

A gender- and sex-oriented perspective on viral infections: insights from human papillomavirus and hepatitis B

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Sex and gender are increasingly recognised as key determinants of health, shaping exposure to infections, access to preventive measures, diagnostic pathways, and long-term clinical outcomes. Nevertheless, public health strategies for viral infection control are often conceived as gender-neutral, implicitly assuming that equal policies lead to equal results. Human papillomavirus (HPV) and hepatitis B virus (HBV) clearly show how this assumption may obscure important inequalities and ultimately weaken elimination strategies, even in the presence of highly effective vaccines.

The aim of this editorial is to illustrate how sex, gender norms, and health-system organisation may shape access to vaccination, screening, diagnosis and clinical outcomes, ultimately influencing the equity and sustainability of elimination strategies. HPV and HBV were selected as complementary models because they represent two vaccine-preventable viral infections with highly effective biomedical tools, yet persistent inequalities remain in prevention and care. These infections show two distinct ways in which sex and gender can influence elimination efforts.

HPV is the most common sexually transmitted infection worldwide and affects both women and men. Persistent infection with oncogenic HPV types is causally associated with a wide spectrum of cancers, many of which are largely preventable through vaccination. Although cervical cancer remains the most emblematic HPV-related malignancy, HPV is also implicated in cancers of the anus, vagina, vulva, penis, and head and neck.

The contribution of HPV to cancer burden varies markedly by anatomical site and sex. HPV infection accounts for approximately 97% of cervical cancers, 88% of anal cancers, 70% of vaginal cancers, 50% of penile cancers, 43% of vulvar cancers, and about 26-30% of head and neck cancers. This heterogeneity is reflected in global incidence patterns: in 2022, according to GLOBOCAN estimates, cervical cancer accounted for approximately 660,000 new cases worldwide, confirming the predominance of the HPV-related cancer burden among females, whereas oropharyngeal cancers showed a markedly higher incidence in males, with an estimated 86,339 new cases and an age-standardised incidence rate (ASR) of 1.90 per 100,000, compared with 20,061 cases, and an ASR of 0.39 per 100,000 in females, indicating an almost fivefold higher risk in males.¹

Despite this clear evidence, HPV prevention has historically been framed almost exclusively as a women-centred issue. Early vaccination programmes were introduced with the primary objective of preventing cervical cancer and therefore targeted girls only. While this approach produced substantial benefits in reducing cervical cancer risk, it also reinforced a gendered perception of HPV infection and disease, contributing to limited awareness of HPV-related cancers in men and to lower attention to male vaccination.^{2,3}

Over time, many countries have moved towards gender-neutral HPV vaccination policies, recognising both the direct benefits for boys and men and the broader population-level impact of herd immunity. However, this transition remains uneven. Not all European countries vaccinate boys, and even where gender-neutral vaccination is recommended, coverage among males often lags behind that of females.^{4,5}

Differences in national immunisation policies, healthcare provider recommendations, organisational models, and communication strategies continue to generate inequalities in access and uptake.

Gender norms also play an important role. Preventive healthcare is often perceived as more relevant to girls and women, while boys and men may be less frequently engaged in vaccination programmes and preventive counselling. Parents and adolescents may underestimate the relevance of HPV vaccination for males, particularly in relation to cancers that are less well known to the general public, such as anal or oropharyngeal cancer.

European collaborative initiatives, such as the Joint Action PartnERship to Contrast HPV-PERCH, have demonstrated that these gaps can be addressed through coordinated, gender-sensitive strategies.⁶ Extending routine HPV vaccination to both girls and boys, strengthening communication strategies that explicitly include male risks and benefits, and investing in healthcare professional training have proven effective in improving awareness and acceptance. Importantly, PERCH also highlighted the need to improve monitoring systems and to link vaccination data with screening and cancer outcomes, allowing sex-based inequalities to be identified and addressed more systematically.⁶

Evidence from national cohorts, including the Italian Platform for the Study of Viral Hepatitis Therapies (Piat-

taforma Italiana per lo Studio della Terapia delle Epatiti Virali, PITER), a nationwide, multicentre prospective cohort collecting standardised demographic, clinical and virological data on patients with chronic HBV, HCV and HDV infection in care in Italy, supports the interpretation that health-system organisation and screening policies strongly shape apparent sex patterns in HBV epidemiology.⁷

In Italy, universal infant HBV vaccination has achieved high coverage in the native population up to approximately 45 years of age; however, sex differences may still emerge among older Italian-born individuals, with women showing an increased risk of progression to advanced liver disease after menopause. In contrast, inequalities are more evident among migrants due to missed vaccination opportunities before migration and fragmented access to prevention and care after arrival. Moreover, systematic HBsAg testing during pregnancy increases the likelihood of identifying HBV infection among women of childbearing age, potentially creating a pregnancy-related detection bias in surveillance systems, while adult men may remain underdiagnosed until later disease stages. Importantly, recent PITER evidence also highlights the role of hepatitis D virus (HDV), which affects only individuals living with HBV and accelerates liver damage, further modifying sex-related risk patterns: migrant women with HBV-HDV infection, often exposed earlier in life in settings with limited access to vaccination, may develop severe liver disease at a young age even in the absence of other risk factors, whereas in men severe disease more frequently reflects the accumulation of multiple concurrent exposures.⁸

Taken together, HPV and HBV offer complementary insights into how sex and gender shape viral infection outcomes. In HPV, the historical focus on women has delayed full recognition of male disease burden and prevention needs, while HBV illustrates how vaccination history and selective screening pathways, particularly pregnancy-based testing, can shape who is diagnosed and therefore how epidemiological patterns are interpreted.

Achieving elimination targets for HPV- and HBV-related diseases will therefore require a more comprehensive and integrated approach. This includes consolidating gender-neutral HPV vaccination across all countries and improving uptake among boys. Achieving equitable and sustainable HBV control requires moving beyond maternal health selective screening, addressing the structural drivers of risk and care and systematically analysing sex-disaggregated data. Healthcare professionals play a crucial role, as their awareness, attitudes, and recommendations strongly influence prevention uptake and equity.

Without the systematic integration of sex- and gender-oriented perspectives into clinical practice and public health policy, viral infection control strategies risk achieving nominal targets while perpetuating avoidable and unjust inequalities.^{9,10}

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