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Review

Global Burden of Human Papillomavirus and Related Diseases

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ABSTRACT

The worldwide prevalence of infection with human papillomavirus (HPV) in women without cervical abnormalities is 11–12% with higher rates in sub-Saharan Africa (24%), Eastern Europe (21%) and Latin America (16%). The two most prevalent types are HPV16 (3.2%) and HPV18 (1.4%). Prevalence increases in women with cervical pathology in proportion to the severity of the lesion reaching around 90% in women with grade 3 cervical intraepithelial neoplasia and invasive cancer. HPV infection has been identified as a definite human carcinogen for six types of cancer: cervix, penis, vulva, vagina, anus and oropharynx (including the base of the tongue and tonsils). Estimates of the incidence of these cancers for 2008 due to HPV infection have been calculated globally. Of the estimated 12.7 million cancers occurring in 2008, 610,000 (Population Attributable Fraction [PAF] = 4.8%) could be attributed to HPV infection. The PAF varies substantially by geographic region and level of development, increasing to 6.9% in less developed regions of the world, 14.2% in sub-Saharan Africa and 15.5% in India, compared with 2.1% in more developed regions, 1.6% in Northern America and 1.2% in Australia/New Zealand. Cervical cancer, for which the PAF is estimated to be 100%, accounted for 530,000 (86.9%) of the HPV attributable cases with the other five cancer types accounting for the residual 80,000 cancers. Cervical cancer is the third most common female malignancy and shows a strong association with level of development, rates being at least four-fold higher in countries defined within the low ranking of the Human Development Index (HDI) compared with those in the very high category. Similar disparities are evident for 5-year survival—less than 20% in low HDI countries and more than 65% in very high countries. There are five-fold or greater differences in incidence between world regions. In those countries for which reliable temporal data are available, incidence rates appear to be consistently declining by approximately 2% per annum. There is, however, a lack of information from low HDI countries where screening is less likely to have been successfully implemented. Estimates of the projected incidence of cervical cancer in 2030, based solely on demographic factors, indicate a 2% increase in the global burden of cervical cancer, i.e., in balance with the current rate of decline. Due to the relative small numbers involved, it is difficult to discern temporal trends for the other cancers associated with HPV infection. Genital warts represent a sexually transmitted benign condition caused by HPV infection, especially HPV6 and HPV11. Reliable surveillance figures are difficult to obtain but data from developed countries indicate an annual incidence of 0.1 to 0.2% with a peak occurring at teenage and young adult ages.

This article forms part of a special supplement entitled "*Comprehensive Control of HPV Infections and Related Diseases*" Vaccine Volume 30, Supplement 5, 2012.

1. Introduction

This paper provides an overview of the worldwide prevalence of human papillomavirus (HPV) infection and the associated burden of cancer. It provides a brief review of the distribution of HPV infection by geographical region and in relation to body sites for which cancer can be an outcome of such infection (cervix, penis, vagina, vulva, anus and oropharynx). For these body sites, information has been extracted from the GLOBOCAN 2008 database on the total number of cancers diagnosed annually worldwide and this has been used to produce estimates of the proportion of these cancers that are associated with HPV. The overall burden of HPV-associated

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cancer has then been stratified by world region and by level of socioeconomic development. Cervical cancer is the most important type of cancer associated with HPV and the chapter provides a review of the current global descriptive epidemiology of this disease, especially in relation to level of development and, where data allows, an analysis of temporal trends. Similar trends are presented for the five other types of cancer associated with HPV infection. Consideration is also given to the epidemiology of genital warts, the major benign condition associated with HPV infection.

2. HPV prevalence

The overall global burden of HPV infection is optimally assessed by the pooling of results from studies in which reliable, quality-controlled methods have been used to detect HPV in women with normal cervical cytology. The most comprehensive such meta-analysis, with data extracted from 194 studies and based on testing over one million women using polymerase chain reaction (PCR) or Hybrid Capture® 2 (Qiagen Gaithersburg, Inc., MD, USA [formerly known as Digene Corp.]) for HPV detection, indicates that the global prevalence of HPV infection is around 11–12% (Fig. 1). [1] There is considerable regional variation in this figure with prevalence highest in sub-Saharan Africa (24%), Eastern Europe (21%) and Latin America (16%). Particularly high prevalence is seen in Eastern Africa and the Caribbean, where rates exceed 30%. In general, there is a division between less and more developed world regions with higher rates observed in the former, although the Eastern European situation represents one exception to this pattern, while rates in Northern Africa (9%) and Western Asia (2%) represent another. There is a relationship between HPV prevalence and age seen globally, which shows maximum rates in younger women (less than 25 years) with a monotonic decline at older ages (Fig. 2). In Europe and Northern America, HPV prevalence rates are very high below age 25 years but tend to become much lower in women over the age of 45 years. No such clear decline with age is found in Asian and African populations, although in some Latin America/Caribbean populations, rates decline and then increase again in middle-aged women [2]. Data from a subset of the studies in the meta-analysis, in which type-specific HPV information could be assessed, showed

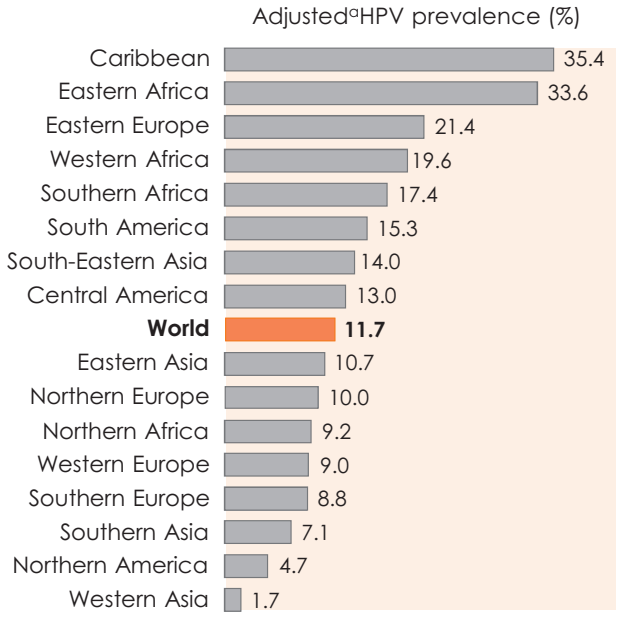

Figure 1. HPV prevalence among women with normal cytology: meta-analysis based on results from 1,016,719 women. [a]Regionally-adjusted HPV (see [1] for adjustment methodology). Redrawn from Bruni L *et al.* [1].

that the five most prevalent types worldwide were HPV16 (3.2%), HPV18 (1.4%), HPV52 (0.9%), HPV31 (0.8%) and HPV58 (0.7%) [1]. All other HPV types had a prevalence of 0.6% or less, including HPV45 (0.5%—along with HPV16 and HPV18—common in invasive cancer), as well as HPV6 (0.5%) and HPV11 (0.2%) (the two most prevalent types found in association with genital warts). All of the above estimates represent point prevalence at the time of sampling and will, therefore, be underestimates of the cumulative exposure to infection.

Another recent meta-analysis included results obtained from 423 studies that evaluated testing with broad spectrum consensus PCR assays and which compared over 260,000 women with normal cytology and 103,000 women with cervical abnormalities

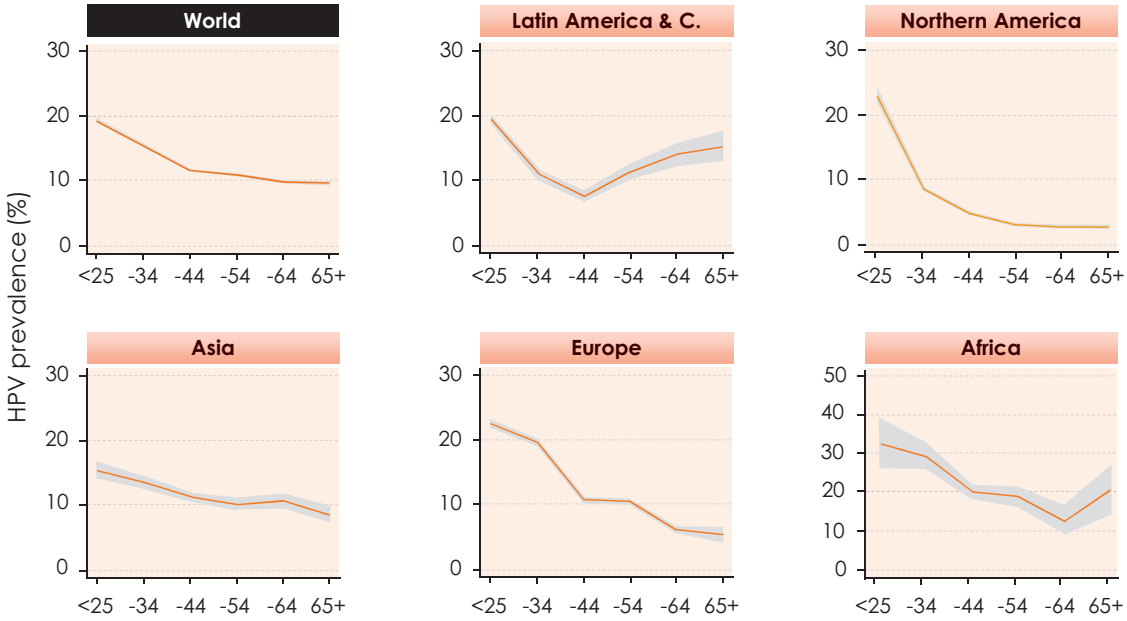

Figure 2. HPV prevalence among women with normal cytology by age group (years). Shaded area reflects 95% confidence intervals. C: Caribbean. Redrawn from Bruni L et al. [1].