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Fitness vs. Fatness on All-Cause Mortality: A Meta-Analysis

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ABSTRACT

The purpose of this study was to quantify the joint association of cardiorespiratory fitness (CRF) and weight status on mortality from all causes using meta-analytical methodology. Studies were included if they were (1) prospective, (2) objectively measured CRF and body mass index (BMI), and (3) jointly assessed CRF and BMI with all-cause mortality. Ten articles were included in the final analysis. Pooled hazard ratios were assessed for each comparison group (i.e. normal weight-unfit, overweight-unfit and -fit, and obese-unfit and -fit) using a random-effects model. Compared to normal weight-fit individuals, unfit individuals had twice the risk of mortality regardless of BMI. Overweight and obese-fit individuals had similar mortality risks as normal weight-fit individuals. Furthermore, the obesity paradox may not influence fit individuals. Researchers, clinicians, and public health officials should focus on physical activity and fitness-based interventions rather than weight-loss driven approaches to reduce mortality risk.

In the past 20 years many prospective studies have described the independent effects of cardiorespiratory fitness[1–8] (CRF) and obesity[9–14] on mortality. Two meta-analytical reviews of these studies reported an independent association of these exposures to mortality.[15,16] Specifically, these reviews found that obesity (assessed as body mass index; BMI) independently increased mortality risk by 20% and 28% in women and men, respectively,[16] while decreasing CRF by 1 MET value increased mortality risk by 13%.[15] Although the independent effects of CRF and obesity on mortality are well established, which factor is more "important" remains controversial and is often debated by researchers.

One theory is the fitness-fatness hypothesis, which suggests a higher level of CRF will substantially reduce the adverse effects of obesity on morbidity and mortality, making obesity a much less important factor for health than is generally believed.[17,18] Numerous studies, including two narrative reviews[18,19] have examined the joint association of CRF and fatness on mortality,[20–42] and the evidence strongly supports the hypothesis that CRF is much more important than fatness as a mortality risk indicator.

However, to our knowledge, no study in the current literature has assessed, meta-analytically, the joint association of CRF and BMI on mortality. Therefore, as suggested by the literature, we hypothesized that mortality levels would be highly correlated to CRF when CRF and BMI were jointly assessed. To quantify this hypothesis, an extensive literature review and meta-analysis was performed on observational studies examining the joint associations of fitness and fatness on all-cause mortality.

Statement of Conflict of Interest: see page 389.

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Abbreviations and Acronyms
BMI = body mass index
CRF = cardiorespiratory fitness
PA = physical activity

Methods

Literature review

The data collection and reporting process were completed following the Meta-analysis of Observational Studies in Epidemiology [43] and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statements. [44] The review of the literature was performed through Pubmed, EBSCOhost, and ProQuest searches by the first author using keywords related to the joint association between CRF and BMI on mortality from all-causes ((“Cardiorespiratory fitness” OR “physical fitness” OR “fitness” OR “maximal oxygen consumption” OR “VO2max” OR “maximal oxygen uptake”) AND (“Body composition” OR “BMI” OR “body mass index” OR “obesity” OR “adiposity”) AND (“mortality” OR “mortalities” OR “death” OR “fatality” OR “fatal” OR “all-cause mortality”)) between January 1980 and May 2013. Articles were included in the analysis if 1) the design was prospective; 2) the main outcome was all-cause mortality; 3) CRF was assessed using a maximal or VO_2peak exercise test; 4) BMI was directly measured; 5) CRF and BMI were jointly assessed on all-cause mortality; and 6) the reference group was the normal weight and fit group. When assessing the ProQuest database, articles were then sorted by their “relevance” to the search terms and the first 300 studies were assessed. No other limits were applied during the search process. These criteria were used to target prospective studies that objectively assessed CRF and BMI and their joint association to all-cause mortality.

Following the database searches, references from relevant review articles and observational studies were assessed for additional reports on fitness and fatness in relation to mortality. Once the data were organized, specific authors were contacted for additional information including hazard ratio, 95% confidence intervals, and sample size and follow-up duration for each comparison group (e.g. normal weight-unfit group). After the data were received and an assessment of the full dataset was completed, three articles were excluded: two because BMI quintiles compared the heaviest quintile to the other four combined groups [34,35] and one for not being able to provide hazard ratios and 95% CI information upon request. [3] In total, 10 articles remained eligible for the current analysis (Fig 1). [27,28,30,32,33,37–41]

Cardiorespiratory fitness and body mass index

The exposure variables for this analysis, CRF and BMI, were categorized into 2 (i.e. unfit and fit) and 3 (i.e. normal weight, overweight, and obese) groups, respectively. The CRF and BMI categories were combined to make 5 comparison groups (i.e. normal weight-unfit, overweight-unfit, overweight-fit, obese-unfit and obese-fit) and a referent group (i.e. normal weight-fit).

Most of the articles in this analysis reported fit and unfit CRF categories. However, three articles further delineated CRF into low, moderate and high. [27,33,39] To account for three CRF groups, we used the Hamling method to combine the moderate and high fit groups. [45] All CRF data were then analyzed and reported in fit and unfit categories. Seven of the 10 included articles used CRF quintiles to define the unfit (1st quintile) and fit (2nd-5th quintile) categories. The three remaining articles determined this threshold using study specific criteria. [27,39,41]

The BMI categories related to normal weight, overweight and obese were <25 kg/m^2, 25 – <30 kg/m^2, and ≥ 30 kg/m^2, respectively. All studies included in this analysis used these thresholds except one. This article, published in 1998, used slightly different threshold values (i.e. normal weight: 19 – <25; overweight: 25 – <27.8; obese: ≥ 27.8). [30] Furthermore, only eight of the 10 articles provided data for all three BMI categories. The remaining two articles provided data for the normal weight BMI category only. [37,38] This particular information (i.e. exposure categorization), along with sample size, number of deaths and average years of follow-up, etc., is found in Table 1.

Article quality assessment

To assess article quality, studies were examined using the Quality Assessment Tool for Quantitative Studies. [41] Sections of this tool were modified to improve the assessment of observational studies. Two new sections were included (i.e. study sample and follow-up period), three sections were removed (i.e. study design, blinding, and withdrawals and drop-outs), and two sections were modified (i.e. confounders and data collection methods). Articles were scored by summing the numeric component ratings (i.e. 1 = weak, 2 = moderate, 3 = strong) and dividing by the highest possible score (i.e. 15).

Statistical analysis

Hazard ratios and 95% confidence intervals were gathered for the five comparison groups (i.e. normal weight-unfit, overweight-unfit, overweight-fit, obese-unfit, and obese-fit). Pooled hazard ratios were estimated using a random-effects model. This model was chosen because of the heterogeneity between studies. This observation was confirmed after calculating the Q score and I^2 statistic.

To assess for possible publication bias, the Begg and Egger tests [47,48] were performed. Furthermore, after completing the aforementioned literature review, data from two research databases (i.e. Aerobic Center Longitudinal Study [ACLS] and Veterans Exercise Testing Study) and one independent article met the inclusion criteria. To account for possible population overlap between studies, a sensitivity analysis was performed using each database or independent article as the unit of analysis. For this analysis two articles [32,40] were chosen from the ACSL dataset (i.e. different population: sex), as these articles provided the largest sample and follow-up years in a healthy population, making the number of studies in this analysis equal to four. [32,39–41]

To examine the effect of study characteristics on risk of all-cause mortality, multiple moderator analyses were performed on possible confounders (mean age [≥50 years or