

Progress and Challenges in Transfusion Medicine, Hemostasis, and Hemotherapy

Modern transfusion medicine is sophisticated hemotherapy. Cellular and humoral blood components can be relevant in virtually every disease, either as a primary determinant in pathophysiology or as a victim of collateral damage, e.g. during treatment with cytostatic drugs, or as crucial substrates in replacement and hemostasis-navigated hemotherapy.

This book highlights major advances in

- hematopoietic stem cells and blood cell engineering
- novel cellular therapeutics and hematopoietic cell transplantation
- molecular immunohematology, immunomodulation, and therapeutic apheresis
- hemostasis in infection and host defense
- platelet-pathogen interactions
- organ- and vascular bed-specific thrombogenesis and genetic research in thrombophilia
- diagnosis and management of bleeding disorders.

It also covers recent challenges in blood donor recruitment and blood supply posed by demographic changes.

With its interdisciplinary approach modern hemotherapy is a paragon of translational research bridging the bench-to-bedside gap in biomedicine. The state-of-the-art contributions collected here aim to stimulate lively discussions – not only among blood center professionals but also with blood and vascular biologists, hematologists, immunologists, anesthesiologists, intensive care specialists, surgeons, cardiologists, nephrologists, hematologists, and pulmonary and infectious disease specialists.

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Progress and Challenges in Transfusion Medicine, Hemostasis, and Hemotherapy

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The Impact of Demographic Changes on Transfusion Demand and Blood Supply: Need for Systematic Blood Donor Research

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Key Words

Demographic changes · Blood supply · Donor research · Transfusion · Red blood cell concentrates · Epidemiology

Summary

The population structure in most European countries is currently changing, with a shift from younger to older age groups. We recently determined the impact of these demographic changes on future blood demand and supply in a well-characterized region in North-East Germany. This indicates two developments. One is the well-known increase in the older population, resulting in an increased demand for blood transfusions of about 12%. The second is the decrease in the number of the younger population due to the decreased birth rate in most of the countries of the former East European block after 1990. This may account for a decrease in blood donations of 25%. We further discuss the reasons for the over-proportional increase in blood demand during the next decades. Prevention of blood shortages will need an increase in the percentage of the population donating blood. To approach new blood donors most efficiently, information about the background of blood donors in comparison to those who do not donate is required. The methodology for performing this type of donor research is presented. As the demographic trends will affect many regions in Europe concomitantly within the next 15 years, coordinated efforts are urgently required to prevent blood shortages.

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Introduction

Blood supply is the transfer of blood from the population of donors to the population of recipients. These two groups differ considerably in their demographic characteristics. The donor population consists primarily of young, healthy individuals. In contrast, most patients requiring blood transfusion are considerably older. Therefore,

blood supply is influenced by the demographic changes in the main age groups of blood donors, while blood demand is influenced by the demographic changes in the age groups of blood recipients.

Blood requirements have steadily increased over the past two decades in Germany and other countries in Europe and North America. This was mainly caused by major therapeutic advances in hematology-oncology and a constant increase in the numbers of major surgical procedures. For example, allogeneic stem cell transplantation in Europe increased by a factor of 4.5 between 1990 and 2000 (from 4,234 to 19,136 procedures) [1], and open heart surgery in Germany increased by a factor of 2.5 between 1990 and 2002 (from 38,712 to 96,194 procedures) [2]. Probably even more important is the extension of the eligibility of older patients for major surgical procedures and the improved (but often still transfusion-dependent) survival following chemotherapy. In Germany, 12% of patients requiring open heart surgery in 1990 were between 70 and 80 years of age, and only 1% was above 80 years. By 2002, however, 39% of patients were 70–80 years old, and 6% were older than 80 years [2]. A less well known factor influencing the number of older patients potentially needing blood transfusions is the sharp increase in life expectancy following the reunification in Germany (mean of 5.1 and 4.8 years for men and women, respectively, since 1989) [3, 4]. The gain in life expectancy was predominantly due to decreases in mortality in men aged 40–64 years and women aged 65 years and older. A variety of reasons for this decrease in mortality after the reunification are assumed: changes in diet with easy access to fresh fruit and vegetables, the modernization of the health care system, the higher availability of modern pharmaceutical drugs and medical technology, a better emergency health care, an increased availability of nursing care, and improvements in overall living conditions especially for the older people [5, 6].

Impact of Demographic Changes on Blood Supply and Blood Demand

Recently, we analyzed how demographic factors will determine future blood demand in Mecklenburg-West Pomerania, a region in Eastern Germany where the demographic change is particularly dynamic, and where detailed donor and recipient data are available from the database of the Department of Transfusion Medicine and the database of the Institute for Community Medicine of the University of Greifswald [7]. This study indicates the potential for a major shortfall of blood supply in the area beginning by the end of this decade, if current age-specific blood donation and demand patterns remain unchanged. The magnitude of this shortfall was calculated to be in the order of 32–35% of red blood cell concentrates (RBCs) required, and is primarily driven by demographics. A major finding of the study was that the expected decrease in blood donations resulting from a relative decrease in the younger donor population has a higher impact than the increase of blood demand. Thus, the impact of demographic changes on transfusion medicine is particularly striking as blood donors

and recipients belong to different age groups and demographic changes affect these populations in the opposite direction. During the next decades, the absolute number of the older age groups will increase. At the same time, the younger adults who donate considerably more blood will decrease by more than 50% by 2015 as compared to the population numbers of 2004, at least in the eastern parts of Germany. The same trend as in Greifswald has been found in Magdeburg, the capital of Saxonia-Anhalt. In this city, the percentage of the population in the age group of 18–68 years, which is the age group of potential blood donors, will decrease from 72 to 65% within 10 years [8]. Thus, the sharply reduced number of potential blood donors, together with increasing demand for blood transfusions in the older population, will result in a growing shortage of RBC units from 2008 onwards.

The shift in the older age groups of the population will have a much more pronounced effect on blood demand than implied by the numbers. This is because malignancies and other diseases, which typically require supportive therapy by blood components, will increase overproportionally in this age group. As a consequence, the incident number of patients with colon cancer will increase by 24.4% until 2012 (+30.9% in 2020), and with myocardial infarction by 27.5% until 2012 (+40.9% in 2020) [9]. Thus, it is very likely that the overall need for blood products will constantly increase although the total population will decrease by 10.5% in Mecklenburg-West Pomerania until 2012.

These demographic changes occur more rapidly in the eastern regions of Germany than in other parts of the country, in which, however, similar demographic changes will manifest with a delay of only a few years. Comparing the demographic data in Germany of 2007 and of 2028 (fig. 1) shows that the peak of the demographic changes that cause the imbalance between blood supply and demand will occur when the 'baby boomer' generation will enter their 7th decade of age. This population group is currently the largest age group in the country and consists of those being between 40 and 50 years of age and therefore currently in the age group primarily donating blood. Thus, the transfusion medicine community has about 15 years to develop strategies to secure blood supply.

As in Mecklenburg-West Pomerania several parameters together have an impact on population numbers, the region may constitute a model region to assess how different approaches may influence blood donation frequency. This may then be transferred to other regions in Germany and Europe which expect similar changes with a delay of just a few years.

Medical advances may reduce RBC demand. However, recent trends indicate the opposite (fig. 2) and indicate that we most likely even underestimate the true need for RBCs in future.

It will be difficult for transfusion medicine specialists to directly achieve a reduction in the transfusion rates, as this is the predominant area of the clinical specialists who are directly involved in patient care. While clinical transfusion medicine can contribute to a reduction in RBC consumption by appropriate clinical trials and on-

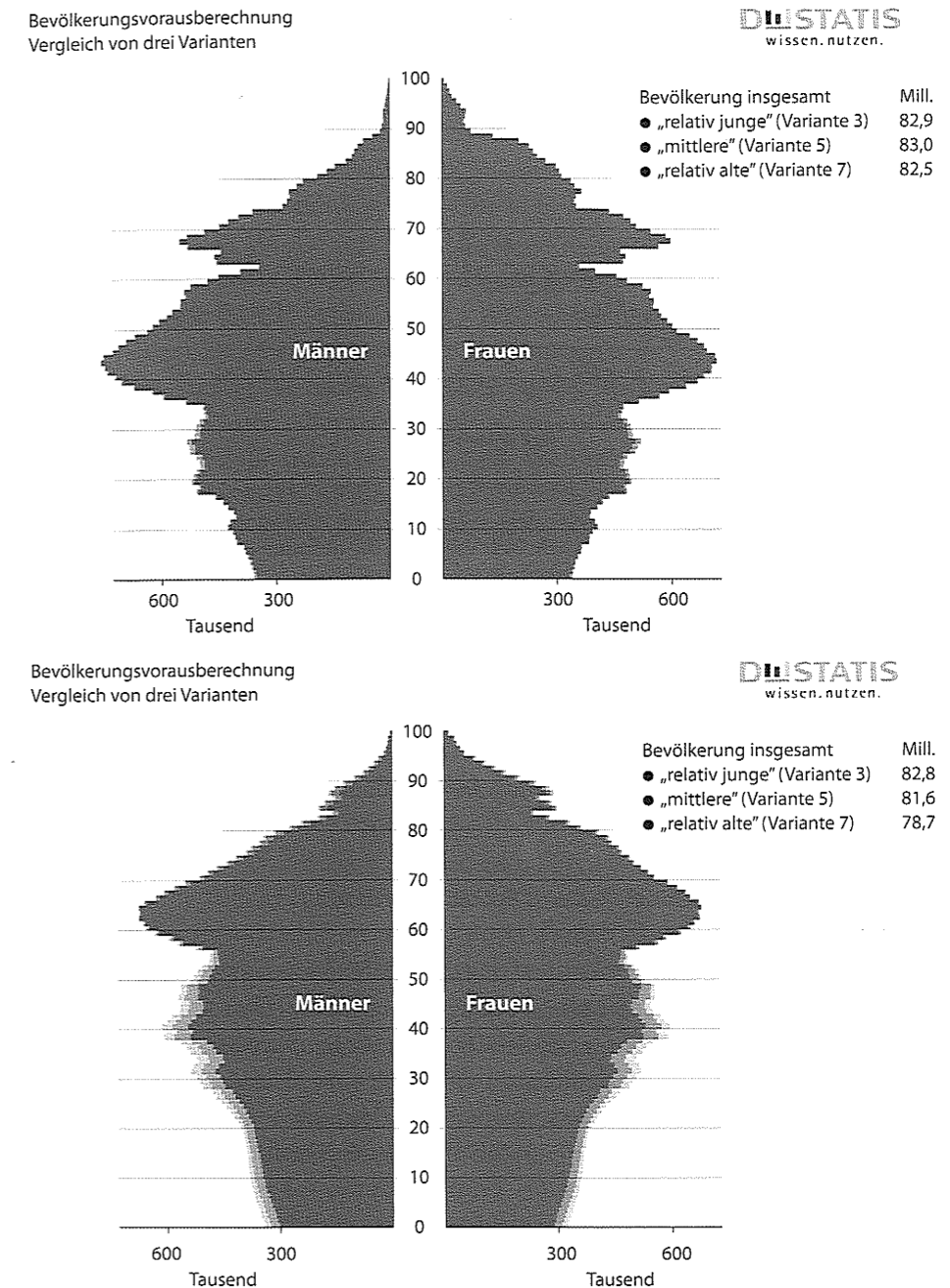


Fig. 1. Demographic pattern of the population in Germany a in 2007 and b in 2028. The decrease in the younger age group as seen in figure 1a for those up to 20 years of age will continue over the next 20 years. The baby boomer generation will remain the biggest age group for the next 20 years. However, they will change from the age group still representing the biggest group of blood donors to the age group with the highest blood demand. This will result in a major shortfall in blood supply if the percentage of blood donors in the younger age group will not be considerably increased within the next 15 years. (©Statistisches Bundesamt)

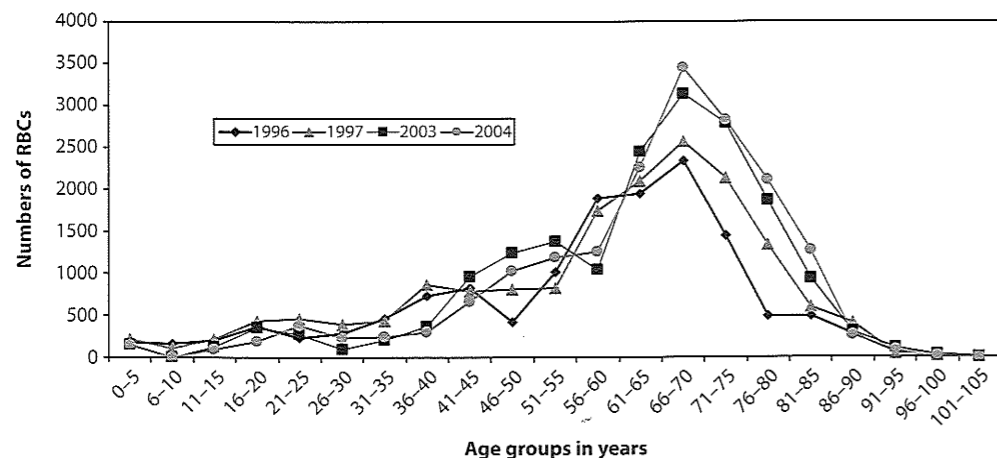


Fig. 2. The figure gives the number of RBCs transfused per age group and year at the University Hospital Greifswald for the years 1996, 1997, and 2003, 2004. While the relative distribution of the age groups of blood recipients remained very similar over the years, the absolute number of transfusions constantly increased. As the University Hospital is the only hospital in the city, these numbers very likely reflect the overall trend of blood demand. It is noteworthy that, during the same time period, major efforts were made to reduce unnecessary RBC transfusions as seen by the reduction of blood transfusions in the younger age groups.

going education on the optimal use of blood products, most blood donation services will have a more important role in obtaining sufficient amounts of blood.

Blood Donor Research: Potential Use and Possible Methods

One approach to counterbalance the threat of a shortfall in blood supply is to increase the percentage of those who donate blood per age group. This will require motivation campaigns, specific advertisement, and identification of those groups in the population who might be addressed most efficiently. However, very little is currently known about the social background and motivation of blood donors. Even more striking is the nearly complete lack of information on the reasons why those who would be eligible for blood donation do not donate.

Such type of studies requires the knowledge and expertise developed in social sciences. Well-planned and scientifically valid donor studies have the potential to provide meaningful data, based on which future activities can be planned and donor recruitment strategies can be designed. 'Self-made' questionnaires are very unlikely to be able to fulfill these requirements. The following section does address how a representative analysis of the blood donor population with regard to their social background and motivation could be designed and analyzed in the context of the regional population. The regional context is of major importance as it is very unlikely that the same criteria and strategies apply for those living in a major city as for those living in a small village.

Methods for Blood Donor Research

Designing interventions for increasing the number of blood donors requires information about the characteristics of those who donate blood and those who do not. The most accurate approach would be a population-representative survey in the region in question. This survey should address the blood donating behavior and, additionally, those variables which are supposed to be relevant to the design of interventions for gaining blood donors. However, if the proportion of blood donors in the population is low, then the sample investigated in such a survey must be very large to have sufficient power. Therefore, population-representative surveys that are specifically designed for assessing the differences between people who donate blood and those who do not are too costly. Alternative approaches are needed. In the following, two possible alternative approaches are discussed. Both rely upon questioning blood donors in the context of the blood donating procedure. The first approach is restricted only to data obtained in this context; the second is based upon additionally applying data from a general population-representative survey performed in the region where the respective blood donating center is located.

Applying Data only from Blood Donors

The survey performed with the blood donors in the course of the blood donating process should fulfill three conditions:

- 1 The survey should last 1 year. This is important because there might be seasonal variations in the behavior of the blood donors as well as in the behavior of the blood donation center. With a survey interval of 1 year, most of these variations will level out.
- 2 People enrolling for donating blood should be approached for study participation in constant intervals over the whole time the donation center is open. The counting should start at the first day of the survey and should be continued from one day to the next. This is important because different groups of people might prefer different times for donating blood, e.g. those donating during morning hours might consist of a totally different group of the population than those donating after regular working hours. It is therefore important that everybody has the same chance of participating in the study.
- 3 For each participant, the number of blood donations given within the study year must be recorded. This is important because this is the central information for determining those features that are associated with the tendency of donating blood.

The data obtained from the blood donors do not contain information about those people who do not donate. They contain, however, information about frequent do-

nors and about sporadic donors. This information, in turn, might be very valuable because there are good reasons to assume that those characteristics that discriminate between people who donate often and those who donate only once or twice also discriminate between people who donate and those who do not. Therefore, the relation between the number of blood donations per year and the characteristics in question should be investigated. If the prevalence of a certain feature increases constantly with the number of blood donations per year, then there is good reason to assume that this feature is underrepresented in people who do not donate at all. If, in contrast, the prevalence of a certain feature decreases constantly with the number of blood donations, then there is good reason to assume that this feature is overrepresented in people who do not donate at all.

Additionally Applying Data from a Population-Representative Survey in the Same Region

Inferring characteristics of people who do not donate blood from characteristics of people who do is associated with a certain degree of uncertainty. This uncertainty can only be reduced by applying data from people who actually do not donate blood. These data can be obtained if there has been a population-representative survey in the region of the blood donating center.

If data of the population-representative survey are to be analyzed together with the data from the blood donor survey, then the latter survey must fulfill three further conditions in addition to the three conditions described above:

- 1 The blood donor survey must contain, at least partly, the same questions as the population-representative survey.
- 2 The information that was relevant to the recruitment procedure of the population-representative survey must also be obtained for the blood donors. In most cases, this is information concerning gender, age and residence. Gender and age are usually registered anyhow. For the residence, in most cases, the postal code will be sufficient.
- 3 Participants of the blood donor survey should be asked whether they have also participated in the population-representative survey.

In most cases, age and residence will be distributed very differently in both data sets merely because of differences in the recruitment procedures. Therefore, those age groups and those residence areas that are represented in only one of the two data sets should be removed before both data sets are merged. Even after removing non-matching groups, there will still be differences between data from the blood donor and the population-representative survey that are merely produced by differences in the recruitment procedures. Usually, these differences will refer to the distribution of

gender, age and residence. These differences should be controlled when both samples are compared in order to identify characteristics that distinguish people who donate blood from those who do not. For this purpose, the comparisons should be performed using multivariate regression analyses with the characteristic in question as dependent variable and gender, age and residence as control variables. Dummy variables for all different frequencies of donating blood per year should be applied as independent variables belonging to the population-representative survey as reference category. Analyses of this kind reveal, specified for each number of donations per year, how blood donors differ from participants of the population-representative survey. Ideally, participants of the population survey who are also blood donors should be excluded to avoid any bias.

Conclusions and Future Directions

Analysis of demographic data indicates increased future demand for blood and blood products that coincides with reduction in blood donations. This process will begin in 2008 in East Germany as in this year the generation affected by the 'post reunification' birth decrease will become 18 and therefore enter the age for blood donation. From now on in the east of Germany, each year the age group of the younger population will be decreased by 50%. In other words, in 2008 the donor population of those being 18 years of age is only half as big as in previous years. In 2009, the donor population of those being 18 and 19 years of age will be reduced by 50%; in 2010 this will affect those being 18, 19, and 20 years of age, and so on. This will inevitably cause shortfalls in blood supply if the transfusion medicine community will not be able to increase the percentage of blood donors in all age groups. Despite some uncertainties in several parameters used in our projection, the threat of major blood shortages is evident. Although these shortfalls might initially be compensated by importing blood from other regions within Germany, this will become increasingly difficult as these demographic trends begin to affect virtually all regions in Europe simultaneously, although to varying degrees. While demographic changes are more pronounced in the eastern states of Germany than in most other areas of Europe, their overall profile resembles that seen elsewhere to various degrees. In Italy and in East European countries, the younger populations decreased markedly during the past decades, whereas in countries like France and England/Wales, the situation is more favorable. Nevertheless, even in the latter countries, the absolute number of the elderly will increase in the future, leading to an increase in blood demand. This has been estimated to be about 30% in Scotland until 2026 [10] and 64% in the USA until 2030 [11, 12]. The latter study also identified the overall population growth, particularly those over 65 years of age as the main cause of the increased demand and also predicted a shortfall between number of donations and number of transfusions required, as the younger age group population will increase less than the one of the older age groups.

It will be increasingly important to motivate younger people to donate blood and to increase the proportion of those who become permanent donors. This needs systematic donor research. We propose that this is an ideal area for a joint approach of experts in social sciences and experts in transfusion medicine. The methodology outlined above might improve the efficacy of donor motivation campaigns. The second major approach to counteract shortfalls in blood supply, which has not been addressed here, is to decrease unnecessary blood transfusion whenever possible.

Disclosure of Conflict of Interests

The authors state that they have no conflict of interests.

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