

## Selected Summaries

### Body-mass index as a robust predictor of mortality in Asian Indians

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#### SUMMARY

This study from the Prospective Studies Collaboration (PSC) is a meta-analysis of individual-level information shared by investigators of 57 primary prospective cohort studies to examine the relationship of body-mass index (BMI) with overall and cause-specific mortality. The primary studies had followed adult subjects, whose baseline blood pressure, blood cholesterol and BMI values had been recorded for 5 years or longer. In these 57 studies, individual records with information about BMI were available for 894 576 adults, 92% of whom were in Europe, Israel, USA or Australia; the remaining adults were from Japan. Eighty-five per cent of participants (763 274) were recruited during the 1970s and 1980s, with median recruitment year being 1979. The participants had a median recruitment age of 46 years, a slight predominance (61%) of men, and mean BMI of 24.8 kg/m<sup>2</sup>. The mean BMI at baseline was greatest for persons 50–69 years of age for both sexes, and in the US and Australian studies (25.6 kg/m<sup>2</sup>) than in European or Israeli studies (24.7 kg/m<sup>2</sup>).

Cause and date of death (or age of death) was routinely sought for all screenees during follow up. The cause-specific mortality was obtained by death records to the greatest detail available and coded up to three-digit International Classification of Diseases coding (ICD-6 to ICD-10). Cross-sectional associations between BMI and risk factors were estimated by multiple logistic regressions with adjustment for study, baseline age-group and baseline smoking status. Associations between baseline BMI and mortality were estimated by Cox regression analysis with stratification for study, sex, age at risk and baseline smoking, but not for blood pressure, blood lipids or diabetes since the latter are mechanisms by which BMI affects the vascular mortality.

To limit the effect of pre-existing disease on baseline BMI (reverse causality), the main analyses excluded all person-years and deaths (total 15 996) in the first 5 years of follow up. In the subsequent mean (SD) follow up duration of 8 (6) years with a total of more than 6.5 million person-years of follow up, 72 749 died. Of these, 75% were men with median age at death of 67 years. Cause of death was unknown for 9% of persons. Of the remaining 66 552 deaths due to a known cause, 30 416 were vascular deaths, 2070 were due to diabetic, renal and hepatic causes, 22 592 neoplastic, 3770 respiratory and 7704 others.

On an average, across all ages (15–89 years), every 5 kg/m<sup>2</sup> higher BMI was associated with at least 5 mmHg (men 5.8 mmHg; women 5.2 mmHg) higher systolic blood pressure (SBP) and about 4 mmHg (men 4.9 mmHg, women 3.3 mmHg or higher) higher diastolic blood pressure (DBP). Up to 30 kg/m<sup>2</sup>, BMI was inversely associated with high density lipoprotein (HDL) cholesterol (men 0.16 mmol/L and women 0.14 mmol/L lower per 5 kg/m<sup>2</sup>) and strongly positively with the ratio of non-HDL to HDL cholesterol (men 0.85 and women 0.54 higher ratio per 5 kg/m<sup>2</sup>). BMI also showed positive association with diabetes, and inverse correlation with smoking and alcohol intake.

Overall mortality was lowest at BMI of 22.5–25 kg/m<sup>2</sup> for both sexes and at all ages. Above this range, increasing BMI was associated with increased overall mortality. BMI showed a positive association with mortality due to specific causes such as ischaemic heart disease, stroke, diabetes and liver disease, and negative association with none of the cause-specific mortality rates. Thus, in the BMI range of 25–50 kg/m<sup>2</sup>, each 5 kg/m<sup>2</sup> higher BMI was on an average associated with about 30% higher overall mortality (hazard ratio per 5 kg/m<sup>2</sup> [HR] 1.29 [95% CI 1.27–1.32]), 40% for vascular mortality (HR 1.41 [1.37–1.45]) including both ischaemic and stroke, 60%–120% for diabetic, renal and hepatic mortality (HRs 2.16 [1.89–2.46], 1.59 [1.27–1.99] and 1.82 [1.59–2.09], respectively), 10% for neoplastic mortality (HR 1.10 [1.06–1.15]) and 20% for respiratory (mainly chronic obstructive pulmonary disease) and other mortalities (HRs 1.20 [1.07–1.34] and 1.20 [1.16–1.25], respectively). Below the range of 22.5–25 kg/m<sup>2</sup>, BMI was associated inversely with overall mortality. This increase in mortality with lower BMI was related to strong inverse associations of BMI with respiratory disease and lung cancer, and was more marked for smokers than for non-smokers.

One of the strengths of this study is the consideration of the confounding factors that may distort the association observed between body weight and mortality. The study appropriately adjusted for confounders such as age, sex and smoking and also rightly, not adjusted for physiological effects of excess body fat through which excess BMI affects the outcome.

In conclusion, this study showed that BMI is a strong predictor of overall mortality, with excess mortality both above and below the apparent optimum of 22.5–25 kg/m<sup>2</sup>. At higher BMI, the increase in mortality progressively increases, is related largely to increased vascular disease and appears to be causal. BMI of 30–35 kg/m<sup>2</sup> is associated with reduction in median survival by 2–4 years, and that of 40–45 kg/m<sup>2</sup> with a reduction by 8–10 years. The excess mortality below 22.5 kg/m<sup>2</sup> is mainly due to smoking-related diseases; the reason for this increase remains unclear.

#### COMMENT

Overweight and obesity have been established as major causes of several disease conditions which can be fatal.<sup>1</sup> With increasing prevalence of obesity and changes in lifestyle, it is important to define cut-off levels for obesity for each ethnic group. The findings of this study have implications for the control of non-communicable diseases (NCDs). Considering that 10% of women and 9% of men in India in the age group of 15–49 years are overweight (BMI 25–29.9 kg/m<sup>2</sup>) and 3% of women and 1% of men are obese (BMI ≥30 kg/m<sup>2</sup>),<sup>2</sup> it is imperative to take a cue from this study towards the control of NCD in India.<sup>3</sup>

Using a screening tool such as BMI to identify at-risk individuals and referring them for preventive intervention could translate into

an effective public health approach to contain the epidemic of NCD. However, we need to review a few issues. First, is BMI an appropriate indicator of obesity in Asians? Interpretation of BMI grading in relation to risk differs for different populations. Since BMI essentially estimates both fat and fat-free mass (bone, muscles and body water) it fails to distinguish between fat and fat-free mass.<sup>4</sup> Moreover, some characteristics of Asians such as short stature, stunting of growth and malnutrition may alter appropriateness of assessing the relationship between height, weight and body composition.<sup>3</sup> Dudeja *et al.*<sup>5</sup> studied 123 subjects and found that native north Indians have a higher proportion of body fat but their BMI may not be high. Some studies suggest that it is the distribution of fat, i.e. subcutaneous fat in the abdominal region, that has a major impact on metabolic variables.<sup>2,3,6</sup>

A consensus statement was proposed on the diagnosis of obesity, abdominal obesity and metabolic syndrome in Asian Indians after consultations with experts from various regions of India belonging to different medical disciplines.<sup>7</sup> This statement gives equal importance to BMI and waist circumference for population- and clinic-based metabolic and cardiovascular risk stratification. The National Family Health Survey (NFHS-3) of 2005–06 reported 57% of men and 52% of women belonging to the so-called 'normal' range of BMI (18.5–24.9 kg/m<sup>2</sup>). Putting this 'normal' range in relation to the finding of this study that BMI in the low-normal range (18.5–22.5 kg/m<sup>2</sup>) has an increased risk of death, would invite enormous public health reaction. This seemingly innocuous statement would translate into a death sentence for people who are still in the 'normal' range. At the same time, overlooking this issue without due assessment may be an act of omission at the policy and public health levels.

Based on the experience from pilot studies in 10 states in India, a national programme for the prevention and control of diabetes, cardiovascular disease (CVD) and stroke is expected to be launched by the Ministry of Health and Family Welfare, Government of India.<sup>8</sup> We propose the creation of a separate cadre of health worker/community-level worker to look after all the ongoing NCD programmes at the grassroots level. From the feasibility point of view, it will be apt to recommend that these grassroots-level workers may measure waist circumference (WC) in a selected section of the population for risk identification.

The aim of the PSC study was to examine the relevance of BMI to cause-specific mortality  $\geq 5$  years after recruitment to those studies. The PSC study reported that BMI is associated with increased total mortality in both men and women, and in all age strata from 35 to 89 years. The findings of the PSC study are important. However, formulation of BMI-based mortality risk for India needs to be informed by geographically representative community-based studies across the country, including follow up studies or the morbidity and mortality outcomes. We believe that measuring BMI is more feasible at a health facility (sub-centre, primary health centre, community health centre and district hospital) and WC at the community level. Such data generated from India would better inform policy-makers and thus help strategically improve the implementation of the NCD programme.

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## Neuraminidase inhibitors for influenza in healthy adults: What we don't know

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and treating influenza in healthy adults: Systematic review and meta-analysis. *BMJ* 2009;**339**:b5106.

## SUMMARY

The authors systematically reviewed and did a meta-analysis of studies that evaluated the efficacy of neuraminidase inhibitors (inhaled zanamavir and oral oseltamivir) for treatment of laboratory-proven cases of influenza, and pre- and post-exposure prophylaxis. Four studies which assessed the efficacy for preventing influenza were included in the study. Two of the 4 studies used oral oseltamivir 75 mg daily while 2 studies used inhaled zanamavir 10 mg daily. The authors found that the current evidence neither supports nor refutes the use of neuraminidase inhibitors for the prophylaxis of influenza (risk ratio 1.28 [CI: 0.45–3.66] for oseltamivir and 1.51 [0.77–2.95]