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The Penrose Inquiry
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Date 29th May 2012
Your Ref
Our Ref DG/ec/Penrose

Enquiries to
Direct Line
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Dear Professor James

Re: Penrose Inquiry - further queries on statistics from Professor Oliver James

Thank you for sharing your ideas relating to the estimates of transfusion related HCV infection, generated by Christian Schnier and myself and submitted to the Inquiry in a document dated March 1, 2012. The delay in responding to you stems from our desire to share these ideas with SNBTS colleagues (Jack Gillon and Brian McClelland); a meeting involving myself, Dr Schnier and Jack Gillon was held at SNBTS on 15th May. Our agreed response to your ideas and suggestions is as follows:

Modelling based on data from the Skipton fund

We appreciate your thinking surrounding the use of Skipton fund survival data to, effectively, back-calculate plausible estimates of the number of individuals who must have been infected in the first place. It is a very reasonable approach but one which can only withstand any test of robustness if the data on which it is based – namely the Skipton fund survival data – are robust themselves. You state that "...we should assume that this figure of 405 has been reasonably verified as "post transfusion" by the consultants who have filled in the information and by the Skipton Fund Expert Assessor Panel SFEAP." As you are aware, I asked the Inquiry for details confirming that the individuals considered eligible for Skipton funding had, indeed, acquired their infections through blood transfusion in Scotland but such information was unavailable. It is my understanding that, for some individuals, such information exists but for others, perhaps the majority, judgements were based "on the balance of probability". Balance of probability is insufficient information for us to make a judgement as to how likely an individual was infected as a consequence of a blood transfusion, without having access to additional information. Even then, such information may be insufficient to narrow the range of uncertainty. This would not be an issue if confirmatory evidence of blood transfusion having been responsible for infection applied to the great majority of the 405 but I suspect the reverse applies. Accordingly, in the absence of any further information which illuminates the Skipton fund data available to me, I advise that the application of such data in the method proposed by you is insufficiently robust for our purposes.

Question 5 and the 344 figure

Under the heading "Question 5" you make reference to individuals diagnosed HCV antibody positive for whom records were entered onto HPS's HCV diagnosis database. You also make reference to estimates of HCV infected injecting drug users for Glasgow and Scotland. You use the above data, along with a statement that 3% of Scottish HCV infected individuals were

attributable to blood transfusion, to generate an estimate of living HCV infected (blood transfusion) individuals and then compare this figure with the Skipton fund one.

I suggest it is inappropriate to undertake such an analysis for the following reasons. My March 2011 submission indicated that "HPS is aware of 304 (*not 344*) individuals known to be HCV antibody positive in Scotland for whom information indicated that the blood transfusion received may have resulted in the acquisition of Hepatitis C infection". I also stated that "as indicated in the HPS notes attached, blood transfusion should only be regarded as a possible, and not a definite or confirmed, route of acquisition for these cases". As you will remember I had a lengthy discussion with Lord Penrose at the Hearing about my take on what was meant by "possible". I recall indicating to him that I was unable to provide a probability figure of an individual, for whom information on an HCV test request form stated "blood transfusion", having acquired his/her infection as a consequence of blood transfusion. If I had used the term "probable" that would have indicated greater than 50% chance; using the term "possible", however, did not, in my view, indicate less than a 50% chance. I did comment that 304 represented only about 3% of all Hepatitis C diagnoses in Scotland but in the absence of information confirming transfusion associated HCV infection, it is not a particularly meaningful proportion.

Accordingly, as stated above, it would be inadvisable to use such uncertain data in any modelling exercise.

Assumption 3

You rightly question the 66% deferral rate assumption and ask whether there should be some degree of gradation between 1984 and 1991, allowing for the policy to take effect. I, Dr Schnier and Drs McClelland and Gillon, spent a considerable amount of time on the generation of this assumption. Initially, to reflect uncertainty surrounding the effectiveness of the deferral policy, we modelled the data using 50% and 75% rates, in addition to the 66% one. We came to the conclusion that the 66% rate was the optimal one, and applying it for all years during 1984 – 1991 seemed reasonable. The SNBTS view was that by mid 1984 everyone was using the same materials to implement the policy and little variation in practice was observed by Drs Gillon and McClelland thereafter till 1991. It is possible that the intervention was less effective during the first half of 1984 but it was felt that adjusting for this would amount to merely tinkering; in other words, it would not have made any appreciable difference. Although the 66% rate was intuitive, it, to a certain extent, was based on the fact that, for both HIV and HCV, the rates of infection among donors, following the implementation of the deferral intervention at the first possible opportunity to access prevalence data through the testing of donor populations for each virus, were very much lower than the rates of infection on non-donor general populations.

We repeated the modelling exercise to ascertain the impact of (i) a deferral policy with no effect and (ii) a deferral policy, the effect of which increased incrementally between 1983 and 1991. For (i) the number infected until 1991 was estimated to be 1110 (90% credibility interval: 876 to1413), the number alive as at 2011 was 230 (178 to 294) and the number alive as at 2011 and chronically infected was 173 (128 to 225). For (ii) the estimated number of those infected was 2212 (1657to 2853), the number alive as at 2011 was 438 (325 to 566) and the number alive and chronically infected as at 2011 was 326 (241 to 435).

Assumption 4

You contest that the change in HCV prevalence among blood donors over the two decades in question would not have mirrored the change in the estimated number of prevalent infections among injecting drug users over this period. While we cannot prove this was indeed the case, our view is that injecting drug use has been the principle driver of HCV infection in Scotland, even going back to the 1960s. As we pointed out, it was not just the direct effect but also the indirect one. What we mean by this is that people who did not inject drugs but acquired their infection through, for example, tattooing, are likely to have become infected with a virus which was originally circulating among individuals who injected drugs. You also mention "prisoners" but most of our studies have indicated that infected prisoners have a history of injecting drug use. Yes, indeed, some individuals who donated may have, themselves, acquired infection through blood transfusion

and some may have been immigrants from higher prevalence areas but it is our view that the numbers in the period of particular concern – the 1970s – are likely to have been small. Even if we had integrated within our model a factor taking into account a higher proportion of infected blood donors in the 1970s not having injected drugs, it would not have made much difference to the final output.

We modified the model, as requested, using a constant HCV prevalence (0.09% antibody positivity); this generated an estimated infected number of 6784 (5027 to 8776), with the number having survived until 2011 being 1050 (789 to 1364) and the number having survived as at 2011 and being chronically infected, 788 (569 to1044).

It is my view that the approach used, i.e. that using the HCV infection IDU estimates, is a novel and scientifically valid one.

Point about the estimated prevalence of HCV positive infectious donors in 1983 and in 1984

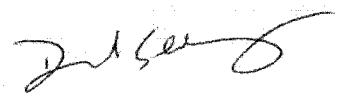
The change in prevalence between 1983 and 1984 takes into account two factors – the 66% deferral factor and a factor to account for the increase in HCV prevalence among potential donors equivalent to the relative increase in the estimated number of HCV infected IDUs in Scotland (i.e. 6401 in 1983 compared to 8316 in 1984).

Conclusion

I appreciate the time you have taken to examine our model and the estimates generated. Your points are very reasonable but, for the reasons given, I do not think that there is a compelling enough case to make any further alterations to our existing approach. Confidence intervals are provided to convey uncertainty. I do accept that slight tinkering at the edges might be merited, but this will not alter the estimates appreciably. This response has the support of Dr Schnier and Drs Gillon and McClelland. Because of time constraints and the uncertainty as to the status of this work, it has not been through the Peer Review process. I am happy to discuss our findings and this response with you and your team if you wish.

Best wishes.

Yours sincerely,



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