

PATIENT INTEREST CORE PARTICIPANTS - ADDITIONAL SUBMISSIONS FOR THE STATISTICS TOPIC

The Inquiry has afforded the patient interest core participants the opportunity to comment on certain additional materials provided to it in connection with the statistics topic. The patient interest core participants have the following comments on these additional materials, in addition to the comments already made in their main submission on this topic¹:

The additional responses of Drs McClelland and Gillon

Further responses have been submitted by Drs McClelland and Gillon in connection with the number of individuals infected with Hepatitis C in Scotland through blood transfusions.² These responses were to specific questions raised by the Inquiry about "data and opinions" which had been provided by Drs McClelland and Gillon to Professor Goldberg & Anr and the impact of that data and those opinions in the formulation of assumptions underpinning the Goldberg analysis of this topic.³

General

We note that both Drs McClelland and Gillon were asked about the extent to which Professor Goldberg's assumptions were based on the "data and opinions" provided by them or whether they were also based on other material. Neither appears to have been able to answer this question, perhaps understandably, which, in our view, requires to be directed to Professor Goldberg directly.

Assumptions 3 and 4

¹ PEN.019.1171

² PEN.019.1315 (McClelland) and PEN.019.1311 (Gillon)

³ PEN.019.0899

In his additional paper, Dr McClelland provides some explanation for the opinion which appears to have formed the basis of Professor Goldberg's assumption 3. He refers to (a) data from the lookback study (b) prevalence estimates suggesting that the population wide prevalence in England & Wales peaked in 1986 at around 1% (Balogun & Ors, 2002) (Dr Gillon confirms that this was actually just over 1%) and (c) a 2011 estimate in the general population in England & Wales of 0.67% on 2005 (the significance of which is unclear). Underpinning all of this is the 0.09% donor prevalence rate from the 1991 - 1992 Crawford study. From this data Dr McClelland suggests that he was able to opine that the HCV prevalence rate in donors was in the order of 10 fold lower than in the general population. That calculation appears to be derived from applying the Crawford prevalence figure to the 1986 Balogun estimate. We note that the 1% figure from the Balogun does not appear to have been used in the Goldberg calculations in his table 1 at all. The discrepancy between the prevalence figure used for 1986 based on the Balogun figure apparently relied upon to a certain extent by Dr McClelland (one tenth of 1% reduced by 75% in accordance with assumption 2 resulting in a prevalence figure of 0.075%) and the figure arrived at in the Goldberg paper (0.045%) would suggest that the reliance on the information (assumption 4) and indeed the starting point from the Crawford paper (0.088%) might not be a reliable way of undertaking the calculation. The use of the 0.075% for 1986 alone would result in an increase in the number of likely infections for that year to 163 - 216,824 units transfused x 0.075% = 163).

Dr McClelland indicates that he gave the opinion that the donor deferral measures introduced in 1983/84, although directed at AIDS, will have indirectly affected the Hepatitis C prevalence rates amongst donors as well. Whilst this is undoubtedly likely as a general proposition, we fail to understand how any of the material to which he has referred can provide any accurate insight into the likely extent of the impact of donor selection policies on HCV prevalence rates in the donor community in 1984, which is what assumption 3 is all about. Although Dr McClelland expresses "opinions" in the absence of data as to prevalence in either the donor or general populations over the relevant period, it does rather seem to us that Professor Goldberg's assumptions are not backed up with anything other than further assumptions for which there is no clear evidential basis.

Dr Gillon expresses the view that he was able to gain some knowledge of the apparent effectiveness of donor selection policies in excluding infected donors in the period between 1984 and 1991 on the basis that he received confidential written reports on every excluded donor. It is not clear what

these reports contained but given that the reports were on donors who had been excluded, they must be deemed to be limited in value in assessing the number of infected donors who were not excluded by the selection policies (ie about whom no such reports would have been written). The approach advocated by assumption 4 in the Goldberg paper would tend to suggest that the number of infected donors coming to donate blood was rising over this period proportionate to the number of intravenous drug users in the population. The number of infected individuals who came to give blood needs to be known (as well as the number of those likely to have been infected who are deferred) before any assumptions can be accurately developed about the effect of the deferral regime on the rates of infected donors being excluded. Further, Dr Gillon makes it clear (lest there were any doubt about the matter) that the exclusion rate of infected donors was "steady" and not instantaneous, as assumption 3 would tend to suggest.

Both Drs McClelland and Gillon make it clear that they played no part in the decision to use assumption 4 and estimate donor prevalence based on the estimated numbers of intra-venous drug users in the population. It seems that questions about the legitimacy of this assumption will require to be directed to Professor Goldberg, if the Inquiry considers that necessary. This assumption has had a considerable impact on Professor Goldberg's overall conclusions about the numbers likely to have been infected over the period he has studied.

The additional responses of Drs Tait and Hay

Further responses have been submitted by Drs Tait and Hay in connection with the number of bleeding disorder patients infected with Hepatitis C in Scotland through their use of blood products.

We note the efforts made to explain the discrepancies in the estimated number of patients so infected provided by (a) Health Protection Scotland (b) the Scottish Haemophilia directors and (c) the UKHCDO. We fail to understand why it is that such considerable efforts have been put into the compilation of the data in this cohort using different methodologies, in particular the separation between the efforts of the Scottish haemophilia directors and the UKHCDO. We would urge those two groups to compare and contrast the data which they have in order to reconcile their conclusions.

Dr Tait suggests in his supplementary submission that a figure of "around 460" should be deemed to be the estimated upper figure for the number of bleeding disorder patients who are likely to have contracted HCV through haemostatic treatment in Scotland. We remain of the view that this figure cannot legitimately represent an upper limit. Dr Hay appears to accept that his figure (447 adjusted to 462 to include the 15 individuals unknown to the UKHCDO identified by Dr Tait) is likely to represent an underestimate of the numbers infected (see page page 5 of his additional report). Further, Dr Hay's report appears to suggest that 19% of the 86 patients treated over the material period with products other than concentrates were likely to be infected. This could result in a further increase of 16 (to 478) (this depends on the extent of any crossover between those 16 and the 15 identified by Dr Tait from local records as Dr Tait's analysis did include consideration of patients who had not been treated with concentrates). Further, on page 2 of his report, Dr Tait does accept that there may be a small number of patients not recorded in the UKHCDO system who may have been infected. Any such patients could increase the total further. Also, the starting point for the Scottish directors' assessment is a figure of 715 which is thought to represent the number of patients treated or registered with a Scottish haemophilia centre between 1970 and 1989. Given that the material provided by Dr Hay would suggest that in 1990 there were 778 patients registered in Scottish centres in 1990⁴, there would appear some difficulty with Dr Tait's starting point. Further, even that number is based on available UKHCDO data which is not complete.

We find ourselves unable to reconcile the claim at page 4 of Dr Hay's additional report that "this risk [of contracting HCV] diminished during 1985/6 when virally inactivated concentrates were introduced" with other evidence available to the Inquiry to the effect that such concentrates virally inactivated for HCV were not available in Scotland until April 1987. Further, evidence is available to the Inquiry of HCV infection occurring in two patients on first exposure to factor VIII concentrate in May 1986 and early 1987 respectively.

Further, at page 4 of his report, Dr Hay discusses the risk of patients contracting Hepatitis C from treatment with cryoprecipitate. This is important in the context of the different approaches taken by him and Dr Tait in their analysis of the number of bleeding disorder patients likely to have been infected in Scotland. He expressed the view that patients with severe haemophilia would have been

⁴ PEN.019.0927 @ 0958

infected anyway as a result of their heavy treatment with cryoprecipitate prior to the advent of concentrates. Therefore, as far as the fact of their infection is concerned, the precise type of treatment which they received does not matter. However, it appears to underlie the analysis conducted by Dr Hay at page 4 that it would be possible to estimate how much cryoprecipitate one would require to have been exposed to to become infected. He makes it clear that increasingly effective donor screening methods after 1984 would appear to have reduced the risk of becoming infected via this route considerably, in his view. Therefore, the timing of exposure to cryoprecipitate would appear to be highly significant in the likelihood of a patient being infected via that treatment route. Given that the treatment records of the 715 patients identified in Dr Tait's analysis appear to be available (the records of those deemed to have been infected in Scotland having been produced to the Inquiry in a spreadsheet), we would anticipate that a more scientific compromise between the approaches of Drs Tait and Hay could be reached by looking at the treatment records of those patients deemed to have been infected by products other than a concentrate (included in Dr Tait's analysis but not in Dr Hay's) and assessing their likelihood of being infected by that route. This would require some analysis of the amount of treatment they received and the timing of that treatment. The validity of the assumptions being made about the amount of such treatment needed to cause an infection could be checked by reference to actual infection data where PCR testing results are available. The reference in the following paragraph of page 4 of Dr Hay's additional report to "18.8% of those patients [being] reported to have been treated with blood components only [having] evidence of exposure to HCV and 14% [having] active HCV infection" would tend to suggest that those not exposed to concentrates have around a 19% chance of infection. It would be of interest to the Inquiry to understand clearly how these figures have been arrived at. Further, it would be of interest to the Inquiry to understand what these figures would be likely to be for bleeding disorder patients exposed only to cryoprecipitate after the introduction of screening measures in 1984, which Dr Hay appears to suggest would have had a significant effect on reducing the infection rate.

Finally, we note from page 6 of Dr Hay's additional report that only 20% of the data which has been sought in connection with the ongoing UKHCDO lookback exercise has been received from the Scottish centres. It does appear that further information is made available to the Inquiry by Dr Hay every time that he has been requested to comment further on this topic. We would suggest that the UKHCDO HCV lookback exercise should be encouraged and that a recommendation be made that it receive extra funding to be completed as soon as possible.

The joint response of Drs Ludlam and Hay

A further joint response has been submitted by Drs Hay and Ludlam in connection with the number of bleeding disorder patients infected with HIV in Scotland through their use of blood products.⁵ This additional report attempts to reconcile the conclusions of the Scottish haemophilia directors and the UKHCDO regarding the number of infections in this cohort. The result is that one further infection is deemed to have occurred in Scotland, resulting in a total of 60. A table has been produced explaining the conclusions of the further investigation into this matter.

As was narrated in our submission on the topic of statistics, the starting point for the UKHCDO analysis here appears to have been the 73 bleeding disorder patients first reported to the national haemophilia database as having been infected by a Scottish centre.⁶ The treatment histories of these patients were analysed in order to deduct from that number patients whose histories suggested that they were more likely to have been infected outwith Scotland. An analysis was done of 11 patients who were reported as infected by Scottish centres and who had received treatment outwith Scotland as well as in Scotland (see table 4) and who therefore may have been infected elsewhere. A similar analysis was also done of 23 patients who were first reported as infected in England but who also received treatment in Scotland and who, therefore, might have been infected here. Dr Hay concluded that a total of 68 - 70 were likely to have been infected in Scotland. The analysis which we undertook of the data which Dr Hay had helpfully provided concluded that 71 infections were likely to have occurred in Scotland. The new analysis undertaken by Drs Ludlam and Hay would suggest that 60 is a more accurate number.

Initially it should be noted that the table attached to the additional submission contains 74 entries.⁷ These are the 73 individuals whose HIV infection was first reported by a Scottish centre, with one additional individual deemed to have been infected in Scotland who was not registered with a Scottish centre (patient 73 in the table)⁸. Therefore, the starting point for the analysis is to increase the previous totals by one. This would mean that of the 74 patients considered Dr Hay would have

⁵ PEN.019.1328

⁶ PEN.019.0927 @ 0961

⁷ PEN.019.1328 @ 1331

⁸ PEN.019.1328 @ 1329, paragraph 1

deemed 63 to have been infected in Scotland (as they had only received treatment there) with 11 to be analysed as possibly having been infected in England (as detailed in table 4 of the original report). The 5 patients from the table 4 whom Dr Hay had considered to have been infected in Scotland (patients 3, 5, 6, 7 and 9 from table 4) are also deemed to have been infected in Scotland according to the new table. This increases the total number to 68. Further, the new table includes as a patient probably infected in Scotland who was patient 1 from table 6 (one of the patients whose infection was first reported in England), who is now patient 63 in the new table. This increases the total infected to 69. With the addition of the missing patient (patient 73) and the patient from table 6, we are unsure why it is that the total number of patients in the new table should not have increased by 2 to a total of 75. It appears that one patient probably infected in Scotland may have been missed. There is then patient 10 from table 4 (now patient 64) who appears to have been deemed to be infected in Scotland but was not included in Dr Hay's original 68. That takes the total number of infections to 71. There are two further patients who, in our original submission, we argued should be included in the Scottish infections list from Dr Hay's table 4, namely patients 2 (patient 8 in the new table) and 11 (patient 1 in the new table). The new table provides no new treatment information in relation to patient 2, merely stating that he was in Denmark. No new information is provided in relation to patient 11. We would continue to suggest that their infections were likely to have occurred in Scotland, taking the total to 73. Further (other than patient 63 referred to above) it is not clear whether any account has been taken of the possibility of other patients from table 6 having been infected in Scotland. They do not seem to have been included in the new table. These were the patients whose first positive test came from England who had also received treatment in Scotland. We would continue to suggest that patient 21 from table 6 is likely to have been infected in Edinburgh. This takes the provisional total to 74.

The controversy between the two reports appears to be based on new local information about patients whom Dr Hay had deemed to have been infected in Scotland (i.e. those included as part of the original 73 not analysed in table 4). This local information is reproduced by Professor Ludlam in the table appended to the new report. It identifies 9 patients who were part of the original 73 but who were not analysed by Dr Hay as having been possibly infected outwith Scotland. The main reason for the failure to analyse them appears to have been that on the information Dr Hay had, it appeared that these patients had only been treated in Scotland.⁹ They were all patients whose first reported positive test came from a Scottish centre. The new table appears to identify 9 patients who

⁹ PEN.019.0927 @ 0964

were not analysed in table 4 but who have been excluded on the basis of a fresh analysis (at times due to the presence of additional information not available to Dr Hay). The "local information" which has been identified is not available to us. We are unsure of its reliability. We are unsure why it was not available to Dr Hay when he provided his helpful report to the Inquiry. The position with these 9 patients appears to be as follows:

1. Patient 25 - deemed to have been infected in Malta due to the fact that he was resident in Malta. He had a first positive test in May 1983. The lack of treatment data outside Scotland for this patient means that, in our view, the fact that he received treatment in Scotland (the details of which are also unknown) means he cannot be excluded.
2. Patient 31 - as above.
3. Patient 41 - deemed to have been infected in France. Treated in Edinburgh in the late 1970s. Returned to Edinburgh in 1984 (treatment details unknown). Given that the date of seroconversion appears to be in late 1984, we think that this individual cannot be excluded.
4. Patient 66 - deemed to have been infected in France due to having received treatment in Edinburgh in 1978 and only returning there in 1993. If this information is reliable, it does appear that this individual is unlikely to have been infected in Scotland. We note that the date of the first positive test is marked as "unavailable" in relation this patient and certain others. We find this hard to comprehend, given the fact that we understand Dr Hay's original 73 patients to have all been patients who had a positive test first reported from a Scottish centre. This would suggest that such a test must have been done and that the date of it should be available.
5. Patient 68 - deemed to have been infected in the USA due to the fact that he arrived in Edinburgh from the USA in 1984. He had a first positive test in January 1985. The lack of treatment data outside Scotland for this patient means that, in our view, the fact that he received treatment in Scotland (the details of which are also unknown) means he cannot be excluded.
6. Patient 70 - deemed to have been infected in the USA due to the fact that he arrived in Edinburgh from the USA in 1987. If this information is reliable, it does appear that this individual is unlikely to have been infected in Scotland.
7. Patient 71 - deemed to have been infected in the USA due to the fact that he arrived in Edinburgh from the USA in 1988. If this information is reliable, it does appear that this individual is unlikely to have been infected in Scotland.

8. Patient 72 - deemed to have been infected abroad due to the fact that he appears to have been treated in Scotland but also usually overseas. If this information is reliable, it does appear that this individual is unlikely to have been infected in Scotland.
9. Patient 74 - deemed to have been infected in France due to the fact that he arrived in Scotland already infected. The first positive test was dated January 1982. If this information is reliable, it does appear that this individual is unlikely to have been infected in Scotland.

Therefore, this new information should in our view result in only 5 patients being excluded from the total figure, resulting in a new total of 69 patients with bleeding disorders who appear to have been infected with HIV by that treatment in Scotland. This analysis is based on the assumed reliability of the additional information which appears to have been added to the material to which Dr Hay had access when he compiled his previous report for the Inquiry.

JTD