

The aspirin conundrum: Navigating negative results, age, aging dynamics and equity

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A new study examining the role of aspirin in breast cancer treatment reveals critical issues related to health equity and aging that have broad implications for cancer and other disease intervention trials, say researchers from Georgetown University's Lombardi Comprehensive Cancer Center. They outline their concerns in an editorial accompanying the study's findings published April 29 in *JAMA*.



The study, called the Alliance trial, was launched after researchers noted that breast cancer survivors taking aspirin as part of another clinical trial for <u>cardiovascular disease</u> lived longer.

To confirm the observation, a Phase III clinical trial randomly assigned volunteers with nonmetastatic, high-risk breast cancer to receive either 300mg of aspirin or placebo daily. The outcome was a disappointment. The study was suspended at the first interim safety analysis because the results indicated futility—aspirin did not decrease the risk of cancer recurrence or improve survival.

In their editorial examining the trial, the Georgetown researchers, Jeanne Mandelblatt, MD, MPH; Candace Mainor, MD; and Barry Hudson, Ph.D., raise several important questions about the outcome.

For example, the authors point out that despite efforts to include various groups in the study, certain subgroups, like <u>racial minorities</u> and those with high exposure to systemic racism, may not have been adequately represented.

"Some individuals from these groups may experience chronic life stressors that affect inflammation, accelerate <u>biological aging</u> and contribute to disparities in cancer risk, recurrence and mortality," they write, noting that these individuals could potentially benefit from aspirin, an anti-inflammatory drug.

Researchers say another issue with this and other trials is how <u>chronological age</u> and biological age might affect implications for a trial's design and its results.

The results in the Alliance trial "raises the question of whether aspirin's lack of benefit could be partly explained by variations in biological age, including heterogeneity in immune and platelet function, <u>inflammatory</u>



responses and host-tumor microenvironment interactions," they write. "Thus, careful consideration of the intersectionality of aging, cancer and disparities will be critical in designing future oncology and other disease trials to advance health equity."

Finally, the researchers say clinicians may find it challenging to integrate new findings into routine practice because the results suggest a lack of intervention efficacy along with the many unanswered questions.

Despite the fairly definitive negative result for use of aspirin to improve invasive disease-free survival among <u>breast cancer survivors</u>, the researchers say, "...oncology and primary care providers may still consider discussing with each other and their patients the potential benefits and harms of aspirin used for other reasons."

More information: The Aspirin Conundrum: Navigating Negative Results, Age, Aging Dynamics and Equity, *JAMA* (2024). <u>DOI:</u> <u>10.1001/jama.2024.4828</u>

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