



**Karolinska  
Institutet**

**Institutionen för Medicinsk Epidemiologi och Biostatistik**

# Human papillomavirus test and vaccination – impact on cervical cancer screening and prevention

AKADEMISK AVHANDLING

som för avläggande av medicine doktorsexamen vid Karolinska  
Institutet offentligen försvaras i sal Petré, Nobels väg 12B.

**Fredagen den 18 januari, 2013, kl 09.00**

av

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**Stockholm 2013**

## **ABSTRACT**

Human papillomavirus (HPV) is the world's most common sexually transmitted infection and its consequence cervical cancer is one of the world's most common cancer forms.

Revolutionary advances in HPV testing and HPV vaccination have the potential to radically change women's health. However, several challenges remain before effective cervical cancer control can be reached.

This thesis has exploited the excellent Swedish register and biobank infrastructure, for studies aiming to inform HPV-based prevention of cervical cancer. To this end, we have combined epidemiological, virological and biostatistical investigation of the use of HPV tests in organized cervical screening. We also investigated awareness of HPV and acceptability of HPV vaccination in the population.

Study I was a molecular epidemiological case-control study, nested within the Swedish cervical screening program, including 515 women with cancer in situ (CIS), 315 women with invasive squamous cervical cancer (SCC), and matched control women. 2772 archival cervical smears were gathered and subjected to full HPV-typing. The median follow-up was 5-7 years. We provide prospective evidence that infection with non-16/18 high-risk HPV types, and persistent infection with HPV16, both confer increased risks for future invasive cervical cancer.

In Study II, we extended this case-control study to include 621 women with CIS and 457 women with SCC; a uniquely large sample. Here, 5665 archival smears were tested for HPV, and HPV16 positive smears further analyzed for HPV16 viral load through realtime-PCR. The median follow-up was 6-8 years. We show that HPV16 viral load predicts risk for both CIS and SCC, but also that the risk functions differ per diagnosis and over time. Thus, HPV16 viral load appears highly complex which may limit its use in HPV-based cervical screening. We further show unexpectedly low viral loads early in invasive disease, which may carry implications for the weighing of sensitivity against specificity in HPV testing.

In Study III, we report results from a cross-sectional population-based survey examining awareness and knowledge of HPV in 24,513 adult Swedish respondents. We show that awareness of condyloma and cervical cancer was high, but that awareness and understanding of their causal factor HPV was poor. The knowledge that men could contract HPV needs to be improved. Education campaigns on HPV should particularly target young men, and those of low education.

Finally, Study IV was also a cross-sectional survey, examining acceptability of HPV vaccination among 10,567 young adults age 18-30 in Sweden. We show that willingness to vaccinate was quite high, but that information on the benefits of vaccinating before sexual debut is important. Few adults stated their health-care related behavior would change after vaccination, but a number were uncertain, suggesting an educational need when vaccinating this group. A perceived risk of side effects was the largest potential barrier to vaccination.

Our findings should assist risk stratification in HPV-based screening, and design of HPV vaccination campaigns. Future research should include investigations of cervical screening attendance, HPV vaccine uptake, and acceptability of HPV-based screening.