Impact of incomplete coverage of neonatal dried blood spot screening on estimating HIV-1 seroprevalence

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SUMMARY

The aim of this study was to determine the extent to which selective under-coverage of births to mothers more likely to be at risk of HIV-1 infection will result in a significant under-estimation of the true neonatal seroprevalence. Census data, local birth statistics, maternity data and data from the prevalence monitoring programme were used to produce a model to predict the effects of under-coverage in the uptake of neonatal metabolic screening which has been observed in babies with a mother of ethnic group black African. The adjustment factor which allows for under-coverage is the relative inclusion ratio (RIR); the probability that samples from a group at different risk of HIV infection were included in the survey divided by the probability of inclusion for samples from all other babies. The RIR was found to be close to unity (0.97), indicating a minimal bias. Under usual conditions only if the relative inclusion ratio (RIR) declined to values of 0.87 or below would there be a substantial bias. Despite some selective under representation, the results obtained from the Unlinked Anonymous HIV Monitoring Programme Dried Blood Spot Survey would seem to identify levels of prevalence in the population of child-bearing women with a good degree of accuracy and remains a useful tool for resource allocation, planning of services, provision of care and counselling.

INTRODUCTION

As part of a national programme unlinked anonymous infant dried blood spot surveys of HIV prevalence are under way in six English health regions and Scotland [1-4]. Objectives including monitoring levels of HIV-1 infection among pregnant women, estimating the proportions of HIV-1 infections clinically identified prior to and during ante-natal care [3, 5-7], and estimating the number of mother to child transmissions preventable by enhancing voluntary confidential HIV testing [8]. The surveys utilize residual dried blood spot (Guthrie card) samples remaining after routine neonatal screening for phenylketonuria and hyperthyroidism. After irreversible unlinking from patient data these residual spots are tested for antibodies to HIV-1 (anti-HIV-1) [2, 3, 9]. Since maternal immunoglobulin crosses the placental membrane in pregnancy, the presence of anti-HIV-1 in neonatal blood spots is a reliable indicator of HIV-1 seropositivity in the mother [10].

National neonatal screening for phenylketonuria began in 1969 and other conditions have been added [11-13]. These programmes aim at 100% coverage at an early age and every live born baby should have a completed screening test by 20 days of age [11]. However, uptake of testing (coverage) is often incomplete [11, 12, 14, 15], with differential coverage...
in ethnic groups. One recent audit survey in two deprived areas in the South of London, England found that coverage levels among babies born to women of ethnic group black african (referred to henceforth as African) was 95.6% compared to 98.2% for babies born to women from all other ethnic groups thus giving a relative inclusion ratio (RIR) of 0.975 for African mothers versus all other mothers for whom ethnic group was known [16]. (The RIR is the probability that a sample with a particular characteristic is included in a survey compared to one without the characteristic). This differential could also have important implications for the unlinked anonymous HIV surveys [17], since HIV-1 prevalence is higher among African women in the UK [18]. A similar study of birth records in New York City suggested that this might, in an extreme circumstance, result in a substantial underestimate in observed compared to true prevalence of HIV-1 [19].

METHODS

The calculation (to determine the difference between true and observed prevalence) was based on the 1991 resident population of Lambeth and Southwark metropolitan boroughs, London, England. HIV-1 prevalence data were obtained from the unlinked anonymous dried blood spot survey and published neonatal screening uptake (coverage) levels were used for the district health authorities which correspond to these boroughs: West Lambeth and Camberwell [16]. Population statistics for the boroughs were obtained from the 1991 Census [20] and fertility statistics for England and Wales from 1991 OPCS Birth Statistics [21].

Differences between estimated true ($P_T$) and observed prevalence ($P_o$) were calculated using the following equations. Observed Prevalence ($P_o$) is derived by the equation

$$P_o = \frac{[C_a \times B_a \times P_a] + [C_r \times B_r \times P_r]}{(C_a \times B_a) + (C_r \times B_r)}.$$  

True Prevalence ($P_T$) is derived by the equation

$$P_T = \frac{[B_a \times P_a] + [B_r \times P_r]}{(B_a) + (B_r)},$$

where: $P_o$, observed prevalence; $P_T$, true prevalence; $C_a$, neonatal screening coverage in babies of African mothers; $B_a$, births to African women, aged 15-44 (1991); $P_a$, HIV-1 prevalence in African women; $C_r$, neonatal screening coverage in babies of all other mothers; $B_r$, births to women in all other ethnic groups, aged 15-44 years (1991); $P_r$, HIV-1 prevalence among women of all other ethnic groups.

The prevalence values of HIV-1 used were 0-20% for African mothers and 0-0.5% for all other mothers of ethnic groups proceeding to have live births as estimates of the extreme ranges for each group. High values for the black african group were used on the basis of high (over 20%) seroprevalences of HIV-1 recorded in pregnant women in some urban areas of Sub-Saharan African countries [22]. Births to African mothers were calculated on the basis of the number of African women aged 15-44 years from the census multiplied by an estimated general fertility rate (the number of births per thousand women) for African women. The corresponding calculation was performed for births to all other mothers. In the UK, no ethnic group specific fertility data is available, rather fertility data are expressed by country of birth. For African women the fertility data used were related to women born in the Rest of Africa category as defined by the OPCS, i.e., excluding women born in East Africa. This was because persons living in London and born in East Africa consist of a mix of ethnic groups unlike those living in London and born in West Africa [20]. Fertility data were taken as 160/1000 for African mothers and 60/1000 for all other mothers respectively as shown in Table 1 [21]. Coverage was taken as 95.6% for African mothers and 98.15% for all other mothers [16].

RESULTS

The differences between observed prevalence and true prevalence were calculated for assumed prevalence values 0-20% for African mothers and 0-0.5% for all other mothers. Figure 1a shows the results for prevalence in all others of 0.3%, as can be seen, no difference occurred between true and observed prevalence until prevalence reached 3% in African mothers and this difference was only 0.01% i.e., it would result in an observed prevalence of 0.34% compared to a true prevalence of 0.35%. The results were very similar for the range of prevalences used for the all other groups, and only started to increase noticeably at prevalences in African women of 8% and above, when the difference reached 0.03%. When coverage in babies born to African women was reduced to 86% (Fig. 1b), the differences were still slight. Therefore, unless HIV-1 prevalence in African women in London
Table 1. Proportion of births to African women, compared to all others

<table>
<thead>
<tr>
<th>Base population (age 15-44 years)</th>
<th>General fertility rate*</th>
<th>Annual births</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>Percentage</td>
</tr>
<tr>
<td>African women</td>
<td>10,336</td>
<td>8.57</td>
</tr>
<tr>
<td>All other women</td>
<td>110,248</td>
<td>91.43</td>
</tr>
<tr>
<td>Combined</td>
<td>120,584</td>
<td>100.00</td>
</tr>
</tbody>
</table>


* The general fertility rate for African women was taken as that given for women born in the ‘Rest of Africa’ as defined by the OPCS (i.e., excluding East Africa).


In a sensitivity analysis (Table 2) the effect of varying the population size and fertility of the African women was limited except when coverage was low. Differences between observed and true prevalence were most sensitive to relative coverage (the relative inclusion ratio, RIR) [17], though only if the RIR was well below that observed in South London.

DISCUSSION

The extent of any bias due to under-coverage is dependent on two variables, the selective under-coverage or relative inclusion ratio (RIR) for African women and the HIV-1 prevalence rates in these and women from all other ethnic groups. Sensitivity analyses suggest that only when coverage falls below 86% (RIR 87%) for African women would there be any significant bias introduced to estimates of HIV-1 seroprevalence from the dried blood spot survey (Table 2). Only if prevalence in African women was implausibly high at 20% and was 0.3% in all others, would there then be a substantial difference between observed and true prevalence (3.65% vs 4.04%). As we have demonstrated prevalence in African women can only be around 2% in South London as the highest estimate. It would seem that the levels of selective under-coverage would, at present, be unlikely to significantly bias the observed HIV-1 seroprevalence. As the areas in the South London study are among the more deprived in the UK and have the...
<table>
<thead>
<tr>
<th>Proportion of African women: all others</th>
<th>Low (1:10)</th>
<th>High (2:10)</th>
</tr>
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<tbody>
<tr>
<td>Observed HIV-1 prevalence (%)</td>
<td>True HIV-1 prevalence (%)</td>
<td>Difference (%)</td>
</tr>
<tr>
<td>Coverage high (95.6%) for African women and low for all others (98.15%)</td>
<td>9.7</td>
<td>9.83</td>
</tr>
<tr>
<td>High prevalence in African women (20%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High African fertility</td>
<td>3.96</td>
<td>4.04</td>
</tr>
<tr>
<td>Low African fertility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low prevalence in African women (0.5%)</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>High African fertility</td>
<td>0.34</td>
<td>0.34</td>
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<td>Low prevalence in African women (0.5%)</td>
<td>0.39</td>
<td>0.40</td>
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<td>High African fertility</td>
<td>0.33</td>
<td>0.34</td>
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<tr>
<td>Low African fertility</td>
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</tbody>
</table>

* Where prevalence for all other women = 0.3% and fertility for all other women = 64 births per 1000 women per year. Where low African fertility = 160 and high African fertility = 640 births per 100 women per year.
† Fertility is based on age specific fertility rates from the 1991 OPCS Birth Statistics, Table 9-4 for women aged 15-44 years. The figures for fertility represent the number of live births per 1000 women by country of birth in 1991.
highest proportion of the African population, it would seem unlikely that effects will be more extreme elsewhere. Of course under-coverage, selective or otherwise, is highly undesirable for the purposes of neonatal screening.

HIV-1 positive mothers aware of their infection might conceivably avoid neonatal screening if they misunderstand the purpose of unlinked anonymous testing. This would create a sub-group of low RIR but very high prevalence and could introduce a substantial bias. However, direct investigations suggest this is not the case [23]. Nevertheless care needs to be taken to ensure that specimens from women known to be HIV-1 infected are included in the programme.

In conclusion, current coverage of neonatal dried blood spot screening in the UK will provide accurate estimates of the prevalence of HIV-1 among pregnant women even in areas where coverage of neonatal screening is incomplete.

ACKNOWLEDGEMENT

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REFERENCES