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# 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.

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## 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

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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 $\hat{\beta}_{ij} \sim N\left(\beta_j, \hat{\sigma}^2_{ij}+\hat{\tau}^2_j\right)$, where $\hat{\sigma}^2_{ij}$ is the within-study variance of $\hat{\beta}_{ij}$ and $\hat{\tau}^2_j$ is the between-cohort variance of $\hat{\beta}_{ij}$, as estimated from the Cox regression model.[4,5] The $\beta_j$ 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 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 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 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.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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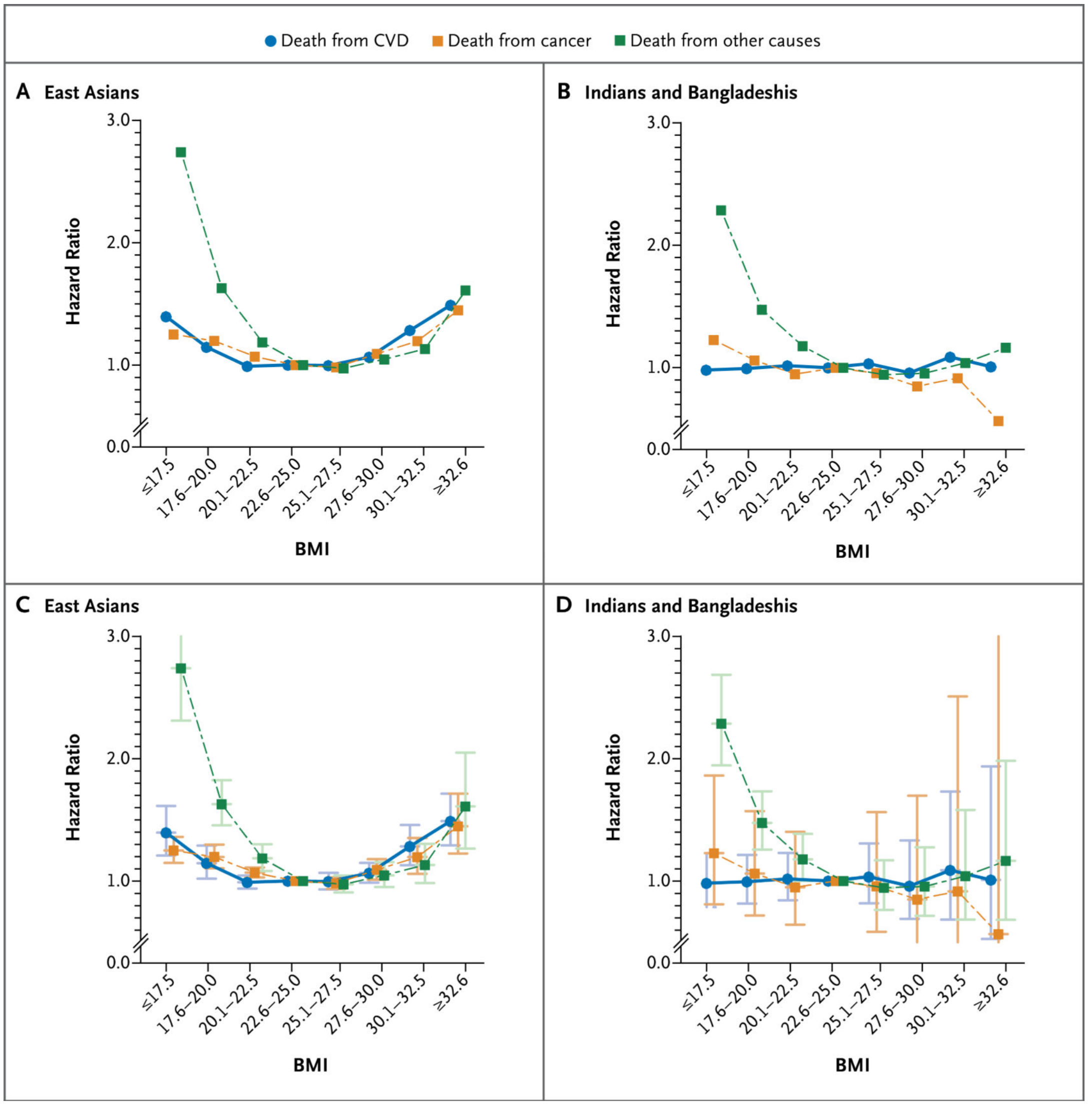


**Figure 1. Association between Body-Mass Index and Risk of Cause-Specific Death in Two Asian Populations**

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.

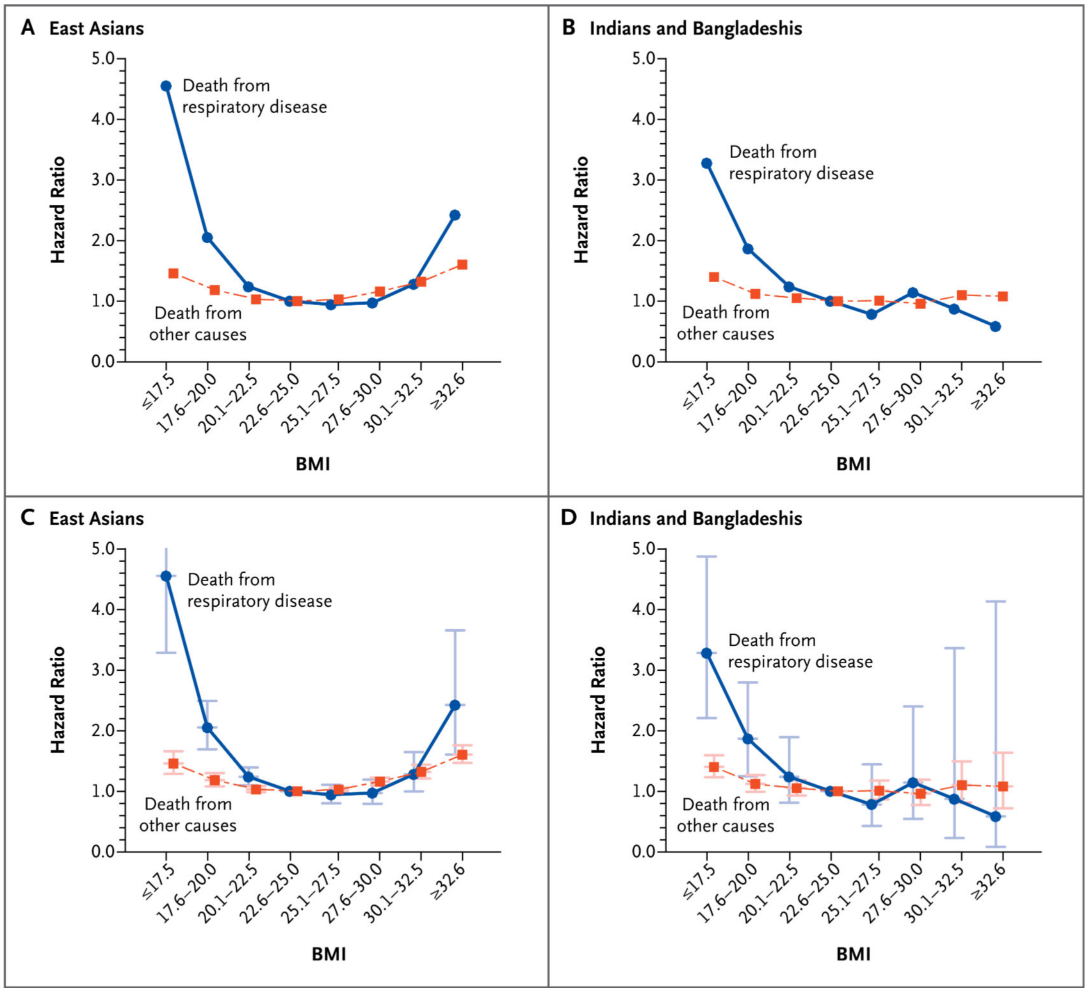


**Figure 2. Association between the Body-Mass Index and the Risk of Death from Respiratory Diseases or Other Causes**

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.

**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‡ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *yr* | | | % | *no.* | Cancer | CVD % | Other |
| 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 |

| 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[‡] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | *yr* | | | % | *no.* | Cancer | CVD % | Other |
| 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) |

NA denotes not available.

*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.

## 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 BM1 | | 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) |

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| Subgroup Analysis | | | All Subjects | | | | | Lifetime Nonsmokers |
|---|---|---|---|---|---|---|---|---|
| | | Low BM1 | | 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)* |
| 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.