Human papillomavirus types in cervical intraepithelial neoplasia in Switzerland: the CIN3+plus study

J. Diebold[1], D. Egli-Gany[2], A. Häfliger[2], A. Spaar[3], V. Masserey Spicher[3], R. Heusser[4], P. Petignat[5], B. Frey Tirri[6], R. Sahli[7], N. Low[2] for the CIN3+plus study group

[1]Institute of Pathology, Lucerne Cantonal Hospital, Lucerne, Switzerland, [2]Institute of Social and Preventive Medicine, University of Bern, Switzerland, [3]Federal Office of Public Health, Bern, Switzerland, [4]National Institute for Cancer Epidemiology and Registration, Zurich, Switzerland, [5]Department of Obstetrics and Gynecology, University Hospital of Geneva, Switzerland, [6]Women's Hospital, Cantonal Hospital Baselland, Liestal, Switzerland, [7]WHO HPV LabNet, Lausanne University Hospital, Switzerland

Background

- Human papillomavirus (HPV) vaccines provide protection against infections that cause cervical cancer. The International Agency for Research on Cancer (IARC) has classified HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58 and 59 as causal agents of cervical cancer. The bivalent and quadrivalent HPV vaccines provide coverage against HPV types 16 and 18. The new nonavalent HPV vaccine covers HPV types 16, 18, 31, 33, 45, 52 and 58.
- Switzerland started a national HPV vaccination programme in 2007 with a quadrivalent HPV vaccine. In order to assess the effectiveness of the Swiss vaccination program and other public health interventions in the future, population-based data about the distribution of HPV types are needed.

Objectives

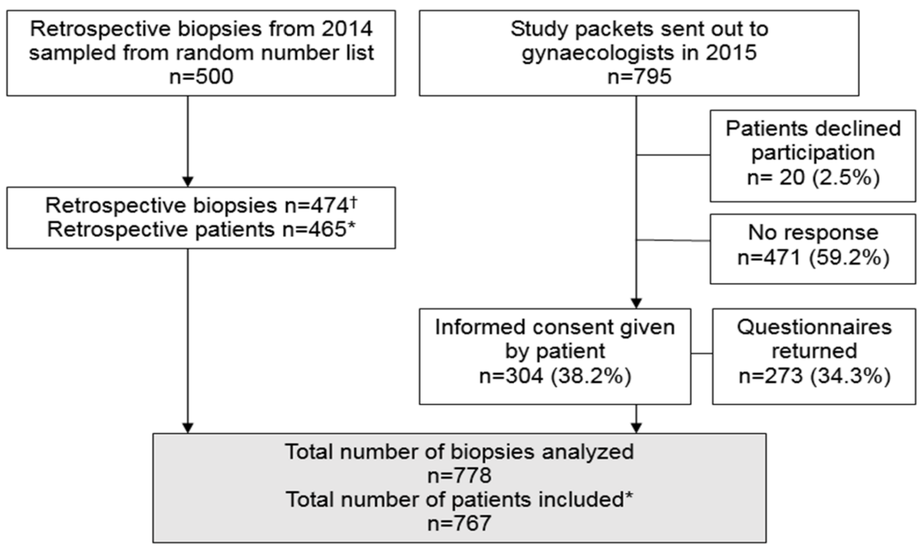
- To examine the baseline distribution of HPV types in women diagnosed with cervical intraepithelial neoplasia and worse (CIN3+) in a representative sample of Swiss women.
- To collect supplementary data about HPV vaccination status and selected factors that might be associated with cervical neoplasia.

Methods

- The project, CIN3+plus, was a cross-sectional study consisting of retrospectively analysed samples from 2014 and samples from prospectively analysed patients from 2015. Ten laboratories from six cantons and three language regions participated in the study.
- We conducted HPV typing on formaldehyde fixed-paraffin embedded (FFPE) specimens. Each laboratory conducted DNA extraction and HPV typing according to their standard practice. Negative and non-evaluable specimens were retested at the WHO Global HPV Reference Laboratory in Sweden.
- We calculated the value for Swiss socioeconomic position (SEP and standard deviation, SD) for patients according to the Swiss neighbourhood index of socioeconomic position and compared this with the Swiss population in the year 2000.

Results 1

- We included 778 biopsies from 767 women aged 17-81 years (Figure 1).

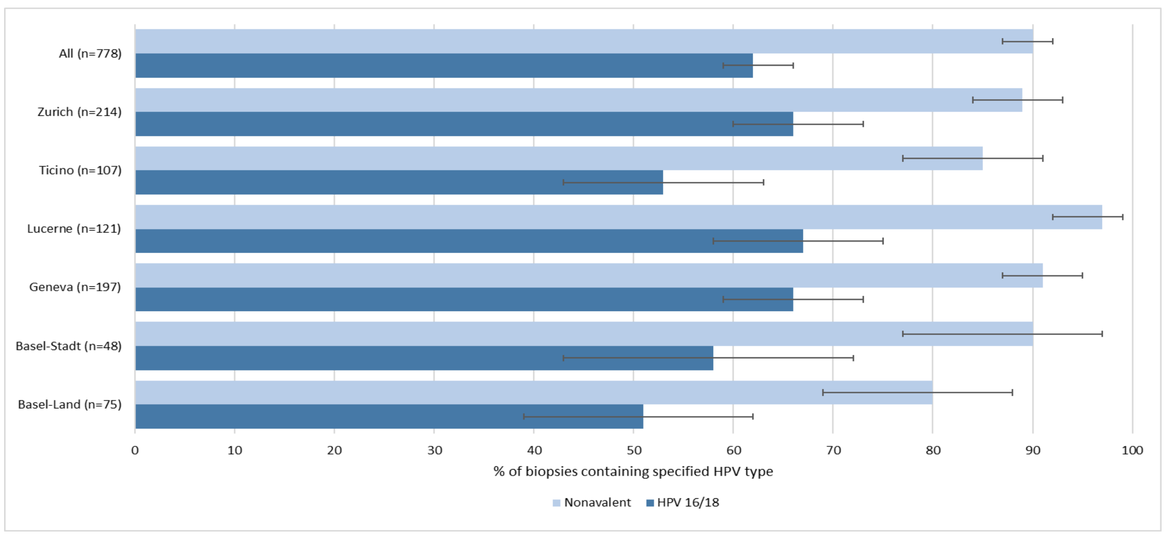


*11 patients were included in the study twice. They were included by different laboratories.
†Laboratories were not able to include all 500 biopsies because not enough tissue was available for testing.

Figure 1. CIN3+plus study flow chart

Results 2

- Overall, the distribution of HPV types was: HPV16, 56.8% (n=442); HPV18, 6.6% (n=51); HPV31, 12.3% (n=96); HPV33, 7.1% (n=55); HPV52, 5.7% (n=44); HPV58, 4.4% (n=34), HPV45, 1.9% (n=15).
- Overall, 94.6% (736/778) biopsies contained one or more IARC defined oncogenic HPV type, 0.6% (5/778) had no HPV detected, 2.4% (19/778 were non-evaluable) and 2.3% (18/778) had other HPV types detected.
- HPV types 16/18 were present in 62.1% (95% CI 58.6-65.5%) of the biopsies; HPV types covered by the nonavalent vaccine were present in 89.5% (95% CI 87.1-91.5%) of the biopsies tested (Figure 2).
- There was no statistical evidence of a difference between retrospectively and prospectively analysed biopsies in the proportions with HPV16/18 (p=0.425) or of those covered by the nonavalent vaccine (p=0.639).
- Some regional differences were seen between cantons. Basel-Land and Ticino had a smaller proportion of high-risk HPV types, but also a higher proportion of non-evaluable biopsies (Figure 2).



HPV 16/18 HPV types 16 and/or 18 detected in any biopsy
Nonavalent Any of the following HPV types detected: 16, 18, 31, 33, 45, 52, 58 in any biopsy
More than on HPV type was detected in 96 biopsies
Error bars represent 95% confidence intervals
Denominator for each canton includes all samples tested
Non-evaluable biopsies: All=19, BL=6, BS=0, GE=3, LU=1, TI=6, ZH=3
HPV negative biopsies: All=5, BL=2, BS=0, GE=2, LU=0, TI=1, ZH=0

Figure 2. HPV types by canton

- 273 women completed a patient questionnaire and 20 (10.3%) reported receiving at least one dose of an HPV vaccine. 14 of the vaccinated women received their first HPV vaccination >25 years of age.
- The SEP value was calculated for 748/767 (97.5%) women. The mean SEP value for the CIN3+plus study group was 64.60 (SD 10.83). The mean SEP value for the entire Swiss population (n=6,979,636) was 62.81 (SD 10.62).

Conclusions

- This first Swiss national study shows a similar HPV genotype distribution to Europe. Some regional differences were observed.
- HPV types covered by the nonavalent vaccine were present in 89.5% of the tested biopsies.
- The SEP index value in the CIN3+plus study group was similar to that of Swiss women in the year 2000.
- This study provides baseline data for monitoring HPV vaccination impact.
- HPV typing of FFPE specimens can be used for surveillance.

3rd Annual Joint Meeting of the Austrian and Swiss Societies of Pathology
Vienna, Austria
November 10-12, 2016

Contact: Prof. Joachim Diebold, joachim.diebold@luks.ch

Funding: Swiss Cancer Research (KFS-3264-08-2013), Swiss Federal Office of Public Health (15.000704)