Probability of receiving testing in a national lookback program: the English HCV experience

The English National Blood Service HCV Lookback Collation Collaborators

BACKGROUND: The HCV lookback program was designed to trace and offer testing to recipients who received transfusion of blood components from donors subsequently found to be anti-HCV positive. Only approximately 20 percent of transfusable components entering lookback did result in a recipient obtaining testing through this program.

STUDY DESIGN AND METHODS: Data from English blood centers were collated to describe the outcomes of the HCV lookback program. The data were used to assess factors affecting the likelihood that recipients of lookback components received testing by the program.

RESULTS: In total, 4424 recipients of 6687 blood components that had been issued for transfusion were identified. The lookback resulted in a tested recipient for 1067 components. Factors positively associated with receiving testing in identified recipients were younger age at transfusion, more recent year of transfusion, certain component types, and transfusion under the care of certain medical specialties; these effects were largely explained by the association of these factors with survival after transfusion.

CONCLUSIONS: Not accepting testing through this program was largely due to death before the lookback and partly due to inability to access information from records and to decisions that testing was not in recipients' best interests. The probability of obtaining testing through this lookback was associated with several factors that could be used to focus the efforts of similar lookbacks in the future.

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The rationale, methods, and outcomes of the HCV lookback in England has been described elsewhere.[1] The outcome in terms of yield of recipients accepting testing, and infections diagnosed, for the effort required per component entering lookback was low compared with many other infection screening programs, but within the range for published HCV lookbacks. This paper presents an analysis of factors associated with accepting testing through this program.

MATERIALS AND METHODS

Data about donors, components, and recipients were linked and collated into a national dataset.[1] Logistic regression models (using STATA 6.0, Stata Corp., College Station, TX) were used to estimate the ORs of the lookback procedure for any component resulting in the testing of a recipient. Univariable and multivariable analyses were performed to investigate the effects of the following variables: recipient's age at time of transfusion, recipient's sex, year of transfusion, time between transfusion and testing, component type transfused, and medical specialty of the clinician prescribing the transfusion. The odds of death after transfusion and before the lookback were investigated similarly.

Chi-square tests were used to test the significance of differences between proportions; t-tests and Kruskal-Wallis tests were used, as appropriate, to test the significance of differences between distributions of continuous variables. Significant results were taken as those with a p value less than 0.05.

RESULTS

Table 1 shows the reported fate of 6687 transfusable components that entered lookback. The fate of 31 percent (2101/6687) of these components was not identified. For those known to have been transfused, recipients were not identified for 3 percent (154/4586). Of components issued for transfusion, 41 percent (2717) had been transfused to recipients known to be dead and 10 percent (648) did not proceed for testing either because they were not traced or because clinicians indicated the recipients were unsuitable for testing (which reason applied for

TABLE 1. Lookback data set: number and fate of lookback components and outcome of lookback for transfusable components

Fate of component	Fate of recipient	Whole blood		RBCs		FFP & cryo		Platelets		Not known		Total	
		n	%	n	%	n	%	n	%	n	%	n	%
Transfused		939	68	2474	73	305	61	844	76	24	8	4586	68
	Not tested	679	49	1868	55	235	47	717	65	14	5	3513	53
	Died	486	35	1391	41	190	38	640	58	10	3	2717	41
	Identified but not tested	181	13	354	10	40	8	69	6	4	1	648	10
	Not identified	12	1	129	4	5	1	8	1	0	0	154	2
	Tested	260	19	600	18	70	14	127	11	10	3	1067	16
Fate not identified	—	438	32	917	27	192	39	267	24	287	92	2101	32
Total transfusable components (% of total)		1377 (21)	100	3391 (51)	100	497 (7)	100	1111 (17)	100	311 (5)	100	6687 (100)	100
To BPL*	—	6		1		1401		0		3		1411	
Discarded†	—	222		443		224		176		59		1124	
Total		1605		3835		2122		1287		373		9222	

* BPL = BioProducts Laboratory, for plasma fractionation.
† Includes donations issued for quality assurance, laboratory use, and research.

each case is not known). Recipients were identified for 4432 components, including eight recipients who received two components (i.e., 4424 recipients were identified). Lookback at 76 percent (3365/4432) of components with identified recipients did not result in recipient testing; 559 HCV infections were detected amongst tested recipients. Overall, for every 100 components that had been issued for transfusion and entering lookback, 26 living recipients were identified, and 8 HCV infections were found.

Figure 1 shows the numbers of lookback components, recipients identified, recipients not known dead, and recipients tested by year of donation.

For 48 (2.3%) of the transfusable components with unknown fate, the component was reported as "transferred" (i.e., to another blood center for issue), but the

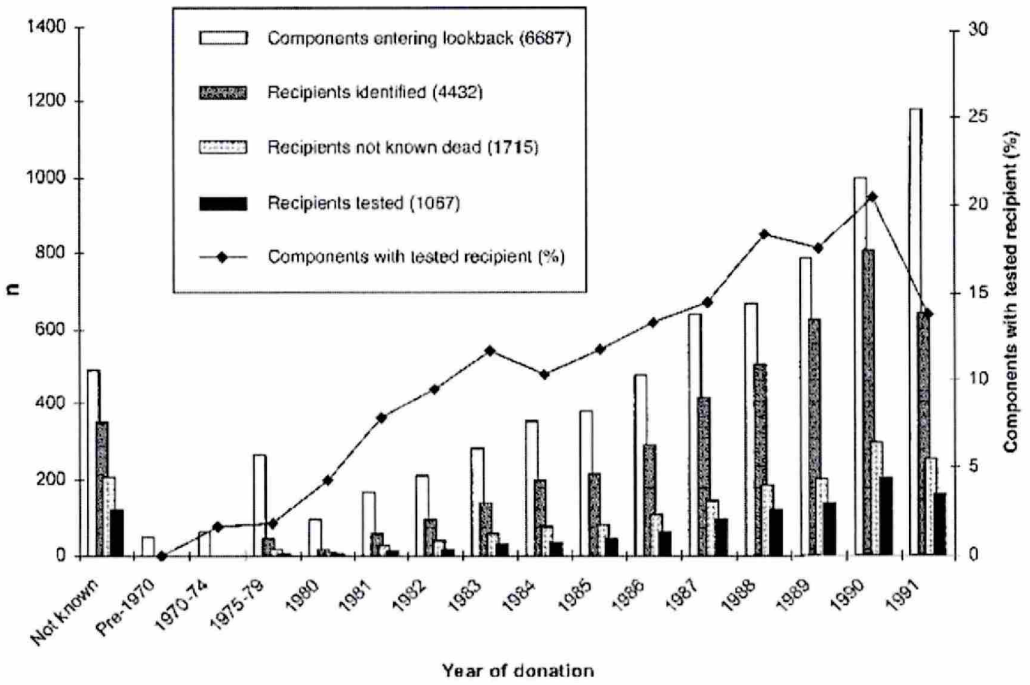

Fig. 1. Transfusable components and outcome of lookback by year of donation.

component was not reported by any other center contributing to the national data set. For the remaining untraced components, information about the fate of the component was not available; it was not reported whether information was unavailable at centers or at hospitals.

The age and sex of the 4424 identified recipients included in the lookback data set, subgrouped by testing status, is summarized in Table 2. The ORs for lookback at transfused components resulting in undergoing testing, for various recipient and donor variables are shown in Table 3. No donor factors (year born, PCR status, sex) had an effect on the probability of recipients accepting testing.

Unknown fate of a unit was significantly associated with earlier year of donation (OR of fate being unknown for year of donation = 0.79 [0.78-0.81]; OR for period of donation, 1990 or later = 1.0 [baseline], 1985-1989 = 2.02 [1.75-2.34], 1980-1984 = 5.31 [4.52-6.25], pre-1980 = 26.50 [20.53-34.22]).

Risk of death before testing

The most common reason for identified recipients not receiving HCV testing was death before tracing through the lookback. The odds of death before tracing associated with recipient and donor variables are shown in Table 4. When the analyses shown in Table 3 of the effects of the recipient and donor variables on the likelihood of obtaining testing were rerun for recipients not known to be dead, age at transfusion (OR = 0.97 [0.96-0.97]), year of transfusion (OR = 1.10 [1.06-1.14]), and specialty at the time of transfusion remained significantly associated with testing in univariable analyses. Age at transfusion (OR = 0.97 [0.96-0.98]) and the specialty at time of transfusion were significant in the multivariable recipient analyses after excluding those known to be dead. The predictive value of component type on whether testing was accepted was completely explained by the risk of known death associated with those component types. This suggests that the risk of death associated with certain component types is a risk of early death in hospital because the effect is fully explained by mortality recorded in hospital notes. The risk of death (assumed to largely account for not being tested) associated with other variables appears to continue acting once the recipient is discharged from hospital care.

Amongst 873 recipients for whom year of death was reported, the interval between year of transfusion and year of death was less than 1 for 47 percent, 1 for 23 percent, 2 for 10 percent, 3 for 4 percent, 4 for 5 percent, 5 for 3 percent, 6-10 for 7 percent, and over 10 for 1 percent.

Some free text about the cause of death was reported for 46 percent (1199) of those known to have died. Of these, 5 percent mentioned liver-related conditions, 38 percent attributed death to hematologic conditions, 19 percent to malignancies, 11 percent to cardiac and peripheral vascular conditions, 3 percent to cerebral vascular problems, 7 percent to respiratory conditions, 4 percent to infectious causes, 4 percent to gastrointestinal conditions, and 7 percent to various other conditions.

DISCUSSION

Overall, approximately one living recipient was identified per four transfusable components entering lookback, and one infected recipient was identified per 12 components entering lookback, per eight recipients identified and per two tests performed.

The strongest associations shown by this data collec-

TABLE 2. National data set: number and fate of lookback components and findings for recipients of transfused components

Recipients	% female	Age (yr) at time of transfusion	Age (yr) at time of tracing	Time (yr) between transfusion and testing*
Identified (4,424)	48 (4047)			
Median		60	68	NA
Mean (SD)		55 (23.0)	62 (22.9)	
N		3746	3784	
Tested (and not known dead) (1067)	51 (1047)			
Median		44	51	6.8
Mean (SD)		42 (21.5)	50 (21.2)	7.6 (2.8)
N		1061	1066	435
Not tested (not known dead)	55 (686)			
Median		65	72	NA†
Mean (SD)		58 (23.2)	65 (23.1)	
N		609	614	
Comparison: tested vs. not tested‡	p = 0.71	**p < 0.001**	**p < 0.001**	NA

* Excluding those known positive at the time of tracing.
† Untested identified recipients had been transfused 4.3 to 21 years (mean, 7.9; SD, 2.9; median, 7) before the median specimen date for the tested recipients.
‡ p value for comparison of age and time variables = result of Kruskal-Wallis rank test; t-tests were also performed, with similar results. Comparisons of variable found significantly different (at 5% significance level) are shown in bold.

TABLE 3. Lookback data set logistic regression results: effects of recipient and donor variables on the likelihood of testing transfused recipient

Variable	Obs (n)	p*	OR of testing if transfused (95% CI)	Obs (n)	p*	OR of testing if transfused (95% CI)
			Univariable	2478		Multivariable
Female	4047	**0.01†**	1.20 (1.04-1.38)		1.00	1.05 (0.86-1.29)
Age at transfusion (yr)	3744	**<0.01†**	0.97 (0.96-0.97)		**<0.01†**	0.96 (0.95-0.96)
Year of transfusion	4204	**0.04†**	1.04 (1.01-1.07)		0.95	1.06 (1.02-1.10)
Period of donation	4204	**0.02†**				
1990 or later			1.0 (baseline)			—
1985-1989			0.86 (0.73-1.00)			—
1980-1984			0.75 (0.59-0.95)			—
pre-1980			0.44 (0.18-1.04)			—
Component type‡	4556	**<0.01**			0.80	
RBCs			1.0 (baseline)			1.0 (baseline)
Whole blood			1.18 (0.99-1.39)			1.02 (0.81-1.30)
Platelets			0.55 (0.45-0.68)			0.66 (0.48-0.91)
Plasma/cryo			0.96 (0.73-1.27)			0.63 (0.43-0.91)
Speciality	2852	**<0.01†**			**<0.01†**	
Cardiothoracic	270		1.0 (baseline)			1.0 (baseline)
Obstetrics/gynecology	204		3.66 (2.48-5.40)			1.44 (0.89-2.31)
Orthopedics	335		1.05 (0.76-1.45)			1.17 (0.79-1.72)
Urology	104		0.56 (0.34-0.92)			0.78 (0.45-1.34)
Gastroenterology	77		0.83 (0.49-1.40)			0.63 (0.35-1.16)
Surgery	608		0.63 (0.47-0.85)			0.62 (0.44-0.88)
Other	103		0.67 (0.41-1.10)			0.50 (0.28-0.89)
Medicine	253		0.41 (0.28-0.61)			0.42 (0.27-0.64)
Hematology	588		0.42 (0.31-0.57)			0.30 (0.20-0.44)
Pediatrics	80		2.07 (1.25-3.44)			0.23 (0.12-0.44)
Oncology/radiology	141		0.12 (0.06-0.24)			0.07 (0.03-0.14)
Care of elderly	89		0.03 (0.01-0.14)			0.02 (0.00-0.17)

* Probability of the observed difference in deviance between the models with and without the variable. Variables with significant effect on the model (at 5% significance level) shown with p value in bold.
† Factors significant when identified recipients who were known to be dead were excluded.
‡ An interaction was observed with the effect of age at transfusion on the odds of testing differing for recipients of different component types.

tion and analyses were the association of failure to trace and test, and of death, with time since transfusion, age at transfusion, and care under certain medical specialties.

Comparability with other lookback studies

The yield of HCV infections detected by published lookback programs has varied along with other factors such as the criteria used to determine components to enter lookback, the procedures used to identify recipients, and the characteristics of the recipients that determine whether testing is performed.

The rates of tracing recipients, and identifying infections, are broadly similar–or within variations to be expected due to different methods–in other published lookbacks and our own. We report identifying 1 HCV infection for every 12 components entering lookback: 1 infection per 9, 10, and 21 components has been reported from Scotland,[2] Northern Ireland,[3] and Canada,[4] respectively. We report identifying 1 HCV infection for every 8 recipients identified: 1 infection per 2, 4, 5, 5, 6, 8, and 22[5] recipients identified has been reported from Eire,[7] Scotland, Northern Ireland, New Zealand,[5] Canada, Denmark,[6] and The Netherlands (for PCR-positive donors only),[8]r espectively. We report identifying 1 HCV infection for every 2 recipients tested: Eire, Northern Ireland, New Zealand, and Canada also report 1 per 2 tests, and Scotland, Denmark, and The Netherlands (for PCR-positive donors) report 1 per 1 test.

At the time of designing the lookback, PCR test results for donors were incomplete and were not considered a robust surrogate of infectivity at the time of previous donations. Had lookback been restricted to PCR-positive donors, the reported data (not shown) suggest that only 10 percent of the components described would have entered lookback, and only 16 percent of the infected recipients identified by the lookback would have been identified. However, under-reporting of donors' PCR test results to our data set was likely.

Mortality of transfusion recipients

Few contemporary data exist on the mortality of transfusion recipients. The recipients traced during this lookback provide a picture of mortality by age, sex, component type, specialty of transfusion, and time since transfusion for recipients of blood transfusions before September 1991. Unfortunately, another variable expected to be strongly associated with mortality—the number and type of all transfusions given during the epi-

TABLE 4. Lookback data set logistic regression results: effects of recipient and donor variables on the likelihood of death of transfusion recipients before lookback

Variable	Obs (n)	p*	OR of recipient death before lookback (95% CI)	Obs (n)	p*	OR of recipient death before lookback (95% CI)
			Univariable	2461		Multivariable
Female sex	3,7889	**<0.01**	0.67 (0.59-0.77)		0.98	0.77 (0.63-0.93)
Age at transfusion (yr)	3555	**<0.01**	1.03 (1.02-1.03)		**<0.01**	1.04 (1.04-1.05)
Year of transfusion (yr)	3986	0.61	0.99 (0.97-1.02)		0.97	0.95 (0.92-0.98)
Period of donation	3986	0.15				
1990 or later			1.0 (baseline)			
1985-1989			1.18 (1.03-1.36)			—
1980-1984			1.08 (0.87-1.35)			—
pre-1980			1.03 (0.53-2.01)			—
Component type	4145	**<0.01**			0.36	
RBCs			1.0 (baseline)			1.0 (baseline)
Whole blood			0.69 (0.59-0.81)			0.99 (0.79-1.26)
Platelets			2.08 (1.72-2.52)			1.85 (1.36-2.51)
Plasma/cryo			1.03 (0.80-1.33)			1.44 (1.02-2.05)
Speciality of transfusion	2832	**<0.01**			**<0.01**	
Cardiothoracic	267		1.0 (baseline)			1.0 (baseline)
Oncology/radiology	141		8.90 (5.13-15.43)			15.9 (8.19-30.86)
Pediatrics	79		0.71 (0.42-1.20)			5.59 (2.91-10.77)
Hematology	588		3.40 (2.51-4.59)			4.15 (2.83-6.10)
Care of elderly	88		5.06 (2.86-8.97)			2.83 (1.50-53.7)
Medicine	251		2.50 (1.75-3.56)			2.30 (1.53-3.45)
Other	101		1.33 (0.83-2.13)			1.69 (0.96-2.97)
Surgery	603		1.72 (1.29-2.30)			1.60 (1.14-2.24)
Gastroenterology	77		1.08 (0.65-1.81)			1.17 (0.64-2.11)
Urology	104		1.85 (1.17-2.92)			1.13 (0.68-1.89)
Orthopedics	331		0.69 (0.50-0.97)			0.55 (0.37-0.81)
Obstetrics/gynecology	202		0.20 (0.13-0.32)			0.52 (0.30-0.89)

* Probability of the observed difference in deviance between the models with and without the variable. Variables with significant effect on the model (at 5% significance level) shown with p value in bold.

sode that including the HCV lookback component—was not recorded. Whether mortality after transfusion has changed since the introduction of anti-HCV testing of blood donations in September 1991 is not known. Unfortunately, information about the cause of death was missing from our data set for 54 percent of those known to have died by the time of tracing for HCV testing.

Factors affecting recipient testing

Analyses of factors associated with accepting testing through this program provide some indication of how lookback activities could be focused to give a higher yield. The exclusion of recipients reported as having had some testing (details unknown) performed outside this program could have affected these findings if these recipients were biased with respect to the factors analyzed; however, this group was relatively small and did not differ significantly in these variables (data not shown).

Year of transfusion and age at transfusion were independently associated with probability of accepting testing through this lookback program.

Restricting lookback to components issued in the last 5 years (or 2 yr) would (assuming no other changes in the lookback procedure's effectiveness) have resulted in 64 percent (or 33%) of the components described entered lookback, and 75 percent (or 45%) of the infected recipients identified by this lookback being identified.

Restricting follow-up to the 72 percent of recipients under 80 years old at the time of tracing (or 52% under 70, or 28% under 50) would have resulted in 93 percent (or 77 or 43%) of the infected recipients identified by this lookback being identified.

Transfusion during care of a medical specialty with high mortality (oncology, care of the elderly, and hematology, with 84, 71, and 69% found "known dead," respectively) was also associated with failure to test. The specialties with lowest mortality (obstetrics and gynecology, paediatrics, cardiothoracic care, and orthopaedics, with 13, 28, 40, and 31% found "known dead," respectively) had the highest yield of identified infected individuals for components transfused: 1 to 2.8, 1 to 3.6, 1 to 4.0, and 1 to 4.1, respectively. Together, these four specialties accounted for 31 percent of the transfusions with specialty known (45% with recipient not known to be dead) and 50 percent of the HCV infections detected.

The variables associated with being "not tested" in those not known to be dead were similar to those associated with being "known dead," suggesting that death, although not recorded in the hospital notes, may have been the major reason for recipients falling into the "not tested" group.

Restriction of the components entered into lookback, and of the follow-up of identified recipients, could improve the efficiency of future lookbacks. Whether re-

strictions could be justified—at the cost of some unidentified infections—would depend on the expected natural history, probability of successful treatment, probability of secondary transmission of the infection, and on the opportunity cost of the process.

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