Does Cardiorespiratory Fitness Attenuate the Adverse Effects of Severe/Morbid Obesity on Cardiometabolic Risk and Insulin Resistance in Children? A Pooled Analysis

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OBJECTIVE

To investigate *1*) differences in cardiometabolic risk and HOMA of insulin resistance (HOMA-IR) across BMI categories (underweight to morbid obesity), *2*) whether fit children have lower cardiometabolic risk/HOMA-IR than unfit children in each BMI category, and *3*) differences in cardiometabolic risk/HOMA-IR in normal-weight unfit children and obese fit children.

RESEARCH DESIGN AND METHODS

A pooled study including cross-sectional data from three projects (n = 1,247 children aged 8–11 years). Cardiometabolic risk was assessed using the sum of the sex- and age-specific z scores for triglycerides, HDL cholesterol, glucose, and the average of systolic and diastolic blood pressure and HOMA-IR.

RESULTS

A significant linear association was observed between the risk score and BMI categories (P trend ≤0.001), with every incremental rise in BMI category being associated with a 0.5 SD higher risk score (standardized β = 0.474, P < 0.001). A trend was found showing that as BMI categories rose, cardiorespiratory fitness (CRF) attenuated the risk score, with the biggest differences observed in the most obese children (−0.8 SD); however, this attenuation was significant only in mild obesity (−0.2 SD, P = 0.048). Normal-weight unfit children had a significantly lower risk score than obese fit children (P < 0.001); however, a significant reduction in the risk score was found in obese fit compared with unfit children (−0.4 SD, P = 0.027). Similar results were obtained for HOMA-IR.

CONCLUSIONS

As BMI categories rose so did cardiometabolic risk and HOMA-IR, which highlights the need for obesity prevention/treatment programs in childhood. Furthermore, CRF may play an important role in lowering the risk of cardiometabolic diseases in obese children.

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Childhood obesity is a great public health problem (1), and this is of serious concern as it is associated with a cluster of cardiometabolic risk factors such as dyslipidemia, hypertension, and insulin resistance (2). Measuring insulin resistance is important as it is a precursor to type 2 diabetes, with the HOMA of insulin resistance (HOMA-IR) being the most common measure of insulin resistance in large-scale studies (3,4). Metabolic syndrome (MetS) has been defined in adults (5); however, no consolidated definition has been created for children and adolescents to date (6). Many studies have investigated the prevalence of cardiometabolic risk scores or factors versus BMI categories in children and have shown that higher BMI categories have a greater prevalence of unhealthy cardiometabolic risk factors (7–10). However, to date, no study has looked at the effect of severe or morbid obesity on cardiometabolic risk in European children.

Cardiorespiratory fitness (CRF) is an important marker of health in children and adolescents (11,12); however, the role of CRF in the aforementioned associations remains to be elucidated. Currently, there is no firm evidence regarding if CRF has an effect on cardiometabolic risk factors irrespective of adiposity (13,14). A mediation analysis investigating the role of BMI on the association between cardiometabolic risk and CRF observed that BMI had a strong effect on the association between levels of CRF and components of MetS in children (8). More studies are needed to better understand the relationship between CRF and cardiometabolic risk throughout BMI categories in children.

The fat but fit paradox denotes individuals who are considered obese but have moderate-to-high CRF (15), and evidence indicates that fat but fit adults do not have a significantly higher risk of mortality from cardiovascular disease than normal-weight unfit adults (15). In children/adolescents, evidence regarding this paradox is inconsistent (8,16–21). It is noteworthy that the majority of studies in this age-group used a median split for both fitness and fatness categories and not standardized cut points. Recently, Tomkinson et al. (22) created sex- and age-specific centiles for CRF from the 20-m shuttle run using over one million children/youth from 50 countries, which will allow for more accurate, universal, and standardized classification of CRF.

Given the inconsistent results regarding the influence of CRF on the association of fatness with cardiometabolic risk in children/youth, we pooled data together from three projects in 8- to 11-year-old Spanish children to investigate the following: *1*) differences in cardiometabolic risk and HOMA-IR across BMI categories (underweight to morbid obesity), *2*) whether fit children have significantly lower cardiometabolic risk scores and HOMA-IR than unfit children in each BMI category, and *3*) differences in cardiometabolic risk scores and HOMA-IR in normal-weight unfit children versus obese fit children (fat but fit paradox).

RESEARCH DESIGN AND METHODS

Study Design and Population

We used a relatively large-scale study (MOVI-2) (23), which included >1,000 children. We then complemented this data with two other projects with children of similar age (ActiveBrains [24] and EFIGRO [25]) where the children were overweight or obese in order to increase the sample size for mild, severe, and morbid obesity (i.e., type I, II, and III obesity), which is the main focus of this paper. This study used the baseline data from the three projects and included a total of 1,247 children aged 8–11 years (n = 1,067 MOVI-2, n = 92 ActiveBrains, and n = 88 EFIGRO). All parents/caregivers provided written, informed consent, and each study was approved by the local authorized institutional review boards and complied with the Declaration of Helsinki. All three trials were registered at clinicaltrials.gov (MOVI-2: NCT01277224; ActiveBrains: NCT02295072; and EFIGRO: NCT02258126).

Measurements

Anthropometry and Covariates

Weight and height were measured when the children were wearing minimal clothing and no shoes using an electronic scale and wall stadiometer, respectively. BMI (kg/m^2) was calculated as weight (kg) divided by height (m) squared. The cut points established by the World Obesity Federation (http://www.worldobesity.org/) were used to classify the children into BMI categories from underweight to morbid obesity (26,27). In regards to percentiles, severe and morbid obesity in children correspond to the 99.8th and 99.95th percentile, respectively (26,27). Parental education was self-reported, and the highest level of parental education in the household was used in sensitivity analyses.

Cardiometabolic Variables

As previously described (23–25), blood samples and blood pressure were collected after an overnight fast according to standardized procedures. Mean arterial blood pressure (MAP) was calculated as diastolic blood pressure + (0.333 × [systolic blood pressure − diastolic blood pressure]). HOMA-IR was calculated as (fasting insulin [μU/L] × fasting glucose [mg/dL])/405.

Using the above components, we calculated two cardiometabolic risk scores (MetS score 1 and MetS score 2) based on sex- and age-specific z scores. Z scores were calculated using data from MOVI-2 that included all BMI categories (23). MetS score 1 for all children was computed using the sum of the sex- and age-specific z scores for the classical variables included in the most-used and well-accepted definition of MetS, i.e., triglycerides (TG), HDL cholesterol, glucose, and the average of systolic and diastolic blood pressure (28). MetS score 2, created by Martínez-Vizcaíno et al. (29,30), has shown good structural validity in cross-sectional and longitudinal studies in children and was calculated as the sum of the sex- and age-specific z scores for TG-to-HDL ratio, MAP, and fasting insulin. Finally, we computed the z score for both cardiometabolic risk scores and HOMA-IR, which were used in the analyses. Higher scores indicate greater cardiometabolic risk.

CRF

CRF was assessed using the 20-m shuttle run test (31). The children ran between two lines 20 m apart with an initial running speed of 8.5 km/h, which increased by 0.5 km/h each minute. The test ended when a child failed to reach the end lines on two consecutive occasions or if the child stopped due to exhaustion. The children were then classified as fit (≥20th centile) or unfit (<20th centile) using the sex- and age-specific centiles created by Tomkinson et al. (22), which is in accordance with the standard definition of fit/unfit in adults (quintile 1 = unfit and quintiles 2–5 = fit) (15).

Statistical Analyses

Linear regression analyses with MetS score 1 or 2 or HOMA-IR as the dependent variable and BMI category, age, and sex as the independent variables were used to estimate the standardized β and the *P* value for trend. Differences between BMI categories for both MetS scores and HOMA-IR were analyzed using a one-way ANCOVA using the Bonferroni adjustment. Differences in MetS scores and HOMA-IR between different BMI categories and CRF levels were analyzed using a two-way ANCOVA to obtain adjusted means, and a one-way ANCOVA was used to test the influence of CRF within each BMI category. Due to the low number of children with severe and morbid obesity, they were merged into one group for this analysis. To test the fat but fit paradox, we divided the eligible children into four categories: normal-weight and fit, normal-weight and unfit, obese and fit, and obese and unfit. Using the two cardiometabolic risk scores and HOMA-IR, we used a one-way ANCOVA to test the differences among the four groups using the Bonferroni adjustment. All analyses were adjusted for age and sex. Differences across the groups for cardiometabolic risk and HOMA-IR *z* scores were interpreted as standardized indicators of effect size. For example, a difference between groups of 0.5 *z* score units means that the two groups differed in 0.5 SD. According to Cohen (32), a standardized mean difference of 0.2, 0.5, and ≥0.8 indicates a small, medium, and large effect size, respectively. This is used for a more meaningful interpretation of the differences observed between groups. Due to the skewed distribution of HOMA-IR, it was log transformed. All statistical analyses were conducted using SPSS version 23 (IBM, Armonk, NY) using the two-sided 5% level of significance.

RESULTS

The characteristics of the study sample are shown in Supplementary Table 1, whereas Table 1 provides the means and SDs for the cardiometabolic risk factors stratified by BMI categories.

Figure 1 shows the differences in MetS score 1, MetS score 2, and HOMA-IR through the different BMI categories. When using regression analysis, every incremental rise in BMI category was associated with a 0.5 SD higher MetS score 1 (β = 0.474, $P < 0.001$) (*P* trend <0.001). When using ANCOVA, compared with normal-weight children, children who were overweight or mildly, severely, or morbidly obese had 0.4, 0.8, 1.3, and 1.6 SD higher MetS score 1, respectively. There were significant differences in MetS score 1 between each BMI category (pairwise comparison range: $P \leq 0.001$–0.036), apart from severe and morbid obesity ($P > 0.9$). Similar linear associations for greater cardiometabolic risk with rising BMI categories were also observed for MetS score 2 (β = 0.517, $P < 0.001$) and HOMA-IR (β = 0.537, $P < 0.001$) (both *P* trend <0.001). In comparison with normal-weight children, underweight children had a lower risk overall; however, it was only significant for MetS score 1 and HOMA-IR (*P* = 0.01 and $P <$ 0.001, respectively).

In a sensitivity analysis, when also adjusting the models for highest parental education (*n* = 679), similar results were obtained. Thus, higher BMI categories were associated with higher MetS scores/HOMA-IR (all *P* trend <0.001).

Figure 2 displays the influence of CRF on MetS score 1 and 2 and HOMA-IR for the different BMI categories. There was a trend for both MetS score 1 and 2 showing that CRF attenuated the cardiometabolic risk scores particularly in the highest BMI categories. For example, for MetS score 1, it was observed that children who were fit and overweight, mildly obese, or severely/morbidly obese had 0.1, 0.2, and 0.8 SD lower cardiometabolic risk score than their unfit counterparts, with this difference only being significant in mild obesity (*P* = 0.048). Similar results were also observed for MetS score 2, where fit children had a significantly lower cardiometabolic risk score than unfit children with mild obesity (*P* = 0.027). The largest differences were observed in the fit severely/morbidly obese children who had 0.8 and 0.5 SD lower MetS score 1 and 2, respectively, than their unfit counterparts. However, this did not reach significance because the sample size was small. For HOMA-IR, there was also a trend showing that CRF attenuated insulin resistance; however, it was only significant in the mildly obese children (*P* = 0.007). When testing for interactions between BMI and CRF in continuous models, the *P* values for MetS score 1, MetS score 2, and HOMA-IR were 0.103, 0.001, and 0.356, respectively. Furthermore, when adjusting for parental education, similar results were obtained.

The differences in the cardiometabolic risk scores and HOMA-IR for the fat but fit paradox are presented in Fig. 3. For MetS score 1 and 2 as well as HOMA-IR, no significant differences for normal-weight

Table 1—Means and SDs for the cardiometabolic risk factors stratified by BMI categories* (*n* = 1,247)

	Underweight (*n* = 76)	Normal-weight (*n* = 567)	Overweight (*n* = 341)	Mild obesity (*n* = 195)	Severe/morbid obesity (*n* = 68)
TG (mg/dL)	54.1 ± 18.4	60.5 ± 27.2	74.6 ± 35.8	92.2 ± 51.0	111.7 ± 55.0
HDL cholesterol (mg/dL)	65.0 ± 13.4	62.3 ± 12.9	56.9 ± 11.9	51.4 ± 11.7	47.4 ± 10.3
LDL cholesterol (mg/dL)†	92.8 ± 19.3	94.7 ± 23.3	100.8 ± 22.4	101.8 ± 24.1	101.8 ± 26.0
TG-to-HDL ratio (mg/dL)	0.9 ± 0.4	1.0 ± 0.7	1.4 ± 1.0	2.0 ± 1.4	2.6 ± 1.7
Glucose (mg/dL)	80.1 ± 6.7	83.4 ± 6.4	84.3 ± 5.8	85.6 ± 6.5	85.9 ± 6.4
Insulin (μU/L)	5.0 ± 2.7	6.6 ± 3.6	9.0 ± 4.2	12.9 ± 7.2	15.9 ± 11.3
Systolic blood pressure (mmHg)	99.3 ± 10.2	99.0 ± 8.3	101.1 ± 9.3	102.1 ± 11.1	106.8 ± 12.5
Diastolic blood pressure (mmHg)	60.9 ± 7.8	60.8 ± 6.8	62.0 ± 7.4	62.6 ± 10.1	66.2 ± 11.5
MAP (mmHg)	73.7 ± 8.0	73.5 ± 6.7	75.0 ± 7.1	75.8 ± 9.5	79.7 ± 11.0

*BMI categories were computed using the cut points established by the World Obesity Federation (26,27). †Nine children had missing data for LDL cholesterol (underweight = 76; normal-weight = 567; overweight = 339; mild obesity = 193; severe/morbid obesity = 63), and the rest of the variables had complete information.

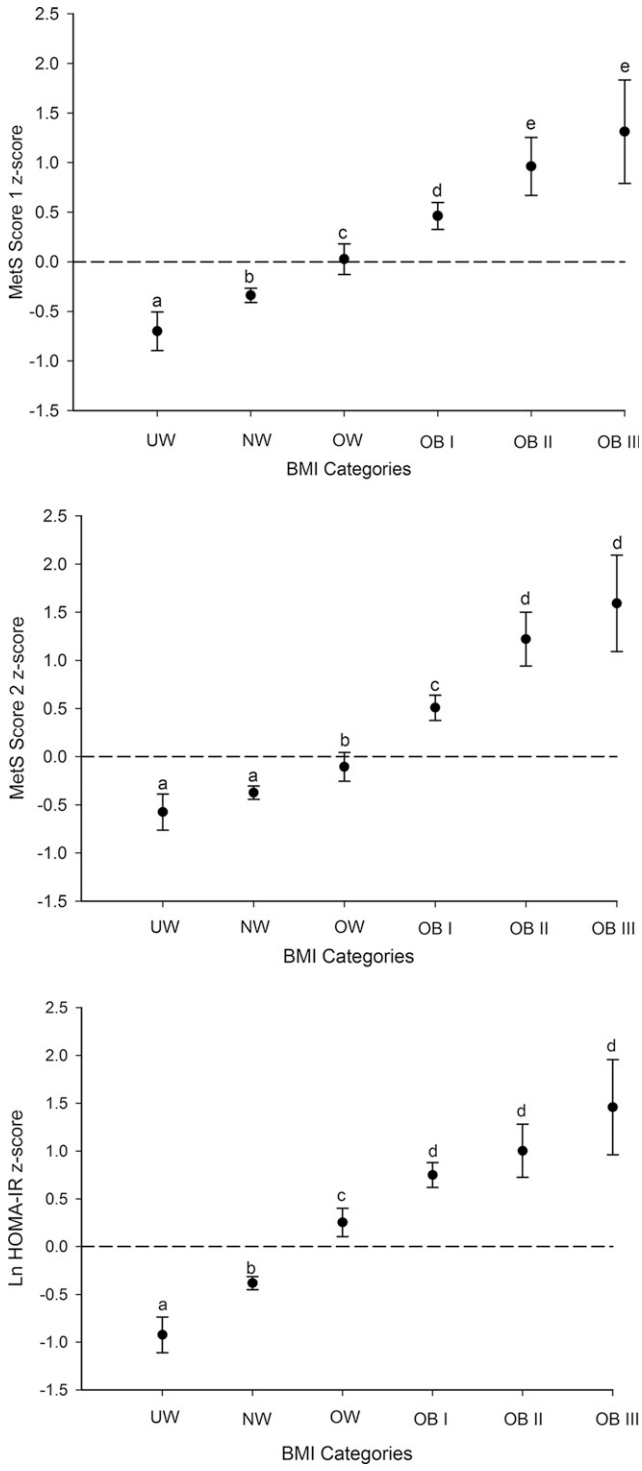

Figure 1—Differences in the two cardiometabolic risk scores as well as HOMA-IR across BMI categories. The figure represents adjusted means from ANCOVA models and 95% error bars, after adjustment for age and sex. The dashed line represents a value of zero for the scores, and a higher score represents greater cardiometabolic risk. Different letters (e.g., a and b) indicate statistically significant differences ($P < 0.05$), whereas the same letters indicate no differences between the two groups, after Bonferroni adjustment. The standardized β for MetS score 1, MetS score 2, and HOMA-IR were 0.474, 0.517, and 0.537, respectively (all $P < 0.001$), and the P value for a linear trend was <0.001 (all models). MetS score 1 was calculated as the sum of the sex- and age-specific z scores for TG, HDL cholesterol, glucose, and the average of systolic and diastolic blood pressure (28). MetS score 2 was calculated as the sum of the sex- and age-specific z scores for TG-to-HDL ratio, MAP, and fasting insulin (29,30). Sample sizes were as follows: UW, $n = 76$; NW, $n = 567$; OW, $n = 341$; OB I, $n = 195$; OB II, $n = 52$; and OB III, $n = 16$. NW, normal-weight; OB I, mild obesity; OB II, severe obesity; OB III, morbid obesity; OW, overweight; UW, underweight.

fit or unfit children (all $P > 0.9$) were observed. There were significant differences in both MetS scores and HOMA-IR between normal-weight fit and normal-weight unfit children as well as between obese fit and obese unfit children (all $P < 0.001$). Interestingly, MetS score 1 and 2 as well as HOMA-IR were lower in obese fit than in obese unfit children (−0.4 SD, $P = 0.027$; −0.5 SD, $P = 0.001$; and −0.4 SD, $P = 0.046$, respectively). Within BMI categories, CRF did not affect the cardiometabolic risk scores in normal-weight children; however, an attenuation in both MetS scores as well as HOMA-IR were observed in the obese children. When further adjusting for parental education ($n = 439$), the statistically significant differences in MetS score 1 and 2 and HOMA-IR between the obese fit and the obese unfit children remained (all $P \leq 0.026$).

CONCLUSIONS

The main findings of the current study are as follows: *1*) cardiometabolic risk scores and HOMA-IR rose linearly throughout the whole spectrum of BMI (underweight to morbid obesity), *2*) CRF attenuates the cardiometabolic risk scores and HOMA-IR, particularly in children within the highest BMI categories, and *3*) fit obese children have significantly lower cardiometabolic risk scores and HOMA-IR than unfit obese children, whereas no significant differences were observed between fit and unfit normal-weight children, suggesting that the effect of CRF in childhood occurs only in the presence of the obesity phenotype. This study adds to the existing literature by investigating the influence of CRF on cardiometabolic risk throughout BMI categories. To our knowledge, the influence of severe and morbid obesity on cardiometabolic risk has only been investigated in American children using individual risk factors (7).

Despite the fact that there is stabilization of childhood overweight and obesity in many countries (33,34), there has been an increase in the amount of children who are morbidly obese (34,35) and thus it is vital to examine the effect of a higher BMI on cardiometabolic risk. Our results are in line with those found in other studies demonstrating that cardiometabolic risk (7–10) and HOMA-IR (4) become greater with BMI status. Nevertheless, it is noteworthy that only one of these studies (7) conducted in American children/youth

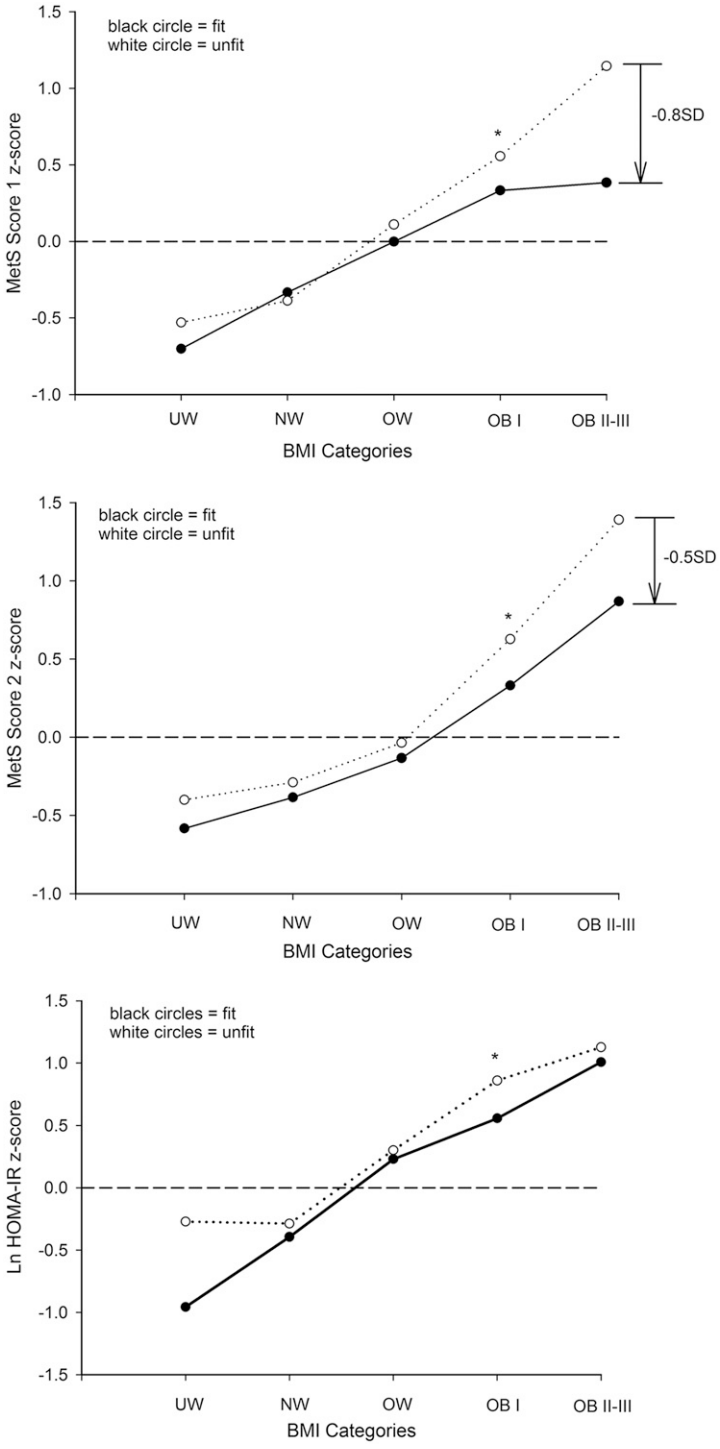

Figure 2—Role of CRF on the two cardiometabolic risk scores and HOMA-IR across BMI categories. The figure represents adjusted means from two-way ANCOVA models after adjustment for age and sex. The dashed line represents a value of zero for the scores, and a higher score represents a greater cardiometabolic risk. The asterisk denotes a significant difference between fit and unfit children in OB I ($P = 0.048$ for MetS score 1, $P = 0.027$ for MetS score 2, and $P = 0.007$ for HOMA-IR). The arrow shows the reduction in the cardiometabolic risk scores (expressed in the number of SDs) for the fit children compared with the unfit children in the OB II-III group, which did not reach statistical significance due to the low number of children in the OB II-III group. MetS score 1 was calculated as the sum of the sex- and age-specific *z* scores for TG, HDL cholesterol, glucose, and the average of systolic and diastolic blood pressure (28). MetS score 2 was calculated as the sum of the sex- and age-specific *z* scores for TG-to-HDL ratio, MAP, and fasting insulin (29,30). Sample sizes were as follows: UW, $n = 72$ (fit) and 4 (unfit); NW, $n = 498$ (fit) and 69 (unfit); OW, $n = 255$ (fit) and 86 (unfit); OB I, $n = 73$ (fit) and 122 (unfit); and OB II-III $n = 13$ (fit) and 55 (unfit). NW, normal-weight; OB I, mild obesity; OB II-III, severe/morbid obesity; OW, overweight; UW, underweight.

was able to classify obesity into mild, severe, and morbid. No European studies in children/youth have been conducted investigating the effect of morbid obesity on cardiometabolic risk. Due to the recently developed cut points to define morbid obesity (27), which were used in this study, new possibilities for further research in this area are now possible.

Very few studies have investigated cardiometabolic risk in relation to underweight in children. One study in Indian children found that underweight children had significantly lower cardiometabolic risk factors in comparison with children who were not underweight (36). Another study in Dutch children found the clustering of cardiovascular risk factors the lowest in the underweight children (37). Our results are in line with these two studies; however, we had a small sample size and therefore these results need to be interpreted with caution.

In this study, we found that BMI had a stronger influence than CRF on the cardiometabolic risk scores, which is in line with previous research (8,14,38). However, there was a trend demonstrating that CRF attenuated the cardiometabolic risk scores the greatest in the most obese children, showing no effect in normal-weight children. It is important to highlight that in general, children are rather healthy, especially if they are normal-weight, which leaves little room for a positive effect from CRF. For instance, 91% of our children have a CRF level above the health-related cut points developed by Ruiz et al. (39), which further supports that our sample is relatively healthy. As an example, a child with normal glycemic levels is not expected to, and perhaps it is not even desirable to, further lower their glucose level no matter if they are fit or unfit. In adults, the metabolic profile, even in normal-weight adults is more altered and it therefore makes sense that being fit versus unfit has a larger effect on the metabolic profile than in children. In fact, it has been demonstrated in adults that unfit normal-weight individuals have a significantly higher risk of all-cause and cardiovascular disease mortality than fit normal-weight individuals (15), a difference not observed in the children participating in this study. Additionally, in adults, the obesity paradox is also being discussed, where it has been found that those who are overweight or mildly obese have improved cardiovascular disease

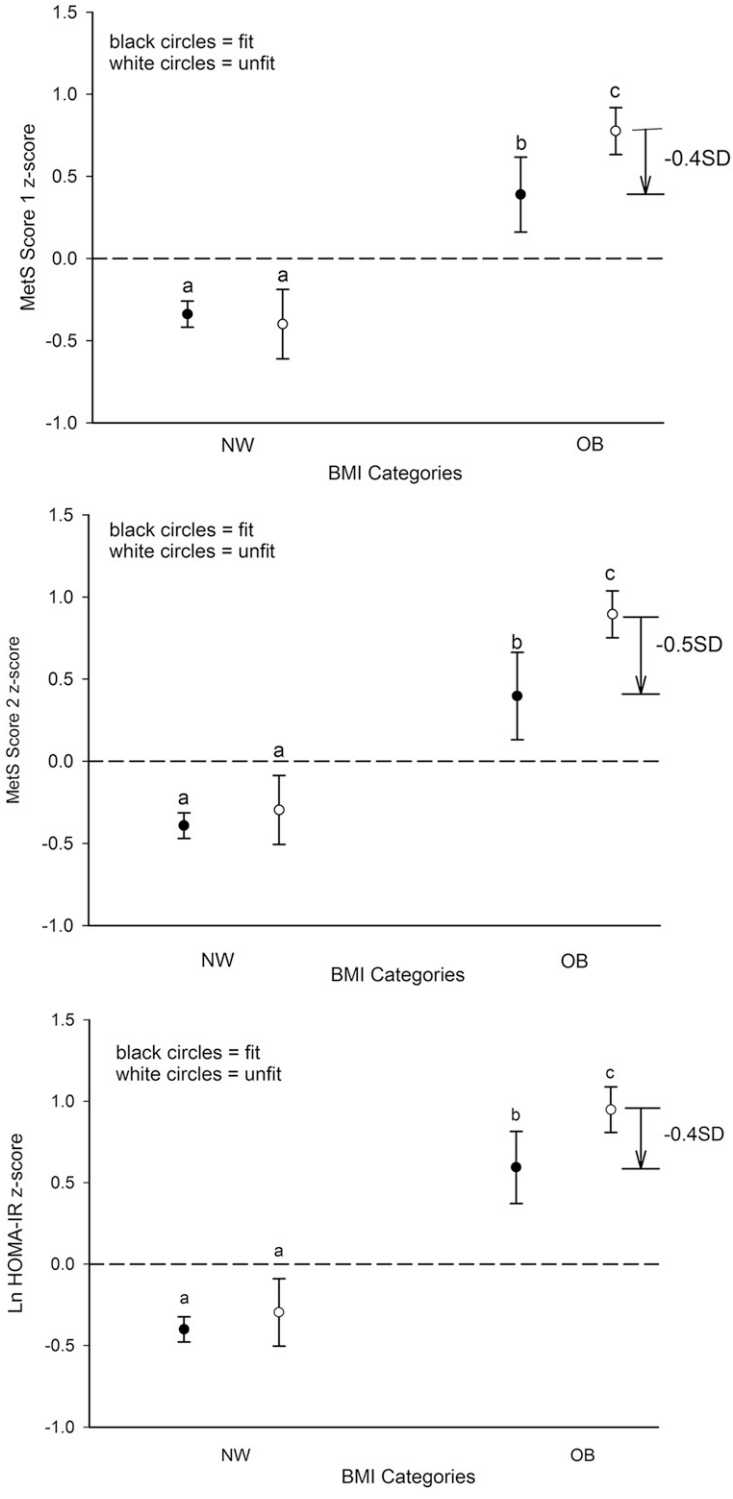

Figure 3—Differences in the two cardiometabolic risk scores and HOMA-IR for the fat but fit paradox. The figure represents adjusted means from ANCOVA models and 95% error bars, after adjustment for age and sex. The dashed line represents a value of zero for the scores and a higher score represents a greater cardiometabolic risk. Different letters (e.g., a and b) indicate statistically significant differences ($P < 0.05$), whereas the same letters indicate no differences between groups, after Bonferroni adjustment. The arrow shows the reduction in the cardiometabolic risk scores (effect size, SD) for the fit children compared with the unfit children in the OB group. MetS score 1 was calculated as the sum of the sex- and age-specific *z* scores for TG, HDL cholesterol, glucose, and the average of systolic and diastolic blood pressure (28). MetS score 2 was calculated as the sum of the sex- and age-specific *z* scores for TG-to-HDL ratio, MAP, and fasting insulin (29,30). Sample sizes were as follows: total ($n = 830$), NW and fit ($n = 498$), NW and unfit ($n = 69$), OB and fit ($n = 86$), and OB and unfit ($n = 177$). NW, normal-weight; OB, obese.

prognosis in the short/medium term than their underweight or normal-weight counterparts, with it being even more prominent in those with low CRF levels (40,41). However, studies in both children and adults agree on the beneficial effect of CRF on the cardiometabolic risk profile in obese individuals. For instance, a recent review indicated that a greater level of CRF should be included as a characteristic of the metabolically healthy phenotype (42).

Comparisons between studies are difficult due to the different methods used to analyze data. However, one study found that CRF in 9 and 15 year olds was significantly associated with cardiometabolic risk factors independent of adiposity (13). On the contrary, another study in 11 year olds reported that higher CRF was associated with a better metabolic profile, but after adjusting for waist circumference, the associations were negligible (14). Nevertheless, these studies did not investigate whether the association of CRF with cardiometabolic risk differed across the whole range of BMI, total body fat, or waist circumference. This may be of importance since our results suggest that CRF attenuates both MetS scores and HOMA-IR, particularly in obese children. Hence, more studies are needed to investigate if CRF has a positive influence on cardiometabolic risk, specifically focusing on children classified with mild, severe, or morbid obesity.

The fat but fit paradox showing that normal-weight unfit children have cardiometabolic risk scores similar to obese fit children is not supported by our results, since CRF showed a beneficial effect on the metabolic profile only in the obese children but not in the normal-weight children, as previously discussed. The significantly lower MetS scores and HOMA-IR observed in obese fit children in comparison with obese unfit children in our study is in line with previous studies using cardiometabolic risk scores (16–19), with no studies, as far as we are aware, having found these results using HOMA-IR. Our study provides evidence that CRF has a positive effect on the metabolic profile in children with severe and morbid obesity, as this effect was actually larger than in children with mild obesity. Two studies in children/youth observed no statistically significant differences in cardiometabolic risk scores between low body fat/BMI and low fit children and high body fat/BMI and high

fit children (16,19). It is important to note that in our study, we used precise cut points for both fatness and fitness, whereas only one of the aforementioned studies (19) used specific cut points. Therefore, more studies using precise cut points for fatness and fitness, as well as studies including only obese children in the high-fat group, are warranted.

This study was strengthened by the fairly large sample size, narrow age range, standardized methods used to collect the data, use of precise cut points to classify children into groups for the fat but fit analysis, and the use of two cardiometabolic risk scores and HOMA-IR. Furthermore, it is important to note that even though BMI has inherent limitations (i.e., inability to distinguish between fat and fat-free mass), in adults it has been found to be a good predictor of mortality from cardiovascular disease, even better than accurate measures of body fat (43). This study was limited by the cross-sectional design, which limits the ability to make casual inferences; the inability to adjust for biological maturity; only having parental education in a subsample of the population (however, sensitivity analyses showed similar results); and a small sample size in underweight and severe and morbid obesity. Even though the number of children classified with severe and morbid obesity was relatively small, the observed results are valuable, because as far as we know, no other study has been able to investigate the combined association of severe/morbid obesity and CRF in cardiometabolic risk in children.

The results obtained in this study have implications for both clinical care and public health. Currently, obesity treatment is focused largely on energy restriction; however, we observed that CRF can attenuate cardiometabolic risk, especially in obese children. Therefore, the promotion of physical activity with the aim to increase CRF from an early age should be incorporated into childhood obesity treatment programs. Even though increasing CRF did not have an effect on cardiometabolic risk scores in the normal-weight population, it is important to promote good CRF, as it has been demonstrated that this reduces the risk of developing overweight/obesity throughout puberty (44). Therefore, from a public health perspective, increasing CRF in all children could reduce cardiometabolic risk, especially in those that need it the most.

In conclusion, our results support that cardiometabolic risk becomes greater throughout the whole BMI spectrum in a linear fashion, with severe and morbid obese children having more than one SD worse metabolic profile than their normal-weight peers. Furthermore, our data suggest that in these generally healthy young individuals, obesity has a larger negative effect on the metabolic profile than low CRF. Nevertheless, it is noteworthy that CRF markedly attenuates the cardiometabolic risk scores and HOMA-IR, particularly in those in the highest BMI categories, and that fit obese children have significantly lower cardiometabolic risk and HOMA-IR than unfit obese children. Further studies with larger sample sizes of severe and morbid obese children and intervention studies are needed in order to confirm or contrast these findings.

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