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Cancer Screening metrics: effective evaluation to balance benefits and harms

Questions and Answers (Q&A)

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*¹ addresses metrics for measuring the benefit of cancer screening. It assessed 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.

1. What methodology was used by the IARC researchers?

The IARC researchers performed a systematic review and meta-analysis. They identified published studies of cancer screening trials and, from these publications, extracted data on the numbers of participants, late-stage cancer diagnoses, and cancer deaths. They analysed these data to compare the effects of cancer screening on the incidence of late-stage cancer versus cancer mortality.

2. What was the objective of the study?

The study aimed to compare mortality from cancer with the incidence of late-stage cancer, as end-points in randomized controlled trials of cancer screening.

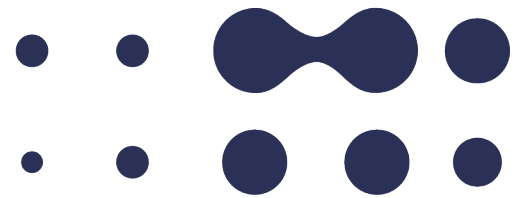
3. What were the results?

The results showed that the degree to which the incidence of late-stage cancer can serve as a suitable alternative end-point to cancer mortality depends on the type of cancer considered. For lung and ovarian cancers, there was a close relationship between the two metrics, and the degrees to which screening reduced cancer mortality and late-stage cancer were similar. For breast cancer, despite a close relationship, the amount by which breast cancer mortality was reduced was much smaller than the amount by which the incidence of late-stage breast cancer was reduced. For colorectal and prostate cancers, the relationship between the two metrics appeared to be weak.

4. Why are these results important?

These results are important because there is interest in using alternative end-points that could allow randomized

¹ 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>.



trials of cancer screening to be completed more quickly. In particular, newly developed blood tests called “multi-cancer” tests aim to detect multiple types of cancer via the same test. It is important to demonstrate that these tests can reduce cancer mortality. This study suggests that it is not possible to use the effects of these tests on late-stage cancer to draw conclusions about their effects on cancer mortality, because the tests combine multiple different types of cancer and the relationship between these two metrics may be different for each cancer type.

5. Why is the choice of metric for screening benefit important?

The choice of metric for screening benefit is important because cancer screening can potentially cause multiple types of harm, and it should be ensured that harms are outweighed by a sufficiently important benefit. In terms of potential harms, some people will have false-positive results, which can lead to unnecessary invasive procedures and psychological stress. Other people may have false-negative results, which may incorrectly reassure them that they do not have cancer, when in fact they should seek care for potential symptoms. There can also be overdiagnosis and overtreatment, meaning that cancers that were not destined to cause symptoms or death are diagnosed and treated, although it would have been better if they had been left undetected.

6. Why would detecting cancer at an early stage instead of a late stage not always lead to avoiding cancer death?

Although it might seem counterintuitive, there are different scenarios in which detecting a cancer at an early stage instead of a late stage might not avoid cancer death. One scenario is for a cancer that is fatal, at the same time, no matter when it is detected. This can happen for cancers for which the available treatments are not very effective at any stage. Another scenario is for a cancer that can be successfully treated regardless of whether it is detected at an early or late stage. In this scenario, earlier detection might facilitate easier or less invasive treatment, but the person does not die from this cancer even if it is detected at a late stage.

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The International Agency for Research on Cancer (IARC) is part of the World Health Organization. Its mission is to coordinate and conduct research on the causes of human cancer, the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. If you wish your name to be removed from our press release emailing list, please write to com@iarc.who.int.