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Moving Beyond the Female-Only Paradigm: Arguments for Accelerating the Global Gender-Neutral Human Papillomavirus Vaccination

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Abstract

Since its adoption into public health programmes in 2006, the Human Papillomavirus (HPV) vaccine has proven its powerful effect in preventing cervical cancer, the most prevalent HPV-associated cancer. Nevertheless, a considerable burden of HPV infection is associated with non-cervical cancers and conditions that, due to a historically gendered narrative around HPV vaccination, are still partially neglected in most preventive agendas. Gender-neutral vaccination (GNV) programmes have been steadily adopted in an increasing number of countries, but global endorsement of this strategy is still being delayed, especially in low- and middle-income countries (LMICs). In this perspective paper, we advocate for an accelerated global shift from female-only to universal, gender-neutral HPV vaccination. This perspective analyses how a GNV strategy addresses the rising burden of non-cervical cancers, promotes gender justice for vulnerabilised groups, and strengthens population-wide herd immunity amidst shifting global funding and healthcare disparities, particularly in LMICs. Further, a gender-neutral approach could also strengthen programme resilience in settings where female vaccination coverage remains far below the elimination targets. The case of HPV vaccination shows that women-only public health interventions can further exacerbate the stigmatisation of women in society and, rather than improving women's health, amplify inequity. We believe that the experience with the HPV vaccine can play a significant role in demonstrating that women-specific vaccination programmes can have unintended consequences: whilst they may improve specific health outcomes, they simultaneously cause social harm to the sex groups they intend to protect, thereby failing to address broader health outcomes across the global society as a whole.

Keywords

HPV vaccination, gender neutral vaccination, gender, equity, vaccination strategies

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Background

Since its initial regulatory approval in 2006, the human papillomavirus (HPV) vaccine has been fully integrated into national immunisation programmes of 161 out of 194 World Health Organization (WHO) member states.[1] The vaccine and its further developed derivatives (most recently Gardasil-9) remain the most effective and economical primary prevention strategy against HPV infection and associated pathologies, particularly within high-burden settings, including low- and middle-income countries (LMICs) when subsidised through programmes like Gavi, the Vaccine Alliance (Gavi), and in high-income countries (HICs).[2]

Historically, HPV immunisation efforts have almost exclusively targeted and prioritised females, who bear nearly 90% of the global HPV-related malignant disease burden, most notably cervical cancer, which has largely shaped the allocation of public health resources towards females.[3,4] This focus neglects non-cervical oncogenic and benign outcomes, while excluding cisgender males (hereafter "males" or "men") and rendering invisible the needs of trans men who retain a cervix and require protection against cervical cancer.[5,6] The advancement of HPV vaccination programmes has shown that vaccinated groups are more likely to undergo secondary prevention that could be even more critical for non-cervical HPV-related cancers, which have a less strong association with the viral infection and a wider and more diverse aetiology.[7]

Admittedly, the initial female prioritisation of HPV immunisation programmes was also partly due to limited vaccine supply, fewer competing manufacturers, and higher costs associated with novel inventions.[8,9] The entry of additional manufacturers alongside commitments to increase production and increasing data on effectiveness of single-dose vaccination have expanded global vaccination possibilities, making GNV increasingly economically feasible, particularly in LMICs.[9-11] Transitioning toward GNV, as has happened in many HICs, requires navigating the historical context of gender-focused policies alongside the ethical challenges of increased costs and limited vaccine availability and accessibility, especially in high-burden, low-resource regions where low female coverage fails to achieve herd immunity.[12]

Therefore, this perspective paper advocates for an accelerated global shift from a female-only to a universal GNV approach, in order to make HPV vaccination accessible to all people in need of protection, irrespective of their sex at birth, gender identity, or expression. In this perspective, we analyse how a GNV strategy addresses the rising burden of non-cervical cancers and outcomes, promotes gender justice for all, and strengthens population-wide herd immunity amidst shifting global funding and healthcare inequalities, particularly in LMICs.

Addressing the Global HPV Burden Beyond the Cervix

HPV (especially the mucosal types) dominates as the most frequently acquired sexually transmitted infection (STI) worldwide, infecting most sexually active individuals through skin-to-skin contact of the genital, anal or oral epithelium at some point in their lives.[13] However, intrapartum and non-sexual transmission are also reported.[13] The virus exhibits tropism for basal cells of epithelial tissues, entering through microlesions of the tissue barrier.[13] Although most HPV infections are temporary and successfully cleared by the immune system, persistent infection with high-risk HPV genotypes (most notably HPV 16 and 18) is an established precursor to multiple malignancies, including cancers of the anogenital tract and a subgroup of head and neck cancers, particularly oropharyngeal squamous cell carcinoma (OPSCC).[13]

The causal link between HPV infection and these cancers is well-established, with more than 5% of all global cancer cases attributable to the virus.[3,14] In 2022 alone, 831,204 reported cancer cases were linked to HPV infection, of which approximately 11.4% occurred in males and around half resulted in deaths.[3] Consequently, the historical focus on cervical cancer has justified the exclusion of non-female populations from many national immunisation frameworks.[1,8] While nearly all cervical cancer cases are attributable to HPV infections,[3,4] the overemphasis on this single outcome has promoted a body of evidence and created an evidentiary bias that has deprioritised the rising global burden of non-cervical HPV-associated malignancies.[14] According to Zhang et al.,[3] while the majority of HPV-attributable malignancies are cervical cancer cases (79.7%), the remaining burden comprising head and neck cancers (7.9%), anal cancers (6.5%), vulvar and vaginal cancers (3.5%), and penile cancers (2.3%), must all be considered if the global HPV burden is to be fully mapped and controlled.[14] Many geographical regions are facing a surge in HPV-positive OPSCC, especially in HICs.[3] In the United States, OPSCC incidence rates now surpass those of cervical cancer, with males having a three-to fourfold higher prevalence than females as HPV infection replaces alcohol and tobacco use as the major risk factor for this cancer.[3,14] In contrast to LMICs, where the disease burden remains higher for females, this trend is reversed in HICs for HPV-attributable cancers.[3] Furthermore, the incidence of HPV-related cancers rises with age, with male rates exceeding female rates after the age of 65.[3]

Certain vulnerabilised groups are at particular risk of seeing their needs for HPV prevention and screening neglected. Persons living with human immunodeficiency virus (HIV), transgender individuals, men and women engaging in same-sex

practice, and sex workers are criminalised, stigmatised and/or discriminated against in many countries.[5,6] In many healthcare settings, individuals of a non-heteronormative identity, expression or practice are not targeted in HPV prevention and screening and are directly prevented from expressing their demand for HPV-related care.[5,6] Yet, some of these groups are at increased risk of certain HPV-related cancers. For instance, a review of epidemiological evidence on anal cancer in the United States has suggested that men engaging in same-sex practice, men having sex with women and living with HIV and women living with HIV must be targeted in anal cancer screening efforts since the incidence of anal cancer is higher in these population groups when compared with the general population.[15]

Recent trend evaluations suggest that vulvar, penile, and anal cancers are among the fastest-increasing HPV-related cancers, particularly in a Sub-Saharan African context, whereas globally anal and OPSCC are on the rise.[3,16] Crucially, current risk stratification often neglects transgender, intersex and gender-diverse populations outside the binary cisgender female/male spectrum.[5,6] These groups are frequently excluded from sexual and reproductive healthcare services, resulting in delayed prevention, screening, and treatment efforts.[6] Meanwhile, regions that implemented GNV programmes early are already reporting a decline in non-cervical outcomes, including precancerous lesions.[17]

HPV Vaccination and the Cervical Cancer Elimination Strategy.

Cervical cancer, which can afflict anyone with female reproductive organs irrespective of their gender identity, remains the HPV-associated pathology causing the greatest morbidity and mortality, with the highest burden concentrated in LMICs.[3,11,14] To address this, the WHO launched the *Global Strategy to Accelerate the Elimination of Cervical Cancer* in November 2020, postulating the "90-70-90" targets to be achieved by 2030: 90% of girls vaccinated between the ages of 9 and 15, 70% of women screened twice by age 45, and 90% of those identified with cervical cancer or precancerous lesions receiving treatment.[18] In this light, the management of cervical cancer uniquely benefits from established screening protocols and gynaecological check-ups, including Pap smears and HPV DNA testing, which enable early detection of cervical intraepithelial neoplasia and foster greater public awareness compared with other HPV-associated cancers.[4] However, the screening and treatment elements of this strategy often fall short or remain inaccessible in resource-limited settings. In sub-Saharan Africa, for instance, the median country coverage for cervical cancer screening is only 16.9% of the population targeted by this WHO strategy.[11,19]

As of 2021, while approximately 133 countries have implemented national cervical cancer screening programmes and 126 published national guidelines on cervical cancer management,[1] the disparity remains stark as nearly all HICs have established such programmes while low-income countries are left behind not only in offering those programmes but also in making them accessible and available to the majority of their population with screening rates often falling under 10%.[1,7,11] In low-resource settings where even cervical cancer screening programmes struggle with funding, ownership and participation, screening for other HPV-associated cancers is even less established, less structured and harder to conceptualise and implement.[4,7,15,20] Thus, while HPV vaccination has significantly reduced cervical cancer prevalence in many HICs and early adopting nations, other HPV-related cancers are on the rise.[3,4,14,16] Meanwhile, cervical cancer rates also continue to be a significant burden, particularly in low-income countries.[3,11] However, non-cervical malignancies suffer from lower public awareness and a lack of internationally standardised global clinical guidelines, which hampers primary prevention and early detection.[4,14,20] Further, it has been suggested that, while a vaccination rate of ≥50% among targeted "girls" can trigger a decline in anogenital warts and genital HPV infections among unvaccinated males and older females, this protection would not extend to males who only engage in sex practice with males who do not engage in sex practice with females.[17,21] Nevertheless, the WHO's 90% cervical cancer elimination remains the benchmark to be aimed for.[18] In this regard, a GNV approach that targets all sex groups irrespective of their sex and gender identities, expression or practice could strengthen the resilience of vaccination programmes if female vaccine coverage among females drops or remains far from expected elimination targets.[8,12]

The Feminisation of HPV and Gender Disease Narratives

The female-oriented HPV vaccination strategy, which remains predominant in LMICs and was amplified by past vaccine shortages, frames HPV strictly as a "women's issue" and has created considerable structural barriers.[8,19] This narrow framing often leads communities to perceive the vaccine as promoting promiscuity because it targets an STI, to spread misinformation claiming that it is used as a mean of population control, to view it as conflicting with their faith, or to develop safety concerns, which in turn leads parents to refuse immunisation for their dependents.[19,22] For example, a qualitative analysis of the 2013 HPV vaccination pilot in Madagascar found that those who refused immunisation expressed concerns that the vaccine promoted non-monogamous sexual activity especially outside of marriage discouraging caregivers to have their female dependants vaccinated.[23]

Generally, female-targeted HPV immunisation programmes have been shown to reduce vaccine acceptance across diverse contexts, whereas in settings where the HPV vaccine has not yet been introduced, and gender-based branding has not

been implemented, vaccine willingness among caregivers is not skewed toward girls.[22,23] When HPV is exclusively portrayed as a "female issue", males regularly remain unaware of it, which is reflected in lower awareness and knowledge of the virus and its associated conditions, as well as a lower perceived risk among males, ultimately discouraging vaccine-seeking non-female individuals.[19,22,24] This situation is particularly challenging in patriarchal structures where men frequently control medical decisions and household expenditures for their family members[25], dependents and the community at large.[19,22] By targeting HPV vaccinations exclusively at girls, campaigns that do not include GNV implicitly portray women as the primary carriers and propagators of STIs.[8,19] In doing so, they reinforce stereotypical associations between female sexuality and disease, whilst avoiding any discussion of males' role in HPV transmission, the risks HPV infection poses to male health, and absolving males of responsibility for HPV-related disease prevention.[8,19] This well-intended strategy of protecting girls and women who bear the brunt of HPV-related morbidity and mortality therefore creates a *boomerang effect*: instead of empowering girls and women, it reinforces communities' misconceptions around STIs and contributes to the stigmatisation and oppression of females who are perceived as active decision-makers regarding their sexuality and sexual practice. Consequently, even in countries that have expanded recommendations to include boys over recent years, vaccination coverage has stagnated; public health messaging often fails to effectively explain the shift, leaving caregivers hesitant to vaccinate their male children due to years of "girls-only" messaging, whilst transgender, intersex, non-binary, queer and other gender minorities remain entirely excluded from the discussion.[8] The example of Germany shows that the national expansion of HPV vaccination to include boys, which began in 2018, has only gradually increased vaccination rates, as previous HPV prevention campaigns targeting girls, as well as gaps in knowledge, continue to impede acceptance, the proactive utilisation of the vaccine by caregivers, and the herd immunity effects sought through a gender-neutral policy.[25] Additionally, in many countries with high disease burdens, populations such as men who have sex with men, transgender and non-binary individuals are often still heavily marginalised, aggravating the neglect and consequences of gender-based prevention strategies.[5,6]

The global political discourse is shifting, precipitating a regressive trend even in countries where gender equity efforts had reached considerable milestones — progress now at risk of being lost.[26] In this climate, neutralising the gendered discourse around HPV vaccination may be essential to successfully move towards eliminating HPV-associated cancers and conditions.[8,20] Furthermore, GNV strategies foster social equity by safeguarding the right of population groups other than cisgender females to demand, access and use protection against HPV and related cancers.[5,6]

HPV and Non-cervical Cancers and Outcomes: Missed Prevention Opportunities

The current state of screening programmes for non-cervical HPV-related cancers, especially outside of high-income contexts, is markedly underdeveloped and largely non-existent compared to cervical cancer screening.[14,15] As of 2026, there are still no validated population-level screening programmes for head and neck, vulvar, vaginal, or penile cancers.[4,15] Clinical protocols for anal cancer screening are also limited. In 2024, the International Anal Neoplasia Society issued guidelines recommending anal cancer screening to populations that the Society suggested as being at increased risk of HPV infection in the United States, such as men engaging in same-sex practice as well as men who have sex with women and live with HIV.[15] Expanding the radius of prevention and screening is critical, as HPV-associated cancers besides cervical cancer generally carry favourable prognoses when detected early, but survival declines sharply at advanced or metastatic stages, even in high-resource health systems.[15,27] In comparison, cervical cancer is unique among HPV-associated malignancies in benefiting from established population-level screening protocols that enable detection at early, highly curable stages.[4,7] In resource-limited settings, where approximately two-thirds of all cancers are diagnosed at advanced stages, and the availability of surgery, chemotherapy, and radiotherapy remains severely limited, outcomes are substantially worse for all HPV-attributable cancers, making prevention efforts even more valuable.[3,28]

Emerging evidence suggests that HPV may be a potential risk factor or influence the clinical course of several other malignancies.[29] Although without strong causality evidence, studies have reported associations between HPV infection and oesophageal, breast, lung, bladder, and prostate cancers.[29,30] Moreover, recent, as yet unconsolidated findings show that HPV vaccination may offer protective or therapeutic advantages against cutaneous squamous cell carcinomas and their precursors, although current vaccines mainly target mucosal HPV genotypes that are suspected to act as co-factors with UV exposure in the development of skin cancer.[31,32] Beyond oncogenic outcomes, HPV infections are associated with increased morbidity. Emerging evidence suggests that HPV may impair reproductive health and fertility, as it is linked to reduced sperm quality, increased risk of miscarriage, and preterm birth.[33] In addition, HPV vaccines such as Gardasil and Gardasil-9, which include the low-risk mucosal HPV types 6 and 11, are highly effective at preventing anogenital warts in persons of any sex at birth.[2]

However, 29 WHO member states have not yet introduced the HPV vaccine at all, and only 31% of targeted girls globally have received the first dose of a HPV vaccine.[1] The gap in access and availability is most pronounced in LMICs, though this

gap is slowly being bridged by the WHO endorsement of a single-dose schedule as an alternative to traditional multi-dose regimens, the entry of additional vaccine manufacturers into the market, and the accelerated implementation of HPV vaccination campaigns in countries that have not yet introduced them.[1,9,10]

Nevertheless, substantial headwinds persist concerning GNV. One could argue that priority should first be placed on completing the vaccine's introduction in every country and on raising female coverage through multi-age cohort (MAC) strategies, above the 50% threshold.[21] Geopolitical instability and declining international support threaten global vaccine delivery and funding, particularly in resource-limited regions.[26,34] Notably, the projected withdrawal of United States funding from Gavi and the potential abolishment of the United States Agency for International Development, alongside anticipated reductions in Official Development Assistance from major contributors including the United Kingdom, France, and Germany, may undermine HPV immunisation campaigns, leaving national programmes to fall victim to these budgetary shortfalls in LMICs.[34] Conversely, the marginal cost-effectiveness of adding gender groups other than females to existing female-only programmes decreases when female coverage is already high, as herd immunity effects reduce HPV transmission to females' unvaccinated sexual partners; however, this finding depends heavily on which HPV-related outcomes are included in cost-effectiveness models.[35] This raises a critical debate: Should limited resources prioritise the highest-burden populations in high-burden settings, or support a broader, resource-intensive universal mandate that has predominantly been adopted by HICs as they can afford it? Nevertheless, Jit, Brisson, and colleagues[35] have shown through modelling that shifting the global effort from elimination of cervical cancer to eradication of vaccine-type HPV is feasible and cost-effective through GNV. Additionally, while MAC strategies might still be more cost-effective, especially in LMICs, they do not address the equity issue in health that is essential to guaranteeing health as a human right in the spirit of universal health coverage.[8,20]

Conclusions and Recommendations

Historically, HPV vaccination campaigns have focused almost exclusively on females, branding the virus a "girls' issue" and neglecting oncogenic outcomes at anatomical sites other than the cervix. This narrow perspective excludes cisgender males, transgender individuals, and other gender minorities from direct protection and has the potential to fuel the societal disparities and inequalities that affect girls and women who remain the primary target of HPV prevention programmes and are uniquely associated with the infection, generating a boomerang effect that amplifies societal disparities. While only 85 reporting countries, mostly HICs, have adopted GNV to date,[1] transitioning toward GNV is a feasible strategy for the global eradication of vaccine-type HPV. Although expanding HPV vaccination programmes to all gender groups may appear less cost-effective where female coverage is already high, a gender-neutral approach strengthens programme resilience precisely in the settings where coverage remains far below the WHO's elimination targets and where non-cervical infection outcomes and considerations of health equity influence the trade-off in both LMICs and HICs. By dismantling the stigma of a "female infection" and acknowledging how all gender groups may be burdened by the HPV infection and participate in its transmission, GNV supports shared responsibility for STI prevention and offers equitable protection for historically underserved groups in HPV vaccination programmes. Furthermore, this broad approach strengthens herd immunity for females and tackles the critical prevention gap for non-cervical cancers, which currently lack standardised screening protocols, while also addressing the HPV-associated consequences on reproductive health of all gender groups. As demonstrated, gender-based strategies risk perpetuating disease-associated social branding rather than dismantling it, while simultaneously neglecting the needs of individuals who are also at high risk of HPV-associated conditions and who may not be eligible in some contexts to receive HPV vaccination due to their sex at birth or gender identity and expression. Therefore, coordinated worldwide efforts, potentially utilising single-dose regimens in times of dwindling international financial support for health programmes, particularly in resource-limited regions, must ensure that vaccine supply does not drive disparities.[10,34] Ultimately, HPV GNV programmes can prove that public health is about the overall well-being of populations and the promotion of health equity among them rather than the mere absence of disease in specific groups in specific parts of the world.

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With this publication, we want to recognise and stand in solidarity with communities systematically excluded and underserved, who navigate ongoing inequities that directly compromise their health and well-being.

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DF and AR conceptualised the article. They have been the main writers. AR curated the literature search. TG and GMP provided a critical revision of the article, given their direct and longstanding experience in the field of human papillomavirus and gender health, respectively.

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