

Will sex differences have to be considered in future studies on health effects of occupational physical activity?

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This editorial refers to ‘Prospective relationship between occupational physical activity and risk of ischemic heart disease—are men and women differently affected?’, by K. Allesøe et al., <https://doi.org/10.1093/eurjpc/zwad067>.

Leisure time physical activity (LTPA) is well known to promote health and reduce the risk of ischaemic heart disease (IHD), one of the leading causes of mortality in Western countries. However, several studies have found this to be different for occupational physical activity (OPA), which appears to adversely affect health and increase the risk of IHD. This phenomenon is called ‘physical activity paradox’.¹ There have been some attempts to explain these differences. Leisure time physical activity is characterized by high-intensity, short-duration, dynamic, and unconstrained postures and activity as well as sufficient recovery time. This has the potential to increase cardiorespiratory fitness and to reduce 24-h heart rate, blood pressure, and inflammation over time. On the other hand, OPA is characterized by low to moderate intensity, long duration, static and constrained postures and activities, and insufficient recovery. This may increase 24-h heart rate, blood pressure, and inflammation, which are associated with detrimental effects on cardiovascular health.²

Literature on health effects of OPA is not consistent, and some of the most recent publications regarding that topic indicate its complexity: A systematic review and meta-analysis covering 23 studies with 655 892 participants showed that higher OPA was not related to overall cardiovascular disease (CVD) mortality but was positively associated with IHD mortality risk.³ Residual confounding by socio-economic status and environmental exposures, however, could not be ruled out completely. Obverse effects of LTPA and OPA on patients with pre-existing CVD were shown in a study on all-cause mortality, recurrent cardiovascular events, and incident type 2 diabetes.⁴ Another recent study examined associations of high OPA with total and cause-specific mortality. A total of 322 126 participants (135 254 women) from the National Institutes of Health—American Association of Retired Persons (HIH—AARP) Diet and Health Study were included.⁵ This large prospective cohort study showed some weak but statistically significant positive associations of a lifetime high OPA with deaths from any cause and some specific causes, including CVD and cancer. However, these associations were strongly attenuated and, in most instances, disappeared after

considering key confounder variables, mainly socio-economic status and smoking. This study highlights the influence of socio-economic status, health behaviours, and environmental factors. It does however not reject the hypothesis of the physical activity paradox, which states that many years of high OPA can increase the risk of CVD and mortality. Whilst study results on the existence of a physical activity paradox are not consistent *per se*, they are even more controversial on the question whether men and women are differently affected.

In this issue of the *EAPC*, Allesøe et al.⁶ explored the prospective relationship between OPA and risk of IHD with the focus on different effects on men and women. They included 1399 women and 1706 men, aged 30–61 years, who have participated in the Danish Monica 1 study from 1982 to 1984. All the enrolled persons were actively employed and without prior IHD. Information about incident cases of IHD was retrieved by individual linkage to the Danish National Patient Registry. Occupational physical activity was assessed by a single question, based on the Saltin and Grimby question and allowing for a classification in sedentary, light, moderate, and strenuous OPA.⁷ Compared with women with sedentary work, who were taken as reference group, women in all other OPA categories had lower hazard ratio (HR) for IHD. Among men, the risk of IHD was 22% higher among those with light OPA, and 42% and 46% higher among those with moderate or strenuous OPA, respectively, compared with men with sedentary work. Compared with women with sedentary OPA, HR for IHD was higher among men in all OPA categories. The interaction between OPA and sex was statistically significant. The authors concluded that demanding and strenuous OPA seems to be a risk factor for IHD among men, whereas a higher level of OPA seems to protect from IHD among women. It was one of the very few studies demonstrating that the association between OPA and IHD differs by sex, which was shown by a statistically significant interaction between OPA and sex.

The Monica study is a prospective study with a high response rate, including a large number of men and women and providing a long follow-up time. This made it possible for the authors to explore sex differences.

Two other studies including both sexes^{8,9} and several studies including either men or women were in accordance with these findings. In contrast, other previous studies showed no association between OPA and heart disease among men or suggested a protective effect. Among

women, some studies suggested an increased risk of heart disease, whereas others found no association between OPA and heart disease.

One of the methodological differences between this study and previous studies with different outcomes for both sexes is that most of the previous papers have not tested for potential interaction between OPA and sex but have merely adjusted for sex or stratified by sex. To reveal sex differences in the relationship between OPA and risk of IHD, it is however necessary to explore potential effect modification by sex.

There are a few caveats in the interpretation of this study. The classification of OPA levels for both sexes was based on a single question in a questionnaire. Although their answer may have placed them in the same OPA category, men and women might have different levels of OPA due to a high degree of gender segregation in the labour market, especially in jobs with high physical demands. This may be true even where men and women have the same occupational titles. A discrimination between walking and standing work was not possible. Workers with high OPA may have retired earlier or may have changed jobs to those with light or sedentary OPA that could have biased the results (healthy worker selection bias). Besides, the response to a question in a questionnaire is partly subjective and may be influenced by physical capacity and health status. It has not yet been clarified, if physiological sex differences like physical capacity and hormone status may influence the impact of a certain workload and how that might change after menopause. As OPA is often associated with a low socio-economic status, the authors performed a sensitivity analysis of the age-adjusted association between OPA and IHD among those with the lowest level of vocational training.

Although the present study by Allesøe *et al.* is a huge step forward in understanding the relationship between OPA and risk of IHD as well as different effects on men and women, some knowledge gaps are still to be filled by future studies. The underlying causes and mechanisms of the effects of OPA on both sexes need to be clarified. In addition, a better understanding of possible confounders and covariates, including socio-economic factors, health behaviours, and environmental influences, is necessary to know what to adjust for in statistical models. Studies with device-worn 24-h measurements of physical activity and physiological parameters would be beneficial to reduce self-reporting bias and to increase precision and specificity of the characteristics of physical activity in different domains. Occupational physical activity should not be regarded in isolation, but as a composition together with other activities and behaviours throughout the whole week, including leisure time. Finally, the impact of OPA on CVD, and specifically IHD, should be studied by interventions on occupational groups to gain a better understanding of varying preconditions on health. Increasing scientific evidence for an increase of the risk of CVD or IHD by OPA in men should then be included for example in the WHO guidelines on physical

activity and sedentary behaviour to avoid the assumption that strenuous OPA may have the same beneficial health effects as LTPA.¹⁰

In conclusion, the study by Allesøe *et al.* is one in very few studies, which has shown a different effect of OPA on IHD risk among men and women. Demanding OPA was associated with a higher risk of IHD compared with sedentary work in men; among women, strenuous OPA seemed to have a protective effect regarding IHD risk compared with sedentary work. Due to the appropriate methodology of this study, these results seem to be valid and reliable. The exact cause and the underlying mechanisms for these differences, however, are still to be clarified in future studies.

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