Comparative effect of physical exercise versus statins on improving arterial stiffness in patients with high cardiometabolic risk: A network meta-analysis

Cavero-Redondo, I.
Deeks, J.J.
Alvarez-Bueno, C.
Jolly, K.
Saz-Lara, A.
Price, M.
Pascual-Morena, C.
Martínez-Vizcaíno, V.

Abstract
Background The comparative analysis of the effect of several doses of statins against different intensities of physical exercise on arterial stiffness (a measure of cardiovascular risk) could shed light for clinicians on which method is most effective in preventing cardiovascular disease (CVD) and be used to inform shared decision-making between doctors and patients. This study was aimed at analyzing the effect, in high cardiometabolic risk patients, of different statins doses and exercise intensities on arterial stiffness (a measure of cardiovascular risk) by integrating all available direct and indirect evidence in network meta-analyses. Methods and findings We systematically searched MEDLINE, Embase, SPORTDiscus, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Web of Science databases from their inception to February 28, 2020; for unpublished trials, we also searched ClinicalTrials.gov. We searched for studies concerning the effect of statins or physical exercise on arterial stiffness, measured by pulse wave velocity (PWV). For methodological quality assessment, Cochrane Collaboration's tool for assessing risk of bias (RoB2) was used. A network geometry graph was used to assess the strength of the evidence. Comparative evaluation of the interventions effect was performed by conducting a standard pairwise meta-analysis and a network meta-analysis (NMA) for direct and indirect comparisons between interventions and control/nonintervention. A total of 22 studies were included in the analyses (18 randomized controlled trials (RCTs) and 4 nonrandomized experimental studies), including 1,307 patients with high cardiometabolic risk from Asia (3 studies), Oceania (2 studies), Europe (10 studies), North America (5 studies), and South America (2 studies). The overall risk of bias assessed with RoB2 was high in all included studies. For standard pairwise meta-analysis and NMA, high-intensity exercise versus control (mean difference (MD) −0.56; 95% CI: −1.01, −0.11; p = 0.015 and −0.62; 95% CI: −1.20, −0.04; p = 0.038, respectively) and moderate statin dose versus control (MD −0.80, 95% CI: −1.59, −0.01; p = 0.048 and −0.73, 95% CI: −1.30, −0.15; p = 0.014, respectively) showed significant MDs. When nonrandomized experimental studies were excluded, the effect on high-intensity exercise versus control and moderate statin dose versus was slightly modified. The main limitation of this study was that the magnitude of the effect of the exercise interventions could be underestimated due to regression toward the mean bias because the baseline cardiometabolic risk profile of patients in the physical

exercise intervention trials was healthier than those in the statins ones; consequently, more modest improvements in physical exercise interventions compared to statins interventions can be expected. Additionally, we might consider as limitations the small study sizes, the heterogeneous patient groups, the focus on a proxy endpoint (PWV), and the high risk of bias. Conclusions In this NMA, we found that although many patients could benefit from statins for reducing CVD risk, our results support that, considering the beneficial effects of high-intensity exercise on arterial stiffness, it would be worthwhile to refocus our attention on this type of exercise as an effective tool for the prevention of CVD.