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**Objective measures of physical performance in women: associations with a cumulative index of hormonal exposure**

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**ABSTRACT**

**BACKGROUND** - Objective measures of physical performance, including walking speed (WS) and grip strength (GS), are associated with increased risk of disability and death. Estrogens are implicated in muscle mass maintenance, bone resorption inhibition, neuro- and cardio-protection and could contribute to explain heterogeneity in physical function in women. However, data on the association of hormonal exposure with WS and GS remain controversial. **Objective.** To investigate the association of a cumulative index of hormonal exposure (CIHE) with WS and GS. **METHODS** - The Constances French prospective population-based cohort included 220,000 subjects aged 18-69 between 2012-2020. Participants aged  $\geq 45$  benefited from functional tests (3-meter fast WS, GS), by trained neuropsychologists at a Health Center. The CIHE included self-reported reproductive life characteristics and exogenous hormonal use. Continuous variables were dichotomized at the median of their distribution; the category associated with the highest or longest duration of estrogen exposure scored 1 point, while the lowest or shortest exposure scored 0 points. Age at menarche $<13$ y, non-nulliparous status, parity $\geq 3$ , ever breastfeeding, duration of breastfeeding $\geq 6$  months, ever pill use, duration of pill use $\geq 5$ y, and being non-menopausal each scored 1 point. In menopausal women, we assigned 1 point to natural menopause (vs artificial), menopause  $\geq 50.2$ y and ever use of hormone therapy. Non-menopausal women were scored 1 for each of these three categories. CIHE was the sum of the points and ranged from 0 to 11. After multiple imputation of missing values, associations of CIHE with WS (N=33,892) and GS (N=37,935) were estimated using linear mixed models with center as a random effect adjusted for a wide range of confounders, including age, education, health behaviours, depression, cognition, or cardiovascular disease. **RESULTS** - Women were 57.1y old on average. Mean WS was 173.5 cm/s and mean maximal GS was 26.6 kg. We found a linear positive association between the CIHE and both WS and GS. Women in the highest quartile of CIHE walked faster ( $\beta_{Q4 \text{ vs } Q1}=1.89$ ; 95%CI=1.07-2.71, p-trend $<0.01$ ) and were stronger than those in the first one ( $\beta_{Q4 \text{ vs } Q1}=0.45$ ; 95%CI=0.29-0.60, p-trend $<0.01$ ). **CONCLUSION** - Women with a higher CIHE walked faster and had higher upper body muscle strength than those with a lower score, suggesting that an intense and longer lifetime estrogens exposure is associated with better physical performances.

**KEYWORDS:** -

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