An analysis of temporal and generational trends in the incidence of anal and other HPV-related cancers in Southeast England

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Patients diagnosed in 1960–2004 with cancer of the cervix, anus, vulva, vagina or penis were identified from the Thames Cancer Registry database, and age-standardised period (temporal) incidence rates calculated by direct standardisation. Age-cohort modelling techniques were used to estimate age-specific incidence rates in the earlier and later cohorts, enabling the calculation of age-standardised cohort (generational) rates. Incidence of anal cancer increased for both men and women over the period studied, mainly in those born from 1940 onwards. Similar generational patterns were seen for cancers of the vulva and vagina, but those for penile cancer were different. For cervix cancer, the steep downward trend in cohort rates due to screening levelled off in women born from 1940 onwards. Our findings are compatible with the hypothesis that changes in sexual practices were a major contributor to the increases of these cancers. Programmes of vaccination against HPV, aimed at reducing the burden of cervical cancer, may also help to reduce the incidence of cancer at other anogenital sites.

Keywords: human papillomavirus; anogenital cancers; cohort effects

RESULTS

Table 1 shows the total number of cancers diagnosed over the study period and the incidence by age for each site. Incidence increases with age at all sites, with few cases (other than cervical cancer cases) occurring before age 55.
Figure 1A shows a modest increase in age-standardised period rates for anal cancer in both men and women. In men, these increased from 0.79 in 1960–64 to 1.06 per 100 000 in 2000–2004. In women, the increase was greater, from 0.45 in 1960–64 to 1.18 per 100 000 in 2000–2004. In both sexes, rates for consecutive cohorts (Figure 1B) remained relatively constant (between 0.5 and 1.1 per 100 000) for individuals born between 1885 and 1935. There was then a sharp increase in rates in the subsequent generations born from 1940 onwards. In men, the rates increased from 0.92 in the 1935 cohort to 1.71 per 100 000 in the 1960 cohort, whereas in women the increase was from 0.97 in the 1935 cohort to 4.18 per 100 000 in the 1960 cohort.

Figure 2A and B show age-standardised rates, by period and cohort, respectively, for cancers of the vulva and vagina. Period rates have remained fairly constant since the early 1990s, whereas cohort rates have been erratic, with no clear pattern emerging (Figure 3A and B).

Figure 4A and B show age-standardised period and cohort rates for cervical cancer. Period rates have shown a dramatic decline from 12.68 in those diagnosed between 1985 and 1990 to 6.66 per 100 000 in 2000–2004. Cohort rates declined from 21.27 in the 1885 cohort to 7.64 per 100 000 in the 1950 cohort; the corresponding rise for vulval cancer was from 1.65 to 2.51. For penile cancer, period rates have remained fairly constant, whereas cohort rates have been erratic, with no clear pattern emerging (Figure 3A and B).

The dramatic decline in rates for cervical cancer from the late 1980s onward is similar to that reported in the West Midlands (Clare et al., 2008), and reflects the introduction of the National Health Service’s screening programme around 1988, which has led to the early detection of precancerous cervical lesions and the prevention of many invasive cancers.

In our study, in both sexes a marked increase was found in the cohort rates for anal cancer in those born after 1940 onwards. Similar generational patterns were seen for cancers of the vulva and vagina, consistent with a common aetiology. The most likely causes are changes in sexual practice and greater exposure to infectious agents such as HPV. For cancer of the cervix, for which HPV is generally recognised as the major cause, the steep downward trend in cohort rates due to screening levelled off in women born from 1940 onwards.

We found no clear-cut change in cohort rates for penile cancer, although on average the rates for generations born after 1940 were

## DISCUSSION

Anal cancer incidence in southeast England increased in both men and women over the study period (1960–2004), by threefold in women and about 1.5-fold in men; the incidence is now higher in women than in men. Similar trends have been seen in Denmark (Frisch et al., 1993), the United States of America (Melbye et al., 1994; Johnson et al., 2004) and Sweden (Goldman et al., 1989). Increases have also been reported in Scotland (Brewster and Bhatti, 2006), where the change in male rates has roughly paralleled that in the female rates from the mid-1970s to the mid-1990s. Male rates have since plateaued, whereas female rates have continued to rise. In Scotland the female rates were higher than the males throughout the period studied, whereas in our population these were initially lower than in men, but became higher from the early 1990s onwards.

Judson et al. (2006) found a 20% increase in invasive vulval cancer in the United States of America between 1973 and 2000. No increase was seen in the period rates for vulval cancer in our data, nor any increase in the period rates for cancers of the vagina or penis.

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### Table 1 Cancer incidence rates per 100 000 by age at diagnosis

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>35 – 44</th>
<th>45 – 54</th>
<th>55 – 64</th>
<th>65 – 74</th>
<th>75 – 84</th>
<th>85+</th>
<th>Total cancers diagnosed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anus, males</td>
<td>0.02</td>
<td>0.39</td>
<td>0.97</td>
<td>2.14</td>
<td>3.41</td>
<td>5.45</td>
<td>7.28</td>
</tr>
<tr>
<td>Anus, females</td>
<td>0.03</td>
<td>0.44</td>
<td>1.18</td>
<td>1.95</td>
<td>3.37</td>
<td>4.75</td>
<td>6.60</td>
</tr>
<tr>
<td>Vulva</td>
<td>0.09</td>
<td>0.74</td>
<td>1.46</td>
<td>3.15</td>
<td>7.44</td>
<td>14.24</td>
<td>22.86</td>
</tr>
<tr>
<td>Vagina</td>
<td>0.04</td>
<td>0.24</td>
<td>0.66</td>
<td>1.06</td>
<td>1.80</td>
<td>3.46</td>
<td>4.19</td>
</tr>
<tr>
<td>Penis</td>
<td>0.04</td>
<td>0.46</td>
<td>0.94</td>
<td>1.92</td>
<td>3.49</td>
<td>6.08</td>
<td>10.24</td>
</tr>
<tr>
<td>Cervix</td>
<td>2.93</td>
<td>16.21</td>
<td>18.34</td>
<td>19.89</td>
<td>20.25</td>
<td>20.34</td>
<td>19.43</td>
</tr>
</tbody>
</table>

A. Age-standardised rates by period

B. Age-standardised rates by cohort

Figure 1 Anal cancer. (A) Age-standardised rates by period. (B) Age-standardised rates by cohort.

higher than in previous cohorts. It may be that the effect of HPV infection is less in penis cancer than in the other cancers, as recently suggested (Tornesello et al., 2008).

Several studies have linked sexual behaviour with cancer of the anus (Daling et al., 1987; Scholefield et al., 1990; Frisch et al., 1993, 1997). In both Denmark (Melbye and Biggar, 1992) and Scotland (Brewster and Bhatti, 2006) a higher prevalence of receptive anal intercourse in women than in men has been reported, and may explain in part the higher incidence of anal cancer in women in these countries. Sexual practices have also been implicated in cancers of the vagina and vulva (Sherman et al., 1991; Madsen et al., 2008) and of the penis (Maden et al., 1993).

It should be noted that the cohorts which show the recent increases in incidence are, of necessity, based partially on modelled data, because observational data in the older age groups are not available. However, the variability introduced by the modelling procedure has been included in the calculation of the standard errors of the estimated rates. As can be seen from Table 2, none of the estimates exhibits excessive variation.

The generational patterns seen in the cohort rates presented in this paper, with a marked change from around 1940, while not constituting proof, are compatible with the hypothesis that changes in sexual practices are a major contributor to the increases in anogenital cancers other than the cervix. Those born around 1940 would have been in their early twenties at the start of the 'sexual revolution' in the early 1960s.

Peto et al. (2004) have estimated that 'cervical cancer screening has prevented an epidemic that would have killed about one in 65 of all British women born since 1950 and culminated in 6000 deaths per year in this country'. Trials of vaccination against HPV in teenage girls are currently underway in the United Kingdom. In Australia, it has been predicted that the public vaccination programme begun in 2007 will result in a reduction in the age-standardised incidence of HPV-16 infections of 56% by 2010 and 92% by 2050 (Smith et al., 2008). Programmes of vaccination, aimed at reducing the burden of cervical cancer, may also help to reduce the incidence of cancers of the vulva, vagina and anus in women.

Figure 2  Vulval and vaginal cancers. (A) Age-standardised rates by period. (B) Age-standardised rates by cohort.

Figure 3  Penile cancer. (A) Age-standardised rates by period. (B) Age-standardised rates by cohort.


REFERENCES


