Short Communication

Age-Specific Occurrence of HPV16- and HPV18-Related Cervical Cancer

Silvia de Sanjose1,2, Cosette M. Wheeler3, Wim G.V. Quint6, William C. Hunt3, Nancy E. Joste3, Laia Alemany1,2, F. Xavier Bosch1,2, on behalf of the Retrospective International Survey and HPV Time Trends Study Group; Evan R. Myers4, and Philip E. Castle5

Abstract

The age-specific occurrence of cervical cancer related to human papillomavirus (HPV) genotypes HPV16 and HPV18, the two targeted by current HPV vaccines, is not well described. We therefore used data from two large, tissue-based HPV genotyping studies of cervical cancer, one conducted in New Mexico (n = 744) and an International study restricted to cancers (n = 1,729) from Europe, North America, and Australia to represent those regions with widely available cervical cancer screening facilities. HPV results were categorized as HPV16- or HPV18-positive (HPV16/18) versus other HPV genotype. We observed a decreasing proportion of HPV16/18-positive cancers with increasing age in the International study (P trend < 0.001) and New Mexico study (P trend < 0.001). There was no heterogeneity in the relationship between age of diagnosis and the proportion of HPV16/18-positive cancers between studies (P = 0.8). Combining results from the two studies (n = 2,473), the percentages of HPV16/18-positive cases were 77.0% [95% confidence interval (CI): 75.1%–78.9%] for women less than 65 years old and 62.7% [95% confidence interval (CI): 58.4%–66.9%] for women aged 65 and older (P < 0.001). In women who are under the age of 25 and have been vaccinated before becoming sexually active, the cervical cancer incidence is expected to be approximately 3.5 per million by 2020. HPV vaccination against HPV16/18 may have a greater impact on cervical cancers in women under 65 than in women aged 65 and older. These data will inform the age-specific impact of HPV vaccination and its integration with cervical cancer screening activities. Cancer Epidemiol Biomarkers Prev; 22(7); 1313–8. © 2013 AACR.

Introduction

Two prophylactic human papillomavirus (HPV) vaccines have been developed, Gardasil (Merck) and Cervarix (GSK), and both have received U.S. Food and Drug Administration approval for women ages 9 to 26 years old. Both vaccines protect against infections by HPV16 and HPV18 (HPV16/18), the 2 HPV genotypes responsible for causing approximately 70% to 75% of all cervical cancer (1). Both HPV vaccines have shown more than 90% efficacy in preventing persistent infections and cervical precancerous lesions caused by HPV16/18 in uninfected women for up to 4 to 6 years with no evidence yet of waning immunity resulting in breakthrough events (2–6); up to 8 years of protection has been observed for a monovalent, research HPV16-only vaccine (7) and 8.4 years for Cervarix (8). However, because the current HPV vaccines do not prevent infections by all carcinogenic HPV genotypes, do not treat preexisting infections or related abnormalities caused by HPV16/18 (3, 4, 9, 10), and the duration of vaccine protection has not been established, cervical cancer screening will be required for the foreseeable future.

To project (i) what degree HPV vaccines will impact age-specific cervical cancer rates and (ii) how screening might be affected and therefore may need to be altered to integrate the 2 interventions in safe and cost-effective manner (i.e., to rebalance the benefits and harms of screening; ref. 11), age-specific data on the occurrence of HPV16/18-related cancer would be very useful. Notably, there is some evidence that HPV16/18-related cervical cancers occur on average at a younger age than cancers due to other HPV genotypes (1, 12). However, detailed, age-specific occurrence of HPV16/18-related cervical cancers has not been described. We therefore combined the data from 2 large studies, one from New Mexico (12) and other from an International study (1), to describe the age-specific patterns of HPV16/18-related cervical cancer in Western countries, where vaccination and screening will need to be integrated in the near future.

Authors’ Affiliations: 1IDIBELL, Institut Català d’Oncologia-Catalan Institute of Oncology, L’Hospitala de, Llobregat; 2CIBER en Epidemiología y Salud Pública, Barcelona, Spain; 3Departments of Pathology and Obstetrics and Gynecology, University of New Mexico Health Sciences Center, House of Prevention Epidemiology (HOPE), Albuquerque, New Mexico; 4Division of Clinical and Epidemiological Research, Department of Obstetrics and Gynecology, Duke University; 5Global Cancer Initiative, Chester-town, Maryland; and 6DDL Diagnostic Laboratory, Voorburg, the Netherlands

S. de Sanjose and C.M. Wheeler contributed equally to this work.

Corresponding Author: Philip E. Castle, Global Cancer Initiative, Chester-town, MD 21620. Phone: 703-772-0611; E-mail: castle.philip@gmail.com
doi: 10.1158/1055-9965.EPI-13-0053
©2013 American Association for Cancer Research.
Materials and Methods
We used data from 2 large cervical cancer studies in this analysis. Both studies had large sample sizes and used tissue-based typing by well-validated assays conducted by expert labs. The 2 studies and their methods have been described in detail elsewhere (1, 12) and will only be summarized here. The institutional review boards of the participating organizations approved these studies.

New Mexico study
The New Mexico Surveillance, Epidemiology, and End Results Registry was used to ascertain all cases of invasive cervical cancer (n = 1,429) diagnosed from January 1, 1980, through September 30, 1999 (12). A total of 808 women (57%) had paraffin-embedded tissue blocks available for analysis, of which there were 744 HPV test results. The HPV genotyping of tissues by PGM09/11 line blot assay (LBA) and SPF10/LiPA25 was described previously (12).

Retrospective international survey and HPV time trends study group study
A retrospective cross-sectional study was designed and coordinated to estimate the prevalence of HPV DNA genotypes in women with invasive cervical cancer during 1949 to 2009 (1). This present analysis was restricted to the 1,729 cases from Europe, North America, and Australia (1), where cervical cancer screening is generally available. The HPV genotyping of tissues by SPF10/LiPA25 was described previously (1).

Statistical and analytical methods
Cancers were classified as positive for HPV16/18 or for other HPV genotypes. We made the a priori assumption that in the context of detecting multiple HPV infections [<10%; (1, 12)], if HPV16 and/or HPV18 were detected, these genotypes were the cause of the cancer. This undoubtedly led to slight overattribution of cancer to these HPV genotypes (12). Age at diagnosis was categorized as <25 years, by 5-year age groups from 25 to 79 and 80 and older.

We used the following statistical procedures and tests in our analysis: (i) exact 95% confidence intervals (95% CI) were calculated for the overall and age group-specific proportions of HPV16/18-positive cervical cancers; (ii) Fisher exact test was used to compare the overall and age group-specific proportions of HPV16/18-positive cervical cancers between studies; and (iii) a nonparametric test for linear trend was used to test for an association of age with group-specific proportions of HPV16/18-positive cervical cancers; (ii) a nonparametric test for linear trend was used to test for an association of age with group-specific proportions of HPV16/18-positive cervical cancers; and (iii) a nonparametric test for linear trend was used to test for an association of age with group-specific proportions of HPV16/18-positive cervical cancers.

We therefore combined the data across studies for greater power (n = 2,473). The age groups with the highest percentage of HPV16/18-positive cases were 30 to 34 years (81.2%) and 40 to 44 years (80.1%). The age groups with the lowest percentage of HPV16/18-positive cases were 70 to 74 years (59.8%) and 80 years and older (60.9%). The percentage of multiple HPV genotypes detected was 7.0% and there was no trend across age groups (P_trend = 0.8).

As a post hoc analysis, we categorized age of diagnosis as less than 65 years and 65 years and older (Fig. 1). Percentages of HPV16/18-positive cases were 77.0% (95%CI: 75.1–78.9%) for women less than 65 years old and 62.7% (95%CI: 58.4–66.9%) for women aged 65 and older.
Table 1. Age group–specific prevalence of HPV16/18 versus other HPV genotypes in cervical cancers diagnosed in Western countries (Europe, North America, and Australia; ref. 1; A), in New Mexico (12; B), and combining data from the 2 studies (C).

### A. Sanjose and colleagues, 2010 (1)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV16/18</td>
<td>N</td>
<td>1294</td>
<td>13</td>
<td>31</td>
<td>91</td>
<td>144</td>
<td>173</td>
<td>165</td>
<td>152</td>
<td>153</td>
<td>119</td>
<td>110</td>
<td>68</td>
<td>39</td>
<td>36  &lt;0.001</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>1.0%</td>
<td>2.4%</td>
<td>7.0%</td>
<td>11.1%</td>
<td>13.4%</td>
<td>12.7%</td>
<td>11.7%</td>
<td>11.8%</td>
<td>9.2%</td>
<td>8.5%</td>
<td>5.3%</td>
<td>3.0%</td>
<td>2.8%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>74.8%</td>
<td>100.0%</td>
<td>73.7%</td>
<td>83.3%</td>
<td>82.3%</td>
<td>80.1%</td>
<td>72.3%</td>
<td>73.4%</td>
<td>81.0%</td>
<td>72.4%</td>
<td>72.5%</td>
<td>60.1%</td>
<td>61.1%</td>
<td>63.2%</td>
</tr>
<tr>
<td>Other HPV Genotypes</td>
<td>N</td>
<td>435</td>
<td>0</td>
<td>11</td>
<td>18</td>
<td>31</td>
<td>43</td>
<td>63</td>
<td>55</td>
<td>36</td>
<td>46</td>
<td>41</td>
<td>45</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>0.0%</td>
<td>2.5%</td>
<td>4.2%</td>
<td>7.1%</td>
<td>9.9%</td>
<td>14.5%</td>
<td>12.6%</td>
<td>8.3%</td>
<td>10.5%</td>
<td>9.5%</td>
<td>10.4%</td>
<td>60.1%</td>
<td>61.1%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>25.2%</td>
<td>0.0%</td>
<td>26.3%</td>
<td>16.7%</td>
<td>17.7%</td>
<td>19.9%</td>
<td>27.7%</td>
<td>26.6%</td>
<td>19.0%</td>
<td>27.6%</td>
<td>27.5%</td>
<td>39.9%</td>
<td>38.9%</td>
<td>36.8%</td>
</tr>
<tr>
<td>Total</td>
<td>N</td>
<td>1729</td>
<td>13</td>
<td>42</td>
<td>109</td>
<td>175</td>
<td>216</td>
<td>228</td>
<td>207</td>
<td>189</td>
<td>165</td>
<td>151</td>
<td>113</td>
<td>64</td>
<td>57</td>
</tr>
</tbody>
</table>

### B. Wheeler and colleagues, 2009 (12)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV16/18</td>
<td>N</td>
<td>5</td>
<td>3</td>
<td>5</td>
<td>9</td>
<td>4</td>
<td>47</td>
<td>0</td>
<td>8</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>64</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>0.0%</td>
<td>2.5%</td>
<td>4.2%</td>
<td>7.1%</td>
<td>9.9%</td>
<td>14.5%</td>
<td>12.6%</td>
<td>8.3%</td>
<td>10.5%</td>
<td>9.5%</td>
<td>10.4%</td>
<td>60.1%</td>
<td>61.1%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>71.9%</td>
<td>0.0%</td>
<td>26.3%</td>
<td>16.7%</td>
<td>17.7%</td>
<td>19.9%</td>
<td>27.7%</td>
<td>26.6%</td>
<td>19.0%</td>
<td>27.6%</td>
<td>27.5%</td>
<td>39.9%</td>
<td>38.9%</td>
<td>36.8%</td>
</tr>
<tr>
<td>Other HPV Genotypes</td>
<td>N</td>
<td>209</td>
<td>6</td>
<td>14</td>
<td>19</td>
<td>26</td>
<td>16</td>
<td>16</td>
<td>11</td>
<td>21</td>
<td>15</td>
<td>25</td>
<td>16</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>2.9%</td>
<td>6.7%</td>
<td>9.1%</td>
<td>12.4%</td>
<td>7.7%</td>
<td>7.7%</td>
<td>5.3%</td>
<td>10.0%</td>
<td>7.2%</td>
<td>12.0%</td>
<td>7.7%</td>
<td>3.4%</td>
<td>3.2%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>28.1%</td>
<td>0.0%</td>
<td>26.3%</td>
<td>16.7%</td>
<td>17.7%</td>
<td>19.9%</td>
<td>27.7%</td>
<td>26.6%</td>
<td>19.0%</td>
<td>27.6%</td>
<td>27.5%</td>
<td>39.9%</td>
<td>38.9%</td>
<td>36.8%</td>
</tr>
<tr>
<td>Total</td>
<td>N</td>
<td>744</td>
<td>15</td>
<td>58</td>
<td>89</td>
<td>106</td>
<td>80</td>
<td>75</td>
<td>53</td>
<td>59</td>
<td>66</td>
<td>45</td>
<td>39</td>
<td>29</td>
<td>30</td>
</tr>
</tbody>
</table>

\[p = 0.018\]

### C. Combined

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV16/18</td>
<td>N</td>
<td>1829</td>
<td>22</td>
<td>75</td>
<td>161</td>
<td>224</td>
<td>237</td>
<td>224</td>
<td>194</td>
<td>191</td>
<td>170</td>
<td>130</td>
<td>91</td>
<td>57</td>
<td>53 &lt;0.001</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>1.2%</td>
<td>4.1%</td>
<td>8.8%</td>
<td>12.2%</td>
<td>13.0%</td>
<td>12.2%</td>
<td>12.6%</td>
<td>10.6%</td>
<td>10.4%</td>
<td>9.3%</td>
<td>7.1%</td>
<td>5.0%</td>
<td>3.1%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>74.0%</td>
<td>78.6%</td>
<td>74.9%</td>
<td>81.2%</td>
<td>79.7%</td>
<td>80.1%</td>
<td>73.9%</td>
<td>74.6%</td>
<td>77.1%</td>
<td>73.8%</td>
<td>66.1%</td>
<td>59.8%</td>
<td>61.4%</td>
<td>60.9%</td>
</tr>
<tr>
<td>Other HPV Genotypes</td>
<td>N</td>
<td>644</td>
<td>6</td>
<td>25</td>
<td>37</td>
<td>57</td>
<td>59</td>
<td>79</td>
<td>66</td>
<td>57</td>
<td>61</td>
<td>66</td>
<td>61</td>
<td>36</td>
<td>34</td>
</tr>
<tr>
<td>%Row</td>
<td></td>
<td>100.0%</td>
<td>0.9%</td>
<td>3.9%</td>
<td>5.8%</td>
<td>8.9%</td>
<td>9.1%</td>
<td>12.3%</td>
<td>10.2%</td>
<td>8.8%</td>
<td>9.4%</td>
<td>10.3%</td>
<td>9.5%</td>
<td>5.6%</td>
<td>5.3%</td>
</tr>
<tr>
<td>%Column</td>
<td></td>
<td>26.0%</td>
<td>21.4%</td>
<td>25.1%</td>
<td>18.8%</td>
<td>20.3%</td>
<td>19.9%</td>
<td>26.1%</td>
<td>25.4%</td>
<td>22.9%</td>
<td>26.2%</td>
<td>33.9%</td>
<td>40.2%</td>
<td>38.6%</td>
<td>39.1%</td>
</tr>
<tr>
<td>Total</td>
<td>N</td>
<td>2473</td>
<td>28</td>
<td>100</td>
<td>198</td>
<td>281</td>
<td>296</td>
<td>303</td>
<td>260</td>
<td>248</td>
<td>231</td>
<td>196</td>
<td>152</td>
<td>93</td>
<td>87</td>
</tr>
</tbody>
</table>

\[p = 0.018\]

NOTE: \(P_{\text{trend}}\), a nonparametric test of trend of the fraction of HPV16/18 with increasing age; \(P\), Fisher exact test for age-group differences in the fraction of HPV16/18 between the 2 studies. Bold type indicates statistical significance (\(P < 0.05\)).
(P < 0.001). The corresponding prevalence ratio of HPV16/18 to other HPV genotypes for less than 65 versus 65 and older was 1.23 (95% CI: 1.15–1.32). Restricted to squamous cell carcinoma histology only (n = 2,204), the percentages of HPV16/18-positive cases were 74.9% (95% CI: 72.8%–76.9%) for women less than 65 years old and 63.5% (95% CI: 58.9%–68.0%) for women aged 65 and older (P < 0.001). The corresponding prevalence ratio was 1.18 (95% CI: 1.09–1.27). Restricted to nonsquamous histology (i.e., primarily adenocarcinoma; n = 269), the percentages of HPV16/18-positive cases were 95.5% (95% CI: 91.6%–97.9%) for women less than 65 years old and 57.1% (95% CI: 44.7%–68.9%) for women aged 65 and older (P < 0.001). The corresponding prevalence ratio was 1.67 (95% CI: 1.36–2.05).

In Fig. 2, we projected what the age group-specific profile of cervical cancer in the U.S. women aged less than 40 years (13) might be without HPV16/18 in the population and screening unchanged. The risks of cervical cancer incidence will decrease from 1.5 per million (0.15 per 100,000) to 0.32 to 0.58 per million in women aged 15 to 19 years and from 14 per million to 3.0 to 4.1 per million in women aged 20 to 24 years. Similar relative reductions are expected in the older age groups.

Discussion

We can only anticipate the HPV vaccine impact based on cervical cancer annual rates and HPV genotype-specific attribution of cervical cancers or wait many years to observe the changes in cancer rates first in the youngest and then later in older women. We therefore empirically projected the impact of removing HPV16 and HPV18 from the population on the age-specific rates of HPV16/18-related cancers in the Western countries, using the best data available from 2 large case series with high-quality HPV genotyping of tissues blocks.

In the United States, where HPV vaccination coverage is poor (15), a broad recommendation for changes in cervical cancer screening in HPV-vaccinated women is not currently appropriate (11). However, we suggest, based on the presented data, that when individual vaccination can be verified through electronic medical records or vaccine registries, or if there is high-population coverage under the age 15 (because women are unlikely to have been exposed to HPV, as most will not yet be sexually active; ref. 16), it will be rational to delay screening until at least age 25. The benefits of screening in unvaccinated women under the age of 25 are already questionable given the very low incidence of cancer (17) in this age group. Time trends of cervical cancer incidence in the United States in women aged 20 to 24 have only declined by approximately 40% over the last 40 years (17), suggesting that the widespread introduction of screening in women aged less than 25 years over that period of time had a minor impact on cancer occurrence. Many European Union countries do not initiate screening until the age of 25 or 30 (18, 19). Likewise, Canadian guidelines now recommend against cervical cancer screening in those less than 25 years of age (20). The population risks in these Western countries are comparable with the United States, indirectly affirming that there is little cancer prevention benefit in screening these young women, even without vaccination. Finally, there is a lack of evidence that screening in this age group prevents these rapidly developing cancers occurring in these very young women (21).

On the basis of this analysis, effective HPV vaccination in primarily unexposed women would be projected to ultimately reduce the incidence of cervical cancer in these vaccinated cohorts of young women up to 80%, or 3 to 4

![Figure 1. The proportions of HPV16/18-positive cancers by age (<65 years vs. 65 and older) and histology type, using data from 2 previous studies of HPV genotyping of cervical cancers (1, 12).](image1)

![Figure 2. An estimation of the impact of HPV vaccination on the annual incidence of cervical cancer (per 100,000) in United States, women under the age of 40 years, assuming vaccination before exposure to HPV16/18 and protective immunity until age 40. The incidence rates were derived on the basis of recently published rates of cervical cancer in the United States (15) and the age group-specific fraction of HPV16/18 cervical cancers (1, 12). The rates of HPV16/18-negative cancers in women less than 20 years and 20 to 24 were based on the fraction of non-HPV16/18 cervical cancers in women under the age of 25. * indicates the estimated fraction for HPV16/18-negative cancers, assuming no impact of HPV16/18 vaccination on cervical cancers with an unknown histology.](image2)
per million in women aged 20 to 24 years, a cancer risk that does not typically warrant population-based screening. In comparison, the age-adjusted, all-ages cancer incidences in the United States in 2009 (22) were 7.5 per million for vaginal cancer, 23.8 per million for vulvar cancer, and 12.0 per million for male breast cancer, none for which we routinely screen. Likewise, we now do not screen women under the age of 21 years for cervical cancer (22, 23) and it may be very reasonable to delay screening until the age of 25 years in those confirmed or highly likely to have been vaccinated before the age of 15 years given the lack of benefit for women aged 21 to 24 years.

In addition, the potential harms of screening these young women are great. HPV infections, and associated cytologic abnormalities, are common in this age group. Testing positive can lead to unnecessary clinical follow-up and treatment, which has been linked to an increased risk of negative reproductive outcomes such as preterm delivery (23).

We noted that the effect of age on the proportion of HPV16/18-positive cervical cancer appeared more like a step function with a decrease around age 65. Although the age-specific effect can be rationalized as a function of the overall greater carcinogenicity of HPV16 and HPV18 compared with the other, weaker carcinogenic HPV genotypes, one would anticipate a more gradual effect over a range of age. It is unclear why this shift occurs at age 65, but it was observed in both sets of independently collected data, lending credence to the observation. One possible contributor to this effect is that screening, which typically stops around age 65, may influence the HPV genotype distribution in cancers. Slowly developing tumors caused by infections by other carcinogenic HPV genotypes might develop after screening has stopped, whereas HPV16 and HPV18-related tumors are more aggressive and cause tumors or precancerous lesions that are detected by screening and treated at an earlier age.

We also cannot rule out that the change in the HPV16/18-attributable fraction of cervical cancer at age 65 is due to a cohort effect. We did not have enough cases to do an age-period-cohort analysis to really understand the origins of this effect. Stratification on women born before and after 1930 showed that in both studies, cancer cases in women over the age of 65 years of age had a lower fraction of HPV16/18 than those under the age of 65 (data not shown), which may suggest that the year a woman was born does not explain the observed decrease in the HPV16/18-attributable fraction in women aged 65 and older.

The age-specific effects observed in this analysis should be considered in mathematical modeling of the impact of HPV vaccination. There may be a greater impact of HPV16/18 vaccination on the occurrence of cervical cancer in women under the age of 65 than in women aged 65 and older. This translates into the possibility of a greater number of years of life (and quality adjusted life years) saved from HPV vaccination than if the fraction of HPV16/18 was constant with age. Our data also emphasize the importance of vaccination in young women before sexual initiation for maximum population impact. Finally, other changes to screening beyond changing the age of initiation of screening to age 25 might be considered, given the reduction in cancer risk and positive predictive value of screening tests for cervical precancer in the absence of the 2 most carcinogenic HPV types, to maintain an appropriate balance of benefits and harms of screening. When vaccination against 7 carcinogenic HPV genotypes becomes available, we anticipate that further adjustments in how and when women are screened will be needed.

Disclosure of Potential Conflicts of Interest
S. de Sanjose has provided expert testimony for Qiagen and MSD. C.M. Wheeler has commercial research support from Roche Molecular Systems and GSK. F.X. Bosch has a commercial research grant and honoraria from speakers’ bureau from MSD, GSK, and SfMPS and is a consultant/advisory board member of GSK and SPMSD. E. Myers has a commercial research grant from GenProbe, Inc and GSK, Inc and is a consultant/advisory board member of Merck. P.E. Castle has honoraria from speakers’ bureau from Roche and is a consultant/advisory board member of BD, Cepheid, GE Healthcare, and Gen-Probe, and Merck. No potential conflicts of interest were disclosed by the other authors.

Authors’ Contributions
Conception and design: S. de Sanjose, C.M. Wheeler, F.X. Bosch, E. Myers, P.E. Castle
Development of methodology: S. de Sanjose, E. Myers
Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): S. de Sanjose, C.M. Wheeler, N.E. Joste, L. Alemany
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): S. de Sanjose, C.M. Wheeler, W.C. Hunt, L. Alemany, F.X. Bosch, E. Myers, P.E. Castle
Writing, review, and/or revision of the manuscript: S. de Sanjose, C.M. Wheeler, W. Quint, L. Alemany, F.X. Bosch, E. Myers, P.E. Castle
Study supervision: C.M. Wheeler L. Alemany

Acknowledgments
The authors would like to thank the Retrospective International Survey and HPV Time Trends Study Group:

1. Australia: Suzanne M. Garland, Sepher Tabrizi (The Royal Women’s Hospital, The University of Melbourne).
2. Bosnia Herzegovina: Ermina Bajzovic (University Clinical Center Tuzla BiH).
3. Croatia: Magdalena Groe, Ivan Sabol (Rudjer Boskovic Institute), Sonja Dzebro, Mara Dominis (Clinical Hospital Merkur).
4. Czech Republic: Ivo Steiner (Faculty of Medicine and Faculty Hospital, Hradec Kralove), Vladimir Vondra (Institute of Hematology and Blood Transfusion).
5. France: Christine Clavel (CHU Reims, Laboratoire Pol Bouin, Hopital Maison Blanche), Massimo Tommasino (International Agency for Research on Cancer).
6. Greece: Maria Tzardi (Medical School of University of Crete), Theodoros Agaratos (Aristotle University of Thessaloniki).
7. Italy: Luciano Mariani, Ferdinando Marandino (Regina Elena Cancer Institute).
8. Poland: Andrzej Marcin Nowakowski (Medical University of Lublin).
9. Portugal: Eugenia Cruz (Centro Regional de Oncologia Coimbra, Instituto Portugues de Oncologia), Manuela Lacerda, Manuel Sobrinho-Simoes (Institute of Molecular Pathology and Immunology of the University of Porto); Ana Felix (Instituto Portugues de Oncologia de Lisboa Francisco Gentil).
References

9. Instituto Catalán de Oncología-Catalan Institute of Oncology, Hospital de Llobregat, Barcelona.
10. The Netherlands: Chris J.L.M Meijer, Peter J.F Snijders (Vrije Universiteit Medical Center); Wim G.V. Quint, Jean-Paul Brunsveld, Joso C. Molijn, Daan T. Geraets (DDI, DDL Laboratory).
11. United States of America: Esther Oliva (Massachusetts General Hospital); Thomas C. Wright (New York Presbyterian Hospital, Columbia University Medical Center).

Received January 17, 2013; revised April 10, 2013; accepted April 11, 2013; published OnlineFirst April 30, 2013.
Correction: Age-Specific Occurrence of HPV16- and HPV18-Related Cervical Cancer

In this article (Cancer Epidemiol Biomarkers Prev 2013;22:1313–8), which was published in the July 2013 issue of Cancer Epidemiology, Biomarkers & Prevention (1), the authors regret that the following financial support was not acknowledged:

Grant Support
The work conducted at the University of New Mexico (awarded to C. M. Wheeler) was supported by the NIH, National Institute of Allergy and Infectious Diseases, U19AI084081, the UNM Interdisciplinary HPV Prevention Center.

Reference

Published online November 4, 2013.
doi: 10.1158/1055-9965.EPI-13-0918
©2013 American Association for Cancer Research.
Age-Specific Occurrence of HPV16- and HPV18-Related Cervical Cancer


Updated version  Access the most recent version of this article at:
doi:10.1158/1055-9965.EPI-13-0053

Cited articles  This article cites 22 articles, 4 of which you can access for free at:
http://cebp.aacrjournals.org/content/22/7/1313.full#ref-list-1

Citing articles  This article has been cited by 2 HighWire-hosted articles. Access the articles at:
http://cebp.aacrjournals.org/content/22/7/1313.full#related-urls

E-mail alerts  Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions  To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions  To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.