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Addressing the Global Challenge: Strategies for Cervical Prevention and Early Detection within WHO's 90-70-90 Framework

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ABSTRACT

Cervical cancer represents a substantial global health issue, standing as the third most prevalent cancer globally and the principal cause of cancer-associated mortality in women, with an uneven burden shouldered by less developed countries. Despite being the most preventable malignancy, with nearly all cases attributed to HPV infection, which has a lifetime cumulative risk of 80% through sexual transmission, cervical cancer remains a pressing issue. National cervical cytology screening programs have been implemented to identify cervical abnormalities, lesions, and early malignancies in eligible women. However, the utilization of screening techniques is declining, and due to resource constraints, screening schemes have not been adopted in less-developed economies. Several nations have embraced alternative screening techniques, such as Visual Inspection with Acetic Acid (VIA), which have shown impacts on mortality and morbidity rates. With the rising accessibility of efficacious HPV screening and self-testing, there will be a necessity to reconfigure existing cervical screening programs. Furthermore, preventative HPV vaccination is an integral part of the World Health Organization's (WHO) Global Strategy to Expedite the Eradication of Cervical Cancer as a Public Health Issue, necessitating the restructuring of vaccination endeavors. This review article evaluates potential techniques for detecting precancerous lesions within the context of the WHO's 90-70-90 global policy for cervical cancer prevention and early diagnosis. The incidence and mortality rates are examined, highlighting the effectiveness of cervical cancer prevention efforts.

Keywords: Cervical Cancer, Prevention Strategies, Global Health Challenge, HPV Vaccination, Cervical Cancer Screening, WHO 90-70-90 Strategy.

INTRODUCTION

Cancer, a relentless and formidable adversary, continues to exact a staggering toll on global health, accounting for nearly 10 million deaths in 2020 alone [1]. Although this number is expected to increase worldwide, the rise is likely to occur mainly in low-middle-income countries (LMICs) as they face challenges in tackling the cancer burden [2]. This multifaceted group of diseases is characterized by uncontrolled cellular proliferation and the potential for metastatic spread, and represents a significant burden on individuals, families, and healthcare systems worldwide [3]. Cancers can arise from various tissue types, including carcinomas (originating from epithelial cells, such as lung [4] breast [5], and prostate cancers [6]), sarcomas (from connective tissues), leukemias (from blood-forming cells), lymphomas (from lymphatic system cells), and others. Among the diverse array of malignancies, cervical cancer remains a formidable global health challenge, cervical cancer is the fourth most common female cancer after breast, and lung cancer [7]. Despite being one of the most preventable malignancies, nearly all cases are attributable to chronic infection with high-risk human papillomavirus (hrHPV) types [8]. The principal causative agent, HPV, is the most widespread sexually transmitted viral infection, with a lifetime cumulative risk of 80% via sexual transmission. Although the majority of HPV infections are temporary and spontaneously eliminated by the immune system, enduring infection with high-risk HPV types, particularly HPV 16 and 18, accounts for approximately 70% of cervical cancer cases globally[9]. These specific types of oncogenic HPV can prompt malignant changes in the cervical cells they infect. This process gradually forms precancerous lesions and, if not identified and addressed, could advance to invasive cervical cancer [10]. In high-income countries (HICs), the proportion of women with cervical cancer who succumb to the disease is typically around 30%, owing to the widespread implementation of effective screening programs and access to timely treatment. However, in many LMICs, this proportion can exceed 60%, more than twice the rate observed in HICs [11]. The significant variation is mainly attributed to limited access to preventive measures such as HPV vaccination and effective cervical cancer screening programs, as well as challenges in delivering prompt and appropriate treatment for precancerous lesions and invasive cancer [12]. Acknowledging the imperative of tackling this preventable

illness, the WHO initiated a thorough Global Strategy in 2020 aimed at expediting the eradication of cervical cancer as a public health issue. This strategy, supported by robust scientific evidence and extensive global consultations, outlines ambitious yet achievable targets, collectively known as the 90-70-90 targets [13]. These objectives strive to attain 90% HPV vaccination coverage for girls by the age of 15, 70% screening coverage for women aged 35 to 45 using high-performance HPV tests, and 90% treatment for precancerous lesions and invasive cervical cancer by the year 2030[14]. Importantly, the WHO's global strategy has been projected to be the most cost-effective approach for cervical cancer control in 95 countries analyzed, promising substantial economic and societal benefits beyond the immediate health gains. By alleviating the immense financial burden imposed by cervical cancer treatment and associated productivity losses, this strategy holds the potential to catalyze broader socioeconomic development, particularly in resource-constrained settings [15]. Despite the compelling evidence and the availability of effective preventive tools, significant challenges persist in the global fight against cervical cancer. Barriers to HPV vaccination uptake, including low acceptability, high costs, inadequate program infrastructure, and the growing anti-vaccine movement, continue to impede progress in primary prevention efforts. This comprehensive review critically evaluates the current landscape of cervical cancer prevention strategies, encompassing primary prevention through HPV vaccination, secondary prevention through various screening techniques, and tertiary prevention through early diagnosis and management of precancerous lesions and invasive cancer. By combining the latest scientific evidence and global trends, this review aims to inform evidence-based policies, identify best practices, and highlight emerging innovations that hold promise in accelerating the global efforts towards eliminating cervical cancer as a public health problem.

ETIOLOGY AND PATHOPHYSIOLOGY

Human Papillomavirus: The Primary Causative Agent

HPV has been firmly established as the primary etiological agent in the development of cervical cancer. HPV is a compact, non-enveloped, double-stranded DNA virus categorized within the Papillomaviridae family. It is a highly prevalent sexually transmitted infection, with a lifetime cumulative risk of acquisition estimated to be around 80% through sexual transmission. To date, over 200 HPV genotypes have been identified, with approximately 14 classified as high-risk or oncogenic types due to their strong association with cervical cancer development [16]. Among these high-risk types, HPV 16 and HPV 18 are the most commonly implicated, accounting for approximately 70% of cervical cancer cases worldwide. The genetic material of high-risk HPV types contains two primary oncoproteins, namely E6 and E7, which are crucial in the development of cervical cancer (Figure 1). These viral oncoproteins possess the ability to interact with and inactivate key cellular tumor suppressor proteins, primarily p53 and pRb, respectively [17]. The E6 oncoprotein binds to and induces the degradation of p53, a critical regulator of cell cycle arrest and apoptosis. By abrogating p53 function, HPV E6 promotes the survival and proliferation of infected cells, even in the presence of genetic alterations that would typically trigger apoptosis[18]. Meanwhile, the E7 oncoprotein binds to and inactivates pRb (retinoblastoma protein), a key regulator of the cell cycle. By disrupting pRb function, E7 promotes the uncontrolled entry of cells into the S-phase of the cell cycle, leading to deregulated cellular proliferation. Together, the concerted actions of E6 and E7 oncoproteins disrupt critical cellular pathways responsible for regulating cell cycle progression, proliferation, and apoptosis, creating an environment conducive to the aggregation of genetic and epigenetic alterations that can ultimately lead to malignant transformation [19, 20]. In addition to E6 and E7, the HPV genome encodes several other proteins that contribute to the viral life cycle and pathogenesis. For example, the E5 protein can enhance cellular proliferation and immune evasion, while the E1 and E2 proteins are involved in viral DNA replication and transcriptional regulation, respectively. The oncogenic potential of high-risk HPV types is further amplified by ability of the virus to integrate its genetic material into the host cell's genome during persistent infection. This integration event frequently disrupts the viral E2 gene, leading to the uncontrolled expression of E6 and E7 oncoproteins and promoting cellular transformation [21, 22].

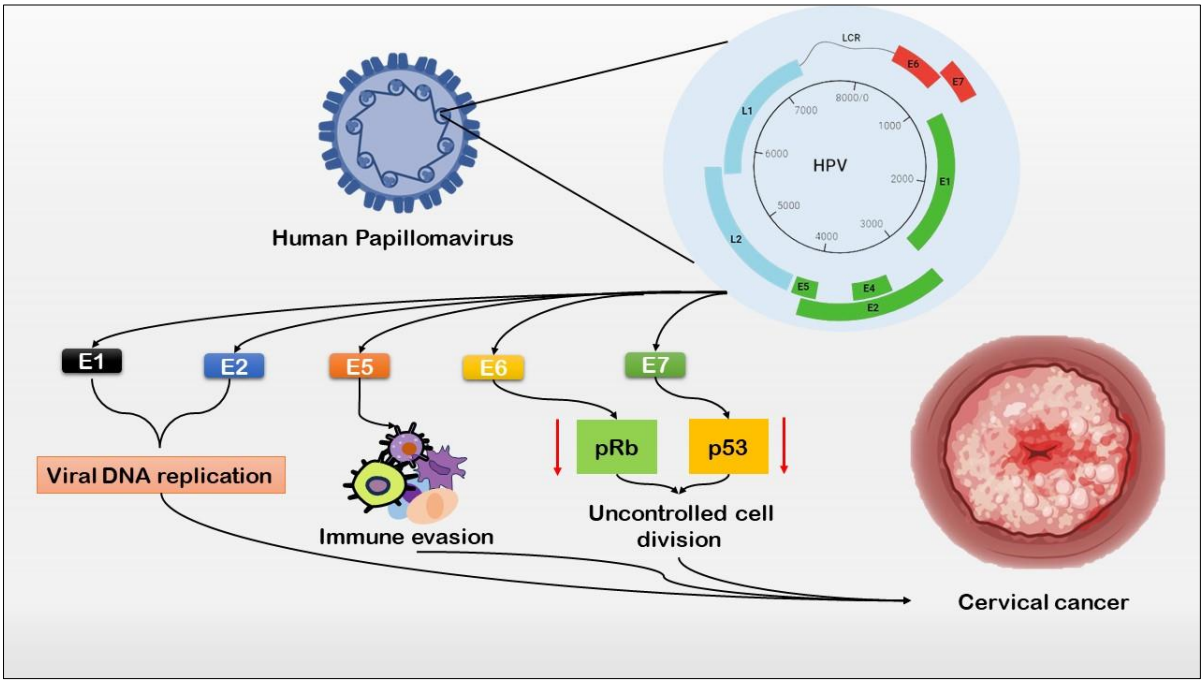

Figure 1: Mechanisms of High-Risk HPV-Induced Cervical Carcinogenesis: High-risk HPV types encode two main oncoproteins, E6 and E7, which drive cervical cancer development. E6 degrades p53, disrupting cell cycle regulation and apoptosis, while E7 inactivates pRb, leading to uncontrolled cell proliferation. Additional HPV proteins, such as E5, E1, and E2, contribute to viral pathogenesis. HPV integration into the host genome, often disrupting the E2 gene, further enhances oncogenic potential, promoting cellular transformation

Immune Dysfunction and Co-Factors

Although persistent infection with high-risk HPV types is an essential condition for the development of cervical cancer, several co-factors can adjust an individual's risk and impact the advancement of the disease. Immune dysfunction, either acquired or inherited, plays a role. Individuals with compromised immune function, such as those living with HIV/AIDS or receiving immunosuppressive therapy, have a susceptibility to persistent HPV infection and subsequent cervical cancer development. This heightened susceptibility is attributed to the impaired ability of the immune system to effectively mount an adequate response against the viral infection, thereby allowing for prolonged viral persistence and the accumulation of genetic alterations in the infected cervical epithelial cells [23]. At a cellular level, the eradication of HPV infections depends significantly on the synchronized efforts of both the innate and adaptive immune systems. The innate immune system, comprising components such as pattern recognition receptors (PRRs), cytokines, and natural killer (NK) cells, provides the first line of defense against HPV infection. PRRs, such as Toll-like receptors (TLRs) and RIG-I-like receptors (RLRs), recognize viral nucleic acids and trigger signaling cascades that lead to the production of type I interferons (IFNs) and pro-inflammatory cytokines, which can inhibit viral replication and promote the elimination of infected cells[24][25]. The adaptive immune response, facilitated by T cells and B cells, holds a vital significance in the subsequent clearance of persistent HPV infections. Cytotoxic CD8+ T cells can directly recognize and eliminate HPV-infected cells through the release of cytolytic granules and the induction of apoptosis[26]. Meanwhile, CD4+ T helper cells orchestrate the adaptive immune response by providing co-stimulatory signals and secreting cytokines that support the expansion and differentiation of cytotoxic T cells and antibody-producing B cells. Impairments in any of these immune components can compromise the host's ability to effectively control and clear HPV infections, thereby increasing the risk of persistent infection and subsequent cervical cancer development [27].

Role of the Vaginal Microbiome

Emerging evidence suggests that the composition and diversity of the vaginal microbiome, the complex community of microorganisms residing in the vaginal environment, has a pivotal role in modulating the risk and onset of cervical cancer. The vaginal microbiome is a dynamic ecosystem comprised of diverse bacterial species, with the most abundant genera being *Lactobacillus*, *Gardnerella*, *Atopobium*, *Prevotella*, and *Sneathia*, among others [28]. In a healthy vaginal environment, *Lactobacillus* species, such as *L. crispatus*, *L. gasseri*, and *L. jensenii*, typically dominate the microbiome, maintaining an acidic pH through the production of lactic acid. This acidic environment helps to prevent the overgrowth of potentially pathogenic microorganisms and promotes a protective mucosal barrier[29]. However, disturbances in the vaginal microbiome, known as dysbiosis, can lead to an imbalance in the microbial community, creating conditions that may facilitate HPV persistence and cervical cancer development [30]. Certain microbial species and their metabolites can interact with cervical epithelial cells and immune cells, influencing the production of cytokines, chemokines, and other immunomodulatory factors. For instance, a study has demonstrated that *Lactobacillus* species can stimulate the generation of anti-inflammatory cytokines like IL-10, while also augmenting the function of natural killer (NK) cells and cytotoxic T cells, which are essential for clearing HPV [31]. The vaginal microbiome contains a diverse array of metabolites, such as short-chain fatty acids (SCFAs), antimicrobial peptides, and enzymes. These metabolites can directly influence cervical epithelial cell function, modulate local inflammation, and potentially impact HPV persistence and cancer development [32, 33]. Certain bacterial species can adhere to and interact with cervical epithelial cells, influencing cellular signaling pathways, gene expression patterns, and susceptibility to HPV infection and oncogenic transformation. The vaginal microbiome plays a role in regulating oxidative stress levels in the cervical environment. Dysbiosis and the overgrowth of certain bacterial species can lead to increased oxidative stress, which can contribute to DNA damage, genomic instability, and cervical carcinogenesis[34]. Studies have revealed associations between specific vaginal microbiome compositions and the risk of HPV persistence, cervical intraepithelial neoplasia (CIN), and invasive cervical cancer [35-37]. For instance, a diverse vaginal microbiome dominated by *Lactobacillus* species is linked to a lower risk of HPV persistence and cervical lesions, while dysbiotic states characterized by the overgrowth of anaerobic bacteria, such as *Gardnerella*, *Atopobium*, and *Sneathia*, have been associated with an increased risk of cervical cancer development [38].

PREVENTIVE STRATEGIES

Preventive measures encompass public awareness, access to information, and timely vaccination. HPV vaccines, targeting high-risk types, have demonstrated efficacy in preventing HPV infection and cervical cancer. Early detection through screening, recommended from age 30 (25 for women living with HIV), coupled with prompt treatment, is crucial. As of 2023, six HPV vaccines globally protect against high-risk types, with priority vaccination for girls aged 9–14. Other preventive measures include maintaining a non-smoking status, using condoms, and voluntary male circumcision [39].

Primary prevention: HPV vaccination

From 2006, when the initial HPV vaccine was authorized, to 2017, more than 100 million adolescent girls worldwide received at least one dose of the HPV vaccine. Furthermore, 95% of these vaccinations took place in high-income countries. However, the accessibility of HPV vaccination has improved over time. By 2019, over 65% of globally vaccinated girls were from LMICs, as reported by the WHO Department of IVB database [40]. Currently, less than 18% of low-income and fewer than 30% of lower-middle-income countries have included the HPV vaccine in their public immunization schedules, while over 85% of high-income countries have done so [41]. Similar patterns are evident in the implementation of cervical cancer screening programs across different income levels. Presently, there are six authorized preventive HPV vaccines. They are all designed to be administered ideally before the onset of sexual activity, thus before exposure to HPV [42]. These vaccines are produced using recombinant DNA and cell-culture technology from the purified L1 structural protein, which self-assembles into HPV type-specific empty shells known as virus-like particles (VLPs) [43]. Notably, HPV vaccines do not contain live biological materials or viral DNA, making them non-infectious. They employ different expression systems, contain adjuvants, and are free from antibiotics or preservative agents. All HPV vaccines include VLPs targeting high-risk HPV types 16 and 18, with the nonavalent vaccine additionally covering types 31, 33, 45, 52, and 58. The quadrivalent and nonavalent vaccines also protect against anogenital warts caused by HPV types 6 and 11 [44, 45]. Indicated for females aged 9 years or older and authorized for use up to 26 or 45 years of age, some HPV vaccines are also approved for males. They are intended for the prevention of cervical premalignant lesions and cancers attributed to high-risk HPV types, which vary by vaccine product. Additionally, specific vaccines have indications against other HPV-related conditions according to their product labels [46]. HPV vaccines are available in prefilled syringes or single or 2-dose vials. To ensure quality, safety, and efficacy, WHO has developed guidelines for manufacturers and regulators, including standards for nucleic acid-based assays and type-specific standards for anti-HPV type16/18 serum. As of now, 125 countries (64%) have introduced the HPV vaccine into their public immunization programs for girls, and 47 countries (24%) have also done so for boys [47].

Optimal Vaccination Schedules for Bivalent and Quadrivalent HPV Vaccines Across Age Groups

Bivalent HPV vaccines, such as Cervarix, are advised for individuals aged 9 to 14 years, delivered as a 2-dose regimen with a gap of 5 to 13 months between doses. For recipients aged 15 years or older at the

time of the initial dose, a 3-dose regimen is recommended, administered at 0, 1 to 2 months, and 5 to 12 months apart [48]. In a similar vein, Cecolin is prescribed for girls aged 9 to 14 years as a 2-dose regimen with a 6-month interval, while a 3-dose regimen is suggested from age 15, with doses administered at 0, 1 to 2 months, and 5 to 8 months apart [49]. Walrinvax adheres to a comparable protocol, initially as a 2-dose regimen for girls aged 9 to 14 years with intervals of 6 months, transitioning to a 3-dose regimen from age 15, with doses administered at 0, 2 to 3 months, and 6 to 7 months apart [50]. Quadrivalent HPV vaccines, such as Gardasil, are appropriate for individuals aged 9 to 13 years, delivered in a 2-dose regimen with a 6-month interval, shifting to a 3-dose regimen from age 14, with doses administered at 0, 1 to 2 months, and 4 to 6 months apart [51]. Similarly, Cervavax is advised for individuals aged 9 to 14 years as a 2-dose regimen with a 6-month interval, while from age 15, a 3-dose regimen is recommended, with doses administered at 0, 2, and 6 months apart [52]. For the nonavalent HPV vaccine, Gardasil9, individuals aged 9 to 14 years are advised to receive a 2-dose regimen with doses spaced 5 to 13 months apart. From age 15, a 3-dose regimen is recommended, with doses administered at 0, 1 to 2 months, and 4 to 6 months apart [53]. These vaccination schedules are designed to optimize immunization against HPV across different age groups, aiming to maximize efficacy and coverage in the prevention of HPV-related diseases.

Table 1: Recommended HPV Vaccine Regimens and Dosing Intervals for Different Age Groups.

Vaccine	Age Group	Dose Regimen	Dose 1 Interval	Dose 2 Interval
Cervarix	9-14 years	2 doses	5-13 months	-
	15+ years	3 doses	0, 1-2 months	5-12 months
Cecolin	9-14 years	2 doses	6 months	-
	15+ years	3 doses	0, 1-2 months	5-8 months
Walrinvax	9-14 years	2 doses	6 months	-
	15+ years	3 doses	0, 2-3 months	6-7 months
Gardasil	9-13 years	2 doses	6 months	-
	14+ years	3 doses	0, 1-2 months	4-6 months
Cervavax	9-14 years	2 doses	6 months	-
	15+ years	3 doses	0, 2 months	6 months
Gardasil9	9-14 years	2 doses	5-13 months	-
	15+ years	3 doses	0, 1-2 months	4-6 months

Single dosage schedule

Findings from immunogenicity trials, post-hoc analyses of efficacy trials, and post-licensure observational studies among women suggest that administering just one dose of the HPV vaccine can prompt a robust response, offering similar protection to multiple doses against both initial and persistent HPV infection. This evidence includes findings from a rigorous RCT80 involving 2250 sexually active women aged 15 to 20 years who were randomly assigned to receive either the bivalent (Cervarix) or nonavalent (Gardasil-9) vaccine or to a control group [54]. At 18 months post-vaccination, the efficacy of a single dose of the HPV vaccine against incident persistent high-risk (HPV16/18) infection was 97.5 percent (95%CI 82 – 100) for the nonavalent vaccine and 97.5 percent (95%CI 82 – 100) for the bivalent vaccine [55]. In a randomized open-label trial81 (DoRIS), 930 women aged 9 to 14 years were randomized to receive 1, 2, or 3 doses of the bivalent (Cervarix) or nonavalent (Gardasil-9) vaccine. At 24 months post-vaccination, over 97.5% of participants in all dose groups for both vaccines were seropositive [56]. Immunobridging demonstrated that a single dose of HPV16/18 elicited antibody responses that were not inferior to those in studies where single-dose efficacy was observed [57]. Meeting the ambitious global cervical cancer control targets set by the WHO for 2030 demands innovative and comprehensive approaches to identify and reach women at high risk [58]. A significant advancement in cervical cancer screening is the adoption of HPV-based self-sampling (SS) strategies. Over the past decade, these strategies have proven to be cost-effective and have achieved success in various settings, overcoming barriers and offering a range of benefits. HPV-based self-sampling, conducted through vaginal samples, provides a practical and accessible screening system. The approach not only reduces costs but also enhances adaptability by allowing sample collection in both healthcare settings and the privacy of one's home [59]. It eliminates the need for uncomfortable pelvic examinations and face-to-face appointments with healthcare professionals, contributing to increased social and cultural acceptability. The success of self-sampling has been significantly stimulated, especially during the COVID-19 pandemic. Challenges such as social distancing, initial lockdowns, and disruptions in healthcare services prompted a shift from clinician-based screens to self-collection strategies. Despite the challenges faced during the pandemic, self-collection emerged as a viable and flexible option. While encouraging data was collected regarding targeted self-sampling bias, sample handling, transport, and storage, challenges remain. Suboptimal rates of clinical follow-up post-SS screen and concerns about overtreatment necessitate effective strategies. Trained health professionals, knowledgeable about HPV biology and operational algorithms, play a crucial role in ensuring proper adherence to follow-up testing and management following positive self-sampling results.

WHO strategy (90-70-90)

WHO has devised a comprehensive strategy called the "90-70-90" targets to combat the global impact of cervical cancer. These objectives aim to achieve the following benchmarks: ensuring that 90% of girls are fully vaccinated against HPV by age 15, screening 70% of women for cervical cancer at least once between ages 35 and 45, and ensuring that 90% of women diagnosed with cervical disease receive appropriate treatment and care [60]. Cervical cancer ranks as the fourth most prevalent cancer among women worldwide, with approximately 604,000 new cases and 342,000 deaths reported in 2020. Nearly 90% of cervical cancer cases stem from persistent infection with high-risk strains of HPV, notably HPV-16 and HPV-18 [61]. Since 2006, effective HPV vaccines have been accessible, protecting the two most carcinogenic HPV types responsible for roughly 70% of cervical cancer cases. Routine screening, whether through Pap smears or HPV testing, can detect precancerous lesions, facilitating early intervention and the prevention of cervical cancer [62]. In high-income nations with robust screening programs, cervical cancer incidence and mortality rates have plummeted by as much as

80% in recent decades. However, in low- and middle-income countries, where access to screening and treatment services is limited, cervical cancer remains a significant public health challenge, accounting for about 90% of global cervical cancer deaths [63]. The WHO projects that meeting the 90-70-90 targets by 2030 could avert over 62 million cervical cancer cases and save 5.5 million lives by 2120 [64]. By adopting this holistic approach, encompassing HPV vaccination, cervical cancer screening, and prompt treatment, countries stand poised to significantly diminish the incidence and mortality associated with this preventable disease, especially in resource-constrained settings where the burden is most acute.

VACCINATION SCHEDULE

Two-dosage schedule.

The available academic literature supports a two-dose regimen for HPV vaccination in the primary target population, starting at the age of 9, and also for older groups eligible for HPV vaccination. It is recommended that there be a minimum gap of 6 months between the initial and subsequent doses. However, a 12-month dosing schedule has demonstrated increased Geometric Mean Titers (GMTs) and is recommended for both programmatic and efficacy reasons. Notably, there is no specified maximum interval between doses, and longer intervals, up to three or five times longer, may be advantageous from a programmatic standpoint [65].

Alternate single-dose schedule

Considering an unconventional off-label approach, a single-dose regimen is being considered for administration in both girls and boys aged 9 to 20 years. Current evidence suggests that a single dose shows comparable efficacy and duration of protection to a two-dose schedule, potentially offering programmatic benefits, increased effectiveness, cost-effectiveness, and improved coverage [66]. From a public health perspective, adopting a single-dose regimen presents significant potential advantages that outweigh the perceived risk of reduced protection if efficacy declines over time, although definitive evidence for this is currently lacking. Vaccinating adolescent girls remains the most effective long-term strategy for reducing the risk of cervical cancer development. Given the substantial long-term benefits associated with HPV vaccination, it is crucial to initiate and sustain this approach universally. The emergence of data indicating sustained protection following a single dose has prompted trials aimed at further validation, paving the way for optimized vaccination programs in the future [67].

SCREENING FOR CERVICAL CANCER

Applicable screen technologies for low–middle-income countries

Despite the significant burden of cervical cancer in LMICs, challenges in implementing and maintaining high-quality cytology screening programs have prompted the exploration and evaluation of alternative screening methods such as visual inspection with acetic acid (VIA) and hrHPV testing-based screening. The effectiveness and cost-effectiveness of VIA have been studied in two randomized controlled trials (RCTs), demonstrating a notable decrease in mortality linked to VIA-based cervical screening [68].

Testing for high-risk human papillomavirus in settings of low to middle-income countries

Although a prior randomized controlled trial (RCT) conducted in rural India showed a substantial reduction in advanced cervical cancers and associated deaths with a single round of screening using hrHPV testing compared to the current standard of opportunistic screening, the feasibility of hrHPV DNA testing as a screening method in low- and middle-income country (LMIC) settings is currently limited. This is primarily due to its high cost, requirement for multiple visits, and laboratory infrastructure, rendering it impractical for community-based screening initiatives [69].

Low-cost rapid-human papillomavirus testing

The advancement of cervical cancer control requires inventive and comprehensive strategies to identify and reach women at elevated risk. A significant development in cervical cancer screening is observed through the implementation of HPV-based SS methodologies. Over the past decade, these methodologies have proven to be cost-effective and successful in a variety of settings, overcoming obstacles and offering numerous benefits. HPV-based self-sampling, performed through vaginal samples, offers a practical and accessible screening technique, reducing costs and increasing flexibility for sample collection in healthcare environments and the privacy of one's home. This method eliminates the need for uncomfortable pelvic examinations and in-person consultations with healthcare professionals, thereby contributing to enhanced social and cultural acceptability [70].

FUTURE PROSPECTS

The battle against cervical cancer presents numerous opportunities and challenges. As we strive to meet the World Health Organization's ambitious targets for cervical cancer elimination, key areas for future progress emerge. Despite the existence of effective HPV vaccines, global coverage is insufficient, particularly in low- and middle-income countries. Efforts are needed to overcome barriers to vaccine access, affordability, and acceptability. The adoption of HPV-based screening strategies, including self-sampling techniques, promises to improve cervical cancer screening coverage and accessibility. However, challenges persist in ensuring robust infrastructure, quality control, and effective follow-up mechanisms. Prevention remains the cornerstone of cervical cancer control, but improving access to early diagnosis and effective treatment is equally vital. Rapid advancements in biotechnology, such as the development of next-generation HPV vaccines and novel diagnostic tools, hold the potential to further enhance prevention efforts. Robust data collection and surveillance systems are crucial for monitoring the impact of interventions, identifying gaps, and informing evidence-based decision-making. Achieving the goal of cervical cancer elimination requires concerted efforts from diverse stakeholders, sustained commitment, resource mobilization, and innovative approaches tailored to local contexts. With a concerted global effort, leveraging scientific advancements, and implementing evidence-based strategies, the elimination of cervical cancer as a public health problem is an achievable goal.

CONCLUSION

Cervical cancer continues to pose a substantial global health issue, with a disproportionate impact on women in low- and middle-income countries. Despite being one of the most preventable forms of cancer, the incidence of cervical cancer continues to escalate, highlighting the pressing need for comprehensive and coordinated action. This review has undertaken a critical assessment of the current state of cervical cancer prevention strategies, which include primary prevention through HPV vaccination, secondary prevention through various screening methods, and tertiary prevention via early detection and management of precancerous lesions and invasive cancer. The evidence presented underscores the significant progress made in the development of safe and effective HPV vaccines, the optimization of vaccination schedules, and the implementation of innovative screening approaches, such as HPV-based self-sampling. However, considerable challenges remain, including obstacles to vaccine access and uptake, inadequate screening coverage, and limited access to timely and effective treatment, particularly in resource-limited settings. Addressing these challenges will necessitate a multifaceted approach, involving robust surveillance systems, enhanced health infrastructure, and collaborative efforts across various sectors. The World Health Organization's ambitious 90-70-90 targets for the elimination of cervical cancer serve as a call to action for global

efforts, providing a clear roadmap for achieving high HPV vaccination coverage, widespread screening, and prompt treatment for cervical disease by 2030. Realizing these targets has the potential to prevent millions of cervical cancer cases and save numerous lives, particularly in low- and middle-income countries where the burden is greatest. Looking ahead, the utilization of emerging technologies, such as next-generation HPV vaccines, point-of-care diagnostic tools, and AI-assisted screening approaches, offers immense potential for enhancing the scope and effectiveness of cervical cancer control programs. Furthermore, the development of robust surveillance systems, the strengthening of health infrastructure, and the promotion of multisectoral collaboration will be crucial in driving sustainable progress. Ultimately, the eradication of cervical cancer as a public health issue is an attainable goal, but it will necessitate steadfast commitment, resource allocation, and innovative approaches tailored to local contexts. By employing evidence-based strategies, addressing social and cultural barriers, and fostering global solidarity, we can collectively make significant progress toward ensuring that no woman is left behind in this battle against a preventable disease.

Conflict of interest

The authors declare that they have no conflict of interest.

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