

CERVICAL CANCER: ITS CONTROL AND EVENTUAL ELIMINATION IN LOW- AND MIDDLE-INCOME COUNTRIES. Douglas R. Lowy, Acting Director, National Cancer Institute, USA

The mission of National Cancer Institute (NCI) of the United States is to “lead, conduct, and support cancer research across the nation to advance scientific knowledge and help all people live longer, healthier lives.” NCI supports a wide range of cancer research, from the most basic to the most applied.

In this morning’s presentation, I will focus on the potential to control and eventually eliminate cervical cancer in low- and middle-income countries (LMICs). There have been many research advances in recent years in the ability to prevent, diagnose, and treat cervical cancer, but these advances are currently being applied unevenly. High-income countries (HICs) of the world have the resources to take advantage of these advances, while LMICs, whose resources are far more constrained, have thus far adopted them to a limited degree. The IAEA can play a critical role in overcoming this serious cancer health disparity because of the key role of radiotherapy in the treatment and cure of cervical cancer. Early stage cervical cancer can have an excellent prognosis, if treated appropriately. Radiotherapy is a key component of this treatment, as I will discuss in a few minutes.

Before going further, I will provide some background and context to the problem of cervical cancer in LMICs. It is estimated that worldwide in 2018 there were 570,000 cases of cervical cancer and 310,000 deaths, and close to 90% of these deaths occur in LMICs. Unless the current approach to cervical cancer changes, it is projected that its incidence and mortality will increase by about 20% every 10 years; the vast majority of this increase will affect women in LMICs.

Despite these demoralizing statistics and projections, there are multiple effective interventions against cervical cancer. They include primary prevention by HPV vaccination, secondary prevention by cervical cancer screening and treatment of cervical precancer, treatment of invasive cervical cancer, and palliation of advanced cervical cancer. Up to now, none of these interventions have been widely implemented in LMICs, but greater commitment to overcoming the problem of cervical cancer together with ongoing research could dramatically improve this situation.

Let’s consider each of these interventions in the context of LMICs. It is now known that virtually all cases of cervical cancer are attributable to chronic infection by the human papillomavirus (HPV), and population-wide approaches to primary and secondary prevention of cervical cancer depend on this critical observation. Primary prevention by HPV vaccination will have the greatest impact on reducing the incidence and mortality of cervical cancer in the long term. However, the vaccine only prevents new infections, and it usually takes 20-30 years for the infection to result in cancer. This means that the impact of the vaccine on cancer will not be seen until many years after beginning a vaccination program. Although it is important to begin widespread vaccination in LMICs now or in the near future, the potential to save lives and improve quality of life in a shorter time frame will depend on cervical cancer screening, treatment of invasive cancer, and palliation of advanced cancer.

High quality cervical cancer screening can have an impact on incidence and mortality more rapidly than vaccination because the interval between detection of cervical precancer, which is the main goal of screening, and development of cervical cancer is many years shorter than the interval following vaccination. Screen-detected precancer can usually be treated effectively by local ablative therapy. In the United States (US), thanks to population-wide cervical cancer screening, the incidence of cervical cancer in the US is about one-fifth what it was in the 1950's. By contrast, the high rates in LMICs have not decreased because population-wide screening is relatively complicated and expensive to implement.

For LMICs, the main barrier to widespread primary and secondary prevention is that current standard of care is not yet sufficiently cost-effective. However, current research, if it is successful, has the potential to change standard of care and make both interventions substantially more cost-effective. Several coordinated HPV vaccine trials are testing the hypothesis that a single HPV vaccine dose may be sufficient to induce strong protection. The decreased cost and simplified logistics of a single dose could be transformative for vaccine deployment in LMICs.

Cervical cancer screening research studies are testing potentially scalable HPV detection technology that is less expensive and can provide results more rapidly than current technology, as well as an artificial intelligence (AI) approach to a low-tech procedure, visualization of the cervix with acetic acid (VIA). The experimental AI algorithm, which is called automated visual evaluation (AVE), is simple enough that it can be stored in a smart phone, which would first take a photo of the cervix and then quickly analyze the photo to determine if the cervix has a lesion that should be treated.

Most lesions that are detected by screening will be precancers, which can be treated locally. However, some of the screened women will turn out to have invasive cervical cancer, which requires more extensive treatment. In screened women, invasive cancer is more likely to be diagnosed in post-menopausal women than in pre-menopausal women. The importance of screening both pre- and post-menopausal women provides a strong rationale for having sufficient infrastructure for the effective treatment of cancers detected by screening. In principle, early stage cancer is highly treatable, and many such cases can be cured. In the US, for example, the 5-year survival rate for women who present with stage I cervical cancer is greater than 90%, while about two-thirds of women with stage II disease live at least 5 years after their diagnosis. Even with stage III disease, one-half of the women in this category will live at least 5 years. It is only women who present with stage IV disease who have a poor prognosis, as only about one-fifth of them will live at least 5 years.

As might be expected, the outlook is much worse for most women in LMICs who present with cervical cancer. Depending on the LMIC, between one-half and two-thirds of the women who develop cervical cancer will succumb to their tumor. By contrast, fewer than one-third of women in the US will die from their cancer. This large disparity is mainly attributable to two factors: 1) women in the US tend to be diagnosed with earlier stage cancer, thanks to widespread screening in the US, and 2) better treatment is available in the US.

There are three main modalities for treatment of early stage disease: surgery, radiation and chemotherapy. The precise combination of these interventions will depend on the stage of disease and their availability; the best results are usually seen when all three approaches are combined. Investment that enables greater access to these three treatment approaches can improve the outlook for women with cervical cancer. Palliation of advanced disease does not need to be expensive and can have a major impact on quality of life. However, Most LMICs do not offer pain management, such as opioid treatment. The benefits of increasing the availability of this modality can extend far beyond cervical cancer to virtually all serious chronic disease where pain is a prominent manifestation. In addition, strengthening the infrastructure for surgery, radiotherapy, chemotherapy, and palliation can have positive impact on the treatment of other diseases.

I hope it is clear from what I have said that there are enormous opportunities to reduce the burden of cervical cancer in LMICs, but that to do so requires more research, greater commitment, and increased investment.