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Joint association of physical activity and body mass index with cardiovascular risk: a nationwide population-based cross-sectional study

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The prevalence of overweight and obesity has reached pandemic proportions, and people with these conditions present with an increased cardiometabolic risk.[1] Some evidence suggests, however, that a high cardiorespiratory fitness (CRF) might mitigate the detrimental effects of excess body weight on cardiometabolic health, termed the 'fat but fit' paradox.[2] For instance, a recent meta-analysis concluded that although both overweight/obesity and a low CRF can increase the risk of mortality from cardiovascular diseases (CVD), low CRF is actually a stronger predictor.[3] Thus, it has been proposed that health policies should focus on physical activity (PA)-based interventions aimed at improving CRF rather than—or at least as much as—on weight loss strategies,[3] although some controversy remains.[2]

To clarify the existence of the 'fat but fit' [or 'elevated body mass index (BMI) but active'] paradox, in this observational study, we assessed the joint association between different BMI categories and PA levels, respectively, and the prevalence of major CVD risk factors.

Participants (18–64 years, all insured by a large occupational risk prevention company) provided oral consent and the local ethics committee (reference#CEIC_2019_001) approved the protocol, which conformed to the Helsinki Declaration. Participants underwent routine medical examinations (~1/year) as part of their health insurance coverage. The data obtained by the physician-directed examinations (2012–16) were collected during the last available examination.

Participants were categorized as normal weight (BMI, 20.0–24.9 $kg \cdot m^{-2}$), overweight (BMI, 25.0–29.9 $kg \cdot m^{-2}$), or obese (BMI $\geq$ 30.0 $kg \cdot m^{-2}$). Self-reported leisure-time PA levels were assessed as previously described,[4] and participants categorized as 'inactive' (performing neither moderate nor vigorous PA), 'insufficiently active' (not meeting WHO minimum PA recommendations for adults, i.e. < 150 min/week and < 75 min/week in moderate and vigorous PA, respectively), or 'regularly active' (meeting WHO guidelines of $\geq$ 150 min/week of moderate PA or $\geq$ 75 min/week of vigorous PA, or a combination thereof). We retrieved information from medical examinations on the prevalence of diabetes (medicated or glycaemia > 125 mg/dL), hypercholesterolaemia (medicated or total blood cholesterol $\geq$ 240 mg/dL), and hypertension (medicated or systolic/diastolic blood pressure $\geq$ 140/90 mmHg).

We used logistic regression to determine the association between each BMI/PA group and the prevalence of CVD risk factors, with the model adjusted by demographic/descriptive variables including date of the medical examination, and participants' home address, age, sex, and smoking status. The level of significance was set at $P < 0.05$.

Data from 527 662 participants [32% female; age (mean ± SD): 42.3 ± 9.4 years; BMI: 26.2 ± 4.3 kg/m^2] were analysed. About 42%,

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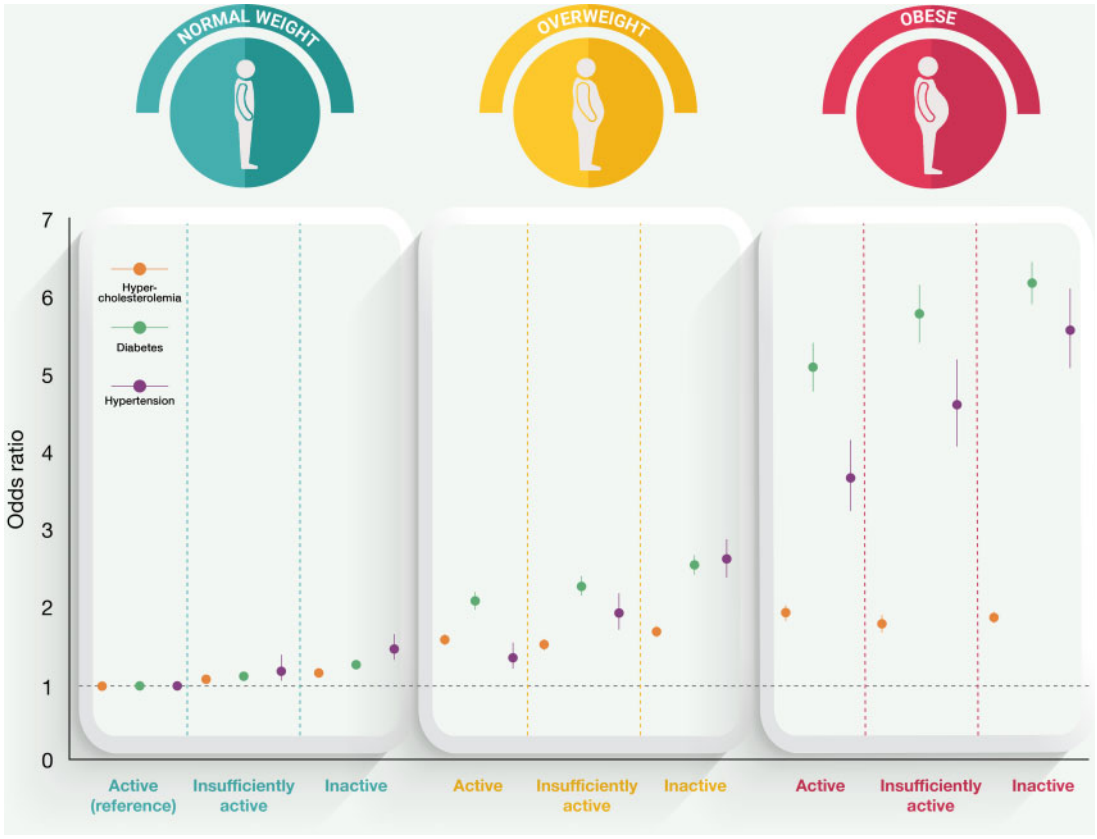

Figure 1 Joint association between physical activity levels and body mass index categories with cardiovascular risk factors. Data are expressed as odds ratio and 95% confidence interval.

41%, and 18% of the participants had normal weight, overweight, or obesity, respectively; 63.5%, 12.3%, and 24.2% were inactive, insufficiently active, and regularly active; and 30%, 15%, and 3% had hypercholesterolaemia, hypertension, and diabetes. Being either regularly or insufficiently active conferred protection compared to inactivity against all the studied risk factors within each BMI category, which was evident in a PA dose-response manner for diabetes and hypertension (*Figure 1*). However, regular/insufficient PA did not compensate for the negative effects of overweight/obesity, as individuals with overweight/obesity were at greater CVD risk than their peers with normal weight, irrespective of PA levels (*Figure 1*). Similar results were found overall when analysing men and women separately (*Table 1*).

Our study suggests that, although PA mitigates—at least partly—the detrimental effects of overweight/obesity on CVD risk, excess body weight *per se* is associated with a remarkable increase in the prevalence of major risk factors, as reflected by approximately two-, five-, and four-fold higher odds for hypercholesterolaemia, hypertension, and diabetes among active but obese individuals compared with their inactive peers with normal weight.

While the health benefits of increasing PA and maintaining an optimal body weight are widely known,[5] whether the cardioprotective role of PA can counteract the detrimental effects of obesity remains controversial. In a recent prospective study involving 5344 adults, individuals with overweight/obesity who were physically active showed a similar risk of CVD events in a 15-year follow-up than their physically active peers with normal weight.[6] A recent study involving 22 476 participants concluded that PA was associated with a larger reduction in the odds of 10-year CVD risk than having a normal weight.[7] However, in line with our findings, a systematic review concluded that an excess BMI is associated with increased CVD risk irrespective of PA levels.[8] Moreover, a study conducted in 2196 participants reported that although PA was associated with a lower CVD risk within each BMI category during a 30-year follow-up, individuals with overweight or obesity presented with an increased CVD risk regardless of their PA levels.[9] Indeed, even 'metabolically healthy' obese individuals (i.e. those without cardiometabolic conditions, such as diabetes, hypertension, or hyperlipidaemia) present with a higher CVD risk than their peers with normal weight, as supported by a meta-analysis of 22 prospective studies.[10] With the cross-sectional design we used, our analyses were not controlled for diet, and leisure-time PA levels were self-reported, representing potential study limitations. Nevertheless, the present findings, which are based on data from

Table 1 Joint association between physical activity levels and body mass index categories with cardiovascular risk factors separately by sex

	Hypertension				Hypercholesterolaemia				Diabetes			
	Men		Women		Men		Women		Men		Women	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Normal weight												
Active (Reference)	—	—	—	—	—	—	—	—	—	—	—	—
Insufficiently active	1.08 (1.00–1.17)	**0.039**	1.15 (1.02–1.31)	**0.027**	0.97 (0.93–1.02)	0.240	1.06 (1.00–1.12)	0.053	1.18 (1.00–1.39)	0.046	1.18 (0.90–1.53)	0.233
Inactive	1.25 (1.18–1.31)	**<0.001**	1.30 (1.18–1.44)	**<0.001**	1.16 (1.13–1.20)	**<0.001**	1.05 (1.00–1.09)	**0.044**	1.56 (1.40–1.74)	**<0.001**	1.27 (1.03–1.57)	**0.024**
Overweight												
Active	1.98 (1.89–2.08)	**<0.001**	2.46 (2.14–2.82)	**<0.001**	1.61 (1.58–1.66)	**<0.001**	1.41 (1.31–1.52)	**<0.001**	1.33 (1.18–1.49)	**<0.001**	1.91 (1.40–2.61)	**<0.001**
Insufficiently active	2.23 (2.10–2.36)	**<0.001**	2.29 (2.00–1.61)	**<0.001**	1.54 (1.48–1.60)	**<0.001**	1.44 (1.34–1.54)	**<0.001**	1.92 (1.70–2.17)	**<0.001**	1.89 (1.41–2.54)	**<0.001**
Inactive	2.46 (2.35–2.57)	**<0.001**	2.80 (2.53–3.08)	**<0.001**	1.78 (1.73–1.83)	**<0.001**	1.43 (1.34–1.49)	**<0.001**	2.58 (2.33–2.84)	**<0.001**	2.71 (2.20–2.33)	**<0.001**
Obesity												
Active	4.93 (4.64–5.24)	**<0.001**	5.45 (4.62–6.44)	**<0.001**	2.03 (1.94–2.13)	**<0.001**	1.36 (1.21–1.54)	**<0.001**	3.62 (3.18–4.12)	**<0.001**	4.18 (2.96–5.92)	**<0.001**
Insufficiently active	5.71 (5.34–6.10)	**<0.001**	5.92 (5.10–6.88)	**<0.001**	1.90 (1–80–2.01)	**<0.001**	1.44 (1.30–1.60)	**<0.001**	4.44 (4.91–5.98)	**<0.001**	5.45 (4.06–7.31)	**<0.001**
Inactive	5.94 (5.68–6.21)	**<0.001**	7.28 (6.59–8.04)	**<0.001**	2.0 (1.96–2.08)	**<0.001**	1.50 (1.43–1.58)	**<0.001**	5.42 (4.91–5.98)	**<0.001**	6.26 (5.10–7.69)	**<0.001**

Significant *P*-values are in bold.
CI, confidence interval; OR, odds ratio.

insured active workers across Spain, represent one of the largest studies to date ($n = 527\ 662$) and refute the notion that a physically active lifestyle can completely negate the deleterious effects of overweight/obesity.

In summary, increasing PA levels appear to provide benefits in an overall dose-response manner (regularly active > insufficiently active > inactive for the risk of hypertension or diabetes) across BMI categories and should be a priority of health policies. However, weight loss *per se* should remain a primary target for health policies aimed at reducing CVD risk in people with overweight/obesity.

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