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Anal cancer risk: HPV-based cervical screening programmes

Similar to cervical cancer, most anal cancers (89–100%) are induced by persistent infections with high-risk human papillomavirus (HPV), especially HPV16.[1] Anal cancer accounts for only 4% of all malignancies of the lower alimentary tract, but its incidence is rising in high-income countries. For the USA, increasing average annual percentage changes of 2·1 for men and 2·9 for women have been reported.[2] About 8300 new anal cancer cases are diagnosed in the USA each year, with higher incidence rates in women than in men.[3] Similar numbers have been estimated for Europe.[4] More than one-third of patients with anal cancer die within 5 years after diagnosis.[3] Several risk groups for anal cancer have been identified, such as men who have sex with men, transplant recipients, people with HIV/AIDS, and women with a history of HPV-induced cervical, vaginal, or vulvar cancer.[3] The latter group has an increased incidence (three to 22 times) of anal cancer, compared with the general population.[3]

Anogenital HPV-induced cancers are largely preventable by prophylactic vaccination of HPV-naive individuals (primary prevention) or by screening for precancers (secondary prevention).[5,6] For cervical cancer, population-based cytology screening has been replaced by primary HPV screening or by co-testing (HPV and cytology) in several countries.[6] By contrast, anal cancer screening has been recommended only for high-risk groups, such as HIV-positive individuals, especially men who have sex with men.[7,8] However, the evidence of benefit has yet to be established in ongoing prospective studies.[7]

In a study in *The Lancet Infectious Diseases*, Chunqing Lin and colleagues[9] have shown that data available from routine HPV-based cervical screening programmes can be used to define anal cancer risk profiles in the participating women. Lin and colleagues did a retrospective collaborative pooled meta-analysis, including individual-level data from 36 studies with 13 427 women for whom paired anal and cervical samples were available. They found that cervical HPV16 is strongly associated with anal HPV16. 41% of HIV-negative women with cervical HPV16 also had anal HPV16, compared with 2% of those without cervical HPV16 (prevalence ratio [PR] 16·5); in HIV-positive women, these values were 46% and 11% (PR 4·4). Anal precancer (high-grade squamous intraepithelial lesion [HSIL]) was associated with cervical high-risk HPV and with cervical HSIL, regardless of HIV status. One quarter of older women (aged ≥45 years) with cervical HPV16 had anal HPV16-associated HSIL (25% of HIV-negative women, 23% of HIV-positive women).[9]

Notwithstanding the divergent progression rates of anal HSIL to invasive cancer reported in the literature[7], the findings of Lin and colleagues[9] have important public health implications. Anal cancer screening might be advisable in all women with cervical high-risk HPV infection (irrespective of their HIV status), particularly if the detected HPV-type is HPV16. Furthermore, a diagnosis of cervical HSIL or cancer seems to be a strong determinant for anal HSIL, also in HIV-negative women (PR 23·1). In HIV-positive women, anal HSIL was found in 25% of patients with cervical HSIL, but also in 7% of those with normal cervical cytology. Similarly, 8% of HIV-positive women without cervical high-risk HPV infection had anal HSIL. This finding could argue for anal cancer screening in more HIV-positive women than only in those with HPV-associated dysplasia.[8] Anal cancer screening algorithms for both HIV-negative and HIV-positive women could possibly be further refined by incorporating additional risk factors, such as smoking or sexual practices.[3]

Similar to anal cancer, incidence rates of HPV-associated oropharyngeal cancer are steadily increasing, especially in men, but also in women.[2] It would be interesting to analyse whether the cervical markers described by Lin and colleagues (HPV16 positivity, HSIL, and cancer)[9] are also associated with an increased risk for HPV-induced oropharyngeal cancer. Such studies could be done in countries that maintain comprehensive

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health databases and cancer registries. However, viable screening tests for HPV-associated oropharyngeal cancer do not yet exist.[10] High-resolution anoscopy is the gold standard for diagnosing anal precancer, but high-resolution anoscopy is not widely available, which could hamper comprehensive screening of high-risk groups beyond HIV-positive individuals.[7] HPV vaccination has already led to significant changes in cervical high-risk HPV infection and precancer rates in younger women.[11,12] The decrease of cervical (and anal) HPV16/18 infection and precancer could make targeted secondary anal cancer prevention feasible despite insufficient resources, especially if high-resolution anoscopy could be preceded by anal high-risk HPV testing. Hopefully, the findings presented by Lin and colleagues[9] will encourage the initiation of prospective trials evaluating screening programmes for all women with an elevated risk for anal cancer.

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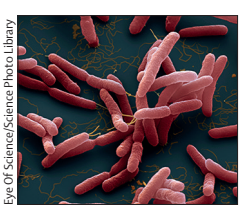
Reducing the melioidosis burden: public health, chronic disease prevention, or improved case management?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Melioidosis, which often presents as an acute, fulminant illness and has a case fatality rate of 10–50%, is caused by *Burkholderia pseudomallei*. In *The Lancet Infectious Diseases*, Emma Birnie and colleagues[1] describe the global burden of melioidosis in terms of disability-adjusted life-years (DALYs) for the first time. The analysis is based on a modelled estimate of the global incidence and mortality of melioidosis,[2] with additional data from a systematic review of the clinical impact of melioidosis. This is an important and well executed study. With these findings, we can compare the burden of melioidosis across regions of the world, and to some extent, compare the global burden of melioidosis with that of other infectious diseases.

Two findings of the study warrant special mention. First, 99% of the DALY burden of melioidosis was attributed to deaths from melioidosis (years of life lost [YLL]). Second, a high DALY burden for melioidosis was estimated in countries with few or no reported melioidosis cases. This finding was driven by a predictive modelling study of the global distribution of melioidosis,[2] in which Limmathurotsakul and colleagues estimated 165 000 melioidosis cases and 89 000 deaths worldwide in 2015. Of note, Limmathurotsakul and colleagues suggested that melioidosis was "severely under-reported in 45 countries in which it is known to be endemic" and "probably endemic in a further 34 countries that have