## Incident cardiovascular disease events in metabolically benign obese individuals.

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- **Authors**: Ogorodnikova, AD, Kim, M, McGinn, AP, Muntner, P, Khan, U, Wildman, RP
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### Abstract

Nearly one-third of obese individuals are classified as metabolically benign; however, whether this subgroup is at a lower risk of cardiovascular disease (CVD) is unclear. Using pooled data from the Atherosclerosis Risk in Communities and Cardiovascular Health Studies, we assessed incident CVD (coronary heart disease and stroke) using three definitions of the metabolically benign phenotype: (i) the ATP-III metabolic syndrome definition (≤2 of the ATP-III components, excluding abdominal obesity (ii) the expanded ATP-III definition (≤1 of: any ATP-III components, insulin resistance (IR), or systemic inflammation), and (iii) the IR-based definition (sex-specific lowest quartile of the HOMA(IR) distribution). The sample included 6,106 normal weight, 7,115 overweight, and 4,323 obese participants. Among obese, 27.0%, 18.1%, and 20.4% were metabolically benign by the three definitions, respectively. The CVD incidence rates (mean follow-up 11.8 years) were 7.1, 5.8, and 8.4 per 1,000 person-years in metabolically benign obese via the three definitions, respectively, compared to 14.3, 13.8, and 13.3 in at-risk obese, and 7.5, 6.7, and 8.2 in metabolically benign normal weight participants. Multivariable-adjusted hazard ratios of incident CVD in metabolically benign obese compared to their at-risk obese counterparts were 0.59 (95% CI 0.47-0.73), 0.52 (0.39-0.68), and 0.71 (0.57-0.90), respectively; and 1.24 (0.99-1.57), 1.16 (0.86-1.56), and 1.28 (1.01-1.62) compared to metabolically benign normal weight individuals. Only 28.7% of obese participants classified as metabolically benign by at least one
definition were "metabolically benign" by all three definitions. Despite similar CVD risk estimates, the three definitions identified different subgroups of the obese population, perhaps suggesting distinct etiologies.

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