# A prospective study of body mass index and mortality in Bangladesh

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- **Background** Body mass index (BMI) (kg/m<sup>2</sup>) has a U- or J-shaped relationship with all-cause mortality in Western and East Asian populations. However, this relationship is not well characterized in Bangladesh, where the BMI distribution is shifted towards lower values.
- **Methods** Using data on 11445 individuals (aged 18–75 years) participating in the Health Effects of Arsenic Longitudinal Study (HEALS) in Araihazar, Bangladesh, we prospectively examined associations of BMI (measured at baseline) with all-cause mortality during ~6 years of follow-up. We also examined this relationship within strata of key covariates (sex, age, smoking, education and arsenic exposure). Cox proportional hazards models adjusted for these covariates and BMI-related illnesses were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for BMI categories defined by the World Health Organization.
- **Results** Low BMI was strongly associated with increased mortality in this cohort (*P*-trend < 0.0001). Severe underweight (BMI < 16 kg/m<sup>2</sup>; HR 2.06, CI 1.53–2.77) and moderate underweight (16.0–16.9 kg/m<sup>2</sup>; HR 1.39, CI 1.01–2.90) were associated with increased all-cause mortality compared with normal BMI (18.6–22.9 kg/m<sup>2</sup>). The highest BMI category ( $\geq$ 23.0 kg/m<sup>2</sup>) did not show a clear association with mortality (HR 1.10, CI 0.77–1.53). The BMI–mortality association was stronger among individuals with <5 years of formal education (interaction P = 0.02).
- **Conclusions** Underweight (presumably due to malnutrition) is a major determinant of mortality in the rural Bangladeshi population.
- Keywords Arsenic, Bangladesh, body mass index, mortality, survival analysis

# Introduction

A large body of epidemiological research suggests that body mass index (BMI) (kg/m<sup>2</sup>) has a U- or J-shaped relationship with all-cause mortality in Western<sup>1-3</sup> and East Asian<sup>4-6</sup> populations. In other words, underweight (<18.5 kg/m<sup>2</sup>; also referred to as 'chronic energy deficiency'<sup>7</sup>) and obese (>30 kg/m<sup>2</sup>) individuals tend to die earlier than individuals with intermediate BMI values. However, the relationship between BMI and mortality is not well characterized in many developing nations, which may have unique BMI distributions, environmental exposures and genetic backgrounds.

Compared with Western populations, the BMI distribution in East Asian countries is shifted towards lower values, although the prevalence of obesity and overweight has increased in recent years.<sup>8</sup> In South Asian countries, such as India, the BMI distribution is shifted even further towards low values, especially in rural areas,<sup>8–11</sup> likely reflecting poor nutritional status.<sup>12</sup> In Bangladesh, recent estimates<sup>7,13,14</sup> of the population mean BMI range between 19 and 20 kg/m<sup>2</sup>, lower than estimates in the USA (~27 kg/m<sup>2</sup>),<sup>15</sup> Japan (~23.5 kg/m<sup>2</sup>)<sup>6</sup> and India (21.7 kg/m<sup>2</sup>).<sup>10</sup>

In this article, we examine the relationship between BMI (measured at baseline) and all-cause mortality using  $\sim$ 6 years of follow-up data from a large prospective cohort study of individuals chronically exposed to arsenic though drinking water in Araihazar, Bangladesh. We examine the BMI–mortality association within strata of key covariates (sex, age, smoking, education and arsenic exposure).

# **Methods**

#### Study area and study population

The Health Effects of Arsenic Longitudinal Study (HEALS, described by Ahsan *et al.*<sup>16</sup>) is a prospective investigation of health outcomes associated with arsenic exposure through drinking water in a cohort of adults in Araihazar, Bangladesh, a rural area east of Dhaka with relatively homogenous socio-cultural characteristics. Between October 2000 and May 2002, we recruited individuals (aged 18–75 years) who were (i) married, (ii) residents of the study area for at least 5 years and (iii) primarily drinking water from a local well. Using a pre-cohort survey, we enumerated a total of 65876 individuals residing in Araihazar, from which we identified a sampling frame of 14828 eligible residents. Of these 14828 individuals, 2778 were not at home during any of the three attempted recruiting visits. Of the 12050 remaining eligible residents, 11746 (97.5% response rate) men and women (4801 married couples and 2144 married individuals whose spouses did not participate) enrolled into the HEALS cohort. All 5966 tubewells in the study area were tested for arsenic. Trained study physicians, blinded to the arsenic measurements,

conducted in-person interviews and clinical evaluations and collected urine and blood samples from participants in their homes using structured protocols. The study protocol was approved by the Institutional Review Boards of The University of Chicago, Columbia University, and the Bangladesh Medical Research Council. Informed consent was obtained from all participants prior to the initial interview.

Follow-up in-person interviews were conducted for the entire cohort during the following periods: follow-up 1 during September 2002 to May 2004, follow-up 2 during June 2004 to August 2006 and follow-up 3 during January 2007 to February 2009. Follow-up interviews were conducted using the same data collection procedures developed for the baseline interview. At each follow-up an attempt was made to find each participant (or an informant who could confirm the vital status of that participant) not determined to be deceased in a prior follow-up. At follow-up 1 we identified 103 deaths, at follow-up 2 we identified 116 deaths and at follow-up 3 we identified 181 deaths. At each follow-up we were unable to ascertain death status for some individuals; however, at the end of follow-up 3 we were able to determine vital status for all but one participant.

### Assessment of mortality

From 2000 to 2009, vital status was determined at each biennial follow-up interview. Date of death was ascertained by relatives (n = 396) or neighbours (n=3) of deceased participants. The relationship status of one informant was unknown. An extensive verbal autopsy procedure was used to investigate and assign the causes of death (previously validated in a Bangladeshi population<sup>17-20</sup>). For deceased individuals, survival time was calculated as the number of days between the date of the baseline interview and date of death. Follow-up time for participants who completed (or were reported to be alive at) all three follow-up interviews was calculated as the number of days between the baseline interview and last interview with the participant or the informant. Participants lost to follow-up with no informant or vital status data were censored at the last point of contact (n = 1).

#### Assessment of BMI and covariates

At the baseline interview, trained study physicians measured height and weight using a locally manufactured tape measure and a Misaki (Japan) scale (calibrated weekly), respectively. Both height and weight were measured three times at baseline and averaged. BMI was calculated as average weight in kilograms divided by average height in metres, squared. Socio-demographic factors including sex, age (years) and education (years) were obtained. Smoking status was categorized as current, former and never. Participants self-reported experiencing the following health-related symptoms in the 6 months prior to baseline (yes or no): nausea, vomiting, weight loss, hyperhydrosis, asthenia, weakness, diarrhoea and dyspnoea.

#### Exclusions

Of the 11 746 enrolled study participants, we excluded subjects lacking data on age (n = 1) and BMI (n = 279) from all analyses. An additional 21 individuals were excluded who lacked data on smoking, education or BMI-related symptoms reported at baseline. These exclusions resulted in an effective analysis sample size of 11 445, including 393 deaths.

#### Arsenic exposure assessment

Nearly half of the Bangladeshi population (approximately 150 million) has been chronically exposed to arsenic through drinking water for >20 years, an exposure known to increase mortality risk in this cohort at levels  $>150 \mu g/l$  (unpublished data). At baseline, participants identified the well they primarily used for drinking water. Arsenic concentrations of all 5966 tubewells in the study area were measured by graphite furnace atomic absorption spectrometry (detection limit of 5 µg/l). Samples below the detection limit (669 wells) were re-analysed by inductively coupled plasma-mass spectrometry (detection limit of  $0.1 \,\mu g/l$ ).<sup>21</sup> We were unable to ascertain well-water arsenic concentration for one tubewell; participants drinking from this well (n=3) were excluded from analyses of water arsenic.

#### **Statistical analysis**

Baseline characteristics were examined stratified by the World Health Organization's (WHO) International BMI categories<sup>22</sup> (kg/m<sup>2</sup>): <16 (severe underweight), 16.0-16.9 (moderate underweight), 17.0 - 18.4(mild underweight), 18.5-22.9 (normal-low), 23.0-24.9 (normal-high), 25–29.9 (pre-obese) and  $\geq 30$ (obese). Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for mortality by BMI categories, using the 'normal-low' category  $(18.5-22.9 \text{ kg/m}^2)$  as the reference group. For all analyses, the three highest WHO BMI categories (normal-high, pre-obese and obese) were combined into a single category to avoid having categories with sparse data. Combining the data in this way is further justified by the WHO's designation of 23.0 kg/m<sup>2</sup> as a 'public health action point', above which health risks have been observed in Asian countries.<sup>22</sup> Trend tests were conducted by including BMI in regression models as an ordinal variable, i.e. 1 (severe underweight) to 5 (normalhigh to obese).

Analyses were first conducted adjusted for age and sex only and then with additional adjustment for smoking status, education and self-reported history of BMI-related symptoms experienced <6 months prior to baseline. Confounding by other markers of socio-economic status (SES) (land and television ownership) and arsenic exposure was also explored. BMI-related symptoms were included as potential confounders if they were associated with both BMI and mortality at a modest P = 0.15 level (weight loss and weakness met these criteria). These symptoms serve as surrogates for prevalent medical conditions that may confound the association between BMI and mortality. To further protect against such confounding, we separately analysed deaths occurring >2 years after baseline, under the assumption that individuals who are seriously ill at baseline are more likely to die in years 1 and 2 of follow-up.

Associations were evaluated in subgroups defined by sex, education (<5 and  $\geq$ 5 years of formal education), age ( $\leq$ 50 and >50 years), smoking status (ever and never smokers) and water arsenic exposure ( $\leq$ 150 and >150 µg/l). We tested for multiplicative interaction between ordinal BMI and each of these subgroup variables by including interaction terms between BMI and stratifying variables in the Cox models. Additive interaction was assessed using the 'relative excess risk due to interaction' (RERI) measure (CIs determined using 5000 bootstrap samples).<sup>23</sup>

Cox regressions were performed using the Statistical Analysis System's (release 9.2) PHREG procedure (SAS Institute, Inc., Cary, NC). The proportional hazards assumption was tested by modelling interaction terms of time and covariates in the model. Since most HEALS participants are married couples drinking from the same tubewell, we accounted for clustering (on tubewell) using robust standard errors for the proportional hazards model<sup>24</sup> analogous to performing a generalized estimating equations analysis in other regression models.<sup>25</sup>

## Results

Distributions of key covariates within WHO BMI categories are shown in Table 1. The mean BMI was 19.8 kg/m<sup>2</sup> (19.4 for males, 20.0 for females) with a 3.2 standard deviation (SD). A total of 81 (0.7% of cohort) and 722 individuals (6.3%) were obese and pre-obese, respectively. The proportion of underweight individuals was higher among older individuals, males, less-educated individuals and current smokers, compared with the total cohort. Compared with females, males had a higher mean age and proportion of current and former smokers. Individuals with and without (n = 279) a BMI measure were similar with respect to age, sex, smoking and mortality rate (data not shown).

The mean follow-up time was 6.4 years (75 225 total person-years); 393 deaths were observed. Common causes of deaths were related to the circulatory system (International Classification of Diseases (ICD)-10 codes I00–I99, n = 170), neoplasms (C00–D48, n = 65), the respiratory system (J00–J99, n = 33) and infection (A00–B99, n = 29). Other deaths were related to the

	BMI (kg/m <sup>2</sup> )								
	Underweight			Normal		Overweight			
Characteristic	Severe <16.0	Moderate 16.0–16.9	Mild 17.0–18.4	Low 18.5–22.9	High 23.0–24.9	Pre-obese 25–29.9	Obese ≥30.0	Full Cohort	
Individuals	846	1128	2571	5214	883	722	81	11445	
Percent of total	7.4	9.9	22.5	45.6	7.7	6.3	0.7	100.0	
Sex (%)									
Female	56.4	50.5	49.7	60.1	63.5	63.0	72.8	57.1	
Age in years (%)									
18–30	20.6	26.1	31.2	35.3	29.9	29.2	23.5	30.1	
31-40	29.8	33.5	34.4	35.9	40.1	42.7	40.7	35.7	
41-50	30.7	27.3	24.2	20.5	22.2	26.0	28.4	23.3	
51–75	18.9	13.1	10.2	8.4	7.8	8.0	7.4	10.0	
Mean	41.1	38.7	37.1	35.9	36.8	37.7	37.8	37.1	
SD	10.9	10.5	10.2	9.9	9.3	9.0	8.5	10.1	
Age for males, yea	ars								
Mean	46.1	43.1	41.1	40.7	41.9	41.7	41.2	41.6	
SD	10.3	10.0	10.0	9.8	9.3	8.8	8.1	9.9	
Age for females, y									
Mean	37.2	34.5	33.1	32.8	33.8	35.3	36.5	33.6	
SD	9.7	9.1	8.9	8.7	8.0	8.2	8.3	8.8	
Years of education		<i>,</i> ,,,	017	017	0.0	0.12	015	010	
0	58.4	54.6	51.0	43.3	26.2	21.7	19.8	44.4	
1-4	17.6	14.8	16.5	14.2	14.0	8.7	4.9	14.6	
5–7	15.0	18.5	20.9	22.7	26.8	25.1	27.2	21.8	
8–16	9.0	12.1	11.7	19.8	33.0	44.5	48.2	19.2	
Smoking <sup>a</sup> (%)	2.0	12.1	11.7	17.0	<u> </u>	11.2	10.2	17.2	
Never	48.6	53.6	55.7	69.2	77.5	78.1	88.9	64.5	
Current	39.3	40.9	37.6	24.8	15.4	15.8	7.4	28.9	
Former	12.0	5.5	6.7	5.9	7.0	6.1	3.7	6.6	
Smoking <sup>a</sup> in male		5.5	0.7	2.7	7.0	0.1	5.7	0.0	
Never	9.7	15.3	20.1	29.2	42.9	43.5	68.2	25.6	
Current	74.9	75.9	69.9	58.5	40.4	40.5	27.3	62.4	
Former	15.4	8.8	10.0	12.4	16.8	16.1	4.6	12.0	
Smoking <sup>a</sup> in fema		0.0	10.0	12.1	10.0	10.1	1.0	12.0	
Never	78.8	90.6	91.8	96.0	97.5	98.5	96.6	93.7	
Current	11.7	7.4	4.9	2.4	1.1	1.3	0.0	3.8	
Former	9.4	2.3	3.3	1.7	1.1	0.2	3.4	2.5	
Weight loss <sup>b</sup>	7.4	2.9	).)	1.7	1.4	0.2	9.4	2.)	
Yes	41.6	39.4	39.1	31.5	19.7	11.6	8.6	32.4	
Weakness <sup>b</sup>	41.0	J7.4	59.1	51.5	19.7	11.0	0.0	92.4	
Yes	59.9	58.1	55.1	48.8	41.0	36.8	28.4	50.5	
Water arsenic con			<u>ارر</u>	40.0	41.0	0.00	20.4	20.5	
0.1–10		23.8	21.0	<b>12 2</b>	24.0	<u> </u>	15 7	<b>12</b> 4	
0.1–10 10.1–50	22.5	23.8 20.0		23.3	24.9	28.2 21.0	45.7 19.8	23.4	
	21.6		22.2	21.2	23.8			21.5	
50.1-150	28.6	30.1	30.7	30.9	31.6	29.5	18.5	30.5	
150.1-854	27.3	26.2	26.1	24.5	19.7	21.3	16.0	24.6	

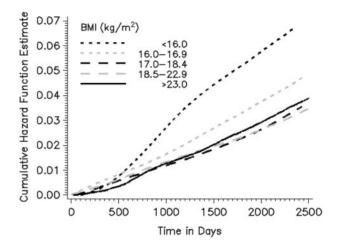
<sup>a</sup>Cigarettes or *bidi*. <sup>b</sup>Self-reported symptoms experienced within the 6 months prior to the baseline interview.

nervous system (G00–G99, n=4), digestive system (K00–K99, n=27), genitourinary system (N00–N99, n=8), pregnancy complications (O00–O99, n=10), diabetes (E00–E99, n=4) and musculoskeletal disorders (M00–M99, n=1), whereas 39 deaths were not related to any specific health problem (R00–R99, n=27; S00–T98, n=2; V01–Y98, n=10). For three cases, an ICD-10 code was not available.

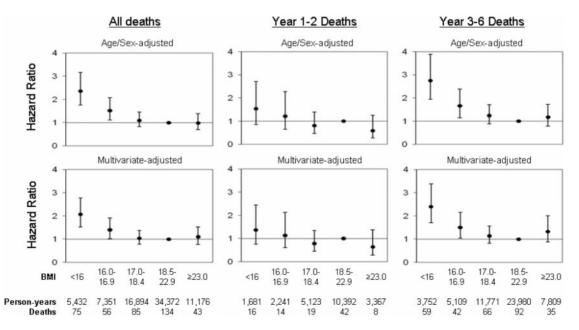
HRs presented in the text are from the multivariate model; P-values are two-sided. Both severe underweight (BMI <16 kg/m<sup>2</sup>; HR 2.06; CI 1.53–2.78) and moderate underweight (16.0–16.9 kg/m<sup>2</sup>; HR 1.40; CI 1.02-1.91) were associated with increased mortality when compared with normal-low BMI  $(18.5-22.9 \text{ kg/m}^2)$  (*P*-trend <0.0001) (Figure 1). These associations were stronger for deaths occurring during years 3-6 of follow-up than for deaths in years 1-2. Further adjustment for water arsenic exposure and other SES-related factors (land ownership and television ownership) did not change the magnitude of these associations (data not shown). The multivariate-adjusted cumulative hazard function for each BMI group is plotted in Figure 2. The hazard rate for each group is fairly constant (supporting the proportional hazards assumption), and clear separation of cumulative hazard functions for severe and moderate underweight groups occurs near the second year of follow-up.

Table 2 shows BMI–mortality associations by gender and education. Males accounted for 43% of total person-time and 74% of deaths (n = 289). In males, both severe (HR 2.31; CI 1.34–3.25) and moderate underweight (HR 1.62; CI 1.13–2.33) were associated with increased mortality. Increasing BMI showed a trend towards decreased mortality (*P*-trend <0.0001), although we observed a borderline association with increased mortality for individuals with BMI  $\geq$ 23 kg/m<sup>2</sup>. In females, increasing BMI was modestly associated with reduced mortality (*P*-trend = 0.03).

Individuals with <5 years of education (59% female) accounted for 59% of total person-time and 69% of total deaths (n = 271); individuals



**Figure 2** The multivariate-adjusted cumulative hazard function (of mortality) plotted against time (in days) by BMI (kg/m<sup>2</sup>) category for the HEALS (Araihazar, Bangladesh; n = 11445). Curves are adjusted to represent non-smoking males (age 18–30 years) with <5 years of formal education (experiencing no weight loss or weakness in the 6 months prior to baseline). Robust standard errors were used to account for clustering on tube well.



**Figure 1** HRs and 95% CIs for mortality, by BMI categories in the HEALS (Araihazar, Bangladesh). Multivariate estimates were adjusted for age, sex, smoking status, education and BMI-related symptoms experienced in the 6 months prior to baseline (weight loss and weakness). Robust standard errors were used to account for clustering on tube well.

		Deaths	All-cause mortality				
	Person-years of follow-up		Age/sex-adjusted <sup>a</sup>		Multivariate-adjusted <sup>a,l</sup>		
			HR	95% CI	HR	95% CI	
Men	32 151	289					
BMI (kg/m <sup>2</sup> )							
<16.0	2317	55	2.61	1.86-3.66	2.31	1.34–3.25	
16.0–16.9	3567	46	1.78	1.24–2.54	1.62	1.13-2.33	
17.0–18.4	8480	67	1.21	0.88-1.67	1.14	0.82-1.57	
18.5–22.9	13 762	87	1.00	Ref.	1.00	Ref.	
≥23.0	4025	34	1.31	0.88-1.94	1.49	1.00-2.23	
P for trend				< 0.0001		0.0004	
Women	43 075	104					
BMI (kg/m <sup>2</sup> )							
<16.0	3090	19	1.89	1.12-3.21	1.58	0.92-2.69	
16.0–16.9	3708	10	0.97	0.49-1.92	0.89	0.45-1.77	
17.0–18.4	8262	18	0.90	0.52-1.56	0.84	0.49-1.4	
18.5–22.9	20136	48	1.00	Ref.	1.00	00 Ref.	
≥23.0	6979	9	0.49	0.24-0.99	0.54	0.27-1.12	
P for trend				0.003		0.03	
<i>P</i> for BMI–sex interaction <sup>c</sup>				0.91		0.78	
Education <5 years	44 140	271					
BMI (kg/m <sup>2</sup> )							
<16.0	4116	63	2.65	1.88-3.74	2.43	1.72-3.44	
16.0–16.9	5048	49	1.87	1.30-2.69	1.80	1.25-2.59	
17.0–18.4	11 360	65	1.28	0.91-1.80	1.23	0.87-1.73	
18.5–22.9	19708	76	1.00	Ref.	1.00	Ref.	
≥23.0	3910	18	1.27	0.76-2.12	1.32	0.78-2.22	
P for trend				< 0.0001		< 0.0001	
Education ≥ 5 years	31 084	122					
BMI (kg/m <sup>2</sup> )							
<16.0	1317	12	1.56	0.83-2.92	1.42	0.75-2.69	
16.0–16.9	2303	7	0.66	0.31-1.44	0.62	0.29-1.35	
17.0–18.4	5534	20	0.77	0.46-1.29	0.74	0.44-1.25	
18.5–22.9	14665	58	1.00	Ref.	1.00	Ref.	
≥23.0	7266	25	0.84	0.53-1.35	0.88	0.55-1.41	
P for trend				0.54		0.85	
P for BMI–education				0.02		0.02	

Table 2 HRs and 95% CIs for associations between BMI categories and mortality in the HEALS cohort (Araihazar Bangladesh) stratified by sex age smoking and education levels

<sup>a</sup>Robust standard errors were used to accounted for clustering on tubewell.

<sup>b</sup>Multivariate estimates were adjusted for age, sex, smoking status, education and BMI-related symptoms experienced in the 6 months prior to baseline (weight loss and weakness).

<sup>c</sup>The multiplicative interaction term tested was ordinal BMI multiplied by the dichotomous strata variable (a one degree of freedom test).

with  $\geq 5$  years of education were 54% females. Increasing BMI was strongly associated with reduced < 0.0001), but there was no clear trend-based in the

interaction<sup>c</sup>

high-education group (P-trend = 0.85), suggesting that education modifies the association between mortality in the low-education group (P-trend BMI and mortality (multiplicative interaction P = 0.02). The RERI was 0.22 (CI 0.10-0.33), indicating that the relative risk of mortality per 1 category decrease in BMI in the low-education group is 0.22 more than that in the high-education group.

No clear evidence of multiplicative or additive interaction with BMI (ordinal) was observed for age, smoking or arsenic exposure (data not shown).

### Discussion

In this prospective cohort study of 11445 residents of Araihazar, Bangladesh, severe underweight (BMI  $<16 \text{ kg/m}^2$ ) and moderate underweight (BMI 16.0–  $16.9 \text{ kg/m}^2$ ) were associated with increased mortality. The prevalence of overweight  $(25-29.9 \text{ kg/m}^2)$  and obesity ( $\geq 30 \text{ kg/m}^2$ ) in this cohort was 6.3 and 0.7%, respectively, lower than prevalences reported from a rural Indian cohort (15.8 and 2.8%, respectively).<sup>10</sup> In this study, overweight and obese BMI categories were combined with the normal-high BMI category (23.0- $24.9 \text{ kg/m}^2$ ) for analysis purposes, and this combined category ( $\geq 23.0 \text{ kg/m}^2$ ) was not strongly associated with increased mortality. Females had a higher average BMI than males, but prior research does not provide clear support for sex-based differences in BMI in Bangladesh.<sup>26–29</sup> The association of mortality to BMI was stronger for individuals with <5 years of education compared with individuals with  $\geq 5$  years of education (multiplicative interaction P = 0.02, additive interaction P = 0.0002), suggesting that individuals of lower SES are more susceptible to adverse health effects associated with low BMI.

Previous research in Bangladesh<sup>30</sup> supports an increased mortality risk for severely and moderately underweight (<17.3 kg/m<sup>2</sup>; lowest quartile) individuals compared with individuals in the low end of the normal-low BMI category (18.4-19.6 kg/m<sup>2</sup>; third quartile), consistent with the results of this work. However, this previous result was based on a smaller cohort (n = 1888) of women only, followed for a longer time period (19 years). In addition, this previous research did not show statistically significant increased risk for the highest average BMI quartile (>19.6 kg/m<sup>2</sup>; compared with third quartile) or decile (>21.7 kg/m<sup>2</sup>; compared with 10th through 89th percentile), consistent with our results. Similarly, data from a large rural Indian cohort<sup>10</sup> suggest that severe  $(<16.0 \text{ kg/m}^2)$  and moderate-mild  $(16.0 - 16.0 \text{ kg/m}^2)$  $18.4 \text{ kg/m}^2$ ) underweight, but not overweight (25.0– 27.4 and  $\geq 27.5 \text{ kg/m}^2$ ), are associated with increased mortality compared with normal-low BMI (18.5-22.9 kg/m<sup>2</sup>). Data from China,<sup>4</sup> Korea<sup>5</sup> and Japan<sup>6</sup> support a similar relationship between underweight  $(<18.5 \text{ kg/m}^2)$  and mortality, but show a clear increase in mortality for the obese  $(>30 \text{ kg/m}^2)$ , when compared with BMI categories of 24.0-24.9 kg/m<sup>2</sup> (China) or  $23.0-24.9 \text{ kg/m}^2$  (Korea and Japan).

BMI is a marker of nutritional status,<sup>12</sup> and low BMI (i.e. chronic energy deficiency) may increase susceptibility to a wide range of diseases, both chronic and infectious, thereby increasing mortality risk. However, associations between low BMI and increased mortality are often controversial, due to the potential confounding effects of smoking, age and SES. In this cohort, female sex, decreasing age, never smoking and increasing education were independently associated with increased BMI and decreased mortality. We attempted to account for these factors by using adjustments and stratified analyses. SES was controlled using education as a proxy; additional adjustment for land ownership and television ownership did not change the results of our education-adjusted analyses, suggesting that education captures the confounding effects of other SES-related factors.

It is also possible that associations between low BMI and increased mortality are confounded by prevalent medical conditions that decrease BMI and increase mortality risk. Although we did not have data on diagnoses of specific medical conditions at baseline, the HEALS cohort consisted of individuals who were apparently healthy at the time of enrolment. Nevertheless, we accounted for potential confounding effects using two strategies: (i) adjusting for baseline symptoms that were associated with both BMI and mortality at a modest P = 0.15 level; and (ii) excluding deaths occurring in the first 2 years of follow-up. Adjustment for symptoms resulted in an attenuation of most significant HRs reported in this analysis, suggesting some partial confounding was present. However, associations between underweight and mortality were stronger in years 3-6 than in years 1-2, suggesting confounding by prevalent medical conditions is not a serious limitation of this analysis.

The low prevalence of overweight/obesity (7%) in this cohort and the lack of a clear association between mortality and BMI  $\geq 23 \text{ kg/m}^2$  suggest that overweight/obesity is not a paramount public health issue in this rural Bangladeshi population, a finding consistent with previous reports from rural India<sup>10</sup> and Bangladesh.<sup>30</sup> However, our ability to observe increased mortality risks for individuals with high BMI may be limited by residual confounding,<sup>31</sup> as individuals with high BMI tended to have low mortality-risk characteristics (i.e. female, high education, non-smoking), although we attempt to adjust for these characteristics. The observation that loweducation subgroups have the lowest prevalence of overweight/obesity is also consistent with data from other Indian<sup>32</sup> and Bangladeshi<sup>7</sup> cohorts. However, it is critical to acknowledge that the prevalence of overweight/obesity in South Asian countries may be increasing,<sup>7,32</sup> even among low SES subgroups.

Further complicating our conclusions regarding high BMI and mortality is the fact that the relationship between BMI and body composition (i.e. percentage of body fat) is known to vary across populations. For example, for a given BMI value, Asians tend to have a higher body fat percentage and more

Caucasians.<sup>33</sup> with abdominal fat, compared Consequently, harmful levels of adiposity may be captured at lower BMI values in Asians than in Caucasians.<sup>34</sup> Data on waist circumference and waist-hip ratio (measures of abdominal adiposity) were not collected in this study. Due to the limited number of deaths observed in the 6-year follow-up period (n=393), we were unable to examine the effects of BMI on specific causes of death. Our power was also limited in subgroups experiencing few events, such as women and never smokers. As long-term follow-up data accumulate, we will be able to better assess the relationship between BMI and mortality for specific causes of death and within strata.

In conclusion, severe underweight and, to a lesser degree, moderate underweight are associated with

increased mortality in this Bangladeshi cohort, and these associations are stronger among individuals with <5 years of education. We did not find strong evidence of a U- or J-shaped relationship between BMI and mortality in this cohort, emphasizing that underweight (presumably due to malnutrition), is a major determinant of mortality in this rural community.

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#### **KEY MESSAGES**

- The relationship between BMI and mortality is not well characterized in Bangladesh, where the population's BMI distribution is shifted towards lower values.
- In a large rural Bangladeshi cohort, severe underweight (BMI <16.0 kg/m<sup>2</sup>) and moderate underweight (16.0–16.9 kg/m<sup>2</sup>) were associated with increased mortality when compared with normal-low BMI (18.6–22.9 kg/m<sup>2</sup>).
- There was not strong evidence for an association between the highest BMI category (≥23.0 kg/m<sup>2</sup>) and increased mortality.
- The association between low BMI and increased mortality was stronger among individuals with <5 years of education than in those with ≥5 years of education.

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# Commentary: Optimal body mass index cut points

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A standard body mass index (BMI)-based definition of overweight and obesity is essential to the monitoring and comparing obesity trends, yet the choice of BMI thresholds continues to excite considerable debate.<sup>1–3</sup> Since the early 1990s, the World Health Organization (WHO) has recommended using BMI