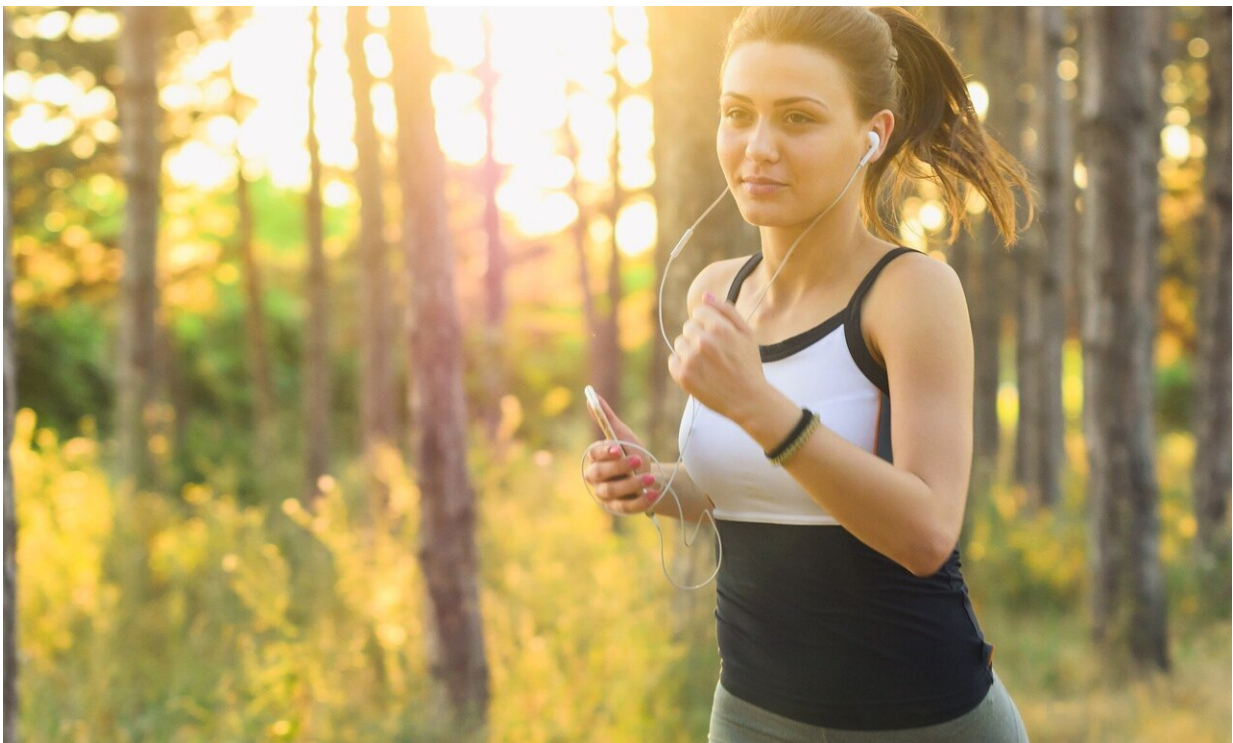


Boosting physical activity and curbing sitting time are highly likely to lower breast cancer risk

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Boosting physical activity levels and curbing sitting time are highly likely to lower breast cancer risk, finds research designed to strengthen proof of causation and published online in the *British Journal of Sports*

Medicine.

The findings were generally consistent across all types and stages of the disease, reveals the Mendelian randomization study, prompting the researchers to recommend a stronger focus on exercise as a way of warding off breast cancer.

Mendelian randomization is a technique that uses genetic variants as proxies for a particular risk factor—in this case lifelong [physical activity](#) levels/[sedentary behavior](#)—to obtain genetic evidence in support of a causal relationship.

Observational studies show that physical [inactivity](#) and sedentary behavior are linked to higher breast cancer risk, but proving they cause breast cancer is another matter.

The researchers therefore used Mendelian randomization to assess whether lifelong physical activity and sitting time might be causally related to breast cancer risk in general, and specifically to different types of tumor.

They included data from 130,957 women of European ancestry: 69, 838 of them had tumors that had spread locally (invasive); 6667 had tumors that hadn't yet done so (in situ); and a comparison group of 54,452 women didn't have breast cancer.

The women were participants of 76 studies under the aegis of the Breast Cancer Association Consortium (BCAC), a forum of investigators interested in the inherited risk of breast cancer.

The researchers then drew on previously published studies that had used the vast repository of UK Biobank data on potential genetic explanations for overall predisposition to physical activity, vigorous physical activity,

or sitting time—as measured by wrist-worn activity trackers—to genetically predict how physically active or inactive their own study participants were.

Next, the researchers estimated overall breast cancer risk, according to whether the women had or hadn't gone through the menopause; and by cancer type (positive for estrogen or progesterone, or HER-2, or positive/negative for all 3 hormones), stage (size and extent of tumor spread), and grade (degree of tumor cell abnormality).

These case-control groups comprised: 23,999 pre/peri-menopausal women with invasive breast cancer and 17,686 women without; 45,839 postmenopausal women with breast cancer and 36,766 without.

In all, there were 46,528 estrogen receptor positive tumors and 11,246 controls; 34,891 progesterone receptor positive tumors and 16,432 controls; 6945 HER2 positive tumors and 33,214 controls; 1974 triple positive cases; and 4964 triple negative cases.

And there were 42,223 cases of invasive ductal/lobular cancers and 8795 controls, and 3510 cases of ductal carcinoma in situ; 17,583 stage 1 cancers, 15,992 stage 2, and 4553 stage 3-4; 34,647 moderately abnormal cell tumors and 16,432 highly abnormal cell tumors.

Analysis of the data showed that a higher overall level of genetically predicted physical activity was associated with a 41% lower risk of invasive breast cancer, and this was largely irrespective of menopausal status, tumor type, stage, or grade.

Similarly, genetically predicted vigorous physical activity on 3 or more days of the week was associated with a 38% lower risk of breast cancer, compared with no self-reported vigorous activity. These findings were consistent across most of the case groups.

Finally, a greater level of genetically predicted sitting time was associated with a 104% higher risk of triple negative breast cancer. These findings were consistent across hormone-negative tumor types.

The findings were unchanged after factoring in the production by a single gene of two or more apparently unrelated effects (pleiotropy), such as smoking and overweight, for example.

There are plausible biological explanations for their findings, say the researchers, who point to a reasonable body of evidence indicating numerous causal pathways between physical activity and breast cancer risk, such as overweight/obesity, disordered metabolism, sex hormones, and inflammation.

"Mechanisms linking sedentary time and cancer are likely to at least partially overlap with those underpinning the physical activity relationship," suggest the researchers.

Their findings provide "strong evidence" that more overall physical activity and less sitting time are likely to reduce [breast cancer risk](#), they say.

They conclude, "Increasing physical activity and reducing sedentary time are already recommended for cancer prevention. Our study adds further evidence that such behavioral changes are likely to lower the incidence of future [breast cancer](#) rates.

"A stronger cancer-control focus on physical activity and sedentary time as modifiable cancer risk factors is warranted, given the heavy burden of disease attributed to the most common cancer in women."

More information: Physical activity, sedentary time and breast cancer risk: a Mendelian randomisation study, *British Journal of Sports Medicine*

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