

International Study of Cancer with Full Genotyping for Cervical Screening

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Editorial

The ATHENA (Addressing the Need for Advanced HPV Diagnostics) trial was a large registration trial for Roche's Cobas human papillomavirus (HPV) test in primary cervical screening and triage of atypical squamous cells of unclear importance (ASC-US). Over 42,000 women aged 25 and up were surveyed enrolled. The research has proven that HPV is a serious infection. Testing as the sole mode of screening is more sensitive. At all ages, it is more sensitive than cervical cytology and is as sensitive as HPV contesting with cytology in women over 30 years old. Cobas has been approved by the Food and Drug Administration (FDA) in the United States for primary screening in women aged 25 and older, as well as ASC-US triage in women aged 21 and older, as a consequence of this research. The Cobas test detects HPV 16 and 18 independently with a consensus pool for 12 other high-risk HPV types and is based on polymerase chain reaction (PCR) amplification of HPV DNA utilising liquid-based cervical cytology samples. This study found that HPV 16 positive is associated with a higher risk of high-grade cervical intraepithelial neoplastic than a group of other high-risk types (CIN). However based on data it stated that typing for HPV types 16 and 18 is all that is required to determine the risk of high-grade cervical intraepithelial neoplastic (CIN grade 2 (CIN2) or CIN grade 3 (CIN3)) in a screening context, based on data from this trial. While essential, this is a huge oversimplification based on currently available data, given there is clear evidence of further risk discrimination based on extended HPV type.

HPV 33 has a significant risk of invasive cervical cancer and has a similar predictive potential for diagnosis of high-grade CIN (CIN2 and CIN3). A number of additional major studies investigating HPV genotype-specific cervical disease risks have found the same thing. In all studies, HPV 33 has a larger positive predictive value for CIN2 and CIN3 than HPV 18, with the exception of a Kaiser Permanente Northern California (KPNC) research, where the risk was nearly similar. In most of the studies it reported, HPV 31 consistently stands out as having a higher risk than other 'high risk HPV types' and has a higher risk than HPV 18. HPV 16 is definitely dominant in squamous malignancies, with HPV 18 performing slightly better. In terms of relative risk, it is usually ranked second. HPV 45 is one of the top four HPV genotypes linked to invasive cervical cancer, yet it ranks lower when it comes to high-grade precursor lesions. In some tests, this strain has been paired with HPV18. HPV 18 is only associated with adenocarcinoma (including adenosquamous cancer) and adenocarcinoma (including adenosquamous cancer). For adenocarcinoma in situ (AIS), data on complete HPV type is few, however in the limited data available, HPV 18 carries the highest relative risk. Presented a big multinational

study of cancer with complete genotyping comprising 10,575 cases. Although no control data were provided in that study, many of the same authors reported on a recent investigation of negative cytology. There was insufficient data to calculate confidence intervals, so the ranks for squamous cancer would be 16, 45, 33, 18, and 31, and for adenocarcinoma, 45, 18, 16, 33, 31 [1-5].

Individual HPV genotypes within commonly grouped categories of "other" high-risk HPV genotypes do not carry equal risk, and some – notably HPV 39, 56, 59, 66, and 68 – would be better classified as "intermediate risk" and require less active clinical management than other high-risk HPV genotypes, for example, repeat screening at 2–3 years rather than one year if cytology negative. Further research and new data suggest that type 66 has little or no harm, and that it should be removed from the list of 'high risk' HPV types. In 2009, the International Agency for Research on Cancer (IARC) decided that there was insufficient evidence for HPV66 to be carcinogenic. Finally, it makes no distinction between types 16 and 18, but multiple studies have shown that they are distinct. These two HPV genotypes appear to play very different roles in disease management, according to research. While HPV 16 is associated with an increased risk of CIN2 or greater (CIN2) at screening, HPV18 is not. Its unique significance stems from the fact that it is more common in cancer patients and is linked to adenocarcinoma and CIN lesions in the end cervical canal.

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