Appendix

For each transformed density measure, Y, we fitted a regression for the mean as a linear function of age and BMI and the other fitted covariates. For individual i, $E[Y_i] = b_0 + b_{age}.age_i + b_{BMI}.BMI_i + b_1X_{1i} + \ldots + b_nX_{ni}$, where Y_i is their observed value; E[.] represents the expected value; and age_i, BMI_i, X_{1i}, …, X_{ni} are their age, BMI_i, and other fitted covariates; and b_0, …, b_n are the corresponding regression coefficients. We then divided the residuals, $R_i = Y_i–E[Y_i]$, by the standard deviation of the residuals, $SD(R_i)$, to give Y' = Ri/SD(Ri).

The different density measures, Y', were fitted independently and then together; the improvement in fit was assessed using the likelihood ratio test. When we fitted two density measures, Y1' and Y2', into the same model, we presented the risk estimates in terms of the change in the standard deviation after adjusting also for the other measure, to be consistent with the OPERA concept. Let *r* be the correlation between Y_1' and Y_2'. Because the standard deviation of Y_j' adjusted for Y_k' is $SD' = [(1–r^2)]^{0.5}$, for j,k = 1,2, when Y_j' is fitted with Y_k' we multiplied the log(OR) estimate from fitting Y_j' by SD' and then exponentiated it to obtain the appropriate OPERA. [For *r* = 0.6, 0.7, and 0.8, SD' ~ 0.8, 0.7, and 0.6, respectively.]

We also fitted weighted linear combinations, $Y_p' = pY_1' + (1–p)Y_2'$, and estimated the optimal weight, p, and confidence interval using maximum likelihood theory. Since the standard deviation of Y_p' is $SD_p' = [1–2p(1–r) + 2p^2(1–r)]^{0.5}$, we multiplied the log(OR) estimate from fitting Y_p' by SD_p' and then exponentiated it to give the appropriate OPERA. [If p = 0.5, $SD_p' = (1+r)/2$.]