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REVIEW

Paying for blood donations: still a risk?

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Vox Sanguinis

It is presently disputed whether studies indicating a higher risk of infectious diseases among paid blood donors are lessons of the past, or still hold relevance. Comparative studies published between 1968 and 2001 were assessed for a possible trend of change in the relative risk for infectious disease markers between paid and unpaid blood or plasma donors. Studies reporting that paid donors had lower risk were found, but most studies, including recent ones, continued to report that paid donors have higher rates of infectious disease markers than unpaid donors. By log-linear regression analysis of the relative risk estimates for infectious disease markers among paid and unpaid donors from 28 published data sets, evidence was not found to indicate that the difference in risk for infectious disease markers between paid donors and unpaid donors had diminished over time (P = 0·128, not significant). Paid donors are still more likely than unpaid donors to donate blood in the period during which infectious donations escape detection by blood-screening tests (the 'window-period'). Therefore, paid donations have a higher risk that labile blood components (such as red blood cells and platelets) are infected. Additional safety measures for handling plasma donations, and the preparation, purification and viral-inactivation steps employed for the production of plasma derivatives, may render the difference in infectious disease marker rates in donors irrelevant for plasma products. However, not all viruses are inactivated and paid donors were repeatedly found to have higher frequencies of markers for emerging agents. In a quality system, critical steps of the process should be addressed, and selection of the donor population is one of the first steps in this process. It is advised that blood establishments present yearly reports (with complete and raw data) to authorities on the incidence and prevalence of infectious disease markers among their donors as an ongoing surveillance on the 'quality' of their donor populations. Paid blood or plasma donors still have higher rates for infectious disease markers than unpaid donors.

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Introduction

The ministers of the European Health Council recently reached agreement that unpaid (non-remunerated) blood donations are to be encouraged [1]. This was not achieved without discussion. The European Union (EU) Scientific Steering Committee noted: 'The effect of a payment to donors on the risk of transmitting infectious diseases by blood has been extensively discussed, but it appears that voluntary, non-remunerated donations have the lowest residual risk. Therefore voluntary, unpaid donations seem to offer a higher margin of safety than paid donations' [2]. However, it was also mentioned that studies reporting a higher risk of infectious diseases among paid donors would just be lessons of the past. This raises the question of whether earlier findings should still be considered relevant. The safety of unpaid vs. paid blood donors has been discussed in reviews, comments,

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opinions and editorials, since 1950 [3,4]. Many of these articles focus on the ethical and social aspects, aspects of sufficiency and sometimes include comparative data on the safety of the donor populations. Thus far, one published review has attempted to systematically analyse the published data sets from studies comparing infectious disease risks among paid vs. unpaid donors. Eastlund takes this approach in his review published in 1998, collating published data from 1970 to 1997 [5]. In the current review we present an update of the published data, comparing the risk for infectious disease markers (IDM) among paid donors vs. unpaid donors of plasma or blood. Comparisons of risk are related to the time-frame until recent. The aim was to assess whether there has been a trend over time towards decreasing relative risk (RR) estimates for paid donors when compared to unpaid donors.

Prospective studies on post-transfusion infections among recipients of blood and blood components

The risk of infectious diseases among recipients of blood components from paid vs. unpaid donors may indirectly reflect the risk of the donor populations. However, other factors at collection, testing and processing of the products, and the selection of patients and use of blood products may interfere. Fourteen prospective studies of post-transfusion hepatitis (PTH) among recipients of blood products were published between 1970 and 1996 [5]. In the early 1970s, when no diagnostic tests for viral hepatitis were available, (non-specified) PTH occurred more often in recipients of blood from paid donors in all of four studies published between 1970 and 1977. After introduction of a diagnostic test for hepatitis B surface antigen (HBsAg) for blood donor screening, post-transfusion hepatitis B occurred more often in recipients of blood from paid donors in all of three studies published between 1970 and 1977. When diagnostic tests for hepatitis A and hepatitis B became available, the remainder of post-transfusion hepatitis was named post-transfusion hepatitis non-A, non-B (PTH-NANB). PTH-NANB occurred more often in recipients of blood from paid donors in all of five studies published between 1975 and 1981. One study published in 1996 on the historical effect on 'non-specified' PTH by transition from a paid to an unpaid donor system showed similar results. When the major causative agent of PTH-NANB was cloned and named hepatitis C virus (HCV), a study in 1994 found post-transfusion hepatitis C significantly more often in recipients of blood from paid donors than in recipients of blood from only unpaid donors. After 1996, no new published studies on risk comparison between paid vs. unpaid donors, as measured in the recipients of blood, were found. It is difficult to assess from these PTH studies whether the overall higher risk associated with paid donors would or would not persist after 1996. The reader is referred to the original studies, reviewed by Eastlund, for details [5].

Update of published data sets on infectious disease markers in blood donors

An indicator of the safety of blood donors is the frequency of IDM found when screening blood donors. The review by Eastlund includes 26 published data sets, most of these indicating higher frequencies of IDM among paid donations as compared to unpaid ones, and some data sets indicating the opposite [5]. After retrieval of the original papers referred to in the Eastlund review, four additional studies were found by searching PubMed for publications in medical journals and the web for government reports [4,6–8].

The Kühnl study

A study of 3123 donations, published in 1989, revealed a data set on early anti-HCV screening in Germany [8]. Among paid donations, three of 1249 (0·24%) were found to be anti-HCV positive using a first-generation enzyme-linked immunosorbent assay (ELISA) without a confirmatory test, as compared to 10 of 1874 (0·53%) among unpaid donations. This article was not included in Eastlund's review, possibly because the authors refer to a north–south gradient in the prevalence of HCV in Europe. A higher prevalence of HCV in Southern Europe as compared to the North was later confirmed by others. A confirmatory test for anti-HCV antibodies was not available at the time, which may have rendered the difference in frequency negligible. The data set was included in this assessment, as geographical bias or confirmation strategy was not an exclusion criterion (see exclusion criteria).

The GAO report

In September 1998, a report was presented by the United States General Accounting Office (GAO) to the Subcommittee on Human Resources, the Committee of Government Reform and Oversight and the House of Representatives [6]. The GAO report includes 10 data sets comparing data from paid and unpaid donors. The first data set provides data on antibody to human immunodeficiency virus (anti-HIV) in paid plasma and volunteer whole-blood donations in California from July to December 1996. Although the donation frequency may differ between the two groups, the data set is included in this assessment (see exclusion criteria). The data are part of a study conducted in California from 1990 to 1996, covering the HIV antibody test results on more than 7 million unpaid whole-blood donations and 4·5 million paid plasma donations. Three data sets include anti-HIV, anti-HCV and HBsAg marker rates from unpaid whole-blood donations vs.

paid plasma donations. The time-frames during which both groups were studied were quite different: 1996–97 vs. 1994, respectively. These three data sets were therefore not included in this assessment (see exclusion criteria). Three additional data sets in the GAO report provide data on ≈ 1 million unpaid whole-blood donations and 4 million paid plasma donations obtained in 1996–97, which represent the basis for calculations of the incidence of HIV (by antibody and antigen testing), anti-HCV and HBsAg among repeat donors. Donors represented in the incidence data pass the donor selection and screening procedures and donate, but subsequently seroconvert, and are detected at a later donation. From such donors, potentially infectious donations may enter the transfusion chain [9]. These three data sets are included in this assessment and are represented separately (see exclusion criteria). The data of the GAO report are also used to calculate three data sets on the 'residual risk' for an infectious donation to be included in the production process. However, two additional safety measures are unilaterally included for the paid plasma donations, and are not included for the unpaid whole-blood donations. These extra measures for the paid plasma donors affect the way the donations are handled, and reduce the risk of infectious donations being introduced into the production process; however, they do not reflect characteristics of the donor populations per se (see exclusion criteria). These three data sets are therefore not included in this assessment.

The Strauss studies

In an editorial in 2001, Strauss presented a further update of his earlier studies [4,10,11], considering data sets from a hospital with ≈ 9000 donations per year. Forty-three of 27 872 (0·15%) unpaid whole-blood donations were found to have IDM using a 'positive confirmatory test' (refers to the earlier publication [11]) as compared to four of 23 975 (0·017%) paid trombocytapheresis donations [4]. The paid trombocytapheresis donors are recruited from unpaid whole-blood donors, preselection of the trombocytapheresis donors therefore not being excluded. The original article by Strauss published in 1994 was criticised by Fiedler as being of flawed methodology and too limited power to support the conclusions [12]. However, it is included in the Eastlund review [5], as well as in the present assessment [11], and the recent update in the editorial of 2001 is also included in this assessment [4] (see exclusion criteria).

The German HCV nucleic acid amplification test study

In Europe, a recent data set for a new IDM was presented at a workshop at the Paul-Ehrlich Institut in Germany, in June 2001, and subsequently published [7]. It presents nationwide data from ≈ 12 million unpaid donations and 2·3 million paid donations screened for HCV RNA since the introduction of nucleic acid amplification testing (NAT). After the introduction of anti-HCV blood donor screening, an appeal was made to enhance the sensitivity of blood screening for HCV by NAT [13]. In Germany, HCV NAT screening of all blood donations was implemented at a national level early in 1999, after quality standards for HCV NAT were set [14]. HCV NAT-positive (but anti-HCV-negative) results on blood or plasma donations can be considered as a new IDM, which is related to the incidence of HCV in the donor population. In this study, HCV NAT was positive in 17 of 2 344 030 (0·725 per 100 000) paid donations as compared to 11 of 12 731 554 (0·086 per 100 000) unpaid donations during the 'window period' of anti-HCV testing [7]. The study is included in this assessment (see exclusion criteria).

Sources of bias and exclusion criteria

Given the aim of this assessment and the available published data, apart from overtly unilateral interventions some forms of bias could not be excluded. Most data sets, either showing unpaid donors to be safer, or the opposite, include some form of bias. For this assessment, the assumption is that bias may be present in studies with either outcome (see Fig. 1), and will not systematically influence the overall assessment into one direction.

Safety interventions

Safety interventions implemented after the donation are included in the results of three data sets on 'residual risk' in the GAO report [6]. These measures are only applied for plasma donations, not for cellular components (shelf life 5 and 35 days) derived from whole-blood donations. Paid plasma donations from newly recruited donors are only released if the donor is shown to be negative for IDM 6 months later. In addition, all plasma donations are held for 60 days before release [6]. These extra interventions significantly reduce the risk of infectious plasma entering the production pools for manufacture of plasma derivatives. However, the final – or residual – risk of an infectious unit entering a plasma pool 'remains somewhat higher for paid donors than for volunteer donors', according to the GAO report [6]. These measures are unilateral, greatly influence the comparison and do not reflect characteristics of the donor populations per se, but rather describe the handling of the donations. These three GAO data sets are therefore not included in our assessment.

Definition of paid and unpaid donors

Definitions of paid and unpaid donors have often been disputed [4]. However, for the sake of this assessment, which

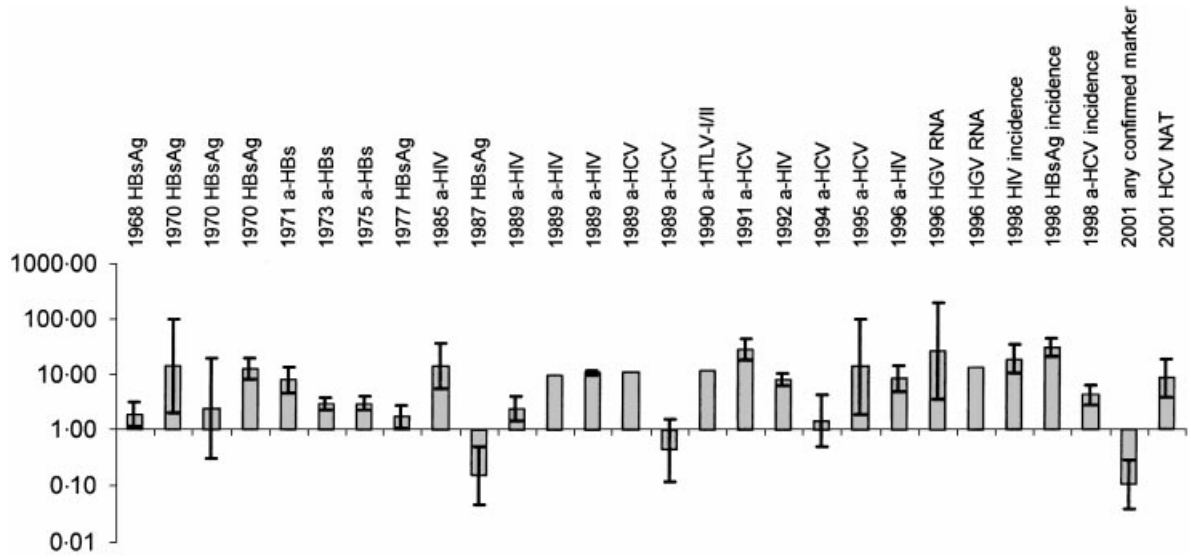

Fig. 1 From 25 studies, comparing the frequency of infectious disease markers (IDM) among paid and unpaid donor populations (definition see text), 28 data sets are included (see Table 1). The relative risks (RR), or risk ratios, were estimated for each data set, in addition to their 95% confidence intervals (95% CI) (GraphPad Instat™). For four data sets, the 95% CI could not be calculated, as only frequencies were given in the original report and data on the population size were lacking. If RR = 1, paid donors had the same frequency as unpaid donors; if RR = 10, paid donors had a 10-fold higher frequency; if RR = 0·1, unpaid donors had a 10 fold higher frequency. a-, anti; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HGV, hepatitis G virus; HIV, human immunodeficiency virus; HTLV-I/II, human T-cell lymphocytotrophic virus I/II; NAT, nucleic acid amplification testing.

reviews RR by time, it is feasible to compare the categories just as given by the authors of the studies, acknowledging that some difference in remuneration of the two donor categories must have been present in their reports. Nuances of remuneration all have some effect on donor behaviour and, in particular, the offering of cash results in a higher risk for IDM [15]. In this assessment the population categories compared are simply referred to as 'paid' or 'unpaid'.

Skewing of the data by donation frequency

The frequencies of risk in many data sets are presented as the number of IDM found among a total number of donations. When first-time blood donors are found to be infected, they are deferred from further donations, and the frequency at which this event occurs is indicative of the infectious disease prevalence among the population the donors are recruited from [16]. However, more important for blood safety is when a previously uninfected donor, while repeatedly donating, becomes infected. The frequency with which this event occurs is indicative of the infectious disease incidence among the population of repeat donors [16]. Early infections may not be detected by screening tests, and the period during which this occurs is referred to as the 'window period'. The risk of blood donations occurring during the window phase ('window-donation') is therefore a function of the length of the 'window period' of the given test and the infectious disease incidence among the population of repeat donors [9].

The skewing effect of presenting IDM frequencies per number of donations is illustrated in the GAO report [6]. The data comprise approximately 1 million unpaid whole-blood donations and approximately 4 million paid plasma donations obtained in 1996–97, the mean interval between donations being very different between the two groups: 5·3 days for paid plasma donors and 154 days for unpaid whole-blood donors, resulting in 68 donations per year, on average, for the paid donors and 2·4 donations per year for the unpaid donors, respectively. Incidence is the rate of new infections over time – usually expressed in person years observed. For the example above, 68 donations from one donor in 1 year contribute 1 person year to the denominator for the incidence among paid donors, and 2·4 donations contribute 1 person year to the denominator for the incidence among unpaid donors. Thus, the correct denominator for the incidence of infection amongst paid donors is actually far smaller than that for the unpaid donors. In this report therefore, the large difference in number of donations per individual donor means that the IDM frequencies presented as number of infections per 100 000 donations provides a misleading comparator. The frequency of infections per 100 000 donations in the GAO report differ by a maximum of twofold; the incidences, however, differ by a maximum of 30-fold. In contrast to the comparisons from the USA, the donation frequencies among German paid and unpaid donor populations [7] are more or less comparable, i.e. with a mean frequency of 1·7–2·8 donations per annum. The RR on the incidence rates for

HCV NAT amongst donors may therefore differ by a maximum of approximately twofold from the RR on the frequencies given for donations.

Also illustrative is the comparison presented by Strauss in 1994, which was criticised by Fiedler as being of flawed methodology [12]. 'The appropriate denominators (numbers of the total observed person-years in each group) are not available, which precludes a valid comparison'. In response, Strauss presents additional information on the issue. One finding was that the paid cytapheresis donors donated about five times per year, i.e. the incidence in paid donors would be five times higher than suggested in the original article. Fiedler's comments are in line with present state-of–the-art risk assessment, as described by Schreiber *et al.* [9], i.e. comparisons of risk in donor populations should be based on the incidence. Notwithstanding the skewing by donation frequency of the IDM data sets provided with donations in the denominator, such data sets are not excluded from this assessment.

Geographical differences in epidemiology

Geographical differences in epidemiology hamper the comparison of paid donors from one country to another [17], or from one region to another [8]. Therefore, it is of importance that comparisons are made from populations within a certain country. For instance, the GAO report, in the USA, and two German studies include data sets that cover approximately the whole country [6,7,18]. In one German comparison, a north–south gradient was acknowledged for HCV among the donors within Germany [8]. This is in agreement with the overall epidemiological data on the spread of HCV, indicating a relatively higher prevalence of HCV in the south of Europe and a lower prevalence in the north [19]. Given the scope of this assessment, it was assumed that the data sets were performed within comparable geographical regions.

Confounding population characteristics

Confounding population characteristics, other than geographical, have rarely been controlled for. There are no reports providing baseline characteristics, let alone that groups are matched. It was discussed that paid donors in Germany are relatively younger, probably more sexually active, and more often students and city dwellers, thus influencing the results of comparison. On the other hand, it could be argued that by paying for donations, populations with risk behaviour (such as drug use) are selected [15]. It could be argued that a relatively greater number of adult and affluent individuals would be less eager to receive cash for donation. It was also considered that €25 per whole-blood donation was adequate for reimbursment of expenses; on the other hand, it could be argued that young students would probably have less expenses to be refunded as compared to adults and affluent individuals. Although small incentives or tokens would probably marginally affect blood safety, the offer of cash results in a significantly higher risk for transfusion-transmitted infections [15]. Interestingly, the Fiedler data on anti-HIV of 1992 are comparable to the Seifried data on HCV NAT in 2001. Although HIV is easily sexually transmitted, HCV is not, and both are frequently spread among drug users [19]. HCV NAT may be a poorer marker of sexual behaviour, rather than drug use, both attributed to the young. It is known that cash payment for blood donations attracts a greater number of drug users [20].

Estimates on incomplete data sets

The GAO report has one systematic flaw, which could render the difference between unpaid donors and paid donors somewhat larger if all data were available. For the paid plasma donors, results of confirmation on the screening test-positive donations were not available, and the number of 'true infections' was extrapolated from the positive predictive value derived from confirmatory test results among the unpaid whole-blood donors. However, the positive predictive value depends on the (donor) population tested and decreases with lower risk of disease [16]. The number of true infections reported among paid donors in the GAO report may therefore have been somewhat underestimated. It was no reason for exclusion in this assessment.

Characteristics of the tests for IDM

Characteristics of the tests for IDM clearly have an influence on the results if the two groups under comparison are screened using tests of considerably different sensitivity. It was discussed whether variability in HCV NAT sensitivity could have caused the difference of frequency observed in German HCV NAT data. HCV replication is very low early after infection and usually below detection levels ('lag phase'), then rapidly increases ('viral burst') to levels of viral load sufficient to be detected by most HCV NAT assays. Germany was the first country where quality standards on HCV NAT were firmly established at a national level [14]. Possible differences in NAT sensitivity would probably not explain the difference in NAT yield [21]. In addition, given the regulations and quality systems for IDM testing, it was assumed (for the scope of this assessment) that serological test methods within a certain time-frame are comparable (i.e. 'state of the art') and would not greatly influence the comparisons.

Different time-frames

Three data sets in the GAO report [6] included anti-HIV, anti-HCV and HBsAg marker rates from unpaid whole-blood donations vs. paid plasma donations. However the time-frames

Table 1 Relative risk and 95% confidence intervals (95% CI) for infectious disease markers of paid vs. unpaid blood donors in population studies between 1968 and 2001

Reference	Year of publication	Marker	Paid donors vs. unpaid donors		
			RR	LL (95% CI)	UL (95% CI)
23	1968	HBsAg	1·88	1·14	3·12
24	1970	HBsAg	14·27	2·03	100·50
25	1970	HBsAg	2·51	0·32	19·90
26	1970	HBsAg	12·75	8·12	20·02
27	1971	a-HBsAg	7·91	4·67	13·38
28	1973	a-HBsAg	2·98	2·30	3·87
29	1975	a-HBsAg	3·00	2.27	3·96
30	1977	HBsAg	1·78	1·11	2·84
31	1985	a-HIV	14·28	5·60	36·41
22	1987	HBsAg	0·15	0·05	0·50
32	1989	a-HIV	2·49	1·52	4·07
33	1989	a-HIV	9·50	*	*
34	1989	a-HIV	10·75	9·87	11·70
35	1989	a-HCV	11·17	*	*
8	1989	a-HCV	0·45	0·12	1·63
36	1990	a-HTLV-I/II	12·09	*	*
37	1991	a-HCV	28·05	18·28	43·04
18	1992	a-HIV	7·96	6·23	10·17
11	1994	a-HCV	1·48	0·51	4·31
38	1995	a-HCV	14·00	1·98	99·26
6	1996	a-HIV	8·39	5·00	14·07
39	1996	HGV RNA	26·00	3·50	193·26
40	1996	HGV RNA	13·00	*	*
6	1998	HIV incidence	18·67	10·07	34·61
6	1998	HBsAg incidence	30·65	20·97	44·30
6	1998	a-HCV incidence	4·26	2·84	6·40
4	2001	Any confirmed marker	0·11	0·04	0·30
7	2001	HCV NAT	8·39	3·93	17·92

a-, anti; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HGV, hepatitis G virus; HIV, human immunodeficiency virus; HTLV-I/II, human T-cell lymphocytotrophic virus I/II; LL, lower limit of 95% CI; NAT, nucleic acid amplification testing; UL, upper limit of 95% CI.

*For four data sets, the 95% CI could not be calculated, as only frequencies were given in the original report and data on the population size were lacking.

during which both groups were studied were different: January 1996 to June 1997 vs. July to December 1994, respectively. Given the aim of this assessment to compare RR trend by time, these three data sets are not included in this assessment.

Selection bias

The Taswell data represent the situation where a hospital-based blood bank changed its donor-recruitment policy from a paid donor system to an unpaid system, by recruiting new, unpaid donors [22]. It is known that new donors are relatively less safe, and HBsAg was found significantly more often in the donations of the newly recruited unpaid donors, than in the longstanding donor base of paid repeat donors. A comparison of two, more stable, donor bases would have been preferred. The Strauss paper of 1994 mentions that the paid cytapheresis donors were recruited among unpaid whole-blood donors; a preselection of the paid cytapheresis donors is therefore not excluded. These were no reason for exclusion from this assessment.

Publication bias

Unfortunately, published surveillance data for paid donor populations are difficult to find [6]. It is not known to what extent, or in which direction, publication bias has affected the apparent higher risk of IDM in paid donors. It is hoped

Table 2 Studies and data sets excluded from relative risk (RR) calculations for mathematical reasons

Reference	Year of publication	Marker	Paid donors		Unpaid donors	
			Marker positive	Denominator	Marker positive	Denominator
22	1987	a-HIV	0	10 414	1	13 304
41	1990	a-HIV	4	1700	0	8000
11	1994	a-HIV	1	1240	0	917
11	1994	a-HBsAg	0	1240	1	917
42	1995	a-HCV	13	100	0	100

These data sets were excluded from the RR estimates in Table 1 and Fig. 1 as a zero value was included in one cell of each data set. Depending on the study, the denominator may represent donors or donations.

a-, anti; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus.

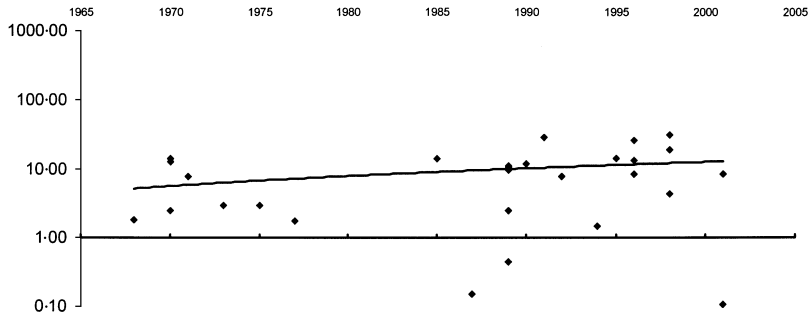

Fig. 2 Trend analysis, by log-linear regression, on the relative risks (RR) for infectious disease markers of paid vs. unpaid blood donors in population studies between 1968 and 2001. No significant trend was identified to indicate that the RR between paid and unpaid donors has shown a decrease over time ($P = 0{\cdot}128$).

that the EU will implement a uniform and scientifically sound system for surveillance on paid as well as on unpaid donor populations, in order to properly compare donor populations. This surveillance should be based on comparable data, e.g. raw data on the incidence and prevalence in these donor populations.

Findings

In total, 33 data sets were included, i.e. 26 from the articles previously reviewed by Eastlund [5], four from the GAO report [6], and one each from Kühnl [8], Strauss [4] and Seifried [7]. The data on IDM rates, as presented in the publications, were used to calculate the RR estimate, including 95% confidence intervals (95% CI) of paid vs. unpaid donations or paid vs. unpaid donors, and are represented in Fig. 1 and Table 1. Five of the 33 (15%) data sets were excluded from the RR calculations owing to the presence of a 'zero' value in one of the nominators. These data sets are summarized in Table 2. Four of 28 (14%) of the data sets included reported only frequencies and failed to include both population sizes, thus hindering the estimate of the 95% CI around the RR. Log-linear regression analysis on the RR estimates from the published data sets did not indicate a trend towards this difference in risk between paid and unpaid donors diminishing over time ($P = 0{\cdot}128$, not significant) (see Fig. 2).

Discussion

Overall, the data available continue to indicate that paid donor populations have higher frequencies of blood-borne infections than unpaid ones (see Figs 1 and 2). Trend analysis does not indicate that the difference in risk between paid and unpaid donor populations has diminished over time. This is in agreement with a Californian study on anti-HIV positivity among paid plasma donors and unpaid whole-blood donors, reviewed in 1998 by the United States GAO to the Subcommittee on Human Resources, the Committee of Government Reform and Oversight and the House of Representatives [6]. The data are part of an ongoing study in California from 1990 to 1996, covering the HIV antibody test results on more than 7 million unpaid whole-blood donations and 4·5 million paid plasma donations. During 1990–96, anti-HIV positivity among unpaid blood donations fell from 0·015% to 0·003% and among paid plasma donations fell from 0·56% to 0·027% [6]. This trend of decreasing risk of HIV in both populations may have contributed to the increasing safety of the blood supply over the last decade [43]. However, it is also clear from these Californian data that the higher RR among paid donors

did not principally change. The GAO reports: 'While the rates of HIV are dropping in both groups, there is a consistent pattern of higher marker rates among paid donors than among volunteer donors' [6].

Paid donors are more likely to donate blood during the 'window-period', when blood-borne viruses may not be detectable in screening tests. Unfortunately, screening tests without a 'window-period' do not exist, and probably never will. New molecular-based technologies (such as NAT) will reduce, but not eliminate, the window period. Paid donations therefore result in a higher risk that labile blood components, such as red blood cell concentrates and platelet concentrates, are infectious. However, the preparation, purification and viral-inactivation procedures employed in the production of derivatives of pooled human plasma may render the difference between the safety of paid and unpaid donors for plasma products irrelevant. On the other hand, viral-inactivation steps may not inactivate all viruses, e.g. non-enveloped viruses, and, in a quality system, all critical steps of the process should be addressed. The selection of the donor population is one of the first steps in this process.

It is important to use clear and standardized epidemiological measurements for infectious-disease risk assessment in blood donors, e.g. the incidence of infectious diseases among repeat donors or regular donors [44]. Blood establishments should present yearly reports to authorities with complete and raw data on the incidence of infectious diseases among their donors. Such ongoing surveillance would contribute greatly to providing absolute and comparative quality assessment of donor populations. In risk analyses, the frequencies of IDM should relate to donors (or donor years) observed, rather than to donations [9,45]. The incidence of infections among repeat or regular donors is a scientifically sound parameter [9,16,45] and a step to be monitored in a quality system for blood transfusions. In addition, the prevalence of IDM in newly recruited donors may provide a transverse picture of the population that the donors are recruited from. Prevalence relates indirectly to incidence, although differently for persistent infections (HIV or HCV) and for transient infections (HBV). In order to allow appropriate comparisons to be made on prevalence, it should reflect the IDM frequency among 'unselected, first-time donors'.

In the light of emerging infections, 'encouragement of unpaid donations' [1] may be justified as a precautionary measure. Two comparative studies are shown, both indicating that in 1996 the newly discovered GBV-C′ virus was found to be considerably more frequent in paid donors. Blood donations are, for various reasons, presently not tested for GBV-C′, mainly because no clear disease association is known. As with HCV, GBV-C′ is readily inactivated by viral-inactivation methods used in the production of plasma derivatives, but this is not the case for cellular products. One lesson of the past may be that any time a new blood-borne infectious disease has emerged, paid donors have had higher frequencies of infection than unpaid ones.

It is concluded that studies on the risks of using paid blood donors are lessons for the future, rather than lessons of the past.

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