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Recommendations on Apheresis Donation in young and first time donors

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1 Remit

The remit of this paper was to evaluate available evidence of the safety or otherwise of accepting apheresis blood donors at 17 in common with whole blood donors and accepting apheresis donors without a prior whole blood donation and make appropriate recommendations. I have **not** considered the need for any changes to existing legislation

2 Summary of recommendations

2.1 Following a review of available evidence outlined below I conclude that:

a) Donors of blood components by apheresis can safely start to donate from their 17th birthday, provided that they meet UK Blood Services' donor acceptance criteria as assessed by routine procedures. (Level B recommendation)

b) Donors may safely donate apheresis components without a prior whole blood donation. (Level B recommendation) However apheresis platelet donors should have a full set of mandatory infection screens performed at least 8 weeks prior to the first donation.

2.3 Implementation of this change of policy must be supported by monitoring and regular review of adverse events in all component donors, together with a prospective study of in younger donors. It is recommended that a study of infective markers in first time apheresis donors is conducted.

3 Background

Current UK legislation and guidance on age limits and frequency for whole blood and component donors are outlined in Appendix 1.[1, 2] The suggested changes to the current donor selection guidelines are consistent with the current legal framework[1] they are also consistent with the guidance form the Council of Europe [28] and the US Food and Drug Administration. [29]

- Would reducing the age limit to match whole blood donation increase the incidence of adverse reactions?
- Would allowing component donors to donate by apheresis without giving a prior whole blood donation increase the incidence of adverse reactions?
- Would allowing component donors to donate by apheresis without giving a prior whole blood donation have any impact on recipient patient safety?
- Approximately how many donations might be gained?

4 Methods

Evidence was obtained from the following sources;

4.1 Demographic data

4.1.1 Population life tables

4.2 Blood service data

4.2.1 Age profiles of NHSBT blood donors

4.2.2 NHSBT and American Red Cross data on donor adverse events

4.3 Review of key literature

4.4 Information from other blood services

5 Results

5.1 Demographic data

5.1.1 Population life tables.

Data published by the Office of National Statistics[3] indicate that 40.1% of the current population of the United Kingdom is between is between 16 and 44 years of age, and gives a current and predicted structure for the 15-18 age group as:

Year	2008 (UK pop. 6.16M)	2018 (UK pop. 65.9M)
Age 15 years	760,900 (1.2%)	687,800 (1.0%)
Age 16 years	788,500 (1.3%)	671,200 (1.0%)
Age 17 years	808,600 (1.3%)	676,900 (1.0%)
Age 18 years	808,600 (1.3%)	701,900 (1.1%)

5.2 Blood Service data

5.2.1 Age profiles of NHSBT blood donors

It should be noted that caution is needed in interpreting these data, as there may be a degree of duplication of records of regular donors.

5.2.1.1 The age profile of the NHSBT active donorbase (Figure1) suggests that currently only a small proportion (0.8%) of our donor base is less than 18 years of age about 1,200 active donors.

5.2.1.2 The age profile of new NHSBT donors (Figure 2) indicates that the ages of 17 and 18 are the most productive of all age groups for new donor recruitment with 12% of all new recruits occurring in that age group. There is a progressive reduction in new donor recruitment in each age group thereafter.

5.2.2 NHSBT and American data on donor adverse events:

The US evidence [4, 11] suggests that platelet and double red cell donors have reduced incidents of fainting when compared to whole blood donation.

Data from 6 million donations (Table 3) taken in 2006 in the United States of which 228,000 were double red cells and 449,594 were platelet apheresis donations given to the American Red Cross have been recently published. This showed a 96% reduction in the rate of symptomatic pre-faints relative to the rate in whole blood donors and a 98% reduction in the rate of loss of consciousness, prolonged faints and other severe vasovagal incidents in double red cell donors while there was a >99% reduction of all events in apheresis platelet donors. Fainting is a significant issue as between 30 and 40% of donors who feel faint or actually faint do not return to donate within a year. The single biggest clinical issue for apheresis is considered to be that of donor venous access. This is the commonest reason for rejecting a donor and bruising is significantly more of an issue in component donors especially in the US (Table 4).

The data from the American Red Cross also looked at the effect of donor age on donor adverse events and demonstrates that in both whole blood (Chart 1) and apheresis donors

(Chart 2), younger donors were more likely to experience complications after apheresis donations than older donors, but the effect of age on the rate of donor complications in apheresis donors was not as pronounced as in whole blood donors (Table 2). It has also been noted that the effect of new donors is much less marked than age on the incidence of donor adverse events in the American Red Cross data (Anne Eder, personal communication).

Data on over a million collections performed by the United Blood Services (US) [11] has also been published this demonstrated no increase in moderate to severe generalized reactions in apheresis donors when compared to whole blood donors. In fact they demonstrated significant reductions in moderate to severe reactions in both double dose red cell and platelet apheresis donors when compared to whole blood donors. It should be noted that the US collects from first time donors and at any age over 16 years thus both of these studies included both first time donors and donors under the age of 18 years.

Review of NHSBT data over four months in 2008 reveals similar trends in donor adverse events when comparing apheresis donors (platelet and a few plasma donors only) with whole blood donations (Table 5). There is a 70% reduction in prefaint events and an 80% reduction in actual faints. Although there is an obvious increase in minor bruising there is no difference in the moderate or severe bruising events, and there have been no ‘more severe’ venepuncture related events (arterial puncture etc) reported in apheresis donors in these 4 months. Citrate reactions have been very few in number, although in the NHSBT we only record those that have stopped the procedure and a number of the mild citrate events may actually be recorded in the prefaint category.

NHSBT does not have any comparative data on donor adverse events in component donors under 18 or over 65 due to current regulations on young donors and the recentness of the changes to regulations for older donors. Due to the smallness of the numbers of component donors NHSBT has no data for the age distribution of the adverse events in platelet donors, most current platelet donors are 45-65 years of age. Data for whole blood donors in NHSBT shows a similar increase in donor adverse events in young (Chart 3) and novice donors (Chart 4) as does the US data. With a first time donor being between 2 and 4 times more likely to have an adverse event than a regular donor depending on the age group. The adverse events are over 70% more likely in younger whole blood donors than those over 40 years of age.

5.3 Literature review

The following databases were searched:

MEDLINE (1950 to present)
EMBASE (1980 to present)
The Cochrane Library, Issue 4, 2008
CINAHL (1982 to present)
BNI (1985 to present)
KOREAMED
INDMED
LILACS
Current Controlled Trials (mRCT)
ClinicalTrials.gov
Clinical Trials Registry – India
Chinese Clinical Trials Registry
German Clinical Trials Register
UMIN-CTR Japanese Clinical Trials Registery
Hong Kong Clinical Trials Registry
Sri Lanka Clinical Trials Registry
WHO International Clinical Trials Registry Platform (ICTRP)
Nederlands Trial Register

The terms used were:

1. BLOOD DONORS single term (MeSH)
2. (blood or plasma or platelet* or granulocyte* or red cell* or autologous) NEAR (donor* or donat*)
3. apheres* or plasmapheres* or plateletpheres* or leukapheres* or hemapheres* or haemapheres*
4. #1 OR #2 OR #3
5. SYNCOPE explode all trees (MeSH)
6. (vertig* or syncop* or faint* or vasovagal* or presyncop* or prefaint* or swoon* or dizz* or ((loss or suspension) NEAR consciousness))
7. sitting or seated or upright or vertical* or lying or horizontal* or supine or reclin*
8. (rais* or elevat* or position*) NEAR leg*
9. (adverse AND (event* or effect* or reaction*)):ti

The search produced 443 papers which were sifted for relevance. The resulting papers are listed in Table 1. The key references were obtained from the US where the FDA does not limit first time donation by apheresis, require any tests over and above FBC before donation and allows the same age donors as for whole blood i.e. above 16 years of age,

The literature on adverse reactions of whole blood donors is large, but there are only a relatively few articles that look at reactions in apheresis donors. There are 2 recent articles from the US[4,8], detailed in the preceding section. These are retrospective observational studies and compare the rate and severity of reactions in whole blood donors to those in the various groups of apheresis donors. The former[4] specifically looked at the age group of the donors and both studies include first time donors and donors under 18 in their data. Like these studies the other papers in the literature are observational studies either of whole blood donors [6,7,10,14,17,21] , apheresis donors [5,8,13,15,16,18] or both [4,11,12,] The studies generally

look at overall reaction rates and/or reaction rates by particular groups of donors. As there is no standard for the definitions in use for adverse reactions it is not possible to compare the various reaction rates between papers. Similarly some papers are only looking at subsets of reactions e.g. only vasovagal reactions [11,14,21] , excluding some reaction types[16] or only looking at the more severe reaction[5,8,17] . There was no paper found demonstrating a higher risk in apheresis donors. The only two papers [4,11] that do compare whole blood donors and apheresis donors demonstrate a reduced risk of reaction in apheresis donors when compared to whole blood donors.

However a number of common themes emerge in the studies of reactions in whole blood donors or both whole blood and apheresis donors. Reactions are more commonly found in young donors [4,6,7,10,11,12,14,17,21] although there is noted to be a marked reduction in this correlation in the apheresis donor [4,11] . First time donors are noted to have increased risk of reaction in both whole blood and apheresis donors [12,14,15,16,17] however this was an effect independent of age. These support the finding in the NHSBT data.

The themes of the observational literature are supported by the three reviews of the literature on apheresis donation [9,119,20] , two of which were published in the early 1980s, all of which conclude that there is no greater risk to donor safety from apheresis donation, and may be less than, from traditional whole blood donation.

5.4 Information from other blood services

Information regarding other blood services' acceptance criteria for platelet apheresis donation was obtained via the individual service's web sites and NHSBT International. Results are summarised in Table 2.

Only the US seems to have an established practice of using first time and young donors for apheresis donation. This results in their experience dominating the literature. They do not require any infection screening prior to a first donation for platelets and say the prevalence of levels of markers are too low to justify it (Celso Bianco, MD personal communication).

6 Discussion

6.1 Would lowering the age limit to 17 increase the incidence of adverse reactions?

Evidence from published experience with apheresis component donors under the age of 18 suggests that they are no more likely and probably less likely than donors in the same age group who currently give whole blood to experience a donor adverse event. Thus there is no reason to presume that this change will increase the likelihood of donor adverse events.

There is some evidence to suggest that haematoma formation may be more common in older component donors but this will not be affected by allowing donors to start at a younger age.

6.2 Would allowing apheresis donors to donate for the first time without a prior whole blood donation increase the incidence of adverse reactions?

The rational for requiring a prior whole blood donation was twofold: to allow evidence that the donor would be able to sustain the physiological challenge of donation and to provide a first set of mandatory infection screen results. The latter will be addressed under the succeeding heading.

The fact that that component donation by apheresis is either an isovolaemic procedure or one in which the fluid volume extracted is done over a longer period than in whole blood donation means that there is virtually no or little physiological challenge to the donor inherent in the procedure. This is supported by the relatively low incidence of fainting or vasovagal adverse reactions in apheresis component donors when compared with whole blood donors. Thus allowing first time donors to donate in this manner should reduce the overall number of vasovagal (the overwhelmingly most common) donor adverse events and thus the total number of donor adverse events will not be increased and may be reduced if the proportion of apheresis to whole blood donations increases. This reduction may be partially offset by a small increase in the number of venepuncture related incidents as the total number of donations by apheresis increases.

6.3 Would allowing component donors to donate by apheresis without giving a prior whole blood donation have any impact on recipient patient safety?

The first whole blood donation allows for a set of mandatory infection screening tests to be performed on a new donor before they are allowed to become a regular platelet donor with a minimum donation interval of 2 weeks. Obviously platelet donors may donate much more frequently than a whole blood donor and as such if they started to donate during the window period for a blood borne viral infection could affect many more recipients than a whole blood donor, minimum donation interval 12 weeks. The current minimum waiting time between the first whole blood donation and subsequent apheresis donations for platelets is 8 weeks. This was set largely due to concerns about iron store depletion.

To maintain the current level of safety for recipients a mandatory infection screening sample could be taken from potential apheresis platelet donors at the same time as the pre-component donation haemoglobin level and platelet count (required for all platelet donors) and the donor not allowed to actually donate platelets until 8 weeks after this sample is taken. This is not an issue for apheresis double red cell donations as the inter donation interval is longer than for whole blood donors.

6.4 Approximately how many additional donations might be gained?

Calculation of possible donations gained is a complex mathematical exercise incorporating several unknown factors. 0.8% of the NHSBT current active donor pool is aged 17 reducing the age limit for apheresis component donation to 17 in line with

whole blood donation would allow these donors to be asked to become platelet donors without waiting for their 18th birthday. It is not known how many would convert but if only 10% do give platelets by apheresis this would give 2,400 additional doses in a year (based on 10 attendances with an average of 2 doses per attendance).

The population statistics would indicate that reducing the age of component donation by a year would give a pool of between 677 and 800 thousand donors year that could be targeted as new donors. If we achieved a penetration of only 0.1% of these 800,000 who are currently 17 years of age donors this would equate to 16,000 platelet doses per annum.

A significant number of young and first time donors faint when giving whole blood. As this faint will result in them not being allowed to donate by apheresis in the future. This results in a significant loss of potential apheresis platelet donors. There is also the potential loss of apheresis donors due to a low haemoglobin deferral when they are screened as an apheresis donor after giving a unit of whole blood, as this screening is currently performed at a minimum of 8 weeks after whole blood donation.

This change will certainly increase the available population of apheresis donors, the magnitude of this change is impossible to calculate with any certainty. In the face of the requirements of the Department of Health to increase the proportion of donations of platelets and potentially red cells by apheresis to reduce donor exposure and the risk of $_{v}$CJD any increase in the available donor pool should be sought to secure the blood component supply.

Table 1: Summary of literature relevant to safety of apheresis, younger and first time donors

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
Eder AF, Dy BA, Kennedy JM, Notari Iv EP, Strupp A, Wissel ME, Reddy R, Gibble J, Haimowitz MD, Newman BH, Chambers LA, Hillyer CD, and Benjamin RJ. **The American Red Cross donor hemovigilance program: complications of blood donation reported in 2006.** Transfusion; 2008. 48 (9): 1809-19.	2008	Observational	Complications recorded at the collection site or reported after WB, apheresis and DDRC donation procedures in 36 regional blood centers in 2006 were analyzed.	Complications after 6,014,472 WB, 449,594 PLT, and 228,183 DDRC procedures were 348.9, 577.5, and 538.3 per 10,000 donations respectively, the vast majority of which were minor presyncopal reactions and small hematomas. Regional center, donor age, sex, and donation status were independently associated with complication rates after WB, PLT, and R2 donation. Excluding large hematomas, the overall rate of major complications was 7.4, 5.2, and 3.3 per 10,000 collections for WB, PLT, and R2 procedures, respectively. Outside medical care was recorded at similar rates for both WB and automated collections (3.2 vs. 2.9 per 10,000 donations, respectively).	B
Yuan, S, Gornbein J, Smeltzer, B, Ziman AF, Lu Q, and Goldfinger D. **Risk factors for acute, moderate to severe donor reactions associated with multicomponent apheresis collections.** Transfusion; 2008. 48 (6): 1213-9.	2008	Observational	Review of 2 years of data on all apheresis donation procedures at a hospital-based donor center over a 2-year period Donor and procedure variables were compared between procedures that did and did not result in moderate to severe AEs.	Moderate to severe AEs occurred in 53 (0.47%) of 11,333 apheresis donation procedures. The majority of events (96.2%) had predominantly features of vasovagal reactions (VVRs). Females were at significantly higher risk (odds ratio [OR] = 2.8, $p < 0.0003$) compared to males. Donors who experienced AEs had significantly lower predonation total blood volume (TBV) and haematocrit (Hct) and higher total RBC loss and net fluid loss at the end of the procedures. Total blood loss was significantly higher among donors who experienced AEs as a percentage of the donor's TBV. Apheresis collections are well tolerated even when multiple components are collected, with a very low overall incidence of moderate to severe AAEs (0.47%). Small, female donors with lower predonation Hct are at higher risk, especially when RBCs are collected.	B
Eder AF, Hillyer CD, Dy BA, Notari EP 4th, and Benjamin RJ. **Adverse reactions to allogeneic whole blood donation by 16- and 17-year-olds.** JAMA; 2008. 299 (19):	2008	Observational	Prospective documentation of adverse events among 16- and 17-year-old donors in 2006. Data were from 9 American	In 2006, 9 American Red Cross regions collected 145,678 whole blood donations from 16- and 17-year-olds, 113,307 from 18- and 19-year-olds, and 1,517,460 from donors aged 20 years or older. Complications were recorded in 15,632 (10.7%), 9359 (8.3%), and 42,987 (2.8%) donations in each corresponding age group. Young age had the strongest	B

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
2279-86.			Red Cross blood centers that routinely collect from 16- and 17-year-olds, a population that provides 80% of its donations at high school blood drives.	association with complications (odds ratio [OR], 3.05; 95% confidence interval [CI], 2.52-3.69; P < .001), followed by first-time donation status (OR, 2.63; 95% CI, 2.24-3.09; P < .001) and female sex (OR, 1.87; 95% CI, 1.62-2.16; P < .001).	
Tondon R, Pandey P, and Chaudhary R. R. Vasovagal reactions in 'at risk' donors: **A univariate analysis of effect of age and weight on the grade of donor reactions.** Transfusion and Apheresis Science; 2008. 39 (2): 95-99.	2008	Observational	A retrospective analysis of 30370 WB donations was done during 15 month study period.	Donor reaction rate of 1.6%. Reaction rate among male and female donors were 1.5% and 3.7% respectively. Female gender was found to be an independent predictor for donor reaction even after nullifying the effect of the blood volume drawn. Age had a significant effect on reaction rate (p = .035) and all grades of reaction decreased with the age of the donor. Age was found to be a significant predictor of the grade of reaction (p = .008).	B
Wiltibank TB, and Giordano GF. **The safety of automated collections: an analysis of more than 1 million collections.** Transfusion; 2007. 47 (6) : 1002-5	2007	Observational	Adverse events in 1,023,682 whole blood donations were compared to those occuing during 249,154 DDRC, 40,870 1+1 and 90,082 platelet collections by apheresis.	Whole blood donation and 1+1 had a low incidence of moderate to severe adverse reactions of 0.47% and 0.37% respectively. While DDRC and platelet collections had a significantly (p < 0.00005) lower rates of 0.16% and 0.15% respectively.	B
Popovsky, MA. **Safety of RBC apheresis and whole blood donation in allogeneic and autologous blood donors.** Transfusion and Apheresis Science; 2006. 34 (2): 205-11.	2006	Review	Automated red cell collection is now a well-established technology. Although widely perceived to be safe, manual collection is associated with a number of potential complications, some of which can be serious, even debilitating. The safety record of 2-RBC and other RBC automated procedures is excellent. Physiologic, cardiovascular, and neurocognitive responses are modest and fall within those seen for manual collection. The long term effects related to erythropoietic response and iron loss are manageable and are similar to the effects of repeated whole blood donation. The collection of whole blood by manual means has been performed for nearly a century and as result the safety of this procedure is assumed. Conversely, the safety of automated collection in general and particularly RBC has had to "prove" itself, primarily because it is much more recent and is a different paradigm. Millions of procedures have been performed using both approaches. This article examines the complications of both manual and automated RBC collection.		D

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
Shehata N, Kusano R, Hannach B, and Hume H. **Reaction rates in allogeneic donors.** Transfusion Medicine; 2004. 14 (5): 327-333.	2004	Observational	Reactions rates in allogeneic whole blood donors who donated at Canadian Blood Services were reviewed retrospectively.	A total of 5478 reactions were available for analysis in 469 837 donors. The highest rate of mild reactions occurred in donors less than 20 years of age. Moderate and severe reactions decreased with increasing age and with donation frequency. Age-adjusted rates for mild reactions were less frequent in donors aged 66-77 years than in donors younger than 20 years. Age-adjusted rates for severe reactions generally did not increase with donation frequency.	B
Tomita T, Takayanagi M, Kiwada K, Mieda A, Takahashi C, and Hata T. **Vasovagal reactions in apheresis donors.** Transfusion; 2002. 42 (12): 1561-6.	2002	Observational	Vasovagal reaction incidence (VVR) was compared between whole blood (WB) and apheresis donation in relation mainly to age and circulatory blood volume (CBV).	In W B donors, the VVR incidence was 0.83 and 1.25 percent, while in apheresis donors it was 0.99 and 4.17 percent in men and women, respectively. The VVR incidence decreased with age in WB donors, but age dependence was very weak in apheresis donors. In elderly women, the incidence increased with repeating cycle of apheresis. Smaller CBV, high sensitivity of low-pressure baroreceptors, and citrate effects on cardiovascular reflex might be major factors involved in the high incidence of VVRs in this group. There was no particular fluctuation in blood pressure in relation to apheresis cycles.	B
Franchini M, Gandini G, Gandini A.R, Crocco I, De Gironcoli M, Bertuzzo D, Giuffrida A.C, Lippi G, Vassanelli A, Bressan F, and Aprili G. **Frequency of adverse events during blood and apheresis donations: A single-center study.** Infusionstherapie und Transfusionsmedizin; 2002. 29 (4): 200-205.	2002	Observational	From January 1998 to June 2001, we recorded at our transfusion center all adverse events occurring during 116,952 consecutive blood and apheresis donations (whole blood donation, plasmapheresis and plateletpheresis)	1,960 adverse events were reported (1.7% of all donations). With a frequency of 1.2%, most commonly mild vasovagal reactions. The frequency of vasovagal reactions was significantly lower in autologous blood and apheresis donations than in whole blood donations. Hematoma at the venipuncture site was the second most frequent adverse effect with a rate of 0.4%. A mild to moderate citrate-related toxicity was observed in 0.3% of apheresis donations. With an overall rate of 0.02%, severe adverse reactions (vasovagal, citrate-related and cardiopulmonary events) were very rare. No life-threatening adverse effect was reported, and no severe adverse event required hospitalization. Those donors who experienced adverse reactions were primarily first-time donors, were younger, and had a lower weight and predonation blood pressure than donors without reactions.	B

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
Moog, R. **Adverse events in peripheral progenitor cell collection: a 7-year experience.** Journal of Hematotherapy & Stem Cell Research. 2001. 10 (5): 675-80.	2001	Observational	In a one centric retrospective study, the data of 540 PPC collections over 7 years were reviewed. Adverse events were subdivided in collection-associated technical problems and patient/donor-related side effects.	Patient/donor-related side effects occurred most often (19.8%); most of them were paresthesias due to citrate toxicity. Paresthesias were treated by oral (20.4%) or intravenous (1.1%) calcium supplementation. Problems with venous access were also seen frequently, resulting in blood flow alarms (11.3%) and blockades in the return line (4.3%). A total of 6.9% of these problems were catheter associated, requiring revision of the central venous line in 2.6%. Technical problems with the blood cell separators were observed in 11.7%. Problems with venous access and technical problems with the cell separators occurred in every tenth PPC collection.	B
Trouern-Trend JJ, Cable RG, Badon SJ, Newman BH, and Popovsky MA. **A case-controlled multicenter study of vasovagal reactions in blood donors: influence of sex, age, donation status, weight, blood pressure, and pulse.** Transfusion; 1999. 39 (3): 316-20.	1999	Case control study	A retrospective case-control study involved 1890 whole blood donors with syncope from 3 United States blood centers during 1994 and 1995. Case controls and random population controls were used in a logistic regression analysis to determine the significance of individual variables to syncopal reactions.	Female donors, young donors, first-time donors, low-weight donors, and donors with low predonation blood pressure had higher absolute donation reaction rates than other donors. When each variable was adjusted for other variables by regression analysis, age, weight, and donation status (first-time or repeat donor) were significant ($p<0.0001$), and sex, predonation blood pressure, and predonation pulse were not. The most important variables, in descending order, were age, weight, and donation status (first-time or repeat donor).	B
Despotis GJ, Goodnough LT, Dynis M, Baorto D, and Spitznagel E. **Adverse events in platelet apheresis donors: A multivariate analysis in a hospital-based program.** V ox Sanguinis; 1999. 77 (1): 24-32.	1999	Observational	A review of the incidence of adverse events during nearly 20,000 apheresis procedures over a 4-year period in a hospital-based program.	Of 19,736 apheresis procedures, 159 (0.81%) were associated with adverse events. In 2,376 first-time donations, 26 (1.09%) developed adverse events compared to 133 (0.77%) of 17,360 repeat procedures ($p = 0.10$). Seventy (0.35%) of 159 donation-related adverse events involved hemodynamic or citrate-related complications and 73 (0.37%) involved venipuncture-related complications, of which 2 required subsequent neurologic consultation. The	B

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
				remaining 23 (0. 12%) adverse events involved procedure-related, nonspecific complications.	
McLeod BC, Price TH, Owen H, Ciavarella D, Sniecinski I, Randels MJ, and Smith JW. **Frequency of immediate adverse effects associated with apheresis donation.** Transfusion; 1998. 38 (10): 938-43.	1998	Observational	In 1995 The AABB devised a uniform questionnaire that asked about 32 specific adverse effects, transient paresthesia and mild vasovagal events were exclude. 17 centers returned 19,611 responses with 250 to 2,000 consecutive apheresis donations per center.	Six hundred adverse effects were reported in 428 donations (2.18% of donations). Pain or hematoma at a venipuncture site was the most common response (1.15% of donations); only 203 donations had other (nonvenipuncture) adverse effects (1.04%). Total and non venepuncture rates were, respectively, 4.84 and 2.92 percent for 2,295 first donations and 1.78 and 0.77 percent for 17,303 repeat donations ($p < 0.001$). Rates of non venepuncture symptoms in first and repeat donations were, respectively, citrate-induced nausea and/or vomiting, 0.87 and 0.27 percent; tetany, 0.09 and 0.04 percent; pallor and/or diaphoresis, 1.87 and 0.32 percent; vasovagal nausea and/or vomiting, 0.87 and 0.13 percent; syncope and/or seizure, 0.39 and 0.04 percent; and chills and/or rigors, 0.31 and 0.01 percent. The overall rate of donor unconsciousness was 0.08 percent. Hemolysis was reported twice. Clotting or leakage occurred in 0.08 percent of donations, and inability to return blood occurred in 0.16 percent. No life-threatening adverse effects were reported.	B
Kasprisin, DO, Glynn, SH, Taylor, F, and Miller, KA. **Mo derate and severe reactions in blood donors.** Transfusion; 1992. 32 (1): 23-6.	1992	Observational	A comparative study of donors who did and not have reactions to whole blood donation	During the period April 1985 to March 1986, 217 blood donors were found to have moderate (syncopal) to severe (convulsive) reactions. This population was compared to 5630 randomly selected donors who did not have reactions. Demographic, physical, and societal/emotional factors were examined determine if any were predictive of reactions in donors. The number of prior donations was inversely proportional to the risk of reaction; the gender of the donor was not predictive; and youth was a predictor of reactions. Donors who reacted were of lower weight than those who did not and that systolic blood pressure was slightly lower in the group with reactions. Finally, the ingestion of caffeinated beverages was associated with a reduced risk of reactions and that the duration between registration and the onset of phlebotomy was directly predictive of reaction status.	B

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
Komatsu F and Shikata M. **Abnormal electrocardiographic findings in apheresis donors.** Transfusion; 1988. 28 (4): 371-4.	1988	Observational	ECG monitoring was performed on 291 donors during apheresis.	Twenty-one donors (7.2%) had clinical symptoms such as discomfort, nausea, chill, numbness, and paresthesia, and 13 of this group exhibited ECG abnormalities, such as tachycardia, bradycardia, and other abnormal wave patterns. The donors with tachycardia and slight bradycardia had no symptoms. Ten donors had moderate to severe bradycardia with pulse rates less than 50 beats per minute; four of them had severe bradycardia (less than 45 beats per minute), and three of the four exhibited severe hypotension, vomiting, fainting, or convulsion. Other abnormal ECG changes, such as supraventricular and ventricular premature contractions, right bundle branch block, ST segment elevation or ST segment depression, and tall, flattened, or inverted T waves were observed in 29 donors (10%). These changes were not associated with symptoms. Only three of these donors complained of discomfort or chest heaviness. The abnormal waves appeared more often in granulocytapheresis donors than in plateletapheresis donors.	B
Grindon AJ. **Adverse reactions to whole blood donation and plasmapheresis.** Critical Reviews in Clinical Laboratory Sciences; 1982 . 17 (1): 51-75.	1982	Review	Whole blood donation is recognized to be extremely safe, yet there have been reports of serious problems stemming from whole blood donation, and so-called "donor reactions" are regularly seen. While the physiologic causes of the common donor reactions are not completely understood, some effects of whole blood donation (such as transient iron deficiency) are understood but probably not significant. In order to avoid accepting any volunteer donor who might be at risk of a serious reaction, we may have been overly cautious in exclusion of potential donors. The apheresis donor is subjected to potential depletion of the protein or cellular elements being removed, problems caused by the device used for automated apheresis, or problems related to the infusion of potentially toxic substances. Documented benefit to the patient must balance these additional risks.		D
Huestis DW. **Adverse effects of granulocyte donations.** Progress in Clinical and Biological Research; 1982. 88: 101-14.	1982	Review	Various reactions occur during cytapheresis by either intermittent or continuous flow centrifugation, because of the nature of the procedures themselves and because of the exposure of the donor to steroids, macromolecular agents, anticoagulants, and saline. Most reactions are vasovagal (commoner in intermittent flow procedures) and citrate-related (commoner in continuous flow). Only very rarely do these require the procedure to be stopped. Other less common reactions are discussed. In addition to actual		D

Reference	Year of publication	Type of study	Methods	Results	Level of evidence of donor safety
			reactions, blood component depletion may occur, especially with frequently repeated procedures in the same donor. Red cell, platelet, and plasma depletion can all force limitation of the frequency of cytapheresis. While most reactions are of little consequence, they can cause procedural failure or refusal of a donor to permit continuation of cytapheresis, and can interfere with donor recruitment.		
Ogata H, Iinuma, N, Nagashima K, and Akabane T. **Vasovagal reactions in blood donors.** Transfusion; 1980. 20 (6): 679-83.	1980	Observational	Review of the records of the WB donors of a hospital blood bank	An incidence of vasovagal reactions: 119 in 10,547 donations (1.13%). Donors of younger age and of lower diastolic blood pressure were more prone to reaction. There was no significant sex difference. Higher reaction rates were also associated with first-time donation, the time of year (spring), and a particular phlebotomist. The low reaction rate and the clearly demonstrated psychologic factors in the present study were attributed to a reflection of the small amount (200 ml) of blood withdrawn.	B

Table 2: Experience of other blood services

Blood Service	Lower Age limit	Do you accept First time donors	Notes
Austria	19 years	No	
Belgium (Flemish)	18 years	Yes	In general platelet donors are already known blood or plasma donors. We don't refuse new donors as platelet donors but it happens rarely.
Belgium (French)	18 years	No	
Denmark	18 years	No	
Estonia	18 years	No	
Finland	Same as whole blood	No	When recruiting blood donors to be platelet apheresis donors, following criteria are used: In past at least 3 whole blood donations, living close to the blood centre, male gender, good veins, BMI<35, platelet count < 170 and age for HLA/HPA – typed donors <45 years. Once accepted as an apheresis donor, the donor can continue donating platelets by apheresis up to 65 years.
Germany	>18 years the same for whole blood donations or plasmapheresis	No	Only experienced blood donors (repeated whole blood donations) for apheresis platelet donations.

Hungary	18 years	No	
Italy	18 years	Yes – it is possible	Besides the infectious tests and haemoglobin or haematocrit test, a platelet count must be performed before each donation (PLTs = 150 x 109/L), and a clotting factor activity assay (PT, aPTT) must be performed before the first donation and then at least every year.
Ireland	18 years in theory	Yes, but only very recently.	Full donor screening: NAT HIV/HepC; HIV, Hep B & C by serology, including anti-core (which we do on every donation), HTLV ½ (ditto), syphilis and ABO/RHD grouping. We also HPA 1 type, and HLA type, but don't need the results of these last two before collection of the first apheresis donation. There's a one month lag before the tests and the first collection: this is to ensure that any precluding testing results are followed up before the donor is scheduled to return.
Malta	18 years	No	Theoretically over 18, but in practice since they must be regular blood donors before becoming eligible for apheresis donation they are always over 20years of age.
Netherlands	18 years – as all blood donors	No	All new donors are interviewed and tested, and more than 2 weeks later invited for their first donation, including testing and interview.

Scotland	18 years	Not at present but this may change	
Slovenia	No age limit	No	One donation of whole blood without adverse reaction
US	Depends on the US state. Most allow donations by individual 17 years of age or older without parental consent. Most require parental consent for a donation by 16 year olds.	Most centres do. Some focus recruitment of plateletpheresis donors on whole blood donors that have donated at least once or twice.	Testing is the same as that performed for whole blood donors plus a platelet count. FDA guidance requires a minimum of 150,000 platelets/ml on the day of donation or in the last donation for eligibility to donate. No prior infection screening required.
Wales	Component donors may donate on their 18th birthday	No	
Australian Red Cross[16]	New donors and repeat donors– 16 requirements for consent dependent on state/territory		
Canadian Blood Services[17]	New donors and repeat donors– 17		
New Zealand Blood Service[18]	New donors and repeat donors– 16		

Figure 1: Profile of NBS active donorbase by age

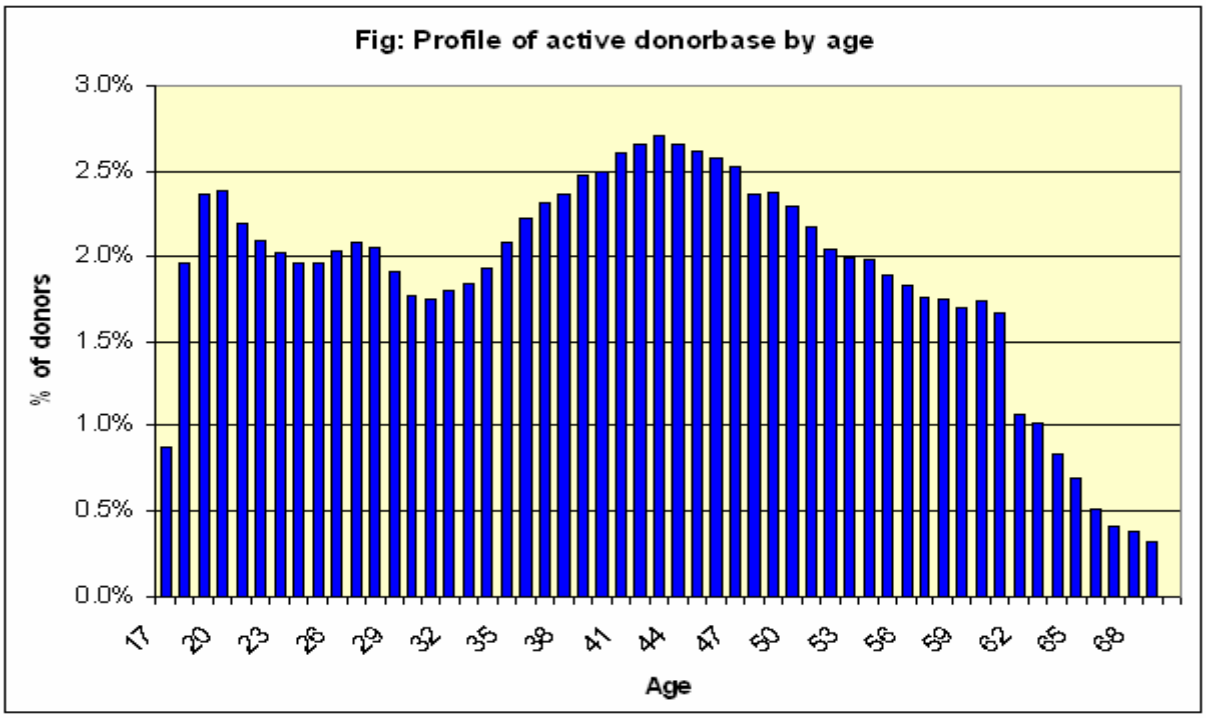


Figure 2: Age profile of new donors

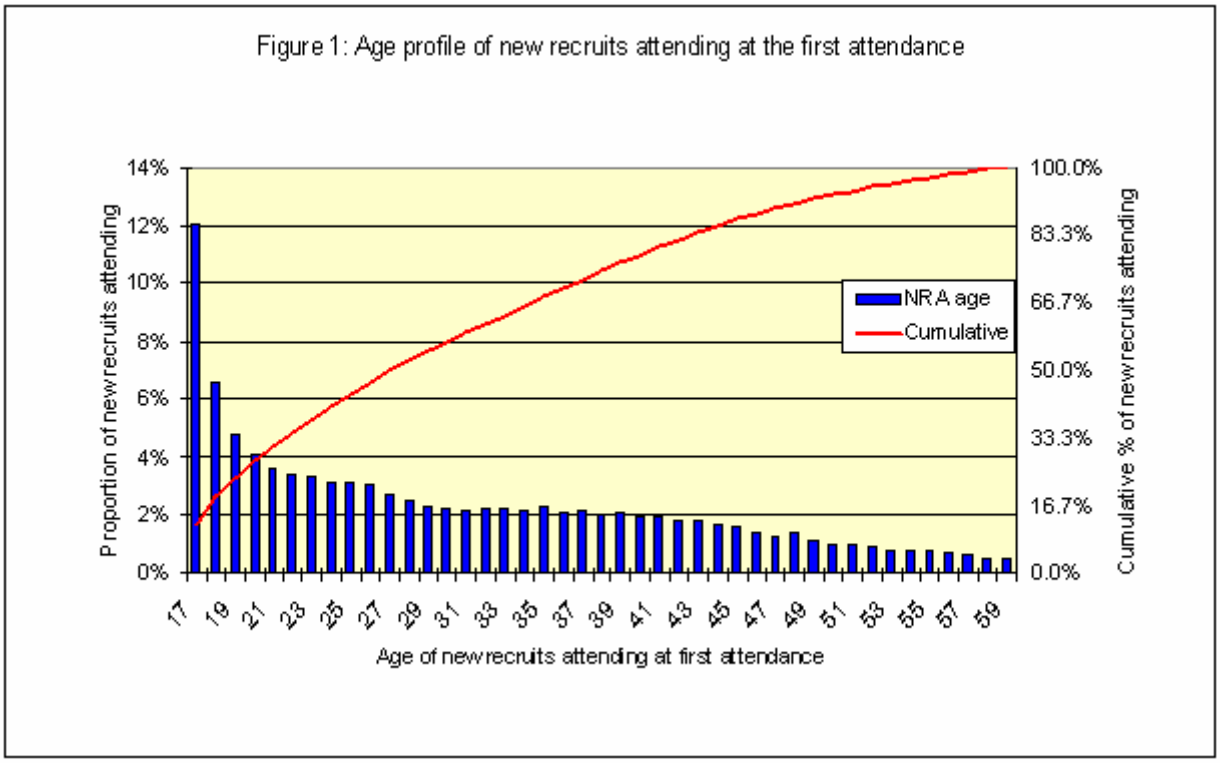


Table 3: Comparative Rates of vasovagal adverse events in Whole Blood and Component donors

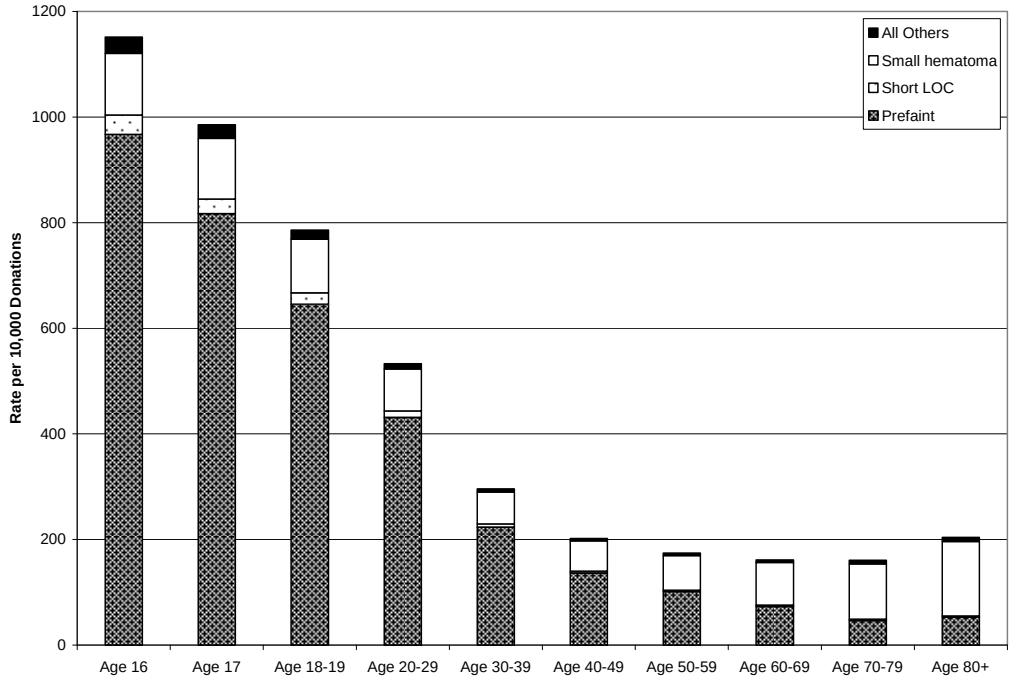
Adverse Event Rates per 10,000 (The American Red Cross Donor Hemovigilance Program: complications of donation reported in 2006. [4])			
	Whole Blood	Apheresis Platelets	Apheresis Double Dose Red Cells
Prefaint	258	1.4	8.6
Faint	13	0.08	0.3

Table 4: Comparative Rates of venepuncture related adverse events in Whole Blood and Component donors

Adverse Event Rates per 10,000 (The American Red Cross Donor Hemovigilance Program: complications of donation reported in 2006.[4])			
	Whole Blood	Apheresis Platelets	Apheresis Double Dose Red Cells
Small haematomas	74.5	377.0	217.9
Large Haematomas and other venepuncture related events	2.2	9.9	2.4
Citrate complications	N/A	123.6	113.2

Chart 1: Rates of Donor Complications Associated with Allogeneic Whole Blood (WB) Donation.

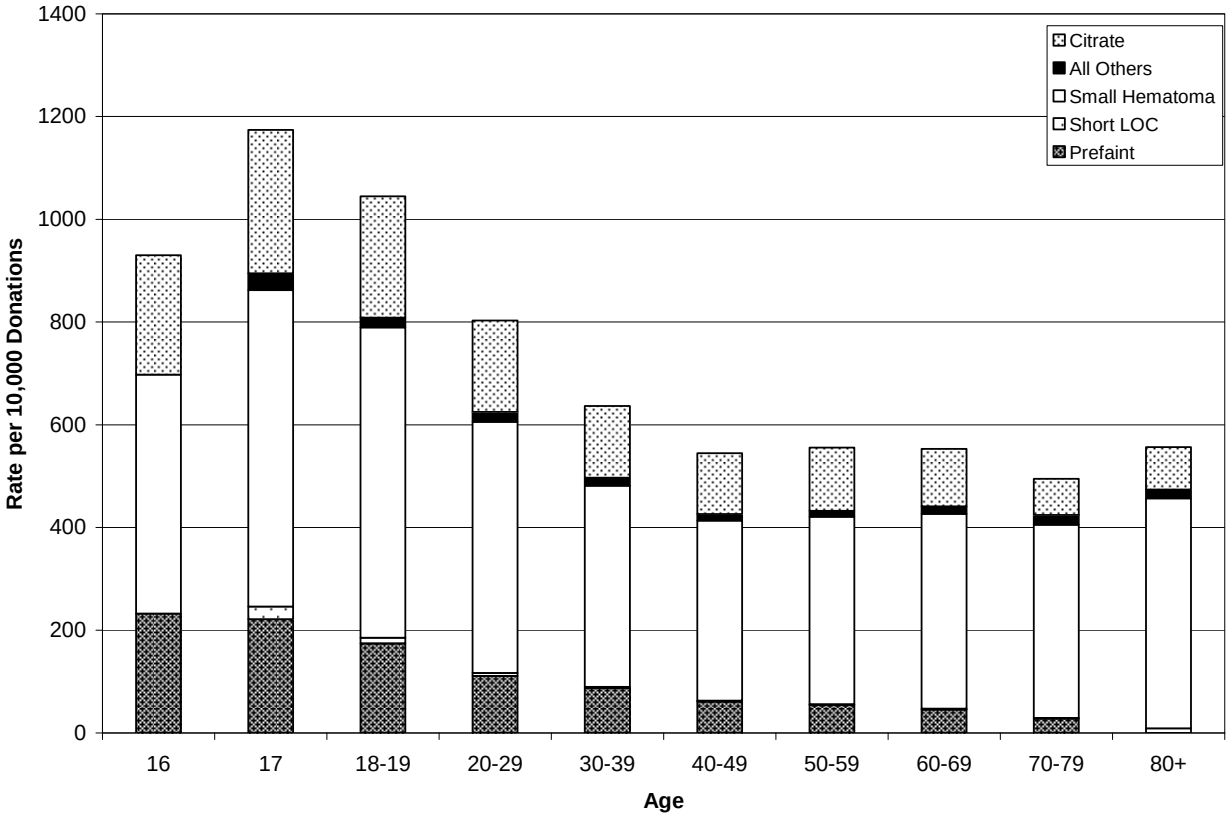
The overall rates are statistically significantly ($p<0.05$) different between each successive age group, except between 60-69 and 70-79 years. (The American Red Cross Donor Hemovigilance Program: complications of donation reported in 2006. [4])



Age	16	17	18-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
Total donations	46,275	404,042	424,624	812,196	822,438	1,319,317	1,314,918	616,879	223,185	30,553

Chart 2: Rates of Donor Complications Associated with Apheresis Platelet (PLT) Donation.

Differences in overall rates between successive age groups are not statistically significant (p<0.05) except for between 18-19, 20-29 and 30-39 years. (The American Red Cross Donor Hemovigilance Program: complications of donation reported in 2006. [4]**)**



Age	16	17	18-19	20-29	30-39	40-49	50-59	60-69	70-79	80+
Total donations	43	1,218	3,560	26,986	44,812	119,535	156,890	72,477	21,771	2,300

Table 5: NHSBT data on adverse events in WB and Component donors

Apheresis Component Donors	Total Donors	Pre Faint	Faint	Bruise Minor	Bruise grade 2 or 3	Citrate reaction	Arterial Injury	Nerve Injury	Thrombo-phlebitis
Aug 2008	6184	34	6	16	0	7	0	0	0
Sept 2008	6557	46	1	26	2	10	0	0	0
Oct 2008	7076	45	4	38	6	10	0	0	0
Nov 2008	6610	42	1	24	1	10	0	0	0
4/12 total	**26427**	**167**	**12**	**104**	**9**	**37**	**0**	**0**	**0**
Rate per 10,000 donations		**63.2**	**4.5**	**39.4**	**3.4**	**14.0**	**0.0**	**0.0**	**0.0**
Whole Blood donors									
Aug 2008	169444	3526	386	63	50	0	8	21	5
Sept 2008	173401	3457	374	66	69	0	5	19	1
Oct 2008	177891	3769	385	99	76	0	7	25	2
Nov 2008	160811	3547	380	78	74	0	9	33	5
4/12 total	**681547**	**14299**	**1525**	**306**	**269**	**0**	**29**	**98**	**13**
Rate per 10,000 donations		**209.8**	**22.4**	**4.5**	**3.9**	**0.0**	**0.4**	**1.4**	**0.2**

Chart 3: Donor adverse event rates for whole blood donors by age group NHSBT October 2008

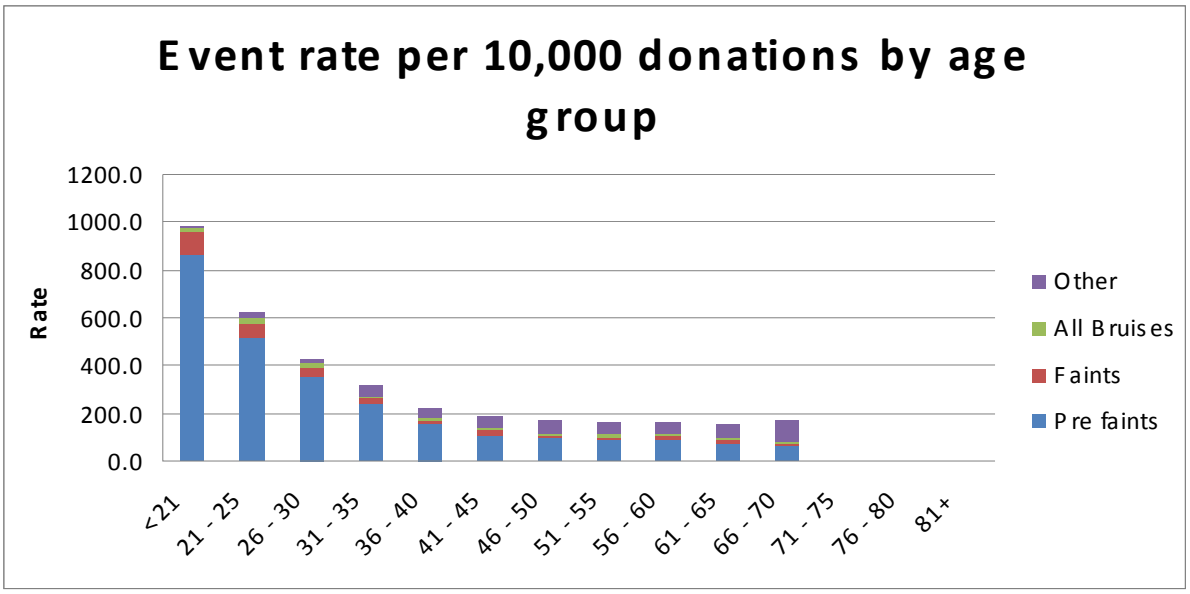
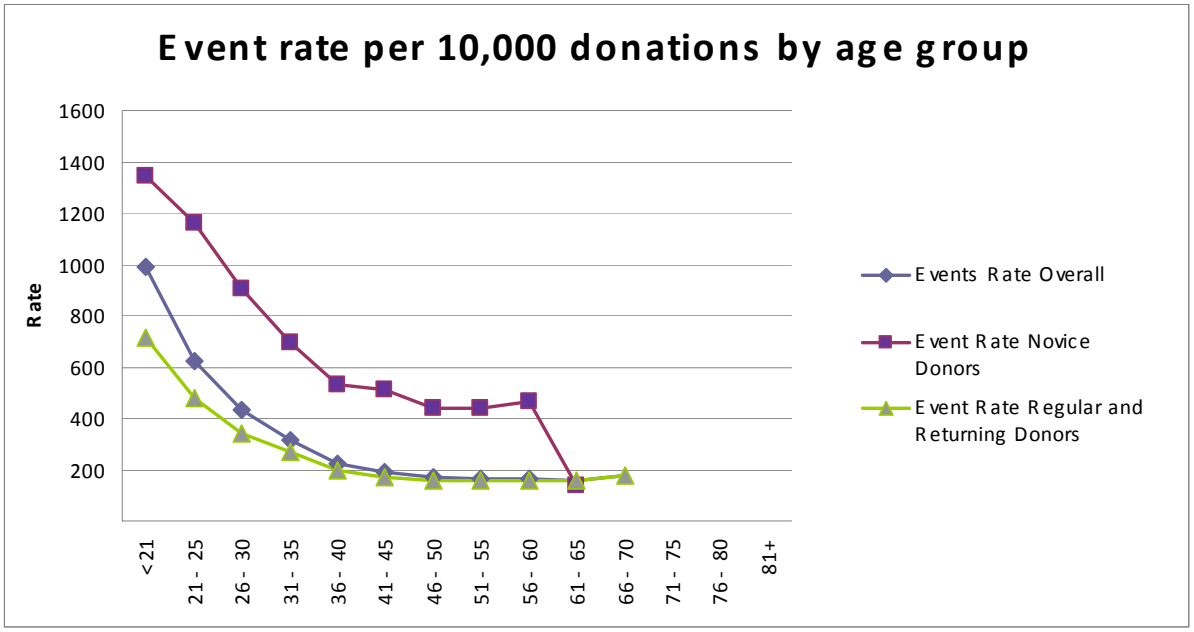


Chart 4: Donor adverse event rates for whole blood donors by donor status NHSBT October 2008



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Appendix 1

Current UK Legislation and guidance on age eligibility of blood donors

Blood Safety and Quality Regulations 2005[1]

Age	18 to 65 years	
	17 years	Where, in the opinion of a qualified health professional, the donor has sufficient knowledge and understanding of what is involved in the process of blood donation to give their informed consent, or otherwise with the written consent of a person with parental responsibility.
	First time donors over 60 years	- at the discretion of the doctor in the blood establishment
	Over 65 years	- with permission of the doctor in the blood establishment, given annually

Guidelines for the Blood Transfusion Services in the United Kingdom[2]

Chapter 3 Care and Selection of blood donors (including donors of pre-deposit autologous blood)

3.1 General Principles

……The age criteria for donors are laid down in the Joint UKBTS/NIBSC Professional Advisory Committee's (JPAC) Donor Selection Guidelines which form a constituent part of this chapter and must be consulted.

Chapter 6 Component Donation: apheresis

6.1 Criteria for acceptance of donors

……..First-time apheresis donors should have given at least one routine blood donation without untoward effect within the last two years (as this may give an indication of their ability to tolerate an apheresis procedure).

Current Joint UKBTS/NIBSC Professional Advisory Committee's (JPAC) Donor Selection Guidelines on age of donors (change notification No.7-2008)

Obligatory

Whole Blood Donors.
Must not donate if:

a) Under seventeen years of age.

b) They are a first time donor who has had their sixty-sixth birthday.

c) They are a returning donor who has had their seventieth birthday.

Component Donors.
Must not donate if:

a) They have not previously given a whole blood donation without untoward effects.

b) They are under eighteen years of age.

c) They are a returning donor who has had their seventieth birthday.

Additional Information

The lower age limit takes account of national laws on age of consent.
Upper age limit on blood and component donation have traditionally been set to protect the health of the donor. There is however little evidence to support this. Audits have shown a decreased incidence of adverse events in older donors compared with younger donors. Further experience in other blood services has shown no harm to donors over the age of 70 years.

A donor must have given at least one donation in the last two years to donate after their 7oth birthday and continue thereafter with no less than one donation every two years to be considered a regular donor.

Provided donors remain in good health they may continue to donate these guidelines.

When appropriate, donors may be accepted on their birthday.

Reason for change:

Within the UK, donors have been accepted until their seventieth birthday since 1998. A full review of the data acquired by the UK Blood Services of donor adverse events by the Standing Advisory Committee for the Care and Selection of Donors suggests that it would be safe to allow older donors to continue to donate past their seventieth birthday.

Donor adverse event data will be monitored closely and further modification of this guideline will be made in light of these findings.