Compared to other risks of other medical therapies, the risks of transfusion are extremely small. Improvements in donor screening, testing and blood processing have reduced the risks far below those of refusing a medically indicated transfusion. Nevertheless, blood is a biological derived from an inherently flawed raw material, and the U.S. General Accounting Office estimates a composite risk of 8 events per 10,000 donated units and 4 events per 1,000 transfused patients (avg. 5 units/patient). In the late 1960's, about one third of multiply transfused patients developed posttransfusion hepatitis. In 1998, the incidence of most transfusion-transmitted infections is so small that rates can no longer be measured practically by prospective studies, but must be calculated from statistical models. Estimates of HIV infection approximate 1/600,000 units transfused, HBV 1/66,000, HCV 1/100,000, and HTLV 1/200,000. The risk of bacterial contamination of blood components is unknown and probably underestimated, although several reports calculate a risk of 1/2,500 per unit of platelets transfused. On a worldwide basis, malaria is the most important transfusion-transmitted disease, although it has been all but eradicated in the United States. There is the ongoing risk of previously unrecognized or "emerging" agents that might threaten the blood supply.

Non-infectious complications of transfusion include the risk of transfusing an incorrect unit (1/12,000), of a hemolytic transfusion reaction (1/6,000), and of a fatal hemolytic reaction (1/500,000). Clinically important acute pulmonary reactions and anaphylaxis occur, but are rare. An area of increasing interest is the immunosuppressive effects of blood and the possible influence of transfusion on postoperative infection and neoplasia.

The availability of hematopoietic cytokines has had an important effect on blood transfusion. Recombinant human erythropoietin (EPO) has eliminated much of the red cell transfusion requirement for patients with end-stage renal disease. This drug is now used widely in the treatment of certain malignancies, in AIDS, and in the anemia of chronic disease. EPO has increased the amount of autologous blood that can be donated preoperatively and dosing schedules have been described to reduce perioperative transfusions in certain patient populations. Cytokines that stimulate granulocytes and platelets are available, but as yet have not had a great impact on transfusion needs.

Red cell substitutes are still not licensed, but several have progressed to Stage III clinical trials. Perfluorocarbon solutions are being tested for intraoperative hemodilution and hemoglobin-based oxygen carriers, derived from human red cells, bovine red cells, and recombinant sources are being tested in several surgical and non-surgical settings. Each of these products has a slightly different therapeutic and safety profile.