International Agency for Research on Cancer

World Health Organization

10 November 2021

IARC Handbooks of Cancer Prevention Volume 18: Evaluation of cervical cancer screening methods

Questions and Answers (Q&A)

A Working Group of international experts was convened by the International Agency for Research on Cancer (IARC) to review and assess all available studies of current methods for cervical cancer screening in terms of their effect on cervical cancer incidence and mortality.

A summary of the findings of Volume 18 of the *IARC Handbooks of Cancer Prevention* series was published today as a Special Report in *The New England Journal of Medicine*.[1]

What is the *IARC Handbooks* series?

The *IARC Handbooks of Cancer Prevention* are a series published by IARC. They provide definitive evaluations about which measures can prevent cancer or can detect cancer at an early stage. To do so, IARC convenes a Working Group of international interdisciplinary experts, who collect all the relevant studies published to date, review the data, and determine how sure we can be that such a measure can reduce the risk of cancer.

Cervical cancer screening was first evaluated in 2005, in Volume 10 of the *IARC Handbooks* series. Therefore, an update of this volume was very timely, to evaluate the methods for cervical cancer screening that are currently in use, such as HPV nucleic acid testing, conventional cytology, and liquid-based cytology, and to compare their effectiveness. The results enabled a determination of which methods are best suited for reducing the cervical cancer burden worldwide in the most rapid and most effective way.

What are the key results from this evaluation?

The Working Group concluded that HPV nucleic acid testing, conventional cytology, and liquid-based cytology are all established to reduce cervical cancer incidence and mortality. Visual inspection with acetic acid (VIA) is established to reduce cervical cancer mortality, whereas the evidence for a reduction in cervical cancer incidence is weaker. When HPV DNA testing was compared with cytology (conventional or liquid-based), with VIA, or with co-testing, HPV DNA testing showed higher effectiveness than any of these methods, with the incremental benefits outweighing the additional harms.

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[1] Bouvard V, Wentzensen N, Mackie A, Berkhof J, Brotherton J, Giorgi Rossi P, et al. The IARC perspective on cervical cancer screening. *N Engl J Med*. Published online 10 November 2021. https://doi.org/10.1056/NEJMsr2030640

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What is new in terms of the evaluation and in terms of the results in this new volume of the *IARC Handbooks*?

First, this *Handbook* used the evaluation scheme developed in 2019 with the new *Handbooks* Preamble.

Second, the evaluations were based on studies conducted in populations where screening takes place, that is, in real-life situations. Previous evaluations were based mostly on trials and test accuracy studies.

Third, the Working Group made an assessment of the comparative effectiveness of those screening methods for which the effectiveness is established (HPV DNA testing, cytology, and VIA).

Finally, the Working Group for this *Handbook* reviewed and evaluated the impact of cytology based on Romanowsky–Giemsa staining, and concluded that the method did not show an effect on cervical cancer incidence or mortality in those countries where the method is used.

What methodology was used to obtain these results?

The *IARC Handbooks* evaluations follow a rigorous and transparent process:

Step 1: Identify which interventions to review and evaluate

Step 2: Identify the relevant literature

Step 3: Screen and perform a preliminary selection of the studies

Step 4: Extract the data and write study summaries

Step 5: Evaluate the quality of each study

Step 6: Peer-review by Working Group members and IARC scientists

Step 7: Synthesize the results and the quality of the studies

Step 8: Interpret the results and evaluate the strength of the evidence

The Working Group reviews and assesses several hundreds of original studies conducted in a large number of countries around the world. The scientific literature is reviewed according to strict criteria as defined in the *Handbooks* Preamble.

How does the *Handbooks* classification system work?

To evaluate interventions of secondary prevention (such as screening methods), the *Handbooks* review studies on cancer incidence or mortality, studies on intermediate outcomes (such as cervical precancerous lesions), and test accuracy studies. On the basis of the criteria defined in the *Handbooks* Preamble, the screening method is classified into Group A, B, C, or D, depending on how effective it is at reducing the incidence of cancer of the target organ or reducing mortality from cancer of the target organ.

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When will the *IARC Handbooks of Cancer Prevention* Volume 18 on Cervical Cancer Screening be available?

Volume 18 is scheduled for publication in the fourth quarter of 2021.

Why is this evaluation important?

Cervical cancer is somewhat unique because it is one of the only cancer types that can be almost fully prevented. The vast majority of cervical cancer cases (99%) are linked to infection with high-risk human papillomavirus (HPV), an extremely common virus that is transmitted through sexual contact.

Effective interventions to prevent cervical cancer, as primary prevention through HPV vaccination and as secondary prevention through screening, are available and have been implemented in many countries. Despite this, in 2020 more than 600 000 new cases of cervical cancer were diagnosed and there were more than 340 000 deaths from this disease worldwide.

This double burden of high incidence and high mortality (>90% for both) occurs mainly in low- and middle-income countries. The preventable nature of cervical cancer and its disproportionate impact on low- and middle-income countries with limited health system resources prompted the Director-General of the World Health Organization (WHO) to issue, in May 2018, a global call for action to eliminate cervical cancer as a public health problem.

In August 2020, the World Health Assembly adopted the WHO Global Strategy to accelerate the elimination of cervical cancer as a public health problem. The *IARC Handbooks* programme responded promptly to the call for action towards elimination of cervical cancer by establishing a close collaboration with the WHO group responsible for updating the recommendations.

How have these results helped advance the WHO Cervical Cancer Elimination Initiative?

Several IARC research teams are involved in the WHO Cervical Cancer Elimination Initiative, and among those, the *IARC Handbooks of Cancer Prevention* programme has played an important role.

In 2018, WHO started the process of updating the recommendations on cervical cancer screening and treatment. *IARC Handbooks* Volume 18 was developed in close collaboration with WHO for the update of the recommendations, to ensure sharing of data and results. The review and assessment conducted by the *IARC Handbooks* of the studies on the comparative effectiveness of the screening methods formed the basis for the updated WHO recommendations.

The *WHO Guideline for Screening and Treatment of Cervical Pre-cancer Lesions for Cervical Cancer Prevention* was launched on 6 July 2021.

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What are the targets set by the WHO Global Strategy for cervical cancer elimination?

To eliminate cervical cancer, all countries must reach and maintain an incidence rate of below 4 per 100 000 women per year. Achieving that goal rests on three key pillars and their corresponding targets:

- Vaccination: 90% of girls fully vaccinated with the HPV vaccine by age 15 years;
- Screening: 70% of women screened using a high-performance test by age 35 years, and again by age 45 years;
- Treatment: 90% of women with cervical precancer treated, and 90% of women with invasive cervical cancer managed.

Each country should meet the 90–70–90 targets by 2030 to be on the path towards the elimination of cervical cancer within this century.

For more information, please contact

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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 and 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.fr.