

ENGLISH SUMMARY

The most common sexually transmitted virus, human papillomavirus (HPV) will affect the majority of sexually active men and women at some point during their lives. Persistent genital infection with HPV can cause diseases with a variety of clinical manifestations; some low-risk (LR) HPVs can cause benign genital warts, whereas persistent high-risk (HR) HPV infections can give rise to more severe morbidity. Extensive research has established that HPV plays a crucial role in the development of cervical cancer as well as anal, penile, vulvar and some head-and neck cancers. Most research has focused on women and the major HPV-related burden, cervical cancer. Studies about genital HPV infection among men, especially men from the general population are limited despite an increasing HPV-related disease burden in men. Thus, it is pivotal to expand our knowledge about the natural history of HPV infection, including prevalence and risk factors in the male part of the population, to prevent the increasing HPV-related disease burden.

This thesis is based on three papers, which together contribute information on the natural history of genital HPV infection among men from Europe, especially men from Denmark. The aim was to investigate the magnitude of male genital HPV infection in Europe and factors associated with HPV prevalence and risk of infection.

Paper I was a review and meta-analysis on genital HPV prevalence among men in Europe. We identified 31 eligible papers, and subdivided them according to the risk-profile of the studied populations into general and high-risk studies. No studies from eastern Europe were eligible for inclusion. The meta-regressions analyses were conducted separately in each risk group. The pooled HPV prevalence in the general population was 12.4% and in high-risk populations, it was 30.9%. A common feature between the two groups was the great between-study heterogeneity. In the general population studies published before 2000, we found a significantly lower pooled HPV prevalence than in the more recently published studies (8.8% vs. 28.5%) ($P = 0.02$). We then investigated whether the factors geographical region, anatomical sampling site and HPV detection method could explain the great between-study heterogeneity. This was done by meta-regression analyses adjusted by publication year. We were not able to identify any factors that could explain the heterogeneity observed between the studies. The most common HPV types detected across studies were HPV6, 16 and 18.

In Paper II, we investigated HPV prevalence among 2,436 men aged 18–65 years, representing the general male population in Denmark. The results were based on the DanMale study, conducted during 2006–2007 at military barracks in Denmark. Penile swab samples from the participants were tested for HPV with two test methods, a polymerase chain reaction (PCR) method and Hybrid Capture 2 (HC2). Overall HPV prevalence was 22.2% in the HC2 test and 41.8% in the PCR test. Prevalence estimates for any, LR and HR HPV peaked among men in the early twenties and remained high despite a slight subsequent decrease. This was regardless of HPV detection method used. In contrast, the prevalence of unclassified HPV infections increased continuously with age. The most commonly detected types were HR HPV51, 16, 66 and 53 and LR HPV6.

In Paper III, we examined the association between HPV infection and circumcision, smoking and alcohol use among men from the DanMale study, after taking sexual behavior into account. In the age-adjusted analyses of sexual behavior, it was apparent that recent and lifetime number of female sex partners was strongly associated with an increased risk for HPV infection. Moreover, young age at sexual debut and sexual intercourse within the past three months increased the risk. In contrast, recent condom use was not associated with altered risk of HPV infection. After mutually adjusting the sexual behavior variables, lifetime number of female sex partners, age at sexual debut and time since last sexual intercourse were all factors significantly associated with risk of HPV. We selected those three variables to use for adjustment in the following analyses. When examining the influence of circumcision we found that it significantly reduced the risk of HPV whereas current smoking was associated with an increased risk of infection after adjusting for sexual behavior. Stratifying the study population by circumcision status revealed a difference in the effect of number of recent and lifetime female sex partners between the two strata; risk of HPV infection among circumcised men did not change despite of an increasing number of female sex partners. In the strata for uncircumcised men, the risk pattern was similar to the results from the unstratified analysis.

This thesis shows that genital HPV prevalence is high among men in European general and high-risk populations, especially men from Denmark, and prevalence estimates vary greatly within and between geographical regions. Some of the commonest HPV types present in the European region are preventable by vaccination. The insights into the natural history of genital HPV infection among men provided here can be used for future prevention strategies; increased awareness about HPV infection and its consequences in the general population is a cornerstone in the prevention of the infection.