RISK OF CANCER FOLLOWING BLOOD TRANSFUSION FROM DONORS WITH SUBCLINICAL CANCER

Gustaf Edgren[1]*, Henrik Hjalgrim[2]*, Marie Reilly[1]*, Trung Nam Tran[1], Klaus Rostgaard[2], Agneta Shanwell[3], Kjell Titlestad[4], Johanna Adami[1, 5], Agneta Wikman[3], Casper Jersild[6], Gloria Gridley[7], Louise Wideroff[8], Olof Nyrén[1], Mads Melbye[2]

[1] Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

[2] Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark

[3] Department of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, Stockholm, Sweden

[4] Department of Clinical Immunology, Odense University Hospital, Odense, Denmark

[5] Department of Medicine, Clinical Epidemiology Unit, Karolinska Institutet, Stockholm, Sweden

[6] Department of Clinical Immunology, Århus University Hospital, Århus, Denmark.

[7] Division of Cancer Epidemiology and Genetics, National Cancer Institute, NIH, Bethesda, Maryland, USA

[8] Division of Cancer Control and Population Sciences, National Cancer Institute, NIH, Bethesda, Maryland, USA

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Correspondence and reprints: Dr Olof Nyrén, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Box 281, SE-171 77, Stockholm, Sweden
Phone +46-8-524 861 95; fax +46-8-31 49 75; e-mail: olof.nyren@ki.se

SUMMARY

BACKGROUND

Whilst mechanisms for detection of short-term complications following blood transfusions are well developed, complications with delayed onset, notably transmission of chronic diseases such as cancer, have been difficult to address.

METHODS

We conducted a register-based retrospective cohort study of cancer incidence among patients who received blood from donors deemed to have a subclinical cancer at time of the donation. These precancerous donors were diagnosed with a cancer within 5 years of the donation.

Data from all computerised blood bank registers in Sweden and Denmark collected between 1968 and 2002 were merged into a common database. Demographic and medical data, including mortality and cancer incidence, were ascertained through linkages with nationwide and essentially complete population and health care registers.

The relative risk of cancer in exposed recipients relative to that in recipients who received blood from non-cancerous donors was estimated using multivariate Poisson regression, adjusted for potential confounding factors.

RESULTS

Out of 354,094 transfusion recipients eligible for this analysis, 12,012 (3·4%) were exposed to blood products from precancerous donors. After necessary adjustments we found no excess risk of cancer overall (relative risk, 1·00; 95% confidence interval, 0·94-1·07) or in crude anatomical subsites among recipients of such blood, compared with recipients of blood from non-cancerous donors.

CONCLUSIONS

This study provides no evidence that blood transfusions from precancerous blood donors are associated with increased cancer risk among recipients.

INTRODUCTION

Continuous attention to transfusion safety has reduced the risk of transfusion-transmitted disease to a current record low.[1] However, while most infectious complications have been comparably easy to identify, possible transmission of chronic diseases with unknown aetiologies and long induction or latency periods has been far more difficult to address.

The hypothesis that a blood transfusion can result in cancer development in the recipient has been tested by several investigators and with various study designs.[2-10] Some reports have described an increased risk of cancer overall[2] and of non-Hodgkin lymphoma in particular,[2,5,8] whereas others found no such associations.[7,9-12] Suggested mechanisms for such an association include immune modulation, transmission of factors etiologically related to cancer development and engraftment of malignant cells of donor origin.[2,8,13-16]

Transmission of both solid[17,18] and non-solid[19-21] malignancies as well as oncogenic viruses such as Kaposi's sarcoma-associated herpesvirus[22] and Epstein-Barr Virus[23] from organ donors to transplant recipients has repeatedly been observed. Transmission of Kaposi's sarcoma-associated herpesvirus via blood transfusions was also recently documented.[24] Further, scattered reports of transmission of cancer cells from needles or surgical instruments demonstrate the ability of tumour cells to be transplanted to, and to develop in healthy recipients.[25,26] The ability of tumour cells to survive in human graft recipients has also been demonstrated in experimental settings.[27] However, the few studies that have addressed the issue of allotransplantation of human tumour tissue through blood transfusion or other blood-borne means have been inconclusive.[14-16,28]

To investigate the possible risk of cancer transmission from blood donors to recipients through blood transfusion, we conducted an epidemiologic investigation based on a bi-national database with long-term detailed donation and transfusion histories as well as information on health outcomes among Scandinavian blood donors and recipients. We hypothesised that the cancer incidence after a transfusion would be higher if one or more units emanated from donors

who were diagnosed with cancer within five years after donation, than if the units came from donors who remained cancer free for at least five years after donation.

METHODS

DATA SOURCES

The assembly of the Scandinavian Donations and Transfusions database (SCANDAT) has been described in detail elsewhere.[29] In brief, we collected selected variables from all computerised registers of blood donations and transfusions maintained by blood banks and transfusion medicine clinics in Sweden and Denmark since 1968 and 1982, respectively. Donor and recipient details, including dates of birth, sex, as well as types, number and dates of donations and transfusions were entered into a common database. Internal codes that uniquely identified each donor, donation, blood component and recipient enabled us to trace each transfused blood unit back to its donor(s). Before de-identification, the database was linked with national population and health registers, including the national registers of migration, death, cancer and in-hospital care, using the unique personal identification number assigned to all residents of Sweden and Denmark.

STUDY POPULATION

Using the SCANDAT database we conducted a retrospective cohort study. We identified all persons with no history of malignant disease who received at least one unit of whole-blood, erythrocytes, plasma or platelets between 1968 and 2002. For each recipient, we considered all transfusions that occurred during the first 30 days following the first recorded blood transfusion in our database, and identified all blood donors who contributed to these transfusions. Donors who, according to the Swedish or Danish cancer registers, were diagnosed with an incident malignancy (7th revision of the International Classification of Disease, 140-207, not counting non-melanoma skin cancer) within five years following a blood donation (henceforth referred to as "precancerous blood donors") were deemed to harbor a subclinical malignancy at the time of donation. Accordingly, recipients of any blood product (henceforth referred to as "blood") from such a donor were thus considered to be exposed, and correspondingly, recipients who received blood products only from donors who were not diagnosed with cancer within five years after

the donation were considered to be unexposed. Recipients of blood from donors with a known prior cancer diagnosis at time of donation were excluded from the main analyses. To ensure correct classification of exposure, all recipients who during the first 30 days received transfusions from unknown blood donors or blood donors for whom we did not have at least five years of follow-up were excluded from the analysis, as were recipients of autologous transfusions. The latest donations that could be considered in this study were thus performed in 1997. We also excluded recipients for whom the area of residence at the time of first transfusion could not be ascertained. The study design with definitions of exposure and outcome, along with inclusion and exclusion criteria is schematically presented in Figure 1.

The recipients were followed for cancer occurrence using the Swedish and Danish cancer registers. Follow-up ended on the date of first malignant cancer diagnosis (excluding non-melanoma skin cancer), death, emigration, or 31st of December, 2002, whichever came first. We also censored individuals who, after the initial 30-day expsure period, received a transfusion originating from a precancerous blood donor, an unknown donor or a donor with less than five years of follow-up. To minimise disturbing noise from incipient cancers that were present in the recipient but indiagnosed at the time of the blood transfusion, we started follow-up six months after the first recorded transfusion. Thus any recipients who died, emigrated or were diagnosed with cancer within six months after the first recorded transfusion were not considered in the analyses.

STATISTICAL ANALYSIS

The relative risk of cancer after transfusion with blood from a precancerous blood donor was assessed as incidence rate ratios estimated from Poisson regression models. In addition to exposure to blood from precancerous blood donors, potential confounding factors included in the analysis were sex, attained age (categorised as <40, 40-59, 60-69, or ≥70 years), area of residence at the time of first transfusion (four Danish and five Swedish geographical regions), ABO-blood type (A, B, AB, O, or unknown), number of transfusions during the first 30 days

following first transfusion (1-2, 3-4, 5-9, or ≥10 transfusions), calendar period (1968-1979, 1980-1989, or 1990-2002) and number of years since first transfusion (<1, 1, 2, 3-4, 5-9, 10-19, or 20-34 years). Attained age, calendar period and time since first transfusion were treated as time-dependent covariates, allowing individuals to move between categories with time.

Since immune responses and thus the possible susceptibility to engraftment of foreign cells may vary by sex and age, and since the potential for transmission may have changed during the study period due to the use of filtered and leukocyte depleted blood and different types of blood components, we conducted sub-analyses stratified by recipient sex and age as well as calendar period of transfusion, number of units that were administered and component type (i.e. whether the exposure-carrying blood unit was cell-containing or plasma). In a sensitivity analysis, we varied our definition of "precancerous blood", and consequentially the definition of exposure, by successively reducing the maximum time span between donation and cancer diagnosis in the donor from 5 years, to 4, 3, 2 and 1 year. Since transfusions from donors with metastatic disease may pose a bigger threat to recipients, we conducted a sub-analysis using only the Danish portion of the data, since only the Danish cancer register records tumour stage. In this additional sub-analysis, recipients of blood from donors who were diagnosed with metastatic cancer were compared to the unexposed group. Similarly, we also assessed whether time to cancer death of the donor who contributed an exposed transfusion somehow was associated with increased cancer risk in the recipient. To test whether the risk of cancer in the recipient depended on type of cancer in the donor, we also conducted analyses with exposure divided into 15 broad groups of cancer in the donor. Correspondingly, we compared site-specific cancer risks among exposed and unexposed transfusion recipients. Finally, we analysed the risk of cancer of the lung, liver, skeleton and central nervous system combined, i.e. anatomical sites deemed to be at highest risk of haematogenous cancer cell transmission.[30-32] Although recipients of blood from donors with a prior cancer diagnosis were excluded from the

overall analyses, we investigated whether the cancer incidence in these recipients differed from that among recipients of donors with no cancer prior to or within 5 years after the donation.

The creation of the SCANDAT database and the conduct of this study were approved by appropriate scientific ethical committees and data protection agencies in both countries.

RESULTS

Of 1,311,079 transfusion recipients in the SCANDAT database, we excluded 373,014 who had a previous diagnosis of cancer and 208,692 recipients who died, emigrated, were diagnosed with cancer within six months of first transfusion, or for whom start of follow-up occurred after 31st of December, 2002. We further excluded 91,959 recipients who received blood from an unknown donor, 230,076 recipients who received blood from a donor who was followed for less than five years, 9,377 recipients who received blood from a donor with a prior cancer diagnosis, 3,760 recipients of autologous transfusions, and 40,107 recipients with an unknown area of residence at the time of first transfusion. Thus 354,094 recipients remained for analysis, of whom 55,871 (15·8%) were censored on receipt of an exposed or unknown unit outside the initial 30-day window. Table 1 presents the general characteristics of the study population. Together these recipients contributed 3,200,800 person-years of follow-up during which 29,651 primary cancers occurred. In total, 12,012 recipients (3·4%) were exposed to blood from precancerous donors. During follow-up for a total of 90,928 person-years among the exposed recipients, 978 incident cancers were recorded in the national cancer registers.

Results from overall and stratified Poisson regression analyses of cancer incidence are presented in Table 2. In the adjusted analysis, we found no excess risk of cancer overall among recipients who had received one or more blood products from a precancerous blood donor, compared with recipients who had only received blood from non-cancerous donors (relative risk, 1·00; 95% confidence interval [CI], 0·94-1·07). The relative risk was not substantially modified by sex, age, calendar period or number of transfusions. However, analyses stratified by sex and follow-up revealed a statistically significantly increased cancer risk among exposed male recipients in the period between 5 and 10 years following the first transfusion (relative risk, 1·19; 95% CI, 1·03-1·38). There was no indication of a corresponding excess risk for exposed women in the same follow-up period (relative risk, 0·93; 95% CI, 0·76-1·12), nor was there any evidence of excess risks in any of the other follow-up intervals for either sex.

A sub-analysis on Danish data comparing recipients of blood from donors who presented with metastatic cancer within 5 years after the donation to unexposed recipients produced a relative risk of 0·99 (95% CI, 0·48-1·79). Analyses according to type of blood component, storage time and time to cancer death of the donor revealed no notable variation. Also, we found no conspicuous pattern when successively reducing the maximum time span allowed between donation and cancer in the donor for the blood to be considered precancerous: for 4, 3, 2 and 1 years, the relative risks were 1·00 (95% CI, 0·93-1·07), 1·00 (95% CI, 0·92-1·07), 0·93 (95% CI, 0·84-1·02) and 0·93 (95% CI, 0·81-1·05), respectively. The cancer incidence among the 9,377 recipients of blood from donors with a prior cancer diagnosis did not differ from that among recipients of blood from non-cancerous donors (relative risk, 0.94; 95% CI, 0.86-1.02).

We found no evidence suggesting variable potential for disease transmission when recipients of blood from donors with cancers at different anatomical sites were considered separately (Table 3). Also, there was little variation in site-specific cancer risk between exposed and unexposed recipients (Table 4). Finally, we detected no excess risk when the anatomically most plausible sites (lung, liver, skeleton and central nervous system) were combined (relative risk, 1·00; 95% CI, 0·85-1·17).

DISCUSSION

In this bi-national retrospective cohort study among Scandinavian transfusion recipients we found essentially no evidence that blood components originating from precancerous blood donors confer an increased cancer risk on the recipients. This was true irrespective of calendar period (which could be seen as a proxy for the declining probability of receiving nucleated cells in addition to red blood cells, platelets and plasma), the recipients' age and sex, and the overall number of transfusions received in addition to the exposed blood component. Moreover, there was no evidence to indicate that the risk of cancer transmission varied by type of cancer in the donor, nor did we observe excess occurrences of any specific cancer sites.

Our data add to the sparse literature, mainly in the form of case reports,[33] that describe the outcome, for the most part short-term, after accidental[33] or deliberate[14,15,34] transfusion of blood from donors with clinically overt malignancies. While our findings should not be over-interpreted, the overall consistency of the negative results does not support the hypothesis that allogenic transfusion of single malignant cells may lead to engraftment and subsequent development of clinical malignancies in human transfusion recipients. The plausibility of such transmission is otherwise supported by reports of long-lasting donor microchimerism following blood transfusion[35-37] and transmission of malignancies through organ transplantation.[17-20] If it does occur, it is so rare that we were unable to capture it with a study that included the total blood bank experience over several years in two countries. Also, since we found no increased cancer risk associated with transfusions from an admittedly limited number of donors with a previous cancer history, it would seem that long-term cancer survivors may be a relatively safe donor group. Since cancer survivors normally are deferred from blood donation, reservations must be made for the representativity of these post-cancerous subjects.

Our study, further, provides a timely addition to a recent report from Uganda demonstrating the transmission of Kaposi's sarcoma-associated herpesvirus via blood transfusions.[24] Despite systematic exclusion of donors at increased risk of HIV infection or

AIDS-related morbidity, our database revealed 14 blood donors with a subsequent Kaposi's sarcoma diagnosis. However, none of the 55 patients that received a blood component from these donors developed Kaposi's sarcoma during follow-up, which ranged from 0 to 26 years. Further follow-up may be needed, though. The last donation made by a donor who later on developed Kaposi's sarcoma was performed in 1991.

The only departure from the generally inconspicuous cancer pattern in recipients of precancerous blood components was the finding of an apparent excess risk of total cancer among male transfusion recipients in the period from 5 to 10 years following the first transfusion. We cannot readily explain this finding, but the absence of a corresponding effect among women and the large number of statistical tests conducted suggests that it is likely to be a spurious result. Also, we are not aware of any biological mechanisms by which only men should be susceptible to such transmission.

Strengths of our study include its design and large sample size. Further, the availability of nationwide population, death, migration and cancer registers of high quality ensures that follow-up is virtually complete and unbiased. Although the geographical coverage of the computerised blood bank registration was less complete in the early years of this investigation, there is little reason to believe that this critically affects the internal validity of our investigation. While we have not been able to assess the validity of the SCANDAT database directly, overall data quality, internal consistency and comparisons with official reports of annual numbers of blood donations and transfusions suggest it to be satisfactory.[29] Both the Swedish and Danish cancer registers are known to have a high degree of completeness.[38,39] Moreover, since the impending cancer of a blood donor was unknown at the time of transfusion, the possibilities for confounding were limited. The number of transfusions administered is an important potential confounder, though, as it is linked to the likelihood of being exposed to precancerous blood and also possibly linked to cancer risk via the disease that prompted the transfusion. Since underlying disease in the recipient can be associated with the probability of being exposed to

precancerous blood only through the number of administered transfusions, there is no need to adjust for indication in the analysis. Other conceivable confounders include cancer risk factors that act on a population level such as calendar time and area of residence, but may also include factors such as blood type. Hence, with proper adjustment for the number of transfusions, calendar period, area of residence and blood type, residual confounding or other confounding due to other unmeasured factors is unlikely. While the restriction to individuals for whom we have at least five years of follow-up of all contributing blood donors is quite conservative and took a heavy toll on the number of study participants, it ensured that the misclassification of the exposure was kept to a minimum.

In our analyses, we restricted our transfusion information to the first 30 days of an individual's recorded transfusion history. This approach could be overly simplistic for handling the problem of widely varying transfusion histories. However, a majority of individuals (69%) received transfusions only within such a 30-day window. It is also possible that the exposure was misclassified due to left truncation of the transfusion history as the introduction of computer registers was staggered. It is reassuring that calendar period did not modify the effect of exposure to precancerous blood. The absence of effect modification by calendar period, despite the changing practice of transfusion medicine is evidence against transfusion-transmitted risk for the various blood products in use: whereas only whole blood and other component types containing significant concentration of leukocytes were used in the beginning of the study period, there has been a gradual shift towards leukocyte depleted or reduced components. Since the practice of transfusion medicine differs substantially internationally, for example with regards to donor suitability criteria and the use of blood filtering and leukocyte depletion, our findings may not be directly applicable to other settings. Nevertheless, the study encompasses more than three decades during which transfusion medicine, as a discipline, has evolved tremendously and shifted from crude whole-blood to specialized components.

We postulated that blood products donated more than five years before the cancer diagnosis in the donor would not be associated with an excess risk. If blood products were associated with risk for more than five years, for instance because of the presence of an infectious agent in the donor's blood, the entailing exposure misclassification would contaminate the unexposed reference group and thus attenuate a true association. Thus, while this five-year cut-off point is somewhat arbitrary and could potentially have masked a true association, we focused on this biologically plausible *a priori* hypothesis to avoid extensive sensitivity analyses and the introduction of further multiple-testing problems. Also, we found no suspicious pattern when the five-year exposure window was shortened. Naturally, we cannot be certain that malignant or pre-malignant cells were present in the donor's blood at the time of the index blood donation, but evidence suggests that the process leading to cancer is indeed lengthy and that circulating tumor cells exist at a relatively early stage.[40] We disregarded the first six months following the first transfusion from the analyses in order to minimize disturbing noise from cancers present already at first transfusion, symptoms of which neccessitated the transfusion. The probability that transfusion-induced cancers would become clinically evident within 6 months is deemed low, based on clinical experiences with transplantation-transmitted cancers.[17]

Our study was not designed to address cancer risks associated with blood transfusion *per se* compared to no transfusion, for instance via an immunomodulating effect, but was specifically focused on the potential transmission of viable cancer cells. Accordingly, the time span between exposure and clinical cancer outcome was assumed to be less than 5 years – an unrealistically short induction period if early-stage carcinogens would be considered. Although the power to confirm excess long-term risks was limited, a point estimate of relative risk slightly below 1 with an upper 95% confidence limit of 1·38 for the follow-up period 20-34 years after first transfusion suggests that hidden long-term excess risks are unlikely, albeit not impossible.

In conclusion, this study provides no evidence that blood transfusions from precancerous blood donors are associated with increased cancer risk among recipients.

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TABLES

TABLE 1

Characteristics of the studied recipient population.

	Unexposed cohort		Exposed cohort		All study participants	
Number of subjects	342,082		12,012		354,094	
Sex						
Female	206,899		6,551		213,450	
Male	135,183		5,461		140,644	
Country						
Denmark	54,848		2,686		57,534	
Sweden	287,234		9,326		296,560	
Age at entry into cohort (year), N (%)						
< 40	81,183	(23·7)	2,419	(20·1)	83,602	(23·6)
40-59	68,199	(19·9)	2,444	(20·3)	70,643	(20·0)
60-69	55,882	(16·3)	2,046	(17·0)	57,928	(16·4)
70-	136,818	(40·0)	5,103	(42·5)	141,921	(40·1)
Mean age at entry into cohort, years (SD)	57·7	(22·7)	59·6	(21·4)	57·8	(22·6)
Median length of follow-up, years (range)	7·0	(0-34)	6·2	(0-33)	7·0	(0-34)
Median year of first recorded transfusion (inter-quartile range)	1992	(1986-1995)	1993	(1989-1996)	1992	(1986-1995)
Median number of transfused units (range)*	2	(1-136)	4	(1-285)	2	(1-285)

*During initial 30 days following first blood transfusion.

TABLE 2

Adjusted rate ratios of cancer among recipients of precancerous blood, relative to recipients of non-cancerous blood; overall and stratified by sex, age at transfusion, calendar period of transfusion, time since exposure and number of transfusions. For each stratum, the reference group is recipients of non-cancerous blood.

Stratum	Number of cancers/person-time among exposed	Number of cancers/person-time among unexposed	Adjusted Rate Ratio (95% CI)*
Overall	978/90,928	28,673/3,109,872	1·00 (0·94 - 1·07)
Sex			
Female	425/51,298	14,290/1,991,245	0·98 (0·89 - 1·08)
Male	553/39,630	14,383/1,118,627	1·03 (0·94 - 1·12)
Age at first transfusion			
0-39	64/29,040	2,450/1,201,474	1·08 (0·84 - 1·38)
40-59	183/23,023	6,589/778,005	0·91 (0·78 - 1·06)
60-69	267/16,028	7,561/482,795	1·03 (0·91 - 1·16)
70-	464/22,837	12,073/647,599	1·02 (0·93 - 1·12)
Calendar period of first transfusion			
1968-1979	74/14,095	4,944/891,022	0·91 (0·71 - 1·13)
1980-1989	283/30,589	8,716/1,036,966	0·96 (0·85 - 1·08)
1990-2002	621/46,244	15,013/1,181,885	1·03 (0·95 - 1·12)
Time since first transfusion			
0-4 years	511/45,181	13,412/1,313,197	0·99 (0·90 - 1·08)
5-9 years	297/26,585	7,705/877,132	1·08 (0·96 - 1·21)
10-19 years	148/16,387	5,874/733,825	0·96 (0·81 - 1·13)
20-34 years	22/2,775	1,682/185,718	0·90 (0·59 - 1·38)
Number of transfusions			
1-2	258/26,845	15,765/1,851,497	1·01 (0·89 - 1·14)
3-4	238/21,703	6,936/701,640	1·02 (0·90 - 1·16)
5-9	252/21,166	4,244/397,543	1·05 (0·92 - 1·19)
>9	230/21,215	1,728/159,193	0·94 (0·81 - 1·07)

*CI denotes confidence interval; Adjusted for sex, attained age, calendar period of observation, number of transfusions, area of residence, ABO blood type and follow-up time.

TABLE 3

Adjusted rate ratios of cancer at any site among recipients of precancerous blood from donors with cancers at different anatomical sites; relative to recipients of non-cancerous blood.

Anatomical site of donor cancer	Number of cancers/person-time among recipients	Adjusted Rate Ratio (95% CI)*
No cancer (unexposed recipient)	28,673/3,109,872	1·00 (ref)
Oral cavity and upper gastrointestinal tract	37/3,614	1·05 (0·75 - 1·43)
Lower gastrointestinal tract	76/7,642	0·94 (0·74 - 1·17)
Liver and gallbladder	6/405	1·26 (0·50 - 2·56)
Respiratory organs	35/3,088	1·11 (0·78 - 1·52)
Breast and mammary gland	160/14,857	0·98 (0·84 - 1·14)
Female genital organs	57/6,243	0·91 (0·69 - 1·17)
Male genital organs, incl. prostate	143/12,756	1·06 (0·90 - 1·25)
Urinary organs	72/7,458	0·91 (0·72 - 1·14)
Melanoma of skin	101/8,387	1·13 (0·92 - 1·36)
Eye and nervous system	48/4,092	1·07 (0·79 - 1·40)
Endocrinal glands	37/3,515	1·20 (0·85 - 1·63)
Bone and connective tissue	11/1,689	0·72 (0·37 - 1·23)
Malignant lymphomas	38/4,164	0·91 (0·65 - 1·24)
Leukemia and myeloma	30/3,003	0·98 (0·67 - 1·38)
Other and unspecified	127/10,016	1·01 (0·84 - 1·20)

* CI denotes confidence interval; Adjusted for sex, attained age, calendar period of observation, number of transfusions, area of residence, ABO blood type and follow-up time.

TABLE 4

Adjusted rate ratios of site-specific cancer among recipients of precancerous blood, relative to recipients of non-cancerous blood. For each anatomical site, the reference group is recipients of non-cancerous blood.

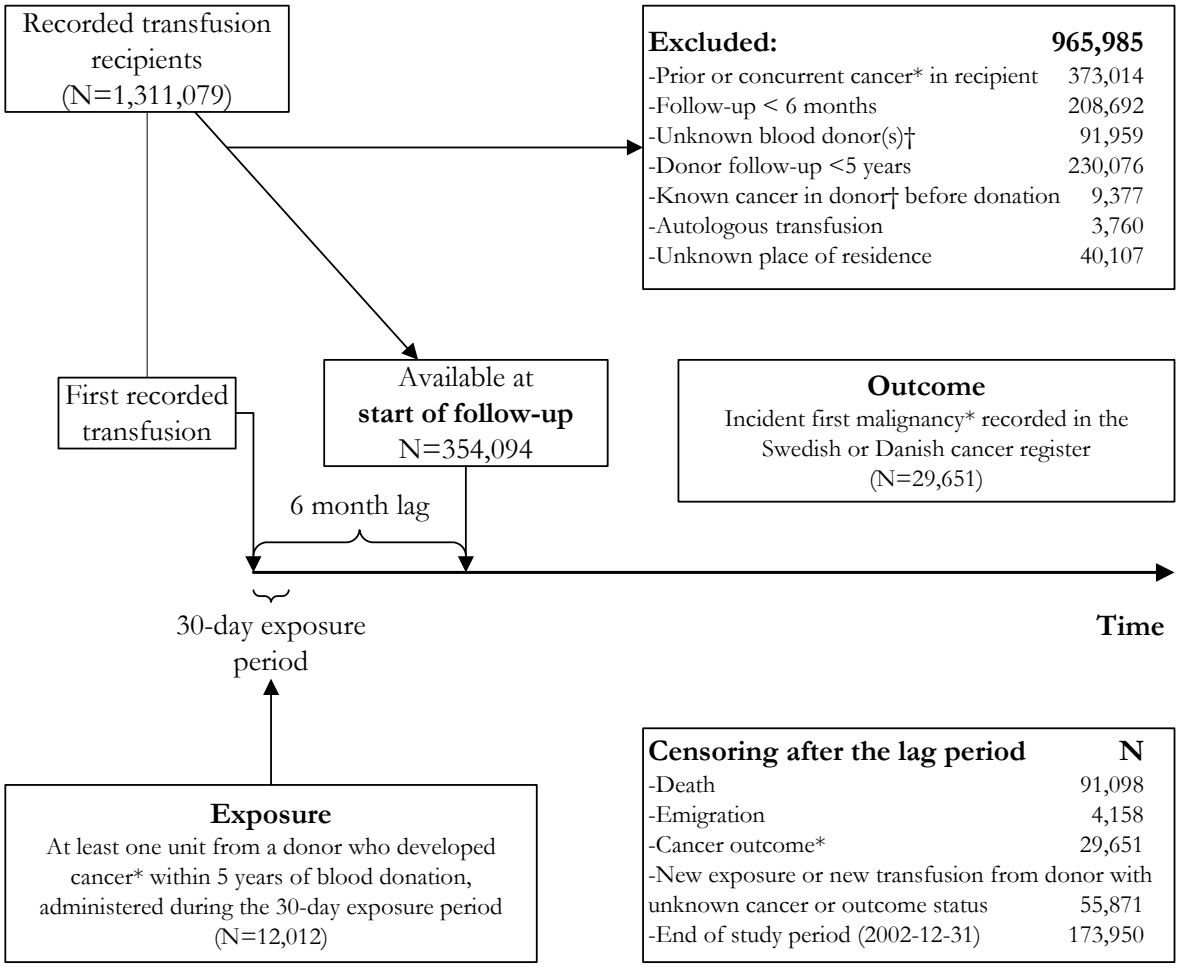
Anatomical site of recipient cancer	Number of cancers among exposed	Number of cancers among unexposed	Adjusted Rate Ratio (95% CI)*
Oral cavity and upper gastrointestinal tract	64	1,789	1·04 (0·80 - 1·32)
Lower gastrointestinal tract	138	3,577	1·13 (0·95 - 1·34)
Liver and gallbladder	27	762	0·96 (0·63 - 1·38)
Respiratory	88	2,363	1·02 (0·82 - 1·26)
Breast	89	3,597	0·90 (0·72 - 1·11)
Female genital organs	49	1,645	1·02 (0·76 - 1·34)
Male genital organs, incl. prostate	160	4,165	1·06 (0·90 - 1·24)
Urinary organs	85	2,240	1·07 (0·85 - 1·33)
Melanoma of skin	80	2,418	1·04 (0·82 - 1·29)
Eye and nervous system	27	649	1·32 (0·87 - 1·92)
Endocrinal glands	14	603	0·82 (0·46 - 1·34)
Bone and connective tissue	9	176	1·51 (0·71 - 2·84)
Lymphomas	30	938	0·92 (0·62 - 1·31)
Leukemia and myeloma	38	1,056	1·05 (0·74 - 1·43)
Other and unspecified	80	2,695	0·78 (0·61 - 0·96)

* CI denotes confidence interval; Adjusted for sex, attained age, calendar period of observation, number of transfusions, area of residence, ABO blood type and follow-up time.

FIGURES

FIGURE 1

Schematic presentation of inclusion criteria and study design.



*According to the International Classification of Disease, revision 7, not counting non-melanoma skin cancer.

†Donors contributing to transfusions given in the 30-day exposure period.