1.14–1.23)	29,964	1.06 (1.03–1.08)	19,425	1.13 (1.08–1.19)	15,529	1.08 (1.05–1.11)
Including only subjects with no CHD, cancer, or stroke at baseline§	27,367	1.19 (1.13–1.25)	20,162	1.06 (1.03–1.09)	11,012	1.13 (1.06–1.20)	9,775	1.08 (1.04–1.12)
Excluding first 5 yr of follow-up	48,187	1.16 (1.13–1.20)	32,353	1.06 (1.04–1.08)	20,078	1.12 (1.07–1.17)	16,124	1.08 (1.05–1.11)
Including all subjects with baseline data on CHD†	39,552	1.17 (1.12–1.22)	28,177	1.06 (1.03–1.09)	17,286	1.12 (1.07–1.17)	14,528	1.08 (1.04–1.11)
Excluding subjects with CHD at baseline†	37,137	1.17 (1.13–1.22)	25,916	1.06 (1.03–1.09)	16,280	1.12 (1.07–1.17)	13,362	1.08 (1.05–1.11)
Excluding subjects with CHD, cancer, or stroke at baseline‡	35,173	1.17 (1.13–1.21)	24,511	1.06 (1.03–1.09)	15,380	1.12 (1.06–1.17)	12,616	1.08 (1.05–1.12)
Including only subjects with no CHD, cancer, or stroke at baseline§	23,000	1.17 (1.12–1.23)	17,010	1.06 (1.02–1.10)	9,267	1.11 (1.04–1.18)	8,209	1.08 (1.03–1.13)
Indians and Bangladeshis								
All subjects	18,988	1.16 (1.12–1.21)	7,295	1.00 (0.93–1.06)	12,155	1.15 (1.09–1.21)	5,392	1.00 (0.93–1.07)
Excluding first 3 yr of follow-up	11,297	1.16 (1.12–1.21)	4,509	1.00 (0.93–1.06)	7,219	1.15 (1.09–1.21)	3,342	1.00 (0.93–1.07)
Including all subjects with baseline data on CHD†	5,876	1.17 (0.99–1.38)	1,962	0.99 (0.73–1.33)	3,410	1.17 (0.94–1.46)	1,437	0.99 (0.71–1.39)
Excluding subjects with CHD at baseline†	5,733	1.17 (0.99–1.39)	1,892	0.99 (0.73–1.34)	3,349	1.17 (0.94–1.47)	1,385	0.99 (0.71–1.39)
Excluding subjects with CHD, cancer, or stroke at baseline‡	5,694	1.17 (0.99–1.39)	1,871	0.99 (0.72–1.34)	3,322	1.17 (0.94–1.47)	1,369	0.99 (0.70–1.40)
Excluding first 5 yr of follow-up	5,459	1.14 (1.08–1.21)	2,154	0.98 (0.90–1.08)	3,398	1.12 (1.04–1.21)	1,599	1.00 (0.90–1.11)
Including all subjects with baseline data on CHD†	3,611	1.15 (0.93–1.43)	1,253	1.01 (0.70–1.47)	2,082	1.16 (0.87–1.54)	904	1.03 (0.68–1.55)
Excluding subjects with CHD at baseline†	3,529	1.15 (0.93–1.43)	1,216	1.01 (0.69–1.47)	2,045	1.16 (0.87–1.55)	875	1.02 (0.67–1.55)
Excluding subjects with CHD, cancer, or stroke at baseline‡	3,512	1.15 (0.93–1.43)	1,206	1.00 (0.68–1.47)	2,033	1.16 (0.87–1.55)	868	1.02 (0.67–1.55)

* The hazard ratios represent the incremental effect per category of BMI relative to the reference category (22.6 to 25.0). Low BMI refers to BMI levels below the reference level (i.e., 20.1 to 22.5, 17.6 to 20.0, and 15.1 to 17.5), and high BMI refers to BMI levels above the reference level (i.e., 25.1 to 27.5, 27.6 to 30.0, 30.1 to 32.5, 32.6 to 35.0, and 35.1 to 50.0). All the models were adjusted for age, sex, educational level, urban or rural residence, marital status, and status with respect to baseline coexisting conditions. Deaths among persons whose BMI was in the reference range were included in the proportional-hazards model for both low-BMI and high-BMI group analyses. CHD denotes coronary heart disease.

† The analysis was restricted to cohorts for which baseline data on prior diagnosis of CHD were collected.

‡ Baseline data on prior diagnosis of CHD were collected in all cohorts included in this analysis. Baseline data on cancer or stroke were not collected in some cohorts; subjects with missing data on prior diagnosis of cancer or stroke were included in the analysis.

§ The analysis was restricted to cohorts for which complete baseline data on prior diagnoses of CHD, cancer, and stroke were collected. This analysis was not performed in the case of the Indian and Bangladeshi subjects, since complete data on these diagnoses at baseline were not collected for any of the cohorts in this population.

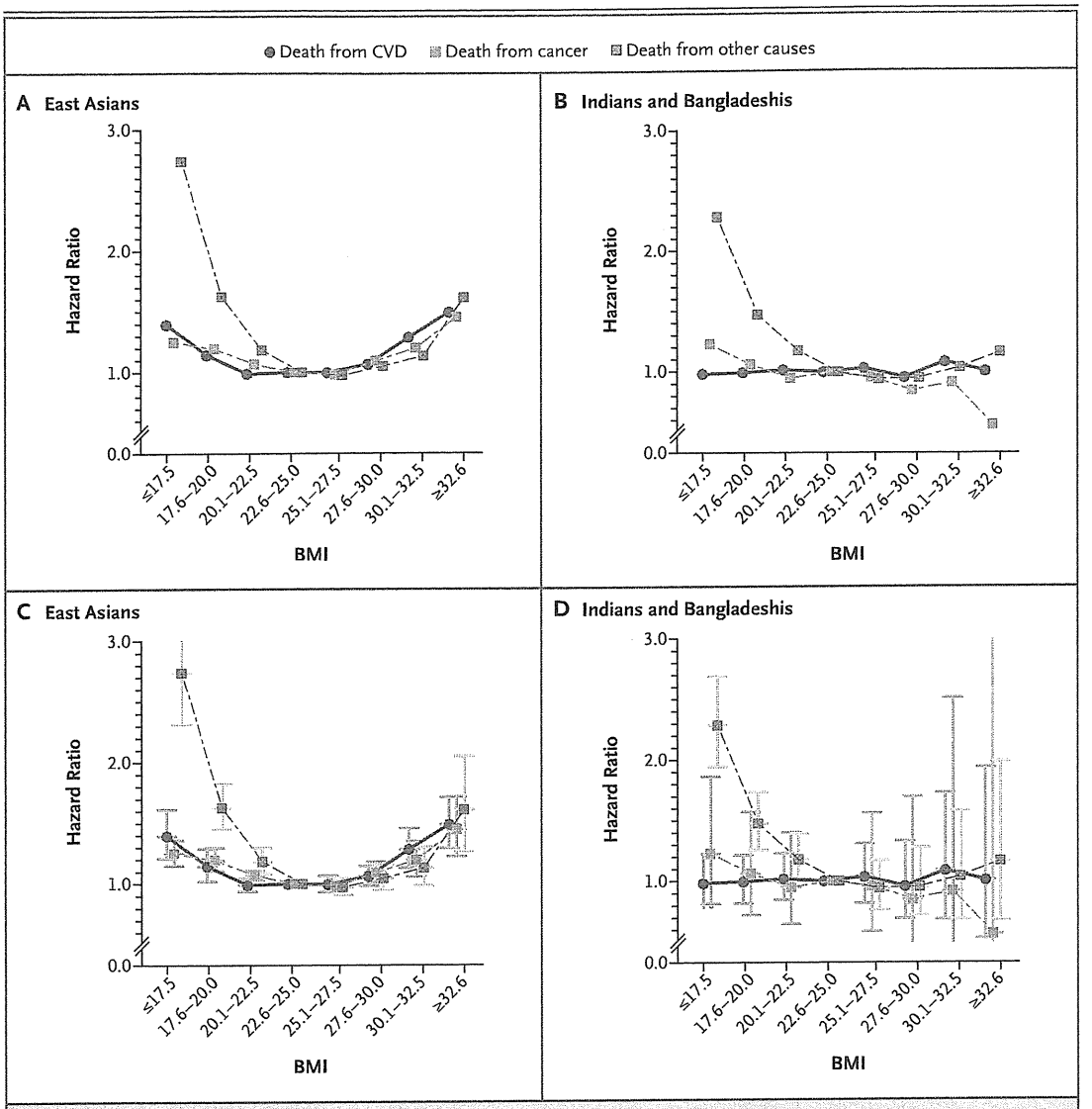

Figure 1. Association between Body-Mass Index and Risk of Cause-Specific Death in Two Asian Populations.

Hazard ratios are shown for the association between body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) and risk of death from cardiovascular disease (CVD), from cancer, and from other causes among East Asians (Chinese, Japanese, and Koreans) and Indians and Bangladeshis. Panels A and B show the hazard ratios without confidence intervals, and Panels C and D show the same data with 95% confidence intervals (I bars). The analyses were adjusted for age, sex, educational level, urban or rural residence, marital status, and status with respect to baseline illnesses; data from subjects with less than 3 years of follow-up were excluded.

the range of 23 to 27, regardless of the study population. The finding that the same optimal weight range is associated with the lowest risk of death both in the current study of East Asians and in previous studies involving populations of European origin argues strongly against the use of race- or ethnicity-specific BMI cutoff points to define overweight and obesity.

In a longitudinal analysis of approximately 1.2 million Koreans in the Korean Cancer Prevention Study (KCPS), Jee et al. reported a J-shaped association between BMI and the risk of death from any cause.[9] The BMI category associated with the lowest overall risk of death was 21.5 to 27.9 in the KCPS, which is similar to the findings among East Asians in our study (Tables 5, 6, and 7 in the Supplementary Appendix). However, for some of the analyses, the magnitude of

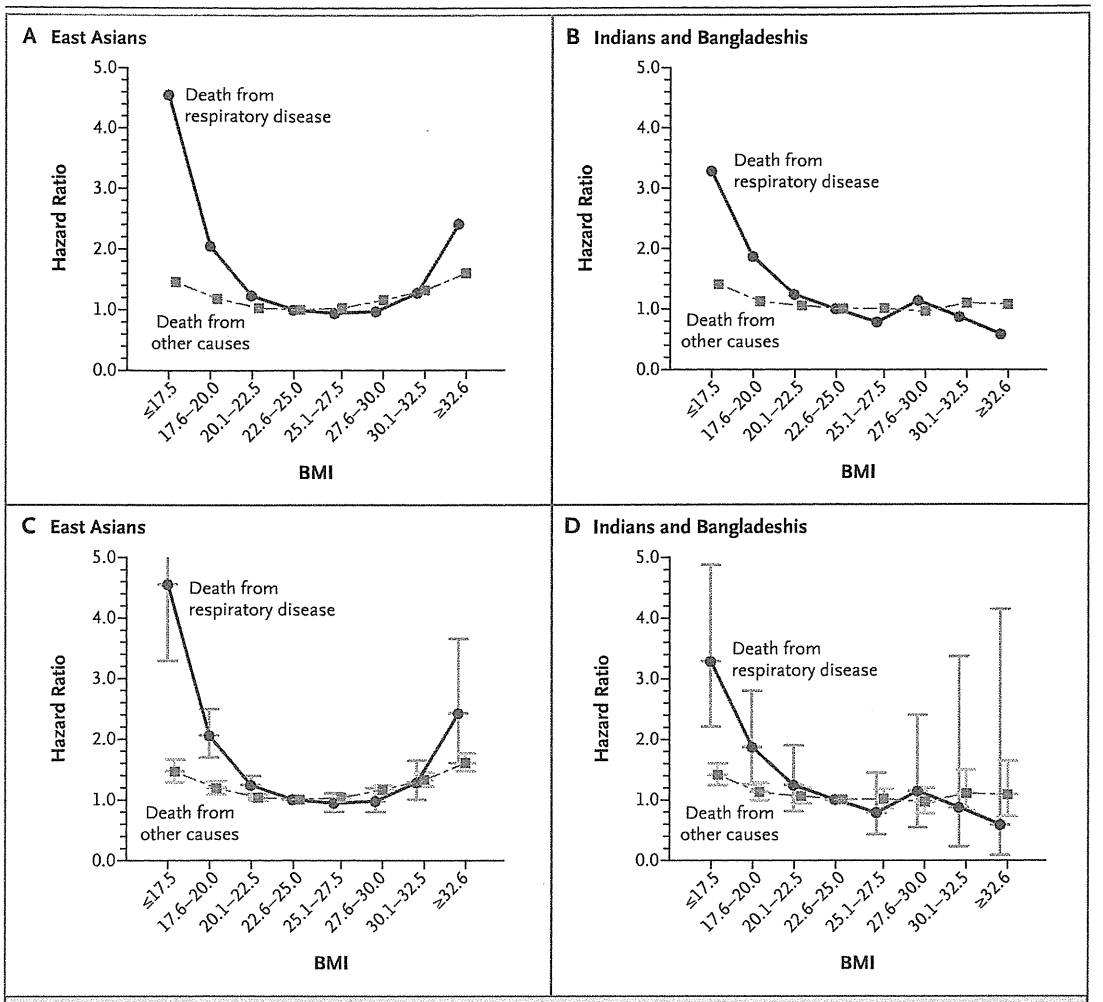

Figure 2. Association between the Body-Mass Index and the Risk of Death from Respiratory Diseases or Other Causes.
Hazard ratios are shown for the association between BMI and risk of death from respiratory diseases and from causes other than respiratory diseases, cardiovascular causes, or cancer (other) among East Asians (Chinese, Japanese, and Koreans) and Indians and Bangladeshis. Panels A and B show the hazard ratios without confidence intervals, and Panels C and D show the same data with 95% confidence intervals (I bars). The analyses were adjusted for age, sex, educational level, urban or rural residence, marital status, and status with respect to baseline illnesses; data from subjects with less than 3 years of follow-up were excluded.

the associations differs between the KCPS and our study. Extensive exclusions were made in the KCPS; subjects with a baseline diagnosis of coronary heart disease, cancer, liver disease, diabetes, stroke, or respiratory disease were not included in that study. Most other cohort studies have not made such extensive exclusions from their analyses, nor did we in our study. Because only about 16,000 Koreans were included in our analysis, the East Asian group in our study consisted primarily of Chinese and Japanese subjects. Therefore, differences in characteristics across these populations could also contribute to inconsistencies between the findings of our study and those of the KCPS.

Although the risk of death is the most critical measure of the health consequences of excess adiposity, epidemiologic studies examining the relationship between body weight and the risk of death are fraught with methodologic challenges.[11,12] The most important of these is the problem of reverse causation, in which weight loss resulting from illness can distort the relationship between leanness and health. An additional

concern is confounding, mainly by smoking status, since smokers often have a lower body mass than do nonsmokers. To address these problems, investigators in multiple studies have performed analyses using data from nonsmokers only and from people who reported no serious underlying illness at the time of enrollment or have excluded from the analyses the early years of follow-up.[13-16] However, in our study, the PSC project, and the KCPS, as well as in some other large cohort studies,[6-10] a J-shaped or U-shaped relation between BMI and the risk of death persisted after major methodologic issues were addressed.

There is substantial evidence supporting the biologic plausibility of a positive association between excess adiposity and the risk of death. Obesity is a well-established risk factor for numerous chronic diseases.[2] Adipose tissue has been increasingly recognized as an active endocrine organ, capable of releasing a large number of cytokines and bioactive mediators that play important roles in the pathogenesis of many obesity-related diseases.[17] In contrast, the increased risk of death associated with a low BMI, observed in our study and in other studies, remains to be fully explained. Inadequate or incomplete control for confounding or reverse-causation bias could in part explain the increased risk.[18] A residual influence of reverse causation may remain in our study, particularly since we did not have information on the presence of infections and on diagnoses of chronic lung disease at baseline; therefore, data from subjects with those conditions could not be excluded from our analysis. A low BMI can be an indicator of certain other chronic medical conditions that were not adequately controlled in the study or an indicator of poor health or a low standard of living, which may contribute to such conditions as undernutrition and may increase the risk of premature death.[19] Several cohort studies have shown that, even among persons with a low BMI, an elevated waist-to-hip ratio or waist circumference (each of which is a measure of abdominal adiposity) was associated with a significantly increased risk of death[10,20]; this suggests that the observed excess risk of death among subjects with a low BMI may be due, in part, to abdominal adiposity, which cannot be assessed adequately on the basis of the BMI.[21]

We did not assess the risk of death in relation to abdominal obesity, which may be a particularly important factor in Asian populations. In the case of several cohorts participating in this consortium, the interval between the assessment of BMI and the ascertainment of the outcome of death was relatively short, raising concern about the effects of subclinical or undiagnosed chronic diseases on the results. Data from subjects with self-reported height and weight measurements were included in our analysis, although the pattern of association between BMI and death from any cause was similar regardless of the method for assessing height and weight (Table 9 in the Supplementary Appendix). Socioeconomic status could confound the association between BMI and the risk of death, since in less well-developed countries, people with a high BMI are more likely to have a high socioeconomic status (and thus better access to health care) than are those with a lower BMI. Although we adjusted for several indicators of socioeconomic status, such as educational level, which is a major measure of socioeconomic status, it is possible that residual confounding effects of socioeconomic status remain that could attenuate the positive association between high BMI and the risk of death.

In conclusion, this large pooled analysis revealed a U-shaped association between BMI and the risk of death in East Asians, with a pattern broadly similar to that seen in previous studies involving mostly North American and European populations. In Indians and Bangladeshis, however, no elevated risk of either death from any cause or cause-specific death was seen in high-BMI groups. Overall, the risk of death among Asians, as compared with Europeans, seems to be more strongly affected by a low BMI than by a high BMI. Given the limitations of the current study, in which the risk of death was used as the outcome, additional studies are needed to quantify the association between BMI and the incidence of disease, in order to better define BMI criteria for overweight and obesity in Asians.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.