The contribution of transfusion to HCV infection in England

THE ENGLISH NATIONAL BLOOD SERVICE HCV LOOKBACK COLLATION COLLABORATORS : K. SOLDAN [1,2]*, M. RAMSAY [2], A. ROBINSON [1], H. HARRIS [2], N. ANDERSON [3], E. CAFFREY [4], C. CHAPMAN [5], A. DIKE [6], G. GABRA [7], A. GORMAN [8], A. HERBORN [9], P. HEWITT [10], N. HEWSON [11], D.A. JONES [11], C. LLEWELYN [4], E. LOVE [12], V. MUDDU [12], V. MARTLEW [13], A. TOWNLEY [14].

1. National Blood Service, Oak House, Reeds Crescent, Watford, WD24 4QN

2. PHLS CDSC, 61 Colindale Avenue, Colindale, London. NW9 5EQ.

3. National Blood Service, Southmead Road, Bristol, BS10 5ND

4. National Blood Service, Long Road, Cambridge, CB2 2PT

5. National Blood Service, Holland Drive, Newcastle upon Tyne, NE2 4NQ

6. National Blood Service, John Radcliffe Hospital, Headington, Oxford, OX3 9DU

7. National Blood Service, Vincent Drive, Edgbaston, Birmingham, B15 2SG

8. National Blood Service, Crescent Drive, Brentwood, Essex, CM15 8DP

9. National Blood Service, Coxford Road, Southampton SO16 5AF

10. National Blood Service, Colindale Avenue, London NW9 5BG

11. National Blood Service, Longley Lane, Sheffield, S5 7JN

12. National Blood Service, Plymouth Grove, Manchester, M13 9LL

13. National Blood Service, West Derby Street, Liverpool L7 8TW

14. National Blood Service, Bridle Path, Leeds, LS15 7TW

* *Author for correspondence:* Dr K Soldan, NBA/PHLS CDSC, 61 Colindale Avenue, Colindale, London. NW9 5EQ.

Running header: Contribution of transfusion to HCV in England

SUMMARY

The English HCV lookback programme has identified some individuals with transfusion-transmitted HCV infection. A model of the path from the collection of donations from HCV infected donors to the identification of infected recipients was constructed using data collected during this programme. Blood components that fell out of the lookback at various stages prior to recipient testing, and components from HCV infected donations that never entered lookback, were entered into the model to produce a complete estimate of infected recipients (dead and alive at the end of 1995). Less than 14,000 recipients were estimated to have been infected with HCV during the decade prior to the start of donation testing. Over 60% of these were expected to have died by the end of 1995. Transfusion has infected a large group of individuals. However, this group constitutes a very small, and declining, proportion of all HCV infections in the population.

(150 words)

INTRODUCTION

The HCV lookback programme in England has attempted to trace patients transfused prior to September 1991 with blood from donors who were found to be positive for hepatitis C virus antibody (anti-HCV) after routine testing for anti-HCV was introduced in September 1991. The aim of this lookback was to diagnose patients with transfusion-transmitted HCV who might benefit from care and treatment. For various reasons including loss of records, movement of patients, death of patients and attention to patients' best interests and wishes, not all recipients of blood from anti-HCV positive donors received testing. Also, as not all HCV infected donors gave blood after anti-HCV testing was introduced, many infected donations collected between 1st January 1980 and September 1991 will not have been subsequently identified and will not have entered the lookback. We have used data collected during the lookback to construct a model of the path from donation to recipient infection in order to estimate the total number of transfusion transmitted HCV infections, and therefore derive the contribution of transfusion to HCV infection in England.

METHODS

Data from all stages of the lookback process - about infected donors, blood components (red cells, platelets, FFP and cryoprecipitate) made from donations by these donors, components transfused, identified recipients, tested recipients, and infected recipients - were collected from eight blood centres that handled 80% of all blood components entering the lookback programme in England. Information about all HCV tested recipients was collected from all centres [1].

These data were used to construct a model of the path followed by a lookback component, with the observed proportion following each branch taken to predict the probability that components with unidentified fate would follow the same route. The number of HCV infections transmitted by components that were included in the lookback programme but did not complete the lookback path to a tested recipient was estimated by assuming that they would have followed the same path as those that completed lookback i.e. by re-entering them into the model at the point at which they fell out of the lookback process.

The number of donations collected between 01/01/1980 and 01/09/1991, and the number of confirmed anti-HCV positive donations collected during the first four months of anti-HCV testing were

obtained from donation testing records. The total number of anti-HCV positive donations collected during the 1980s and until September 1991 was estimated by assuming that the prevalence of anti-HCV observed during the first four months of donor testing (0.066%) existed throughout this time. The number of anti-HCV positive components from donors who were not subsequently tested for anti-HCV (and therefore did not entered into the lookback programme) was then derived by subtraction of the number of components that did enter lookback. These extra (non-lookback) HCV infected components were then entered into the top of the model to estimate the number of infections they are expected to have caused, and the number of those infected recipients expected to have died by the end of 1995.

RESULTS

The observed outcomes at each stage of the lookback process on route to HCV testing for the 80% of components from the eight centres providing full datasets are shown in the middle column of Figure 1. Six-hundred and sixty-seven HCV infected recipients were identified from the 1,062 tested in the eight centres that provided full information about each component and the 271 tested recipients who received other components from anti-HCV positive donors identified in the lookback programme. The infection rate in tested recipients (excluding 124 tested recipients with insufficient test results to determine HCV status) was 55%; 10% of the identified infections had been diagnosed prior to the lookback programme. The median age of these infected individuals in 1995 was 55 years.

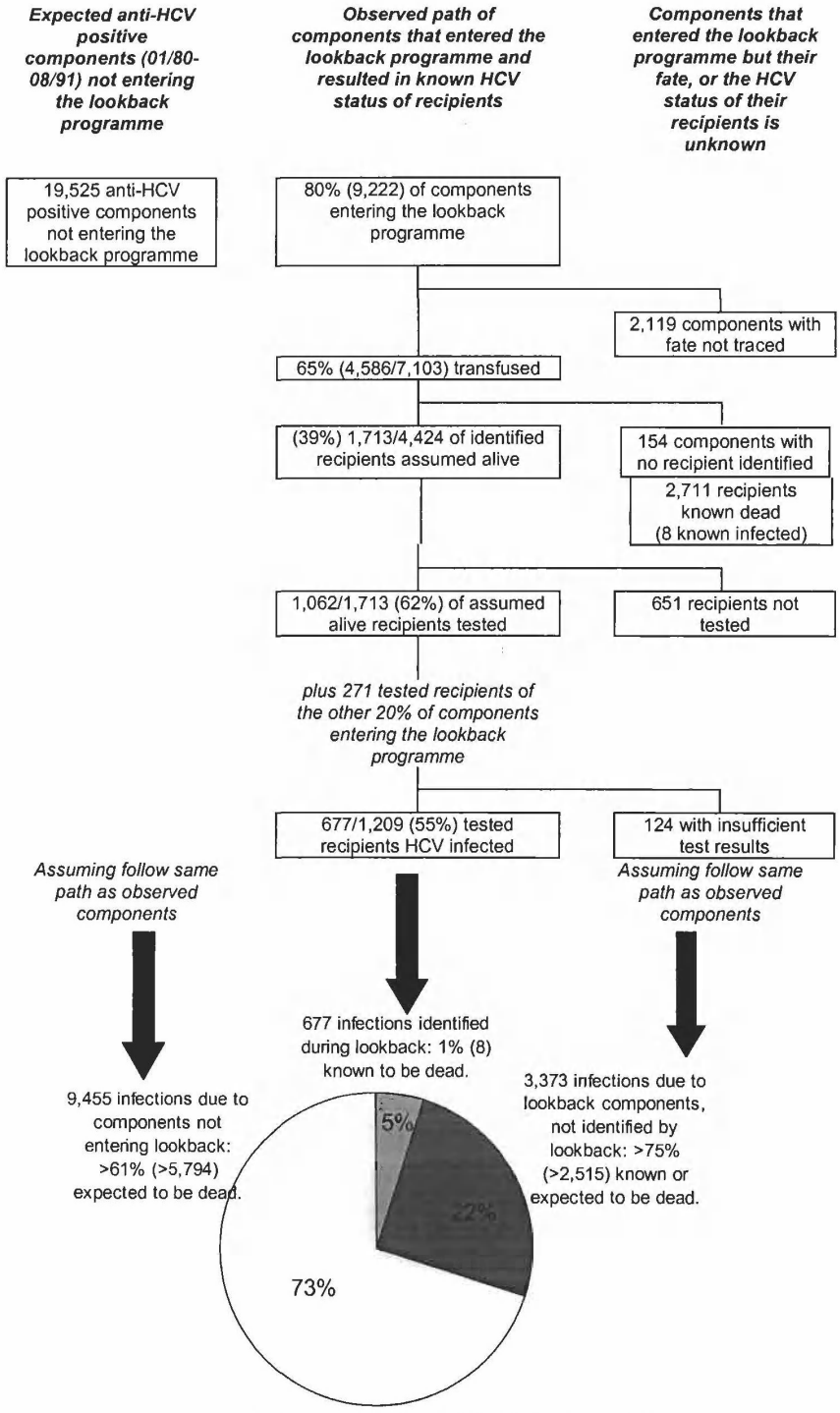
The observed probabilities of the outcome of interest at each stage on the lookback path are also shown on the figure: these formed the model of the path from donation to infected recipient that was assumed to apply to components that did not complete the stages on this path. This model estimated the number of transfusion transmitted HCV infections from components that entered the lookback programme but fell out of the process prior to recipient testing to be 3,373 HCV infections (946 with fate of component not traced, 107 known to have been transfused but with no recipient identified, 1870 known to have been transfused and to have died by end of 1995, and 450 who declined testing). Of these infections, 55% (1870) were known to be dead and an additional 19% (645) were expected to have died by the end of 1995. The median age of the identified recipients in this category in 1995 was 73 years.

A total of 25,864,035 donations were collected over the period 01/01/1980 to 01/09/1991, including an estimated 17,086 anti-HCV positive donations. If - as observed for the lookback donations - each donation resulted in 1.6 components, there were 26,647 components issued from

anti-HCV positive donors. How many of these components were identified to enter the lookback is uncertain; 9,756 of the lookback components were collected between 1st January 1980 and the start of anti-HCV testing. If we assumed that all these lookback components were anti-HCV positive, then they constituted 37% of the estimated total number of anti-HCV positive components issued during this time period, and 16,891 (63%) anti-HCV positive components did not enter the lookback. Entry of these extra anti-HCV positive components into the model predicts an extra 10,905 transfused recipients, and an extra 6,034 HCV infected recipients of which 3,681 are expected to have died by the end of 1995. However, it is unlikely that all the components that were identified for lookback (by subsequent anti-HCV positivity of their donor) were anti-HCV positive. Approximately 75% of confirmed anti-HCV positive donors have been found to be HCV RNA positive by PCR. If we assume that only HCV RNA positive donations transmit HCV infection, we would expect 75% of anti-HCV positive components to transmit. Our observation that only 55% of lookback components result in HCV infection was used to estimate that 73% of lookback components were anti-HCV positive (0.73 x 0.75=0.55). The remaining 27% of lookback donations where presumably collected while the donor was anti-HCV (and HCV RNA) negative. If only 73% of lookback components were anti-HCV positive, then an extra 19,525 (= 26,647-(9,756 x 0.73)) anti-HCV positive components did not enter the lookback. The entry of these extra anti-HCV positive components into the model - with the use of a 0.75 probability of infection transmission for these components - predicted an extra 12,606 transfused recipients, and an extra 9,455 HCV infected recipients of which at least 5,794 are expected to have died by the end of 1995.

In total, we therefore estimated that there have been approximately 13,500 HCV infections transmitted by transfusion from lookback components, and other HCV infected blood components issued between 1st January 1980 and 1st September 1991. Over 8,300 (61%) of these were either known or expected to have died by the end of 1995.

Figure: Observed and estimated transfusion-transmitted HCV infections.



Total estimated transfusion-transmitted HCV infections (01/80-09/91). N=13,500; <5,200 assumed alive in 1995

DISCUSSION

These data, and the model used, give an indication of the likely number of transfusion-transmitted HCV infections, and of the contribution transfusion has made to HCV infection in England. There were, by necessity, many assumptions and extrapolations used in our model, and the results are not therefore expected to be exact.

We estimate that the HCV lookback programme has identified about 5% (677) of the total number of HCV infections transmitted by transfusion from 1st January 1980 to 1st September 1991, and over 13% of infected recipients who survived to 1995. It has been estimated that there are between 200,000 and 400,000 HCV infected individuals living in the UK [2]: if this is so, transfusion since 1980 appears to account for between 3% and 7% of all infections. Laboratory reports of HCV infection – that are biased towards those individuals who are offered testing, are in accord with these estimates. Transfusion was reported as the most probable route of infection for 4.3% (128) of laboratory reports of HCV infection with risk factor information in England and Wales during 1992-1996 [3].

Of the infections identified by this lookback programme, 10% had already been diagnosed. The proportion of infections not identified by the lookback that have already been diagnosed may be lower if individuals not identified by the lookback are less likely to be in contact with health services, or higher if individuals not tested during the lookback were more likely to be known anti-HCV positive.

Other analyses of data from the lookback programme [1] imply that our estimates of the proportions of unidentified infections that have died based on frequency of "known dead" recipients will be conservative. When calculated by year, the majority of the "extra" components (from donors who not did not donate after September 1991) not included in the lookback programme were collected and transfused longer ago - during the first half of the 1980s. Also, there will be some (approximately 1%) multiply transfused recipients who received more than one of these "infections". Our model's estimate of assumed living transfusion transmitted infections (in 1995) is therefore a maximum estimate.

We may have underestimated or overestimated the infections transmitted from 1st January 1980 to 1st September 1991 by using the prevalence of infection at the start of testing without accounting for selective removal of infected donors during the 1980s, or accumulation of prevalence

over time. This uncertainty, and others, prohibit including earlier years. If the prevalence of anti-HCV amongst blood donors during the 1970s was assumed to be the same as at the end of 1991, inclusion of the 1970s would generate approximately 10,000 extra HCV-infected blood recipients. If the average age of transfusion has stayed fairly constant over the years, 60% of these recipients infected during the 1970s would have been born prior to 1920, i.e. would have been at least 75 years old by 1995.

These estimates may be useful for predicting the burden of HCV-related disease, or for assessing how the demand for HCV-related care compares to the burden of infection, particularly amongst the current older age groups that are expected to include a relatively large proportion of these transfusion-transmitted infections.

Only two transfusion-transmitted HCV infections have been reported from anti-HCV tested components during the past six years [4] (up to end 2000), and the risk of infection by transfusion is being reduced further by nucleic acid testing of blood donations. Transfusion-transmission of HCV in UK is therefore largely a thing of the past, although the extent of continuing secondary transmission has not been established, and investigation of the burden of disease amongst infected recipients is ongoing [5].

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