

Response to request for further information on statistics, received from Penrose Inquiry and dated 28 November 2012.

Dr J Gillon

Information is requested in relation to the ten assumptions underpinning the paper written by Dr C Schnier and Professor D Goldberg. My responses are as follows:

Assumption 1 and Assumption 2

I address these two assumptions together, as they relate to different aspects of the same question, namely the likelihood of a recipient developing hepatitis C if they had received a “contaminated unit” (assumption 1), and as a determining factor, the likelihood of an HCV antibody-positive donor being PCR positive, i.e. infectious (assumption 2).

Dr McClelland and I did not provide any local data in relation to these assumptions, but agreed in discussion with the stated position derived from published data as referenced in the paper.

Assumption 3

This assumption was based entirely on such data as were available on the prevalence of HCV and HIV in the donor population as compared with the general population prevalences. The difficulty we encountered with this was the lack of reliable population data for either infection in the period 1984 – 1991, though exact data on blood donors was available for that period for HIV, and at the introduction of testing for HCV in 1991. We knew that the donor selection procedures introduced by November 1984, including as they did a signed declaration by each donor that he or she was not in the defined risk categories, led to the exclusion of a steady number of such donors throughout the period leading up to HCV screening in 1991. I received a written confidential report on every such donor, and therefore had first hand, if somewhat impressionistic knowledge of the apparent effectiveness of the procedures. In order to try to give this a numerical basis, we tried to extrapolate backwards as best we could from the reports on population prevalences published in the early 1990s and subsequently, in order to estimate what proportion of potentially infected donors we were managing to exclude. In the case of HIV there were no screening-based data other than in donors, apart from selective screening of high risk groups. Brettell et al reported that 65% of IVDUs attending for testing in Edinburgh were anti-HIV positive, while the HPS estimates for the number of IVDUs in Scotland between 1984 and 1991 rose from 8,316 to 19,097, averaging around 14,500. Later data suggested that the HIV diagnostic rate was constant during that period at around 3,000 cases per year in the UK, and also that the prevalence in pregnant women was around 0.1%. Thus, while HIV prevalence was extremely high in IVDUs at least in parts of Scotland, the population prevalence, probably around 1:1000, was and remained low by international standards (data from HPA 2011 Report, HIV in the UK). The prevalence in blood donors, however, was much lower still, at around 0.005% in 1985/6, falling to less than 0.001% by 1991 in spite of a population prevalence that has now reached a level of around 0.15% (HPA 2011 Report).

Similarly, we knew that the initial period of screening for HCV in 1991/2 produced a donor prevalence of 0.09%. Balogun et al (2002) estimated that the population prevalence in England and

Wales peaked in 1986, at just over 1%. By 2005 the HPA (Hepatitis C in the UK. 2011 Report) estimated a prevalence in adults of 0.67%.

We interpreted these data as evidence that the entirety of donor selection policies and procedures, including publicity and donor education, reduced the risk of an infectious unit entering the blood supply by at least an order of magnitude. It was no surprise that the effectiveness was greater for HIV than HCV, as the former was exclusively associated with the established high risk behaviours, while HCV could be contracted by other means, including transfusion (Crawford et al, 1984) which, though a recognised means of transmission of HIV, was not numerically as significant as in the case of HCV. We agreed in discussion that it would be appropriate to be very conservative in the final assumption, but we acknowledge that there are residual reservations about the assumptions on population prevalences. It was therefore correct to state that Assumption 3 derived in part from our expert professional opinions.

Assumption 4

Dr McClelland and I provided no data in relation to this assumption, and had no input to the decision to model the retrospective estimation of donor prevalence on the estimated prevalence of IVDU in the general population.

Assumption 5

The assumption that 1.25 components were produced per donation was derived from the data generated by the SNBTS Lookback. This is directly analogous to the data cited by Soldan et al for England and Wales, in their case 1.6 components per donation. The difference between the Scottish and English numbers is most likely due to the fact that during the 1980s blood collection in Scotland was plasma driven: in order to meet the target for self sufficiency in plasma products, an excess of red cells was inevitable, and a higher proportion of collected whole blood units would be used only as plasma for fractionation, with a higher rate of discard of red cells. This is, however, speculative: we do not have data comparing production or usage of other components such as platelets, FFP and cryoprecipitate, nor do we know the relative contribution of plasmapheresis or platelet pheresis north and south of the border.

Since the lookback data were derived from a substantial number of donations over a long period of time, we regard them as factual rather than a matter of expert opinion.

Assumption 6

The assumption that 56% of units were transfused was derived from the data resulting from the lookback in Edinburgh. It was my opinion that, since the Edinburgh lookback was done in “real time”, it would be more reliable as a source of data than the Scottish lookback, which was known to be incomplete. However, on receipt of the present request I have derived similar data from both the Scottish lookback and the English lookback as reported by Soldan et al. The respective figures are 66% for Scotland and 61% for England. These differences, when taken with the assumed prevalence of HCV in donors, are unlikely to be statistically significant, but the inherent unreliability of this set of assumptions, encapsulating as they do significant numbers of components which could not be traced, would make statistical calculations meaningless. It is our expert opinion that the

assumptions are reasonable in the absence of any other source of data, and not amenable to improvement.

Assumption 7

I had no input to this assumption.

Assumptions 8, 9 and 10

I provided no data for these assumptions, but agreed in discussion that they were reasonable interpretations of the published literature cited.

Summary

The summarised responses to the specific questions posed by the Penrose Inquiry are as follows:

1. What data and opinion evidence did Dr McClelland and Dr Gillon provide to Dr Schnier and Professor Goldberg in respect of each assumption?

This is detailed above in relation to each assumption separately.

2. Where opinion evidence was provided in respect of an assumption, on what was that opinion evidence based.

In my responses to the assumptions, above, I have tried to make it clear whether the opinion I provided was based on published data, local data or personal expert knowledge.

3. Are Dr McClelland and Dr Gillon aware of the extent to which the data and opinion evidence they provided to Dr Schnier and Professor Goldberg formed the basis of each assumption, i.e. if some assumptions were based entirely on the data and opinion evidence provided by Dr McClelland and Dr Gillon, are Dr McClelland and Dr Gillon able to identify these assumptions?

I cannot be certain to what extent the formulation of the individual assumptions relied on the data we provided or the opinions we expressed, but I think it is evident that assumptions 5 and 6 relied exclusively on the data provided from the Scottish HCV lookback as described above. These data were published (Ayob et al, 1994).

4. Do Dr McClelland and Dr Gillon have any reservations about the reliability of the data and opinion evidence provided by them in respect of each assumption? If so, please explain the nature of the reservations.

In my comments on each of the assumptions above I have made clear the distinctions between published data, unpublished local data, and opinions based on my knowledge derived from personal experience and observation. Where data were limited or non-existent I have indicated that such is the case. While I would accept that hard numerical data would be the preferred basis for my responses, I am confident that my opinions based on personal experience over many years of practice in donor medicine are valid and reasoned.

5. Do Dr McClelland and Dr Gillon consider that any further steps or investigations can reasonably be undertaken to make the data and opinion evidence they provided to Dr Schnier and Professor Goldberg more reliable?

With a single exception (q.v.) I have not been able to identify any further work that could be done to strengthen the evidence we have provided.

The exception is described in my response to assumption 6 above. I have shown that comparable data for the percentage of units transfused could be derived from the lookback studies in England and Scotland to set against the data we provided from the Edinburgh lookback, which was undertaken prospectively, and in which I therefore had the greatest confidence. I do not consider that this exercise makes the data any more reliable, but it tends to indicate that, given the similarity of the data with England sandwiched between the Edinburgh level and that of the whole of Scotland, the figure used is reasonable in the absence of data collected at the time of the issue and use or non-use of the units of blood in question.

Dr J Gillon, 14 January 2013