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REVIEW

Cost of allogeneic blood transfusion

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Abstract

Blood is a scarce and costly resource to society. Therefore, it is important to understand the costs associated with blood, blood components, and blood transfusions. Previous studies have attempted to account for the cost of blood but, because of different objectives, perspectives, and methodologies, they may have underestimated the true (direct and indirect) costs associated with transfusions. Recognizing these limitations, a panel of experts in blood banking and transfusion medicine gathered at the Cost of Blood Consensus Conference to identify a set of key elements associated with whole blood collection, transfusion processes, follow-up, and to establish a standard methodology in estimating costs. Activity-based costing (ABC), the proposed all-inclusive reference methodology, is expected to produce standard and generalizable estimates of the cost of blood transfusion, and it should prove useful to payers, buyers, and society (all of whom bear the cost of blood). In this article, we argue that the ABC approach should be adopted in future cost-of-transfusion studies. In particular, we address the supply and demand dilemma associated with blood and blood components; evaluate the economic impact of transfusion-related adverse outcomes on overall blood utilization; discuss hemovigilance as it contributes not to the expense, but also the safety of transfusion; review previous cost-of-transfusion studies; and summarize the ABC approach and its utility as a methodology for estimating transfusion costs.

Key words: Transfusion; Red blood cells; Cost; Activity-based costing; Methodology

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INTRODUCTION

Blood and its components are critical health care resources. Globally, around 92 million red blood cell (RBC) units are collected each year[1]. According to the 2009 US National Blood Collection and Utilization Survey, approximately 15 million units of whole blood and RBCs were transfused in the US in 2008, and this was not statistically different from 2006 despite a 15.8% decline in overall blood utilization[2]. If current trends continue, then by 2020 US transfusion demand is projected to exceed collections[3]. Also, past research has long predicted a surplus of blood transfusions *vs* RBC collections in the future of

the US blood supply[4-10], an ideal solution has not been found after decades of intense effort.

Even when sufficient blood is available, collecting and maintaining a supply free of potentially infectious viruses and bacteria is extremely costly[11]. In a cost-effectiveness analysis, Jackson *et al*[12] evaluated the effects of implementing nucleic acid testing (NAT) and found that whole-blood donation NAT for human immunodeficiency virus and hepatitis C virus would cost between $155 million and $428 million per year in the US, with an additional $39 million to $140 million per year by adding hepatitis B virus NAT.

With blood donor pools shrinking owing to an aging population and stringent donor qualifications[13,14]; with costs escalating due to new screening technologies to assure a safe blood supply[15,16]; and with demand increasing from rising hematologic and oncologic diseases[17,18], perioperative procedures[19,20], and myelosuppressive therapies[21,22], blood has become a costly and scarce resource. Additional factors that may contribute to the steadily increasing costs of blood include: processing; collecting and administering blood and blood components; hospital liability insurance and overhead; recruiting and retaining blood donors; and shortages of trained personnel[23].

In a 1991 study, Forbes *et al*[24] examined RBC transfusion costs in a group of randomly selected teaching hospitals and estimated the mean cost of transfusing one unit of blood to be $155 (1991 US dollars). Lubarsky *et al*[25] found similar results and determined that the total cost to Duke University Medical Center of a perioperative RBC transfusion was $151.20 (1991-1992 US dollars). Another study[26] calculated the cost of RBC transfusion either preoperatively or in the operating room during hemodilution. Direct cost of purchasing and indirect costs of preparation resulted in an overall cost of $107.26 (1994 US dollars) for the first unit of allogeneic packed RBC transfused. A second unit was slightly less costly ($100.89), because no type and screen was required and the same delivery set and filter could be used.

Yet, despite rising costs of blood, cost estimation methods have varied from study to study[27]. This is due to the lack of a uniform methodology to completely describe and correctly allocate all the contributing cost elements, "beginning with blood collection, continuing through pretransfusion preparation and transfusion administration, and lasting throughout follow-up[28]". Without a harmonizing tool, we are likely to underestimate the true (direct and indirect) cost of blood utilization. Recognizing these limitations, a panel of experts from blood collection facilities, government agencies, academia, hospitals, and practitioners in transfusion medicine gathered at the Cost of Blood Consensus Conference (COBCON) to identify a set of key elements associated with whole blood collection, transfusion processes, follow-up, and to establish a standard methodology in estimating costs[23]. Activity-based costing (ABC), the proposed all-inclusive reference methodology, is expected to produce standard and generalizable estimates of the cost of blood transfusion and it should prove useful to payers, buyers, and society (all of whom bear the cost of blood)[23].

In this article, we argue that the ABC approach should be adopted in future cost-of-transfusion studies. In particular, we address the supply and demand dilemma associated with blood and blood components. We also evaluate the economic impact of transfusion-related adverse outcomes on overall blood utilization. Hemovigilance is discussed as it contributes not only to the expense but also the safety of transfusion. We then review previous cost-of-transfusion studies. We conclude by summarizing the ABC approach and its utility as a methodology for estimating transfusion costs.

SUPPLY AND DEMAND DILEMMA

By 2020, the US population is projected to increase by approximately 10%; however, the major donor population (aged 16-64 years) will increase by only 5.2%, while those 65 years and older will increase 36.2% from 40.2 million to 54.8 million[3]. The 65 years and older age group will shift from 13.0% to 16.1% of the total population, resulting in a 3.1% increase[3]. Given that this particular group of seniors uses the majority of the blood supply, the US will be facing a major challenge in meeting the transfusion needs of the nation.

Early work performed in a well-defined population in Olmsted County, Minnesota, from 1989 through 1992, showed that 53.3% of RBC units were transfused into patients older than 65 years[29]. More importantly, the probability of receiving a transfusion of RBCs in any year rises by 20-fold within the 40-65 years old age group. Rogers *et al*[30] reported similar findings of blood use in a nationally representative sample of the older US population: 31% of Americans older than 65 years received at least one transfusion within a 10-year period and 5.8% experienced repeated transfusion-related visits to hospitals or health care providers within 30 d. Furthermore, older Americans who lived in the South were most likely to receive a transfusion (34%), independent of demographic and health-related factors, whereas those who lived in the West were the least likely (26%).

Similar results have been observed in other countries. For example, in Finland, RBC consumption markedly increased with increasing age among recipients, beginning at around 50 years of age, and 70- to 80-year-olds have an eight-fold higher RBC consumption than 20- to 40-year-olds[31]. In the German federal state Mecklenburg-Pomerania with a population of 1 707 266 inhabitants, researchers were able to track the vast majority of hospital transfusion and blood bank donation records for a 1-year period[32]. The patient group 65 years and older is predicted to grow by 26.4%, whereas the potential blood donor group aged 18 to 68 years may decline by 16.1% in this region. Assuming no changes in donation patterns and medical indications for blood use, these opposing forces are projected to result in a 47% (56 000 RBC units) shortfall in the blood supply by 2020. Comparable

trends have been observed in Northern England[33], Western Australia[34], and Denmark and Sweden[35]. Unless offset by increased donations or reduced blood use, or an alternative source, blood shortages are likely in the foreseeable future and may revolutionize health care to an increasingly aging population.

TRANSFUSION-RELATED ADVERSE OUTCOMES

A safe and secure blood supply is a prerequisite for the delivery of modern health care, but it is provided at a cost of £500 million per year to the UK National Health Service[36]. This cost, which has doubled over the past 10 years, may further increase as additional precautions are implemented to prevent the risk of transmission of infectious agents[36]. Concerns have been expressed as to whether such large expense for small increments in safety are justified[37], and past research[38-43] has investigated the impact of adverse outcomes on transfusion costs. For instance, using cost-utility analysis, autologous transfusion would be considered an expensive strategy if there were no increased risk of bacterial infection with allogeneic transfusion (relative risk of 1.0)[39]. In contrast, autologous transfusion would result in improved outcomes at a reasonable cost, if the relative risk of bacterial infection after allogeneic transfusion exceeds 1.1. And if the relative risk exceeds 2.4, autologous transfusion would prevail over allogeneic transfusion, leading to both lower costs and better outcomes.

While blood transfusion has been shown to be independently associated with adverse outcomes, such as increased morbidity and mortality, postoperative infections, lung injury, and length of hospital stay[44-47], it is difficult to point to transfusion as the cause of the problem. Hemodynamic instability and other effects of acute blood loss (along with associated patient comorbidities) may contribute to the occurrence of adverse outcomes. However, it is difficult to establish the relative contribution of every possible condition and their interactions.

For example, one study[48] examined patients who received either "newer blood" (blood stored for 14 d or less) (n = 2872) or "older blood" (blood stored for more than 14 d) (n = 3130) during cardiac surgery. Transfusion of red cells stored for more than 2 wk was associated with a significantly increased risk of postoperative complications and reduced short-term and long-term survival, suggesting that RBC age may be the cause of adverse outcomes, and not transfusion itself. Glance *et al*[49] derived a different conclusion, when investigating the association of transfusion and mortality and morbidity in 10 100 patients who underwent general, vascular, or orthopedic surgery. Intraoperative blood transfusion was associated with a higher risk of death in surgical patients with severe anemia [odds ratio (OR), 1.29]. Also, the negative impact on outcome was substantial: transfusions of one or two units of RBCs resulted in more pulmonary complications (OR, 1.76), sepsis (OR, 1.43), thromboembolic events (OR, 1.77), and wound complications (OR, 1.87).

According to the past literature, there are many adverse outcomes to transfusion that may occur, and hypotheses about what causes adverse outcomes in transfusion also vary. But, more importantly, if there is a causal relationship between transfusion and adverse outcomes, then these unintended consequences will translate into additional health care costs and may prove to be one of the most costly contributors to health care expenditures[50].

IMPROVING SAFETY THROUGH HEMOVIGILANCE

Hemovigilance has become an integral part of the safety concept in blood transfusion. Its purpose is to assure surveillance of blood transfusion activities, collect data on sequelae of blood transfusion, inform health policy, improve transfusion standards, assist in the formulation of guidelines in the field, and increase the safety and quality of the entire transfusion process[51,52]. Although increasing attention is being paid to hemovigilance worldwide[53-57], there are significant differences from country to country in terms of definition, organizational schemes, state of development, and implementation[51,52].

For example, in response to past failures in the safety of its blood supply, France has established a national system with two separate parallel institutional avenues: that of the regulator (Agence Française de Sécurité Sanitaire des Produits de Santé) and that of the operator (Etablissement Français du Sang)[52]. Both have centralized head offices and regional agencies. Notification of side effects is mandatory and covers any and all events that reporters may believe to be potentially associated[52]. Because the system involves many players, the French model is considered very complex and perhaps expensive[52]. In contrast, the UK scheme is centralized in the Serious Hazards of Transfusion office at a national level[52]. Notification of side effects is on a voluntary basis and only covers serious reactions[52]. Unlike the French model, the UK system is run by professionals in the field, and thus likely to be more cost-efficient[52].

On February 8, 2003, the European Blood Directive 2002/98/EC ("Directive of the European Parliament of the Council setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2002/83/EC")[58] came into force, and since then has mandated minimum hemovigilance activities to be implemented in the member states of the European Union. Although the objective of hemovigilance is clear and precise, the cost implications are rather less obvious. Presently, no detailed cost studies demonstrating the economic impact of each individual system are available[52]. Future studies are needed to investigate the costs and effectiveness of hemovigilance, determine the economic impact on blood transfusion, and compare the value of the system across countries.

ESTIMATES FROM COST-OF-TRANSFUSION STUDIES

Managing the costs of transfusion requires that we completely understand and accurately quantify the economics of component parts of the transfusion chain. Hofmann *et al*[59] pointed out that there are at least five different problem areas that should be considered when undertaking cost-effectiveness analyses to compare transfusion medicine with competing modalities: (1) determining the true cost of allogeneic blood transfusion and other strategies; (2) determining the true cost of allogeneic blood products; (3) the impact of population dynamics on donor blood supply, demand for blood components and marginal cost of these products; (4) limited evidence for effectiveness of transfusion and competing strategies; and (5) missing impact of existing cost-effectiveness on health economic transfusion policies. Given these challenges, it is not surprising that cost evaluations of transfusion have varied in scope, methodology, and outcomes.

Economic evaluation in health care generally classifies costs as direct, indirect, and intangible[60]. Direct costs include resources associated with the provision of an intervention or treatment for an illness. Because direct costs can often be easily identified and calculated, this cost component has been included in many cost studies. Indirect costs refer to productivity loss incurred by an illness, and are important in cost-of-illness studies given their substantial impact. Although some studies also include intangible costs of pain and sufferings by patients because of a disease, this category of costs (usually in the form of quality of life measures) is often omitted because of the difficulty in accurately quantifying it in monetary terms. Several studies in the US[24,61,62] have estimated the cost of blood transfusion with variations in methodology and have derived different results. Adjusted for 2011 US dollars, the cost estimates of a two-unit RBC transfusion by Cantor *et al*[61] ($841.61 to $845.82) were higher than those by Forbes *et al*[24] ($515.63), but lower than those by Crémieux *et al*[62] ($1303.68 for adults and $1578.87 for pediatric cancer patients).

Cost studies outside of the US have been limited. To better understand the cost consequences of blood transfusion in other parts of the world, we conducted a systematic review of the literature to estimate the population-weighted cost associated with a two-unit RBC transfusion in Europe[27]. The weighted average cost of transfusion, expressed in 2011 Euros, was €877.69 (or USD $1225 at the then prevailing exchange rate). The methodological variation between studies may have influenced the magnitude and precision of our cost estimate, potentially underestimating the true (direct and indirect) cost of transfusion. We learned that differences in cost perspectives, cost categories, cost per unit of RBC, study designs, and study settings can have a substantial impact on the cost estimates, making comparisons across studies and countries difficult. We also believe that if the true cost of blood transfusion can be estimated with accuracy, then cost-effectiveness analyses in transfusion medicine can be used more extensively; for instance, to compare allogeneic *vs* autologous transfusion, or transfusion *vs* other methods of anemia management.

In recognition of these limitations, a panel of experts from blood collection facilities, government agencies, academia, hospitals, and practitioners in transfusion medicine gathered at the COBCON to identify the various elements that contribute to the cost of collecting and transfusion RBCs and other single-donor blood components, and to establish a standard methodology for the US in estimating costs of transfusion[23].

ABC APPROACH

The ABC approach was the final product of this meeting, representing the first step to improve upon blood cost accounting methods. The ABC approach involves a total of six steps[23,63]. The initial step is to identify a cost object, also known as a demand for a service. Then the process needs to be outlined by breaking it down into all activities and sub-activities that must be performed to deliver this service. Outputs, or cost drivers, are to be defined for each activity. Resources needed to produce all the defined outputs are then listed, and they can be either fixed or variable. Subsequently, it is necessary to identify resource inputs (e.g., labor hours, supplies), which are required to perform the activities. Capacity constraints, such as staffing hours, inventory limitations, and equipment can be built into this part of the model. Lastly, cost data are needed to calculate the final cost.

To obtain the total cost per unit transfused from a societal perspective, add up all the costs from the following: (1) total donor cost (average cost incurred per donor × number of donations); (2) total production cost (average cost per unit produced × units produced); (3) total hospital transfusion preparation cost (average cost per unit prepared for transfusion × units prepared); (4) total hospital cost of administering transfusion (average cost of administering per unit transfused × units transfused); (5) total cost of treating adverse events (average cost per adverse transfusion event × events); (6) total cost of transfusion-transmitted illness (average cost per transfusion-transmitted case of illness × cases); (7) total cost of litigation (average cost of litigation per case x cases litigated); (8) total cost of lost productivity (average cost of lost productivity per day × hospital and rehabilitation stay days); and (9) total cost of hemovigilance (average cost per hemovigilance case × cases); and then divide the sum by the total number of units transfused[28].

Although the COBCON[23] has made significant progress in outlining a conceptual model and listing both the direct and indirect cost elements, there is much more work required to complete all the steps of this framework. Upon completion of these steps, data can be entered and the model can be tested for general applicability. In addition, the ABC model will clarify the steps in the process, so that the results are more comprehensive

and generalizable. However, individual researchers will need to choose the most relevant parts of the model: those that help locate necessary values need to populate the model. Initially, users will invest more time and resources, but this approach will lead to a unique end product that can be customized to fit specific circumstances. This methodology will redefine how to use transfusions to better evaluate alternatives to transfusions. It will also assist decision-makers in how to allocate funds more equitably, so that blood resources are used to optimal effectiveness. In the long term, this strategy will help to drastically alleviate shortages in global blood supplies.

CONCLUSION

Blood is a scarce and costly resource to society. It is not an infinite resource to be allocated irrationally, used liberally, or wasted without considering the consequences. However, determining the cost of blood is a challenging undertaking that requires us to account for all relevant cost blood components, from its acquisition, to transfusion, and then through follow-up. In our systematic review, we estimated that the cost of a two-unit RBC transfusion was €877.69 in 2011 Euros (equivalent to USD $1,225). This estimate closely approximates the true cost of blood transfusion, because it is comparable to the European estimates provided by Shander *et al*[28] that utilized the ABC approach. However, further studies should be implemented to properly examine the cost of blood components and blood transfusion. Certainly, it is difficult, to fully evaluate and provide accurate estimates of the economic burden of hemovigilance. There are a number of reasons for this lack of precision: complications from adverse outcomes; administrative errors; and not assessing patient experiences as intangible costs. Nonetheless, to the best of our knowledge, modeling of costs using the ABC approach will optimize blood usage, reduce variability, and minimize waste while enabling more studies and more comparison globally. Therefore, we advocate the use of the ABC approach as an effective methodology to lower overall transfusion costs until better and more effective methods are developed.

REFERENCES

1 **World Health Organization**. Blood safety: Key global fact and figures in 2011. Available from: URL: http://www.who.int/worldblooddonorday/media/who_blood_safety_factsheet_2011.pdf. Updated June 2011. Accessed March 30, 2012
2 **Whitaker B**, Schlumpf K, Schulman J, Green J. Report of the US Department of Health and Human Services. The 2009 national blood collection and utilization survey report. Washington, DC: US Department of Health and Human Services, Office of the Assistant Secretary for Health, 2011
3 **Benjamin RJ**, Whitaker BI. Boom or bust? Estimating blood demand and supply as the baby boomers age. *Transfusion* 2011; **51**: 670-673
4 **Surgenor DM**, Wallace EL, Hao SH, Chapman RH. Collection and transfusion of blood in the United States, 1982-1988. *N Engl J Med* 1990; **322**: 1646-1651
5 **Wallace EL**, Surgenor DM, Hao HS, An J, Chapman RH, Churchill WH. Collection and transfusion of blood and blood components in the United States, 1989. *Transfusion* 1993; **33**: 139-144
6 **Wallace EL**, Churchill WH, Surgenor DM, An J, Cho G, McGurk S, Murphy L. Collection and transfusion of blood and blood components in the United States, 1992. *Transfusion* 1995; **35**: 802-812
7 **Wallace EL**, Churchill WH, Surgenor DM, Cho GS, McGurk S. Collection and transfusion of blood and blood components in the United States, 1994. *Transfusion* 1998; **38**: 625-636
8 **Sullivan MT**, McCullough J, Schreiber GB, Wallace EL. Blood collection and transfusion in the United States in 1997. *Transfusion* 2002; **42**: 1253-1260
9 **Sullivan MT**, Wallace EL. Blood collection and transfusion in the United States in 1999. *Transfusion* 2005; **45**: 141-148
10 **Sullivan MT**, Cotten R, Read EJ, Wallace EL. Blood collection and transfusion in the United States in 2001. *Transfusion* 2007; **47**: 385-394
11 **van Hulst M**, de Wolf JT, Staginnus U, Ruitenberg EJ, Postma MJ. Pharmaco-economics of blood transfusion safety: review of the available evidence. *Vox Sang* 2002; **83**: 146-155
12 **Jackson BR**, Busch MP, Stramer SL, AuBuchon JP. The cost-effectiveness of NAT for HIV, HCV, and HBV in whole-blood donations. *Transfusion* 2003; **43**: 721-729
13 **Vamvakas EC**. Epidemiology of red blood cell utilization. *Transfus Med Rev* 1996; **10**: 44-61
14 **Goodnough LT**, Brecher ME, Kanter MH, AuBuchon JP. Transfusion medicine. First of two parts--blood transfusion. *N Engl J Med* 1999; **340**: 438-447
15 **Goodman C**, Chan S, Collins P, Haught R, Chen YJ. Ensuring blood safety and availability in the US: technological advances, costs, and challenges to payment--final report. *Transfusion* 2003; **43**: 3S-46S
16 **Dzik WH**. Technology for enhanced transfusion safety. *Hematology Am Soc Hematol Educ Program* 2005; 476-482
17 **Wandt H**, Ehninger G, Gallmeier WM. New strategies for prophylactic platelet transfusion in patients with hematologic diseases. *Oncologist* 2001; **6**: 446-450
18 **Schonewille H**, Haak HL, van Zijl AM. Alloimmunization after blood transfusion in patients with hematologic and oncologic diseases. *Transfusion* 1999; **39**: 763-771
19 **Hannon TJ**, Gjerde KP. The contemporary economics of transfusion. In: Spiess BD, Spence RK, Shander A, editors. Perioperative transfusion medicine. 2nd ed. Philadelphia: Lippincott Williams and Wilkins, 2006: 13-38
20 **Ferraris VA**, Ferraris SP, Saha SP, Hessel EA, Haan CK, Royston BD, Bridges CR, Higgins RS, Despotis G, Brown JR, Spiess BD, Shore-Lesserson L, Stafford-Smith M, Mazer CD, Bennett-Guerrero E, Hill SE, Body S. Perioperative blood transfusion and blood conservation in cardiac surgery: the Society of Thoracic Surgeons and The Society of Cardiovascular Anesthesiologists clinical practice guideline. *Ann Thorac Surg* 2007; **83**: S27-S86
21 **Estrin JT**, Schocket L, Kregenow R, Henry DH. A retrospective review of blood transfusions in cancer patients with anemia. *Oncologist* 1999; **4**: 318-324
22 **Ludwig H**, Aapro M, Bokemeyer C, Macdonald K, Soubeyran P, Turner M, Albrecht T, Abraham I. Treatment patterns and outcomes in the management of anaemia in cancer patients in Europe: findings from the Anaemia Cancer Treatment (ACT) study. *Eur J Cancer* 2009; **45**: 1603-1615
23 The cost of blood: multidisciplinary consensus conference for a standard methodology. *Transfus Med Rev* 2005; **19**: 66-78
24 **Forbes JM**, Anderson MD, Anderson GF, Bleecker GC, Rossi EC, Moss GS. Blood transfusion costs: a multicenter study. *Transfusion* 1991; **31**: 318-323
25 **Lubarsky DA**, Hahn C, Bennett DH, Smith LR, Bredehoeft SJ, Klein HG, Reves JG. The hospital cost (fiscal year 1991/1992) of a simple perioperative allogeneic red blood cell transfusion during elective surgery at Duke University. *Anesth Analg*

1994; **79**: 629-637
26 **Roberts WA**, Kirkley SA, Newby M. A cost comparison of allogeneic and preoperatively or intraoperatively donated autologous blood. *Anesth Analg* 1996; **83**: 129-133
27 **Abraham I**, Sun D. The cost of blood transfusion in Western Europe as estimated from six studies. *Transfusion* 2012; **52**: 1983-1988
28 **Shander A**, Hofmann A, Ozawa S, Theusinger OM, Gombotz H, Spahn DR. Activity-based costs of blood transfusions in surgical patients at four hospitals. *Transfusion* 2010; **50**: 753-765
29 **Vamvakas EC**, Taswell HF. Epidemiology of blood transfusion. *Transfusion* 1994; **34**: 464-470
30 **Rogers MA**, Blumberg N, Heal JM, Langa KM. Utilization of blood transfusion among older adults in the United States. *Transfusion* 2011; **51**: 710-718
31 **Ali A**, Auvinen MK, Rautonen J. The aging population poses a global challenge for blood services. *Transfusion* 2010; **50**: 584-588
32 **Greinacher A**, Fendrich K, Brzenska R, Kiefel V, Hoffmann W. Implications of demographics on future blood supply: a population-based cross-sectional study. *Transfusion* 2011; **51**: 702-709
33 **Wells AW**, Mounter PJ, Chapman CE, Stainsby D, Wallis JP. Where does blood go? Prospective observational study of red cell transfusion in north England. *BMJ* 2002; **325**: 803
34 **Shortt J**, Polizzotto MN, Waters N, Borosak M, Moran M, Comande M, Devine A, Jolley DJ, Wood EM. Assessment of the urgency and deferability of transfusion to inform emergency blood planning and triage: the Bloodhound prospective audit of red blood cell use. *Transfusion* 2009; **49**: 2296-2303
35 **Kamper-Jørgensen M**, Edgren G, Rostgaard K, Biggar RJ, Nyrén O, Reilly M, Titlestad K, Shanwell A, Melbye M, Hjalgrim H. Blood transfusion exposure in Denmark and Sweden. *Transfusion* 2009; **49**: 888-894
36 **Stainsby D**, Russell J, Cohen H, Lilleyman J. Reducing adverse events in blood transfusion. *Br J Haematol* 2005; **131**: 8-12
37 **McClelland B**, Contreras M. Appropriateness and safety of blood transfusion. *BMJ* 2005; **330**: 104-105
38 **Blumberg N**, Kirkley SA, Heal JM. A cost analysis of autologous and allogeneic transfusions in hip-replacement surgery. *Am J Surg* 1996; **171**: 324-330
39 **Sonnenberg FA**, Gregory P, Yomtovian R, Russell LB, Tierney W, Kosmin M, Carson JL. The cost-effectiveness of autologous transfusion revisited: implications of an increased risk of bacterial infection with allogeneic transfusion. *Transfusion* 1999; **39**: 808-817
40 **Angus DC**, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med* 2001; **29**: 1303-1310
41 **Orsi GB**, Di Stefano L, Noah N. Hospital-acquired, laboratory-confirmed bloodstream infection: increased hospital stay and direct costs. *Infect Control Hosp Epidemiol* 2002; **23**: 190-197
42 **Liu JW**, Su YK, Liu CF, Chen JB. Nosocomial blood-stream infection in patients with end-stage renal disease: excess length of hospital stay, extra cost and attributable mortality. *J Hosp Infect* 2002; **50**: 224-227
43 **Shermock KM**, Horn E, Lipsett PA, Pronovost PJ, Dorman T. Number needed to treat and cost of recombinant human erythropoietin to avoid one transfusion-related adverse event in critically ill patients. *Crit Care Med* 2005; **33**: 497-503
44 **Karkouti K**, Wijeysundera DN, Beattie WS. Risk associated with preoperative anemia in cardiac surgery: a multicenter cohort study. *Circulation* 2008; **117**: 478-484
45 **Beattie WS**, Karkouti K, Wijeysundera DN, Tait G. Risk associated with preoperative anemia in noncardiac surgery: a single-center cohort study. *Anesthesiology* 2009; **110**: 574-581
46 **Chaiwat O**, Lang JD, Vavilala MS, Wang J, MacKenzie EJ, Jurkovich GJ, Rivara FP. Early packed red blood cell transfusion and acute respiratory distress syndrome after trauma. *Anesthesiology* 2009; **110**: 351-360
47 **Bernard AC**, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg* 2009; **208**: 931-937, 937.e1-937.e2; discussion 938-939
48 **Koch CG**, Li L, Sessler DI, Figueroa P, Hoeltge GA, Mihaljevic T, Blackstone EH. Duration of red-cell storage and complications after cardiac surgery. *N Engl J Med* 2008; **358**: 1229-1239
49 **Glance LG**, Dick AW, Mukamel DB, Fleming FJ, Zollo RA, Wissler R, Salloum R, Meredith UW, Osler TM. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. *Anesthesiology* 2011; **114**: 283-292
50 **Blumberg N**. Allogeneic transfusion and infection: economic and clinical implications. *Semin Hematol* 1997; **34**: 34-40
51 **Faber JC**. Haemovigilance around the world. *Vox Sang* 2002; **83** Suppl 1: 71-76
52 **Faber JC**. Worldwide overview of existing haemovigilance systems. *Transfus Apher Sci* 2004; **31**: 99-110
53 **Andreu G**, Morel P, Forestier F, Debeir J, Rebibo D, Janvier G, Hervé P. Hemovigilance network in France: organization and analysis of immediate transfusion incident reports from 1994 to 1998. *Transfusion* 2002; **42**: 1356-1364
54 **Robillard P**, Nawej KI, Jochem K. The Quebec hemovigilance system: description and results from the first two years. *Transfus Apher Sci* 2004; **31**: 111-122
55 **Siegenthaler MA**, Schneider P, Vu DH, Tissot JD. Haemovigilance in a general university hospital: need for a more comprehensive classification and a codification of transfusion-related events. *Vox Sang* 2005; **88**: 22-30
56 **Stainsby D**, Jones H, Asher D, Atterbury C, Boncinelli A, Brant L, Chapman CE, Davison K, Gerrard R, Gray A, Knowles S, Love EM, Milkins C, McClelland DB, Norfolk DR, Soldan K, Taylor C, Revill J, Williamson LM, Cohen H. Serious hazards of transfusion: a decade of hemovigilance in the UK. *Transfus Med Rev* 2006; **20**: 273-282
57 **Keller-Stanislawski B**, Lohmann A, Günay S, Heiden M, Funk MB. The German Haemovigilance System--reports of serious adverse transfusion reactions between 1997 and 2007. *Transfus Med* 2009; **19**: 340-349
58 **European Commission**. Directive 2002/98/EC of the European parliament and of the council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending directive 2001/83/EC. Official Journal of the European Union, 2003: L 33/30-L 33/40
59 **Hofmann A**, Farmer S, Shander A. Cost-effectiveness in haemotherapies and transfusion medicine. *ISBT Sci Ser* 2009; **4**: 258-265
60 **Drummond MF**, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Basic types of economic evaluation. In: Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL, editors. Methods for economic evaluation of health care programmes. 3rd ed. Oxford: Oxford University, 2005: 7-26
61 **Cantor SB**, Hudson DV, Lichtiger B, Rubenstein EB. Costs of blood transfusion: a process-flow analysis. *J Clin Oncol* 1998; **16**: 2364-2370
62 **Crémieux PY**, Barrett B, Anderson K, Slavin MB. Cost of outpatient blood transfusion in cancer patients. *J Clin Oncol* 2000; **18**: 2755-2761
63 **Asadi MJ**, Baltz WA. Activity-based costing for clinical paths. An example to improve clinical cost & efficiency. *J Soc Health Syst* 1996; **5**: 1-7

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American Society of Pediatric Hematology/oncology 25th Annual Meeting 2012
New Orleans, United States

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SSC 2012 - 58th Scientific and Standardization Committee meeting of the ISTH
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3 **Tian D**, Araki H, Stahl E, Bergelson J, Kreitman M. Signature of balancing selection in Arabidopsis. *Proc Natl Acad Sci USA* 2006; In press

Organization as author

4 **Diabetes Prevention Program Research Group**. Hypertension, insulin, and proinsulin in participants with impaired glucose tolerance. *Hypertension* 2002; **40**: 679-686 [PMID: 12411462 PMCID:2516377 DOI:10.1161/01.HYP.0000035706.28494.09]

Both personal authors and an organization as author

5 **Vallancien G**, Emberton M, Harving N, van Moorselaar RJ; Alf-One Study Group. Sexual dysfunction in 1, 274 European men suffering from lower urinary tract symptoms. *J Urol* 2003; **169**: 2257-2261 [PMID: 12771764 DOI:10.1097/01.ju.0000067940.76090.73]

No author given

6 21st century heart solution may have a sting in the tail. *BMJ* 2002; **325**: 184 [PMID: 12142303 DOI:10.1136/bmj.325.7357.184]

Volume with supplement

7 **Geraud G**, Spierings EL, Keywood C. Tolerability and safety of frovatriptan with short- and long-term use for treatment of migraine and in comparison with sumatriptan. *Headache* 2002; **42** Suppl 2: S93-99 [PMID: 12028325 DOI:10.1046/j.1526-4610.42.s2.7.x]

Issue with no volume

8 **Banit DM**, Kaufer H, Hartford JM. Intraoperative frozen section analysis in revision total joint arthroplasty. *Clin Orthop Relat Res* 2002; (**401**): 230-238 [PMID: 12151900 DOI:10.1097/00003086-200208000-00026]

No volume or issue

9 Outreach: Bringing HIV-positive individuals into care. *HRSA Careaction* 2002; 1-6 [PMID: 12154804]

Books

Personal author(s)

10 **Sherlock S**, Dooley J. Diseases of the liver and billiary system. 9th ed. Oxford: Blackwell Sci Pub, 1993: 258-296

Chapter in a book (list all authors)

11 **Lam SK**. Academic investigator's perspectives of medical treatment for peptic ulcer. In: Swabb EA, Azabo S. Ulcer disease: investigation and basis for therapy. New York: Marcel Dekker, 1991: 431-450

Author(s) and editor(s)

12 **Breedlove GK**, Schorfheide AM. Adolescent pregnancy. 2nd ed. Wieczorek RR, editor. White Plains (NY): March of Dimes Education Services, 2001: 20-34

Conference proceedings

13 **Harnden P**, Joffe JK, Jones WG, editors. Germ cell tumours V. Proceedings of the 5th Germ cell tumours Conference; 2001 Sep 13-15; Leeds, UK. New York: Springer, 2002: 30-56

Conference paper

14 **Christensen S**, Oppacher F. An analysis of Koza's computational effort statistic for genetic programming. In: Foster JA, Lutton E, Miller J, Ryan C, Tettamanzi AG, editors. Genetic programming. EuroGP 2002: Proceedings of the 5th European Conference on Genetic Programming; 2002 Apr 3-5; Kinsdale, Ireland. Berlin: Springer, 2002: 182-191

Electronic journal (list all authors)

15 Morse SS. Factors in the emergence of infectious diseases. Emerg Infect Dis serial online, 1995-01-03, cited 1996-06-05; 1(1): 24 screens. Available from: URL: http://www.cdc.gov/ncidod/eid/index.htm

Patent (list all authors)

16 **Pagedas AC**, inventor; Ancel Surgical R&D Inc., assignee. Flexible endoscopic grasping and cutting device and positioning tool assembly. United States patent US 20020103498. 2002 Aug 1

Statistical data

Write as mean ± SD or mean ± SE.

Statistical expression

Express *t* test as *t* (in italics), *F* test as *F* (in italics), chi square test as χ^2 (in Greek), related coefficient as *r* (in italics), degree of freedom as υ (in Greek), sample number as *n* (in italics), and probability as *P* (in italics).

Units

Use SI units. For example: body mass, m (B) = 78 kg; blood pressure, p (B) = 16.2/12.3 kPa; incubation time, t (incubation) = 96 h, blood glucose concentration, c (glucose) 6.4 ± 2.1 mmol/L; blood CEA mass concentration, p (CEA) = 8.6 24.5 μg/L; CO_2 volume fraction, 50 mL/L CO_2, not 5% CO_2; likewise for 40 g/L formaldehyde, not 10% formalin; and mass fraction, 8 ng/g, *etc.* Arabic numerals such as 23, 243, 641 should be read 23 243 641.

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Quantities: *t* time or temperature, *c* concentration, *A* area, *l* length, *m* mass, *V* volume.
Genotypes: *gyrA*, *arg* 1, *c myc*, *c fos*, *etc.*
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