An age-period-cohort analysis of 50 875 AIDS cases among injecting drug users in Europe

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Background The long average incubation time from HIV infection to AIDS makes it difficult to estimate recent HIV transmission from AIDS incidence data. Age-period-cohort (APC) analysis can separate out the effects of age, calendar time and birth cohort to provide a clearer picture of transmission trends.

Methods AIDS incidence data from 1981 to 1994 among intravenous drug users (IDU) for 12 Western European countries were used. Yearly incidences per 100 000 population or 100 000 person-years were calculated by age at diagnosis and 5-year birth cohort (1950–1954, 1955–1959, 1960–1964, 1965–1969 and 1970–1974), and corrected for reporting delay. Incidence patterns were compared between birth cohorts and countries.

Results For most countries the impact was greatest on the cohort born 1960–1964. Comparing incidence patterns in the 1965–1969 to 1960–1964 cohorts suggest the epidemic has plateaued at low to intermediate levels in Austria, Greece and the North-Western European countries, and at high levels in France, Italy and Switzerland. For most countries transmission amongst the 1970–1974 as compared to the 1965–1969 cohorts could not be assessed due to small numbers and short follow-up time. In Spain the epidemic was uncontrolled with a high incidence among recent birth cohorts. In Portugal the epidemic was still at an early and expanding phase.

Conclusions The APC analysis revealed large country differences in the dynamics of the HIV/AIDS epidemic among IDU. Full interpretation of these differences is dependent on information from other sources about the local public health response and trends in drug injecting behaviours. Earlier introduction of the virus and higher prevalence of injecting drug use may explain some of the generally higher incidence in Southern European countries, but the larger part of it is most likely explained by local characteristics of drug users, such as younger age and more frequent sharing of needles and syringes, and a less effective public health response.

Keywords Age-period-cohort analysis, AIDS, birth cohort analysis, Europe, injecting drug use, public health

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Since 1989 most new cases of acquired immunodeficiency syndrome (AIDS) in Europe have been in injecting drug users (IDU).1 In the early and mid-1980s rapid spread of human immunodeficiency virus (HIV) occurred through injecting drug use, as documented in places such as Amsterdam, Edinburgh, Geneva and Milan.1–5 High levels of risk behaviour and ignorance of the HIV/AIDS threat made possible the rapid spread.6 Because of the long average incubation time, this early pool of HIV infections was still driving most of the epidemics of AIDS cases in the mid-1990s.7–9 Scarcity of HIV incidence data makes it difficult to assess whether adoption of safer behaviours from
the mid to late 1980s has reduced HIV transmission. Current transmission patterns cannot easily be derived from AIDS incidence data, either directly or through back-calculation, again because of the long average incubation time. In these circumstances an age-period-cohort (APC) analysis of AIDS incidence data could provide fresh insights. Age is a strong determinant of HIV infection through age-related sexual and needle-sharing risk behaviours, but the risk may have changed over time. An APC analysis can separate the effect of age from other time factors such as calendar time and year of birth to see the impact of epidemics across generations (birth cohorts). For this article we used APC analysis to study differences in the extent of transmission to young IDU between European countries.

Material and Methods

We used AIDS cases from the 12 Western European countries that reported their cases by age (Table 1) diagnosed between 1981 (first case) and 31 December 1994 and reported as of 31 March 1995 to the European Centre for the Epidemiological Monitoring of AIDS. The analyses were restricted to cases reported in the transmission category of IDU: homo/bisexual men who also inject drugs were excluded. Incidences for 1992–1994 were adjusted for reporting delay using standard methodology and assuming a maximum delay of 12 quarters. The proportions yet to be reported were estimated specifically for IDU and separately for each of the 12 countries. No adjustments were made for underreporting.

A total of 50 875 AIDS cases (53 826 when corrected for reporting delay) among IDU were diagnosed between 1981 and 31 December 1994. Only 69 cases were reported during 1981–1984. Therefore, graphs by calendar time were restricted to cases reported 1985–1994.

To assess age-related time trends we analysed the mean age at diagnosis over time, incidence by year of birth (in 5-year birth cohorts), and incidence by both year of birth and age, overall and by country. Incidence among cohorts born before 1950 and after 1974 was very limited: 1101 people (2.2%) and 52 (0.1%), respectively; so analyses of incidence by birth cohort were limited to those born 1950–1974. For 152 people (0.3%) the year of birth was unknown. AIDS incidences were much higher for men than for women. For the 12 countries combined incidence during 1994 among the cohorts born 1965–1969 and 1970–1974 was similar for male than female IDU, and female AIDS cases on average occurred at ever younger ages in succeeding birth cohorts. Analyses by country compared only the 1960–1964 and 1965–1969 cohorts at ages 25–29 because the numbers were too small in the lower age groups.

Results

Cumulative AIDS incidence (adjusted for reporting delay) per 100 000 population ranged over a 100-fold from 0.4 in Greece to 54.3 in Spain (Table 1). Incidence in Switzerland and France has reached a plateau, but in Italy, Portugal and especially Spain it continues to increase through 1994 (Figure 1). The epidemic curve in Portugal was very different from that of all the other countries as it began to rise only in the late 1980s and was still increasing exponentially in the 1990s.

The IDU with AIDS were relatively old in the Netherlands, Germany, the UK, Austria and Switzerland, intermediate in France, Italy and Greece, but relatively young in Belgium, Ireland, Spain and Portugal. During the 10-year period 1985–1994 mean age at AIDS diagnosis increased by about 5 years for most countries except Greece, where the increase was about 10 years, Spain, where the increase was only about 4 years, and Portugal, where mean age was unchanged (selected countries shown in Figure 2). The fluctuation between 1985 and 1990 for Portugal was due to small numbers.

AIDS has occurred at ever younger ages in succeeding birth cohorts within particular countries, but there are indications that the rate of increase in AIDS by age may be less in the youngest cohorts compared with in the next older cohorts in countries such as France, Italy and Switzerland (Figure 3). A completely different picture was seen in Spain and Portugal where the rise in AIDS incidence by age has been progressively more rapid with succeeding birth cohorts.

In most countries the impact was highest on the 1960–1964 cohort. In Switzerland, Germany, the UK, the Netherlands and Austria, however, incidence in the 1955–1959 cohort was about as high as in the 1960–1964 cohort. Except for Portugal and Spain, AIDS cases among the 1970–1974 cohort at age 15–20

<table>
<thead>
<tr>
<th>Country</th>
<th>Crude n</th>
<th>Adjusted for reporting delay n/a</th>
<th>n/a/10^5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>359</td>
<td>366</td>
<td>4.8</td>
</tr>
<tr>
<td>Belgium</td>
<td>118</td>
<td>122</td>
<td>1.2</td>
</tr>
<tr>
<td>France</td>
<td>8281</td>
<td>8629</td>
<td>15.4</td>
</tr>
<tr>
<td>Germany</td>
<td>1691</td>
<td>1800</td>
<td>2.3</td>
</tr>
<tr>
<td>Greece</td>
<td>41</td>
<td>41</td>
<td>0.4</td>
</tr>
<tr>
<td>Ireland</td>
<td>195</td>
<td>201</td>
<td>5.7</td>
</tr>
<tr>
<td>Italy</td>
<td>17 255</td>
<td>17 816</td>
<td>31.0</td>
</tr>
<tr>
<td>Netherlands</td>
<td>339</td>
<td>348</td>
<td>2.3</td>
</tr>
<tr>
<td>Portugal</td>
<td>701</td>
<td>885</td>
<td>8.6</td>
</tr>
<tr>
<td>Spain</td>
<td>19 577</td>
<td>21 122</td>
<td>54.3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>1720</td>
<td>1862</td>
<td>28.0</td>
</tr>
<tr>
<td>UK</td>
<td>598</td>
<td>634</td>
<td>1.1</td>
</tr>
<tr>
<td>Overall</td>
<td>50 875</td>
<td>53 826</td>
<td>15.3</td>
</tr>
</tbody>
</table>
Figure 1  Annual AIDS incidence per 100 000 people, injecting drug users, selected European countries 1985–1994

* Adjusted for reporting delay.

Figure 2  Mean age at AIDS diagnosis by calendar year, injecting drug users, selected European countries 1985–1994
were extremely few and it was impossible to compare with older cohorts (cases at higher age in this cohort were excluded). In Belgium the numbers of AIDS cases among IDU were too few to be able to distinguish clear patterns by birth cohort.

For the 12 countries combined, incidence at age 25–29 increased from 8.36 per 100 000 among the 1960–1964 cohort to 9.91 among the 1965–1969 cohort, but the rate of increase changed from 2.1 extra cases per 100 000 per calendar year in the

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**Figure 3** AIDS incidence per 100 000 person-years in 5-year birth cohorts 1950–1974, by age at diagnosis, injecting drug users, 12 European countries 1981–1994. Adjusted for reporting delay.
1960–1964 cohort to 1.5 among the younger cohort (Figure 4). At age 20–24 incidence dropped from 2.61 per 100 000 in the 1965–1969 cohort to 2.07 in the 1970–1974 cohort and the rate of increase changed from 0.63 to 0.43 extra cases per 100 000 per calendar year.

Large contrasts between countries in the underlying intensity of HIV transmission were indicated by the size of the difference in AIDS incidence, and the percentage change in the slope of the incidence curve at age 25–29 between the 1960–1964 and 1965–1969 birth cohorts (Table 2). A deteriorating situation in

Table 2 AIDS incidence$^a$ at age range 25–29 (per 100 000 people per year) in two 5-year birth cohorts and rate of increase (extra cases per 100 000 people per year) by country

<table>
<thead>
<tr>
<th>Country</th>
<th>Incidence 1960–1964$^b$ (per 100 000 people per year)</th>
<th>Incidence 1965–1969$^c$ (per 100 000 people per year)</th>
<th>Change (%)</th>
<th>Rate of increase 1960–1964$^d$ (extra cases per 100 000 people per year)</th>
<th>Rate of increase 1965–1969$^e$ (extra cases per 100 000 people per year)</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Austria</td>
<td>2.90</td>
<td>1.25</td>
<td>–57</td>
<td>0.67</td>
<td>0.13</td>
<td>–81</td>
</tr>
<tr>
<td>Belgium</td>
<td>0.38</td>
<td>0.42</td>
<td>+11</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>France</td>
<td>9.48</td>
<td>7.15</td>
<td>–25</td>
<td>2.32</td>
<td>0.71</td>
<td>–69</td>
</tr>
<tr>
<td>Germany</td>
<td>0.87</td>
<td>0.51</td>
<td>–41</td>
<td>0.21</td>
<td>0.10</td>
<td>–52</td>
</tr>
<tr>
<td>Greece</td>
<td>0.14</td>
<td>0</td>
<td>–100</td>
<td>0.00</td>
<td>0.00</td>
<td>0</td>
</tr>
<tr>
<td>Ireland</td>
<td>6.18</td>
<td>2.17</td>
<td>–65</td>
<td>2.21</td>
<td>0.00</td>
<td>–100</td>
</tr>
<tr>
<td>Italy</td>
<td>17.17</td>
<td>16.28</td>
<td>–5</td>
<td>4.25</td>
<td>2.44</td>
<td>–43</td>
</tr>
<tr>
<td>Netherlands</td>
<td>0.78</td>
<td>0.37</td>
<td>–53</td>
<td>0.26</td>
<td>–0.03</td>
<td>–112</td>
</tr>
<tr>
<td>Portugal</td>
<td>1.91</td>
<td>14.36</td>
<td>+652</td>
<td>0.39</td>
<td>3.24</td>
<td>+731</td>
</tr>
<tr>
<td>Spain</td>
<td>29.65</td>
<td>45.70</td>
<td>+54</td>
<td>7.36</td>
<td>7.13</td>
<td>–3</td>
</tr>
<tr>
<td>Switzerland</td>
<td>20.81</td>
<td>6.58</td>
<td>–68</td>
<td>4.73</td>
<td>1.02</td>
<td>–78</td>
</tr>
<tr>
<td>UK</td>
<td>0.39</td>
<td>0.68</td>
<td>+74</td>
<td>0.13</td>
<td>0.15</td>
<td>+15</td>
</tr>
<tr>
<td>All</td>
<td>8.36</td>
<td>9.91</td>
<td>+19</td>
<td>2.06</td>
<td>1.50</td>
<td>–27</td>
</tr>
</tbody>
</table>

$^a$ Adjusted for reporting delay.

$^b$ Cases diagnosed in 1989.

$^c$ Cases diagnosed in 1994.


Spain and Portugal and marked improvements in France and Switzerland were apparent.

Discussion

Age-period-cohort analysis of trends in AIDS incidence suggests by 1994 the epidemic among IDU had stabilized at low to intermediate levels in Austria, Greece and the North-Western European countries, and at high levels in France, Italy and Switzerland. In Spain, however, the epidemic seems uncontrolled with high incidence among recent birth cohorts. In Portugal the epidemic started later and was still at an early and expanding phase.

Can these differences in incidence between birth cohorts and countries be explained by limitations of the data? In general, available AIDS incidence data are more reliable and complete than HIV incidence data, especially in western countries. Differences in underreporting of AIDS cases and misclassification of IDU exposure group may influence comparisons between countries, but it is not likely that they would vary by birth cohort or age group. Age at HIV infection is a strong determinant of progression towards AIDS, and age-related host factors or therapies may have influenced AIDS incidence patterns over time. This effect, however, is probably overcome by comparing AIDS incidences between successive birth cohorts at the points in time when they were of the same age.

Inclusion in the AIDS-surveillance case-definition of pulmonary tuberculosis from January 1994 may have inflated recent AIDS incidence. In 1994, 11.9% of all AIDS cases were reported with pulmonary tuberculosis and this proportion was higher in Portugal (32.4%) and in Spain (20.2%), reflecting the relatively high prevalence of tuberculosis in these two countries. The extension of the case definition was visible as a greater than expected incidence for 1994 in Figures 1 and 4 and may have influenced the last data point of each curve in Figure 3. How- ever, there were no great differences in the proportions of early infections at the start of the epidemic, diagnosis in the countries that we studied probably reflect no clear picture of a markedly earlier introduction or spread in the South can be derived from them. Yet, it cannot be ruled out that earlier introduction in the Southern countries plays some role in explaining North-South differences. However, Edinburgh and Amsterdam, both cities in North-Western European countries that now have low incidence of AIDS, were among the first to report a rapid spread and by 1985 the prevalence was 38% and over 25%, respectively. This indicates that in North-Western European countries also the potential for rapid spread existed then.

Prevalence of injecting drug use itself may explain part of the differences. Estimates for hard drug use, however, are difficult to obtain and specific estimates for injecting drug use are not available. Available estimates of hard-drug users in Europe range from 120–180 per 100 000 in Germany, 100–210 in Finland, 130–190 in Austria, 160–180 in the Netherlands, 160–230 in Sweden, 240 in Denmark, 280 in France, 330–550 in Italy to 460–550 in Luxembourg. These estimates, produced by the countries, are based on very different methods and are subject to different types of biases. Altogether, differences in the estimated prevalence of hard drug use are much smaller than differences in AIDS incidence. However, whereas smoking heroin has become increasingly widespread in North-Western Europe from about 1980, injection has remained the dominant route of administration in Southern countries. Moreover, among IDU in Southern European countries generally much higher levels of sharing needles and syringes have been reported.

The increase in mean age over time contains information on the proportions of early infections at the start of the epidemic, that could not be influenced by prevention, and later infections. If all the AIDS cases came from a pool of people who were infected with HIV when the epidemic began with very few infections thereafter (and there was no age effect on the AIDS incubation time), mean age at diagnosis would increase by about one per calendar year. If, however, many AIDS cases also come from infections after the initial epidemic wave, mean age at diagnosis would rise less or might decrease. The increase of about 5 years in the mean age at AIDS diagnosis in most countries during the 10-year study period suggests transmission has diminished overall in these countries, but relatively less so in Spain (4 years increase) and not at all in Portugal (no increase). The absolute differences in the mean age at AIDS diagnosis in the countries that we studied probably reflect differences in the age distribution of all IDU in these countries. Since age itself is a determinant of HIV infection through age-related risk behaviours, the average younger age of IDU in most Southern European countries may explain part of the higher AIDS incidence in these countries.

A review of the literature suggests that content and timing of the public health response may be significant in explaining the large differences between countries. The single most important prevention factor is the availability of clean needles and
syringes. In general, North-Western European countries have more often endorsed needle exchange programmes, whereas France, Italy, Portugal and Spain, introduced them largely after 1993. A French study to evaluate the effects of the liberalization of syringe sales at pharmacies in 1987–1988 showed the mere availability of needles and syringes, not embedded in a wider programme of HIV prevention, is insufficient to eliminate needle sharing: about half of the participants continued to share in a variety of ways. However, availability of clean needles and syringes may have reduced overall levels of HIV transmission, and this might partly explain the considerably lower AIDS incidence among young IDU in France as well as in Italy in recent years. The lower incidence has come about in the absence of widespread prevention programmes other than the availability of needles and syringes through pharmacies. AIDS incidence, however, was high and this in itself may have encouraged IDU to adopt safer behaviour already in early years. In Edinburgh the rapid and extensive spread of HIV infection followed the sudden withdrawal of a needle exchange programme, but timely introduction of a prevention programme including needle exchange probably prevented a major epidemic in nearby Glasgow. In the Netherlands, needle exchange programmes were set up relatively early in all parts of the country, and although this was not in time to prevent a major epidemic in Amsterdam, HIV prevalence has remained low in nearby regional towns. Switzerland is another example that it may be possible to reduce transmission to younger IDU in more recent birth cohorts, even when the epidemic has become well established. Here, AIDS incidence was high in the 1955–1959 and 1960–1964 cohorts in the late 1980s, but it is relatively low in the more recent cohorts. This may partly be explained by large-scale prevention programmes that were initiated in the late 1980s after a dramatic spread of HIV infection in the mid-1980s.

In conclusion, there is a scarcity of quantitative data on local public health response and trends in drug injecting behaviours which explain the large differences between countries. Earlier introduction of the virus and higher prevalence of injecting drug use may explain some of the generally higher incidence in Southern European countries, but the larger part of it is most likely explained by local characteristics of drug users, such as younger age and more frequent sharing of needles and syringes, and a less effective public health response.

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References


