

## **'Further Questions on Statistics'**

### **Response to Penrose Inquiry**

#### **from Professor Ludlam and Dr Hay**

The Inquiry is seeking an explanation for differing estimates of the number of people with haemophilia who were likely to have been infected by HIV in Scotland and posed the following questions:

- 1. What is the explanation for the discrepancy between the figures?*
- 2. Is one set of figures more likely to be correct and, if so, why?*
- 3. Has any further work been undertaken in an attempt to reconcile the figures or arrive at more definitive figures?*
- 4. Do Professor Ludlam and Dr Hay consider that any further work can reasonably be undertaken to try and reconcile the figures or arrive at more definitive figures?*

To address the reasons for the differing estimates Professor Ludlam and Dr Hay have collaborated and reviewed the HIV and treatment records held by Haemophilia Centres in Scotland (in conjunction with Professor Lowe and Dr Tait, Glasgow and Dr Watson, Aberdeen) and the UK National Haemophilia Database (NHD).

The patient data held locally contained details which were not recorded in the National Haemophilia database (NHD). In particular, local data included many more HIV test results than had been reported centrally, permitting greater localisation of the most likely time (and therefore place) of initial infection. On the other hand, the National Haemophilia Database recorded particularly treatment, records at Haemophilia Centres other than at the one each patient is registered. Therefore using both sets of data it has been possible to make a more accurate estimate of the time each patient contracted HIV and which centre administered the treatment responsible for the infection. Furthermore, scrutiny of the NHD has identified a Scottish patient not registered or treated at any the Scottish Haemophilia Centres but infected in a non-specialist Scottish Centre.

In their original submission Haemophilia Directors in Scotland reported to the Inquiry a total of 59 patients which were considered 'infected by HIV in Scotland' (this included two patients who had also been extensively treated in England and in whom there was uncertainty as to where infection occurred (patients 63 and 64 in attached table)). In Dr Hay's report of April 2012 from the NHD a total of 74 patients were identified as possibly being infected in Scotland. On reviewing the individual data held at NHD Dr Hay concluded

that a number of these patients (perhaps about 5) may have been infected out with Scotland (Table 4 and 6).

Professor Ludlam and Dr Hay together have reviewed the available information on all the 74 patients in the NHD April 2012 Report. The attached table summarises information on each of the 74 patients and indicates the likely country of infection. It was agreed that the 59 patients identified by Scottish Haemophilia Directors were all included within the 74 patients highlighted by the NHD and all were probably or likely infected in Scotland. Of the other 15 patients, after reviewing all available data, the following has been agreed:

1. One additional patient (no. 73) was identified on the NHD who had lived and received treatment in Scotland but he was not registered or treated at any Scottish Haemophilia Centre. As a result of reviewing the records it has been concluded that it is probable that he was infected in Scotland.
2. Three patients, on reviewing their treatment records and HIV blood test results, were considered probably infected in England (nos. 1, 5 and 40).
3. There were 11 patients who all arrived from abroad direct to Scottish Haemophilia Centres. Review of their data indicated that 10 were HIV positive when they arrived in Scotland (nos. 8, 25, 31, 66, 68, 69, 70, 71, 72, 74).
4. A further patient was found to be anti-HIV negative upon arrival in Scotland and became anti-HIV positive shortly thereafter (no.41). This individual had severe haemophilia, required frequent infusions of factor VIII and came from a country that had a high prevalence of HIV in factor VIII concentrates. The details of the Scottish transfusion records of this patient have been reviewed. On the balance of probability it is concluded that this patient was probably infected abroad and was 'incubating' HIV on his arrival in Scotland. This fits better with the known incubation period of HIV than the alternative hypothesis, which would have him infected in Scotland immediately after arrival and with an unusually short incubation time.
5. In conclusion 11 patients were therefore considered to have been infected out with Scotland.
6. **In summary** we are agreed that 60 (59 plus (1) above) were probably infected in Scotland and that of the others considered in the NHD Report of April 2012 estimate, 3 were infected in England and 11 infected out with the UK.

Health Protection Scotland (HPS) recorded 76 patients with haemophilia being infected with HIV. The patients notified to HPS were those with a positive HIV test who were classified on the request form to the virology laboratory in Scotland as either having haemophilia or being a recipient of a clotting factor concentrate (see statement to Penrose Inquiry from Professor David Goldberg dated 1<sup>st</sup> February 2011). HPS does not have access to, or knowledge of, where the patients are likely to have acquired their infection. Thus the total of 76 will include patients infected in Scotland as well as those infected out with, and who came to live in, Scotland.

We would point out that 60 patients with bleeding disorders infected with HIV in Scotland further reduces the estimated incidence of HIV in Scotland relative to Dr Hay's earlier report and relative to the incidence reported for the rest of the United Kingdom. This is an infection rate slightly less than half of that observed in the rest of the UK, in fact. The Scottish cohort is less than 5% of the UK cohort. Had they been infected on the same per capita basis as the rest of the UK, twice as many HIV infections would have been observed in Scottish patients with bleeding disorders.

**The Inquiry also posed the following questions;**

7. *Has any further work been undertaken on the number of patients with bleeding disorders who were infected with HIV as a result of NHS treatment in Scotland who have died (including any further work in respect of the cause of death)?*

No significant further work has been undertaken into causes of death of HIV infected individuals. The additional patient described above who was treated out with a Haemophilia Centre in Scotland is recorded as having died of AIDS. It is unlikely that such investigation would reveal significant further information.

8. *The Inquiry is unaware of any evidence that any patients with von Willebrand's Disease were infected with HIV as a result of NHS treatment in Scotland. For the avoidance of doubt, can Professor Ludlam and Dr Hay confirm that that is also their understanding of matters?*

It is our understanding that there are no patients with Von Willebrand disease who acquired HIV in Scotland.

Dr Charles RM Hay

Date 20/2/2013

Professor Christopher A Ludlam

Date 27/2/2013

## Country of Probable HIV infection

Patient Number	Diagnosis	Country of probable Infection	Table 4 & 6 NHD Report April 2012	Comments from Tables 4 and 6 of the NHD Report April 2012 <i>Additional information in italics</i>	Date Last Negative	Date First Positive
1	Haemophilia A	England	11	The first reported HIV positive test dates from 5/7/1985, when the test became available and no negative tests have been reported. The date of seroconversion is therefore quite uncertain. During the period of risk he was treated extensively in Oxford and was treated for three years there with Factorate. <b>On the balance of probabilities, he was probably infected with HIV in Oxford</b> from Factorate, or Koate (Cutter USA), but there can be no certainty of this.		05/07/1985
2	Haemophilia A	Scotland				15/05/1984
3	Haemophilia A	Scotland			15/05/1982	15/01/1984
4	Haemophilia A	Scotland	5	This patient first tested positive in September 1982 and was negative when tested in May 1981. This shows that he was not infected with HIV from commercial concentrate administered in Belfast in 1980 but <b>infected in Glasgow, either from commercial concentrate administered in 1981 or from PFC concentrate administered in 1982.</b>	15/05/1981	15/09/1982
5	Haemophilia A	England	1	This patient was treated mainly in Coventry during the period of risk and was treated with Factorate (Armour) in 1981, 1982 and 1983, in each case in Coventry. This patient was first reported positive when the HIV test became available in 1985 and so the date of seroconversion is uncertain. However, given that most of his treatment was in Coventry, and that he was treated extensively there with commercial concentrate, I would say, <b>on the balance of probabilities, that he was infected with HIV in Coventry and not Scotland.</b>		12/07/1985
6	Haemophilia A	Scotland			16/04/1984	20/07/1984
7	Haemophilia A	Scotland			01/01/1982	15/02/1984

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8	Haemophilia A	Denmark	2	This patient, who has severe haemophilia A was first tested HIV-positive in 1984, presumably from a stored sample. We have no record of any negative sample in this patient. That is therefore likely to be the year of seroconversion, particularly since no treatment is recorded for the years 1980, 1981, 1982 and 1983. Prior to 1980, the patient was treated in London, only occasionally, and exclusively with BPL products or cryoprecipitate. The database also indicated that he was resident overseas, which probably accounts for the years when no treatment was issued in the UK. On that basis and on the balance of probabilities, and assuming that the first available sample tested positive, <b>I would say that this patient was infected with HIV overseas prior to 1984.</b> ( <i>Arrived from Denmark to Edinburgh 1984 no UK treatment records 1980-83</i> )		14/11/1984
9	Haemophilia A	Scotland			01/01/1985	17/11/1986
10	Haemophilia A	Scotland			14/07/1983	18/12/1984
11	Haemophilia A	Scotland			28/11/1983	20/06/1984
12	Haemophilia A	Scotland			16/08/1984	19/11/1984
13	Haemophilia A	Scotland	3	This patient also first tested positive in Edinburgh in October 1984 and negative in April of that year, presumably from a stored sample. <b>This shows that he was infected in Edinburgh from PFC factor VIII</b> , which is all that he received in that year.	05/04/1984	06/10/1984
14	Haemophilia A	Scotland			13/09/1983	13/06/1987
15	Haemophilia A	Scotland			26/10/1983	08/05/1984
16	Haemophilia A	Scotland			27/03/1984	29/05/1984
17	Haemophilia A	Scotland				22/08/1984
18	Haemophilia A	Scotland			09/04/1984	29/05/1984
19	Haemophilia A	Scotland			26/06/1984	10/08/1984
20	Haemophilia A	Scotland			14/12/1983	17/04/1984
21	Haemophilia A	Scotland				15/09/1983
22	Haemophilia A	Scotland			15/05/1984	11/10/1984

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23	Haemophilia A	Scotland	7	The first HIV positive test for this patient was reported for 15/10/1985 and last negative for 15/10/1984. <b>The patient was therefore infected between late 1984 and late 1985 from PFC factor VIII administered in Glasgow.</b>	15/10/1984	15/10/1985
24	Haemophilia A	Scotland			29/03/1984	24/05/1984
25	Haemophilia A	Malta		Resident of Malta		03/05/1983
26	Haemophilia A	Scotland			01/02/1984	29/05/1984
27	Haemophilia A	Scotland			16/03/1981	01/12/1981
28	Haemophilia A	Scotland			06/08/1984	23/10/1984
29	Haemophilia A	Scotland				15/04/1981
30	Haemophilia A	Scotland	6	This patient first tested positive in 1985, when the test became available and we have no record of any stored samples testing negative. The date of seroconversion in this case therefore remains uncertain but certainly antedates his treatment at the Royal Free Hospital. <b>He was therefore infected in Glasgow</b> , possibly from PFC products but also possibly from Factorate (Armour) administered in 1980 and 1981.		15/05/1985
31	Haemophilia A	Malta		Resident of Malta		Unavailable
32	Haemophilia A	Scotland				01/01/1985
33	Haemophilia A	Scotland			18/01/1983	26/06/1984
34	Haemophilia A	Scotland				15/01/1985
35	Haemophilia A	Scotland			17/04/1984	23/04/1984
36	Haemophilia A	Scotland			01/01/1982	01/01/1983
37	Haemophilia A	Scotland			01/01/1982	15/09/1986
38	Haemophilia A	Scotland			15/12/1984	15/11/1985
39	Haemophilia A	Scotland			15/07/1982	15/12/1983
40	Haemophilia A	England	8	The first positive sample in this case dates from 1/1/1981 presumably from a stored sample. There are no negative tests reported to us for this individual. <b>This implies that on the balance of probabilities, he was infected in 1980 from commercial concentrate administered in Basingstoke or Luton.</b> This patient died in 2009 from liver failure secondary to HCV.		01/01/1981

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41	Haemophilia A	France		<i>French. Visited Edinburgh 1978 and 1979 treated cryo and PFC VIII returned to Edinburgh 1984</i>	15/10/1984	27/11/1984
42	Haemophilia A	Scotland			29/05/1984	22/11/1984
43	Haemophilia A	Scotland			13/09/1984	30/10/1984
44	Haemophilia A	Scotland			24/02/1982	06/04/1983
45	Haemophilia B	Scotland				15/11/1985
46	Haemophilia A	Scotland			01/01/1980	01/01/1981
47	Haemophilia A	Scotland			15/04/1981	15/05/1982
48	Haemophilia A	Scotland	9	This patient first tested positive on 15/2/1983. We have no record of any negative tests reported to us. This shows that he was infected with HIV in Glasgow, either from Factorate administered in 1980, 1981 or 1983 or from PFC factor VIII administered in 1980, 1981 or 1983. On the balance of probabilities, infection from Factorate (Armour) is more likely during those years.		15/02/1983
49	Haemophilia A	Scotland			15/06/1981	15/10/1981
50	Haemophilia A	Scotland				15/12/1982
51	Haemophilia A	Scotland			29/01/1982	10/03/1983
52	Haemophilia A	Scotland				15/01/1985
53	Haemophilia A	Scotland			01/01/1981	19/03/1982
54	Haemophilia A	Scotland				01/01/1985
55	Haemophilia A	Scotland			01/01/1991	15/11/1982
56	Haemophilia A	Scotland				15/02/1983
57	Haemophilia A	Scotland			21/05/1982	08/08/1984
58	Haemophilia A	Scotland			08/04/1981	11/03/1983
59	Haemophilia A	Scotland				01/09/1982
60	Haemophilia A	Scotland			17/11/1982	06/04/1983
61	Haemophilia A	Scotland			15/05/1981	15/11/1982
62	Haemophilia A	Scotland				18/10/1984
63	Haemophilia A	'Included as infected in Scotland'	1	First reported positive 15/4/1985. No negative test. Seroconversion date uncertain. Probably infected in Basingstoke but one cannot exclude infection in 1982 from Factorate administered in Glasgow.		15/04/1985

Patient Number	Diagnosis	Country of probable Infection	Table 4 & 6 NHD Report April 2012	Comments from Tables 4 and 6 of the NHD Report April 2012 <i>Additional information in italics</i>	Date Last Negative	Date First Positive
64	Haemophilia B	'Included as infected in Scotland'	10	The last HIV-negative test reported to NHD in this case dates from 15/10/1985 and first positive from 15/7/1986. This patient with severe haemophilia B was therefore <b>probably infected from commercial factor IX concentrate administered in Glasgow in 1985 (Immuno, Vienna) or in Manchester in the same year (Cutter factor IX, USA)</b> . Infection from PFC and BPL IX administered in the same year cannot be excluded. Although we can pinpoint the year of HIV seroconversion to a single year, this does not enable us to determine where or from which product he was infected since he was treated with four products in two centres during that time.	15/10/1985	15/07/1986
65	Haemophilia A	Scotland				29/11/1982
66	Haemophilia A	France		<i>Treated Edinburgh 1978. Returned to Edinburgh 1993</i>		Unavailable
67	Haemophilia A	Scotland			15/01/1980	01/01/1981
68	Haemophilia A	USA		<i>Arrived direct from USA in 1984 - no UKHCDO records before 1984</i>		15/01/1985
69	Haemophilia A	Malta	4	This is an occasional visitor from Malta, who has been treated very occasionally in Edinburgh and Oxford over the years. <b>Almost all of his treatment has been in Malta, however, and that is probably where he contracted HIV.</b>		Unavailable
70	Haemophilia A	USA		<i>Direct from USA to Edinburgh in 1987</i>		15/10/1987
71	Haemophilia A	USA		<i>Arrived direct from USA in 1988</i>		Unavailable
72	Haemophilia A	Abroad		<i>Arrived from overseas - UKHCDO database records 'Scotland but usually overseas' - no treatment records 1980-86</i>		Unavailable
73	Haemophilia A	Probably infected in Scotland		<i>Treated Scotland, outwith a haemophilia centre</i>		01/01/1983
74	Haemophilia A	France		<i>Arrived direct from France HIV positive</i>		01/01/1982