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Letter to the editor

Association between physical activity and cardiovascular risk factors: Dose and sex matter

Alejandro Santos-Lozano [a,b,*], Alberto Torres Barrán [c], Pablo Fernández-Navarro [d,e], Pedro L. Valenzuela [f], Adrián Castillo-Garcia [g], Luis M. Ruilope [h], David Ríos Insua [c], José M. Ordovas [i], Victoria Ley [j], Alejandro Lucia [b,k]

[a] i+HeALTH, Department of Health Sciences, European University Miguel de Cervantes, Valladolid 47012, Spain
[b] Research Institute of the Hospital 12 de Octubre (imas12, PaHerg group), and (CIBER en Fragilidad y Envejecimiento Saludable - CIBEFES), Madrid 28041, Spain
[c] Institute of Mathematical Sciences (ICMAT-CSIC), Madrid 28049, Spain
[d] Cancer and Environmental Epidemiology Unit, National Center for Epidemiology, Carlos III Institute of Health, Madrid 28029, Spain
[e] Consortium for Biomedical Research in Epidemiology & Public Health (CIBER en Epidemiología y Salud Pública - CIBERESP), Madrid 28029, Spain
[f] Department of Systems Biology, University of Alcalá, Madrid 28801, Spain
[g] Fissac-Physiology, Health and Physical Activity, Madrid 28801, Spain
[h] Hypertension Unit and Cardiorenal Translational Laboratory, Research Institute of the Hospital 12 de Octubre (imas12), Madrid 28041, Spain
[i] Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University, Boston, MA 02111, USA
[j] Spanish State Research Agency, Ministry of Science, Innovation and Universities, Madrid 28046, Spain
[k] Faculty of Sport Sciences, Universidad Europea de Madrid, Madrid 28670, Spain

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Dear Editor,

Failure to meet World Health Organization (WHO)-determined minimum physical activity (PA) levels is an established risk factor for cardiovascular disease (CVD),[1] but evidence is still scarce on its effects on other CVD risk factors. Furthermore, whether or not there are sex-specific effects on the association between PA and CVD risk is a matter of controversy, with some authors observing a protective effect of PA in men but not in women,[2] and others finding the opposite trend.[3]

We studied the association between different PA levels and major CVD risk factors, along with potential sex effects on this association, in a European (Spanish) cohort of workers (aged 18−64 years) insured by a large occupational risk prevention company. Participants underwent routine (~1 time/year) medical examinations as part of their health insurance coverage, and their data were registered over a 5-year period (2012−2016). Participants provided their oral consent, and the local ethics committee of the European University Miguel de Cervantes approved the protocol.

We collected data from the last available medical examination for each participant during the study period. Demographic/descriptive variables included date/location of the medical examination and participants' postal code, age, sex, body mass index (BMI), and smoking status. Data were enriched with National Census data using the postal code, from which we obtained average socioeconomic and education information.

We retrieved information on the following CVD risk factors: diabetes (medicated or glycaemia $\geq$ 125 mg/dL), hypercholesterolemia (medicated or total cholesterol $\geq$ 240 mg/dL), hypertension (medicated or systolic/diastolic blood pressure $\geq$ 140/90 mm Hg), and obesity (BMI $\geq$ 30 kg/m^2).

Participants' self-reported levels of leisure-time PA were assessed as explained elsewhere,[4] using a questionnaire about PA frequency/intensity during a typical week. Accordingly, participants were considered "inactive" (performing neither moderate nor vigorous PA), "insufficiently active" (not meeting WHO guidelines,[5] i.e., <150 min/week and <75 min/week in moderate and vigorous PA, respectively), or "regularly active" (meeting WHO minimum guidelines, i.e., $\geq$150 min/week of moderate PA or $\geq$75 min/week of vigorous PA, or a combination thereof).

We used logistic regression to determine the association between PA levels and CVD risk factors—the model was

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* Corresponding author.
E-mail address: asantos@uemc.es (A. Santos-Lozano).

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adjusted by sex, age, smoking status, year, and month of data collection, province, and socioeconomic and education variables ($\alpha = 0.05$).

Data from 527,662 participants (32% female) were used for analysis. Approximately one-half of the participants (47%) were free of the CVD risk factors studied, and 63.5%, 12.3%, and 24.2% were inactive, insufficiently active, and regularly active, respectively. Regression analyses for the whole cohort (both sexes combined) showed a significantly lower prevalence (between 10% and 42%) of all the studied CVD risk factors in those individuals who were regularly active compared with their inactive referents. We found a PA-dose benefit with a lower CVD risk in regularly active individuals when compared with their insufficiently active peers. The latter group, nonetheless, also had a lower prevalence of all CVD risk factors (between 9% and 30%) compared with inactive individuals (Fig. 1).

The inverse association between CVD risk factors and regular activity (*vs*. inactivity) was confirmed in both sexes, with the exception of obesity in women. The PA-dose benefits that were found for the whole cohort were also corroborated in both sexes separately, with the exception of the aforementioned case of obesity and hypercholesterolemia risk in women. Barring hypertension, the benefits of PA (whether sufficient or insufficient) *vs*. inactivity against CVD risk factors appeared to be more marked in men than in women, although statistical comparisons were not performed between sexes for the sake of simplicity.

Our findings are in line with previous studies reporting that even PA levels below WHO guidelines are associated with a lower risk of CVD and mortality.[5,6] Thus, even performing minimum amounts of PA will be beneficial compared to being inactive. Our results showing a high proportion of inactive adults are in agreement with recent findings from the same European country.[4] This highlights the need to educate the population and promote PA at the national level, particularly given the fact that even "insufficient" PA is associated with a significantly lower CVD risk.

Controversy exists regarding the presence of a potential sex effect on the association between PA levels and CVD risk. A 40-year follow-up study reported that, although long-term PA exerted a global protective effect against CVD incidence and CVD mortality, the benefits were significant in men but not in women.[2] By contrast, El Saadany et al.[3] reported that both regular and irregular PA prevented CVD-attributable mortality risk in women but not in men.[3] Our findings that PA was significantly associated with a reduced prevalence of most CVD risk in both sexes suggest that increasing PA could be a beneficial strategy against CVD independently of sex. It must be noted, however, that we found that higher PA levels were strongly associated with a lower prevalence of obesity in men but not in women. Differences in sex hormones and other particular situations (e.g., pregnancy, menopause, or hormonal contraceptive use) could partly explain the potential sex-specific effects on the association of PA with obesity risk and metabolic health.[7] There is some evidence suggesting that men lose more weight than women do in response to exercise interventions,[8] which may support our findings. Future

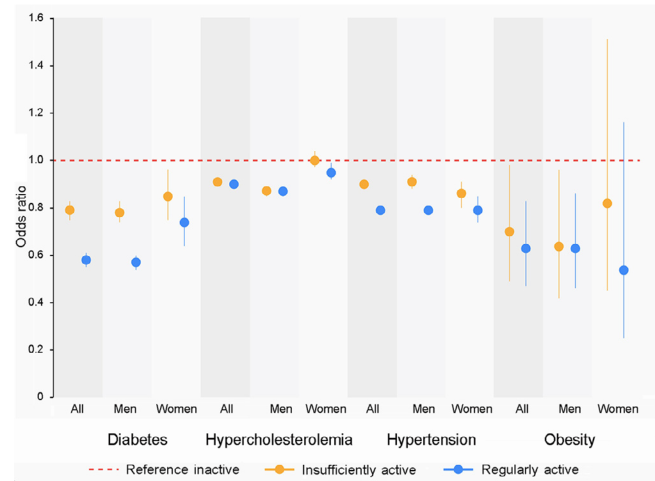

Fig. 1. Association between physical activity levels and cardiovascular risk factors.

research examining the association between PA levels and obesity in women should consider potential confounding factors such as diet as well as hormonal or fertility status. Moreover, the amount of vigorous PA might be more important than meeting or not meeting WHO guidelines for preventing obesity in women.

In summary, despite the cross-sectional nature of the present study, our findings suggest that PA—especially but not exclusively when performed above WHO-recommended minimum levels—is associated with a lower prevalence of major CVD risk factors in a large cohort of European working adults. Some sex-specific trends were found, notably for obesity, which was not actually associated with PA in women.

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Authors' contributions

ASL, PFN, and AL conceived the study, participated in its design and coordination, and helped to draft the manuscript; ATB, ACG, and DRI helped to analyze the data; PLV helped to draft the manuscript; LMR and JMO conceived the study and participated in its design; VL conceived the study and participated in its design and coordination. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interest. The funders had no role in the design of the study in the collection, analyses, or interpretation of data; in the writing of the manuscript; or in the decision to publish the results.

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