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## Cancer screening metrics: effective evaluation to balance benefits and harms

**Lyon, France, 8 April 2024** – A new study led by researchers at the International Agency for Research on Cancer (IARC) and published today in the *Journal of the American Medical Association*<sup>1</sup> assesses whether the incidence of late-stage cancer could be a suitable alternative end-point in randomized clinical trials of cancer screening, in place of cancer-specific mortality, the gold-standard end-point.

Based on 41 randomized clinical trials evaluating the effectiveness of screening tests, the findings suggest that the rate of late-stage cancers may be a suitable alternative metric to cancer deaths for some types of cancer but not for others.

"The choice of metric is critical in assessing the effectiveness of cancer screening tests," says Dr Hilary Robbins, a scientist in the Genomic Epidemiology Branch at IARC. "Study results showed that, for some cancer types, there is not a strong link between avoiding late cancer diagnosis and preventing cancer deaths. If late-stage diagnoses are used as a metric, it may provide misleading evidence on whether benefits outweigh harms."

For years, the gold standard for proving the effectiveness of a cancer screening test has been a decrease in the rate of deaths from the form of cancer targeted by the test, in a type of study called a randomized controlled trial. This stringent standard is in place because cancer screening is generally carried out among healthy people; most of these people will not benefit from screening and some might even experience harm, such as invasive procedures or psychological stress. Therefore, recommendations to screen for breast, colorectal, and/or lung cancers have in most countries been made on the basis of trials showing that screening successfully reduced cancer mortality.

A potential alternative metric is the rate of people diagnosed with cancer at a late stage, also called the incidence of late-stage cancer. "Using a reduced rate of late-stage cancer as the metric for screening effectiveness could speed up trials of new 'multi-cancer' screening tests, which aim to detect many types of cancer with a single blood test. Already, a large trial is under way in England that will evaluate a multi-cancer test based on its ability to reduce late-stage diagnoses," says Dr Robbins. "However, there are concerns that even if this trial is successful, we cannot be certain that the test saves lives. This is because avoiding late diagnosis may not

<sup>&</sup>lt;sup>1</sup> Feng X, Zahed H, Onwuka J, Callister ME, Johansson M, Etzioni R, et al. (2024). Cancer stage compared with mortality as end points in randomized clinical trials of cancer screening: a systematic review and meta-analysis. *JAMA*, Published online 7 April 2024; https://doi.org/10.1001/jama.2024.5814.







always prevent cancer death. Our study used data from prior cancer screening trials to compare these two metrics of screening effectiveness."

## **Cancer sites**

In the study, IARC scientists found that reductions in the rate of late-stage diagnoses for lung and ovarian cancers led to similar reductions in cancer deaths. For breast cancer, the reduction in deaths was smaller than the reduction in the incidence of late-stage cancers, and for colorectal and prostate cancers, the relationship between the two metrics was weak.

IARC scientists noted that new multi-cancer screening tests target many types of cancer that were not included in previous trials. Therefore, even if these tests are effective in reducing the incidence of late-stage cancers, it is not currently possible to conclude that they reduce cancer deaths.

The researchers are planning additional studies to improve the evaluation of cancer screening tests in the future.

## For more information, please contact

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