Blood Safety and Resource Allocation:
Economic Analyses of Donated Blood Safety Initiatives

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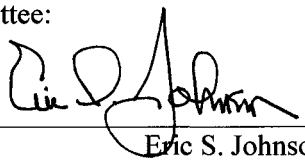

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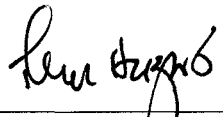

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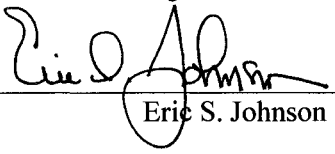

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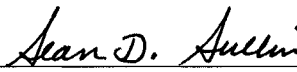

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Abstract

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Risk management at any cost has become the apparent policy of blood banks and regulators because of transfusion-transmitted HIV and hepatitis. However, blood bank opinion leaders suggest economic analyses of new interventions are increasingly important for choosing between competing interventions. In this document we explore these issues and describe a new model to assess blood policy decisions. First, we provide a systematic review of blood supply policy evaluations and discuss improvements that can increase the usefulness of economic evaluation for decision makers. Researchers should: (1) provide more detail on cost parameters and methods used to obtain them; (2) adopt a clear analysis perspective relevant to decision makers that captures all important costs and consequences; (3) at minimum, conduct one-way sensitivity analyses; and (4) place greater reliance on graphical results presentation. Next, we describe a new model developed to evaluate factors that influence the safety, sufficiency, and cost of producing a blood supply. The model was developed using data from Blood Centers of the

Pacific, San Francisco. The model is a cohort simulation that tracks blood donation beginning with the population of persons presenting for donation and ending with units of blood cleared for release to health care providers. We used the blood supply policy model to assess the impact of the U.S. Food and Drug Administration's expanded donor deferral criteria for European travel due to possible exposure to variant Creutzfeldt-Jakob disease. Expanded European travel deferral will lead to the permanent deferral of 3,271 donors (95% Confidence Range, 2,600 – 3,973 donors) reducing the supply of blood by 3,141 units out of an approximate 94,000 unit annual supply produced by this blood bank. The cost of each blood unit increases by $0.53 from the blood bank perspective and by $1.22 from the societal perspective. 2.8% of blood units that would have been available before the policy will be lost from the supply unless recruitment efforts are enhanced to bring in new donors and increase the frequency of repeat donation. This evaluation and other economic analyses provide a valuable approach for assessing the trade-off between safety and sufficiency for the blood supply.

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Glossary

Allogeneic blood	Blood that is donated for use by anyone in the community requiring transfusion
ALT	Alanine aminotransferase
Anti-HBc	Antibodies to Hepatitis B virus core antigen, a specific component of HBV
Autologous blood	Blood that is collected prospectively for administration to the same person at a later time
Directed donation	Blood that is specifically intended for administration to one person, typically a relative or friend
HBsAg	Hepatitis B virus surface antigen, a specific component of HBV
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HIVp24	Human immunodeficiency virus antigen p24, a specific component of HIV
HTLV	Human T cell lymphotrophic virus
NAT	Nucleic acid testing
Pheresis donation	Donation where a specific component of blood (platelets, plasma, or red cells) is collected with the other components intravenously returned to the donor at the time of donation

Preface

The specific aims for this dissertation are:

1. To conduct a systematic review of the cost effectiveness literature for HIV, hepatitis C virus (HCV), and hepatitis B virus (HBV) blood safety initiatives over the last 20 years for the United States setting, report on the quality of the literature, and summarize the cost effectiveness of blood screening in the United States.

2. To construct an economic model of a community blood supply based on the currently required behavioral deferrals and serologic screens. This simulation model addresses determinants of a safe and sufficient blood supply.

a. The epidemiologic portion of the simulation model includes the demographic characteristics of blood donors, the prevalence of behaviors that lead to deferral in the population of persons who present for donation, and the prevalence of screening results in the donor population. Outcome results include both the number of donors who provide blood and number of donated blood units that are cleared for release to providers. In addition, tallies of the number of donors and blood units deferred are generated.

b. The economic portion of the community blood supply model includes both direct and indirect cost contributors. The model includes all costs that are incurred in producing a blood supply. Costs are calculated using actual blood bank costs and estimated indirect costs.

3. To use the community blood supply model to conduct an analysis of a blood supply safety initiative. European travel deferral serves as the case study to show the impact on safety and supply with the implementation of this initiative. The comparator is the required behavioral deferrals and serologic screens prior to the adoption of the expanded travel deferral policy. Results are reported as the impact on supply and costs in cost consequence tables.

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Chapter 1: Systematic Review of Blood Safety and Transfusion Medicine Interventions

Abstract

Economic evaluations are increasingly common in blood safety and transfusion medicine. We sought to summarize and review economic evaluations of blood policy interventions conducted for the United States. Using computer database searches, we identified 19 studies that reported results as both costs and health benefits, and relative to each other, we rated the quality of their design and reporting using an instrument developed by the *U.S. Preventative Services Task Force*. We classified six of the studies as having high quality, 10 as having fair quality, and 3 as having poor quality. Several strengths and limitations in economic evaluations of blood safety and transfusion medicine interventions were identified. Four key improvements can increase the quality of literature in this discipline: we believe researchers should (1) provide more explicit detail on cost parameters in each study and the methods used to obtain them; (2) adopt a clear analysis perspective relevant to decision makers that captures all important costs and consequences, such as the societal perspective; (3) use a consistent approach to reporting sensitivity analyses; and (4) place greater reliance on graphical presentation of results including sensitivity analyses because a large amount of information can be conveyed in relatively simple figures, thus leaving space to discuss the impact of important analysis assumptions and applicability of the results to other settings.

Introduction

Economic evaluations can be one of several important contributors to decision making in health and medicine. The purpose of these evaluations is to provide decision makers with quantitative measures of the efficiency of health care interventions to help guide resource allocation. There are two general categories of economic evaluation that consider both the costs and consequences of interventions. The first is cost effectiveness analysis where, in its simplest form, results are expressed as cost per natural unit, such as infection prevented or years of life saved. A subset of cost effectiveness analysis is cost utility analysis where results are expressed as cost per quality-adjusted life years saved (QALYs) or disability-adjusted life years saved (DALYs). Cost utility studies account for morbidity in addition to mortality when measuring comparative effectiveness by using health state-specific weighting factors. The second category of economic evaluation is cost benefit analysis where both health outcomes or consequences and costs are expressed in monetary units. Typically, health care interventions are evaluated using cost effectiveness or cost utility methods because cost benefit analysis requires that health consequences, such as death or disability, be assigned controversial monetary values.[1]

Although each type of economic evaluation has been conducted and published for blood supply policy interventions, the impact these analyses have had on decision making appears limited. AuBuchon and colleagues have discussed some of the reasons why economic evaluations have not informed blood policy decisions.[2] As a result of HIV and HCV transmission, the safety of the blood supply is held to a level of public, political, and legal scrutiny that few areas of health care endure. This scrutiny, along with the general population's fear of transfusion-transmitted viruses, may explain why economic evaluations of blood safety interventions have had little influence on policy decisions: The search for "zero-risk" (of HIV and HCV transmission) in donated blood creates an atmosphere where no intervention seems too expensive. AuBuchon provides a good review of both economic evaluation methods and some of the social

and political factors that have contributed to the adoption of some blood safety policies, while other policies that cost less and produce greater health gains have not been adopted.[3] In addition, recently, van Hulst and colleagues conducted a systematic review of economic evidence related to blood transfusion safety. The purpose of their article was to consider whether any further increase in transfusion safety is worthwhile and whether the increased costs justify the health gains achieved.[4] Their review included studies from several more developed regions (North America, Japan, and Europe) and therefore did not focus on evidence that is necessarily comparable.

However, another reason economic evaluations have not contributed to blood policy decision-making may be the studies themselves. The clarity of the research and reporting, and the quality of the evidence may limit the inclusion of economic evaluations in health policy decisions. Researchers have evaluated the quality of economic evaluations throughout health care as part of an ongoing effort to examine adherence to recommended methods and to improve future economic studies.[5-8] In addition, systematic reviews of economic evaluations for specific disease categories have been published.[9-13] For economic evaluations to provide decision makers with information they can employ, all groups (clinicians, patients, public health officials, government regulators, and others) must have confidence in the study results. Recognizing the need for standard techniques and reporting, researchers have developed evaluation techniques to assess the quality of economic studies and to compare the methodological validity of such studies.[14-17] We sought to review the results for blood policy evaluations and to evaluate the quality of blood policy evaluations with the belief that a greater understanding of the quality of these studies can help to explain apparent variation in study findings, improve future studies, and increase the inclusion of economic analysis results in blood policy decision making.

As background, Table 1.1 provides a description of donated blood safety policies in the United States. Efforts to increase blood safety begin with donor medical and behavioral eligibility assessments used to select donors believed to confer a lower risk to the blood supply and end with

good manufacturing practices for donated blood that screens negative for all disease markers. Today the focus of donated blood screening is transfusion-transmissible viruses. However, blood banks continue to screen for syphilis as well as alanine aminotransferase (ALT) testing. Both of these screens are used to assess specific conditions and also serve as non-specific surrogates for general ill health. Three transfusion-transmissible viruses (HIV, HCV, and HBV) are of such great health concern that multiple screens are conducted for each virus in order to identify different stages of infection.

Methods

We conducted computer searches of databases to identify all English language economic evaluations of blood supply safety interventions for the United States published between 1982 and 2003. We searched in PubMed, EconLit, Embase, Lexis Nexus, and Cochrane Library databases. Search algorithms consisted of combinations of both terms in group 1, below, with at least one of the words or phrases from group 2 and one from group 3. We conducted both keyword and medical subject heading (MeSH) searches where possible.

Group 1:	blood, United States
Group 2:	HIV, HCV, HBV, blood donor, blood donation, blood collection, or blood screening
Group 3:	economic evaluation, cost, efficacy, effectiveness, cost benefit, cost effectiveness, or cost utility

We excluded all studies related to umbilical cord blood banking. We also excluded studies that evaluated either cost or consequences alone. To be included in this review, study results had to present both cost and consequence results specific to the United States. Examples of important blood safety interventions that could not be included in the review because full economic evaluations have not been published for the U.S. include; HBV surface antigen, HBV core antibody, confidential unit exclusion, HCV antibody, and HCV lookback, where following seroconversion in a blood donor blood products from previous donations by that donor are identified and transfusion recipients notified of possible exposure. Several blood donor and

transfusion medicine economic evaluations from other countries, particularly from Spain, France, Australia, Canada, and the United Kingdom, have been published but were not included in this review because results from these studies may not be applicable in the U.S. due to differences in health care systems, currencies, demographics, disease prevalence, and the ways policies are implemented.

We assessed the quality of each economic evaluation using questions developed by the *U.S. Preventative Services Task Force* for overall quality.[14] We assessed the quality of the reporting for each decision analysis or mathematical model using a set of questions developed by Sculpher and colleagues.[15] The evaluation questions are listed in Figure 1.1. We used a common, printed abstraction and assessment form for all studies. For the evaluation, a total of 22 questions were answered for each study, ranging from the basic study design to methods for mathematical model validation. The *U.S. Preventative Services Task Force* questions and the Sculpher and colleague questions include overlapping content. However, because the focus of the questions is different, overall study versus model-specific, we answered the questions independently. Following abstraction of all studies, we compared the adequacy of the reporting based on our perceived ability to reproduce the study from the publication. Subjective quality ratings (high, fair, or poor) were assigned. For example, if a study appeared reproducible from the report, contained sufficient evidence to support the modeling assumptions and parameter values, and adhered to accepted economic evaluation methods we gave the study a high rating.

Results

Over 400 studies were identified using the search algorithm. Many of the studies could be excluded based on title alone because the evaluations were specific to clinical blood tests or screens that did not involve blood donation or banking. Based on title, 67 studies were candidates for inclusion in the systematic review. We read the abstract for each of these 67 studies to assess eligibility for inclusion in the systematic review. Most of these studies were excluded for one of

two reasons (1) they measured only cost or consequences alone, or (2) the U.S. was not the study setting. Of the 67 studies, 19 publications met our inclusion criteria. In addition, we reviewed the reference lists for each economic evaluation we included in the review to check for any studies that were not identified using the computer-based search strategy. No additional studies were identified.

Here, we review the content and results for each blood safety or transfusion medicine evaluation using an approach similar to the systematic review of Graham and colleagues.[13] Then we discuss the overall quality ratings, summarized in Table 1.2, and use the evaluation results to discuss potential improvements for future studies. Tables 1.3 through 1.6 provide a detailed review of the content and results for each of the 19 economic evaluation studies.

Cost Benefit Analysis of Blood Safety Interventions

Although most economic evaluations of health and medicine interventions use cost effectiveness methods, we identified three cost benefit studies of blood safety interventions. In 1982, Hornbrook and colleagues evaluated the use of alanine aminotransferase (ALT) screening as a surrogate for non-A, non-B hepatitis in blood donors.[18] The results suggest that, based on the avoidance of hepatitis infection, the ratio of benefit to cost of ALT screening varied from 1:3, assuming a low non-A, non-B hepatitis prevalence, to 8:1 assuming a high non-A, non-B hepatitis prevalence.

The two other cost benefit studies of blood safety interventions examined HIV antibody screening. The first study, published in 1988, considered HIV antibody screening compared to no screening.[19] In this study Eisenstaedt and colleagues estimated a benefit to cost ratio of 1.2:1. This translated into a net benefit of $0.73 per blood donor for HIV antibody testing in 1988 dollars. In the other HIV antibody study, published in 1993, Gelles considered HIV-1 antibody screening compared to non-specific HIV screening.[20] Benefit valuation is based on the value of a

human life from work by Fisher and colleagues.[21] Results suggest a benefit to cost of ratio between 44:1 and 12:1 per HIV-1 infection prevented depending on the cost of HIV-1 screening.

Cost Effectiveness Analysis of Blood Safety Interventions

We identified eight cost effectiveness evaluations of blood safety interventions. Four are cost effectiveness studies with infections averted as the denominator of the cost effectiveness ratio.[22-25] In the first of these studies, published in 1990, Schwartz and colleagues compared seven HIV antibody screening strategies from no screening to various combinations of enzyme immunoassay and western blot screens.[22] For all other strategies, the comparator was the no screening strategy. The results suggest all strategies were cost effective depending on the prevalence of HIV, if $55,000 per life year ($50,000 per quality adjusted life year) is used as a benchmark.[17] None of the strategies exceeded $62,000 per HIV infected donation detected when compared to no screening. For all strategies the incremental costs did not exceed $2.18 per blood unit, but individual incremental cost effectiveness ratios comparing each strategy to all others were not calculated. This study was conducted from the blood bank perspective and focused on donors and blood availability as opposed to the clinical consequences of transfusion-transmission of HIV.

The next study in this group was also published in 1990 and compared HIV antigen screening to HIV antibody screening.[23] Mendelson and colleagues estimated that adding HIV antigen testing would be extremely expensive at approximately $20 million per HIV infection prevented in persons living at least four years after transfusion. Although by current standards the study design may be considered incomplete because it does not include important health outcome and cost contributors, this study indicated very early that the addition of HIV antigen testing to HIV antibody testing would have very poor cost effectiveness. A more formal subsequent study by AuBuchon and colleagues confirmed the findings from Mendelson and colleagues.[26]

In the third study in this group, published in 1993, McCarthy and colleagues considered HIV antibody screening in different sub-populations from intravenous drug users to first time blood donors.[24] For blood safety, the relevant results of the study are a cost effectiveness of $290,000 per life year gained for first time male blood donors with no reported risk factors and $1,277,000 per life year gained for first time female blood donors with no reported risk factors. This study only considered the impact of screening on blood donors and did not include the impact on transfusion recipients.

In the last study in this group, published in 1997, Herrera and colleagues evaluated the role of the serologic test for syphilis as a surrogate for window period viral infections in donated blood.[25] The window period is the time between the transmission of an infectious agent and a host's measurable immune response to the infectious agent—this time period is different for different infectious agents. Herrera and colleagues used only blood bank test costs and did not consider transfusion recipient health outcomes. For HIV, HCV, HBV or HTLV the cost effectiveness of surrogate syphilis testing ranged between $6 million and $19 million per corresponding viral infection averted.

The other four blood safety intervention studies are cost utility evaluations with quality-adjusted life years as the denominator in the results ratio.[26-29] All four of these cost utility studies come from a group of researchers who frequently collaborate on economic evaluations. All of these cost utility studies of blood safety interventions were conducted from the hospital or third party payer perspective. Birkmeyer and colleagues developed the core decision analysis model used in all of these studies for the evaluation of autologous blood donation.[30] In the first blood safety intervention evaluation, published in 1995, Busch and colleagues examined the impact of ALT screening following the introduction of HCV antibody screening.[28] This study follows the work of Hornbrook and colleagues and examines ALT screening alone, HCV antibody screening alone, and a combination of both screens compared to no ALT or HCV antibody screening. The

focus of the study was to assess ALT screening with the advent of HCV antibody screening. The results suggest that if ALT was added to a screening regimen already including HCV antibody, the cost effectiveness would be $7.93 million per QALY, whereas each screen alone is cost saving, with estimates between $92,000 and $95,000 saved per QALY. The study highlights the redundancy of ALT screening in the presence of HCV antibody screening.

In the next cost utility study, published in 1997, Busch and colleagues evaluated the use of HBV core antigen as a surrogate for window period HIV infection.[27] Comparators in this study included HIV antibody alone and HIV antibody combined with HIV p24 antigen screening. Results suggest a cost effectiveness of approximately $1.0 million per QALY or more for HBV core antigen screening as a surrogate for early HIV infection.

In the third cost utility study of blood safety interventions, also published in 1997, AuBuchon and colleagues compared HIV p24 antigen screening or HIV RNA screening to HIV antibody screening alone.[26] The purpose of the evaluation was to demonstrate the impact of expanded HIV screening. The cost effectiveness ratio for HIV p24 is $2.28 million per QALY compared to HIV antibody screening alone, and for HIV RNA the ratio is $1.97 million per QALY compared to HIV antibody screening alone.

The final study was published in 2003. In this study, Jackson and colleagues examined nucleic acid testing (NAT) for HCV and HIV compared to all currently required screens.[29] The base case result for HCV/HIV NAT conducted on pooled samples from a small of number donors is $5.8 million per QALY. In addition, the study considers the addition of HBV NAT to the HCV/HIV NAT screen. The base case result for the HCV/HIV/HBV NAT conducted on pooled samples from a small of number donors is $7.6 million per QALY. In scenario analyses, the researchers provide a valuable exploration of different screening protocols and the removal of redundant tests such as HIV p24 antigen and HBV core antibody with the advent of HCV/HIV/HBV NAT.

Cost Effectiveness of Transfusion Medicine Interventions

We identified eight studies comparing different blood or blood component preparations or methods intended to minimize transfusion complications. All of these studies used a health care provider (hospital) perspective to assess costs. The studies focus on the reduction of infectious disease transmission risk, except one study, published in 1996, where AuBuchon and colleagues examined the use of mechanical barriers to prevent mistransfusion.[31] AuBuchon and colleagues' base case result of $197,000 per life year saved is consistent with the cost effectiveness results of other adopted transfusion medicine interventions, although mechanical barriers have not been required by the U.S. Food and Drug Administration.

Two other transfusion medicine studies in this group used cost utility analysis to evaluate specific blood component preparations. In the first of these studies, published in 1994, AuBuchon and colleagues compared solvent detergent treated frozen plasma to standard untreated plasma.[32] Solvent detergent treatment specifically targets all lipid enveloped viruses such as HIV, HCV, and HBV. The base case result of $289,000 per QALY suggests the technology is not cost effective but also not outside the realm of consideration for transfusion medicine interventions. However, Jackson and colleagues published an update of this analysis in 1999, after more reliable information on the cost of the process and new data on the decreased viral transmission risk in the U.S. setting were available.[33] The cost effectiveness of this technology jumped dramatically with a new result of $9.74 million per QALY.

In another component preparation study published in 1999, Lopez-Plaza and colleagues compared the cost effectiveness of single donor platelets collected by pheresis with random donor platelets from whole blood pools.[34] The collection of platelets by pheresis decreases the risk of transfusion-transmitted infections for recipients because recipients are exposed to the blood of one donor as compared to the blood of seven donors when whole blood is pooled for platelet

preparation. The results of this study ranged from $170,000 to $520,000 per QALY depending on the plasma transfusion requirement for four different medical procedures.

We identified five other transfusion medicine studies that evaluated the impact of autologous blood compared to allogeneic blood in elective medical procedures.[30,35-38] Questions about the costs and consequences of autologous blood are well-suited to economic evaluation. All of these studies were published between 1993 and 1999. The results from these studies vary from autologous blood being a dominant strategy (costs less and is more effective) to having very poor cost effectiveness. Birkmeyer and colleagues, Etchason and colleagues, Sonnenberg and colleagues, and Healy and colleagues included hip or knee replacement surgery as the surgical intervention requiring transfusion, allowing for the direct comparison of results between these studies with base case results of $557,000 per QALY in 1993 dollars, $235,000 per QALY in 1992 dollars, $2,470 per QALY in 1997 dollars, and cost savings in 1992 dollars, respectively. To provide a single estimate for the Birkmeyer study we calculated a simple average of the results for the two separate institutions in that study. In addition, Sonnenberg, Etchason, and another Birkmeyer study report results for elective coronary artery bypass grafting (CABG) with results of $1,470 per QALY in 1997 dollars, $494,000 per QALY in 1992 dollars, and $508,000 per QALY in 1992 dollars, respectively.

Figure 1.2 is a plot of the incremental effectiveness and incremental cost results for each autologous blood donation study of hip or knee replacement surgery and coronary artery bypass surgery. For results to be included on this plot, researchers had to report both incremental cost and incremental effectiveness results separately. For hip or knee replacement, the figure shows that three studies have incremental cost results that are similar with the other study result indicating autologous blood is cost saving (annotated on figure). In comparison, three studies have incremental effectiveness results that are similar with the other study having a much larger incremental effectiveness result (annotated on figure). The results for the two CABG studies that

provide incremental cost and effectiveness results are similar to each other. Several factors contribute to the variability of hip or knee replacement results. First, the analysis perspective is not consistent for all studies—one study was conducted from a health provider perspective[30], two studies conducted from a third party payer perspective[37,38] and the other study stated a societal perspective.[36] Each perspective leads to the inclusion of different cost estimates. Second, the assumptions in each analysis are different. For hip or knee replacement, the most critical difference between the studies was whether bacterial infection risk resulting from immunomodulatory effects of allogeneic blood was included in the analysis. The two analyses that included bacterial infection risk suggest prospective autologous blood donation is either a dominant strategy[37] or a highly cost effective strategy with a base case result of $2,470 per QALY[38] compared to allogeneic blood. Neither of the two studies that specifically reported both incremental cost and effectiveness result for CABG included bacterial infection risk. However, one would expect a similar pattern on the incremental cost and effectiveness graph with relatively similar costs but a much larger incremental effectiveness.

Over the 1990s, the viral prevalence trends in donated blood show a decrease for HIV, a decrease for HCV, and a slight increase for HBV.[39] Figure 1.3 provides a comparison of the currency year used in each economic evaluation and the cost effectiveness results for blood safety interventions specifically targeted to reducing the risk of HIV, HCV, or HBV in blood. Because some results overlap and would not be evident, we have slightly modified the currency year so that all results are visible. Results are plotted in terms of the currency year used in each evaluation and also updated to year 2002 dollars using the Consumer Price Index – Medical Care Component.[40] Therefore, each result has two data points on this graph. When the impact of inflation is minimal the points overlap, otherwise the two points lie on the same vertical line but the results in year 2002 dollars are above the results for the currency year when the study was conducted. The dashed line represents $50,000 per QALY in 1991 and is adjusted for inflation, so

that the value is $80,500 per QALY in year 2002 dollars. However, this increase is not evident on the plot because the vertical scale increases in $2,000,000 steps. In this plot, the comparison intervention is not consistently a "no screening" or "no intervention" strategy because multiple screens are conducted for HIV, HBV, and HCV, so the typical comparator is the most recently adopted screen. The plot demonstrates the variation of cost effectiveness results for blood safety interventions, from cost saving (results below the horizontal axis) to very poor cost effectiveness (over $11 million per QALY after adjusting for inflation). All of the results shown on this graph come from interventions that are currently required or used voluntarily by some blood banks in the U.S.

Discussion

The U.S. Federal Aviation Authority uses a threshold of $2.7 million per life saved for economic acceptability, which corresponds to $60,000 to $70,000 per life year saved for the average air traveler 35 to 40 years in age.[41] This cost effectiveness range is elevated compared to the often stated $55,000 per life year ($50,000 per QALY) for medicine, but may serve as a useful guide for defining cost effective interventions in blood supply safety. Many of the interventions that have been adopted far exceed $70,000 per life year saved. In this discipline, decision makers seem insensitive to the concept of limited resources. However, it is unlikely this approach to managing blood supply safety can continue indefinitely. But even if it can, making good decisions between competing, expensive alternatives will rely on the quality and completeness of assembled evidence.

Our review of economic evaluations of transfusion medicine and blood safety interventions reveals several common themes. Overall, there is insufficient economic evaluation of each new blood safety intervention. We were unable to locate published articles on the cost effectiveness or cost benefit of many interventions for example, HBV surface antigen and HCV antibody. In order for economic evaluations to be useful for decision makers, the relative

incremental merits and costs of each blood safety and transfusion medicine intervention must be reported for meaningful comparison. We cannot provide a complete picture of the history of cost effectiveness of blood safety interventions because formal studies have not been conducted or reported for many adopted interventions.

Figure 1.4 illustrates a hypothetical relationship between viral prevalence and cost effectiveness, portraying the expectation that as the prevalence of a disease or condition decreases in the blood donor population the projected cost effectiveness of an intervention will be poorer (meaning more costly with relatively little health benefit). The cost effectiveness ratio is positive above the horizontal axis and negative below the axis (cost saving). When prevalence is high (near the vertical axis) the screening cost effectiveness may even be cost saving because identifying infections will produce greater efficiency as many donated units are interdicted thus preventing infection transmission. Also, earlier identification of infections in the blood donor population may lead to earlier treatment (greater quality-adjusted health at lower cost). As prevalence decreases, the cost effectiveness ratio becomes unfavorable because the increment of infections identified by a screening test is smaller, even though the screening test is still performed on every donated blood unit. When the prevalence is very low, the cost effectiveness ratio will be very unfavorable. At very low viral prevalence it may be too expensive to screen because the positive test yield is so small. This figure may help us understand the cost effectiveness results reported in the literature for blood safety interventions because the prevalence of many viruses in the blood donor population is now quite low when compared to the prevalence in the late 1980s and early 1990s. In addition, because multiple tests are conducted for HIV, HCV, and HBV, the increment of infection identified solely by each additional test is smaller leading to increasingly unfavorable cost effectiveness ratios.

In our subjective assessment, we classified six of 19 studies as having high quality, ten as having good quality, and three as having poor quality. How do these ratings compare to other to

other quality assessments? The largest overall assessment to date was conducted by Neumann and colleagues. They assessed the quality of reporting in cost utility analyses for 228 articles published between 1976 and 1997. Over time they found a steady improvement in reporting based on their subjective quality score, and these results are consistent with the other systematic reviews. Whether broad in scope or focused on specific health care disciplines, researchers report an improvement in the quality of articles over the last 10 years likely reflecting an increase in adherence to recommended reporting requirements.[8,9] We observe this trend in blood policy evaluations with articles from the late 1990s forward providing more details on the evaluation process, and generally having higher quality than studies from the 1980s and early 1990s.

We identified several strengths in the majority of economic evaluation articles. First, researchers provided very clear descriptions of the true or hypothetical study population, including the sources of data used to identify or define the study population. Second, researchers provided a thorough description of the rationale for the evaluation and clearly stated the intervention under evaluation and its comparator(s). Third, researchers discussed the assumptions directly related to the performance of the intervention and the impact these assumptions have on the results of the analysis. Fourth, researchers provided good descriptions of and references for the literature-based estimates incorporated into the effectiveness or benefit parameters of the evaluation. Fifth, in over half of the articles, researchers provided good discussion of the sensitivity analysis results.

However, we also identified limitations in the articles we reviewed. We speculate that some of these limitations contribute to the apparently narrow role economic evaluations have in blood policy decisions. Standard reporting approaches such as those recommended by the *Panel on Cost Effectiveness in Health and Medicine*[42] could address these limitations and increase the role of economic evaluations in blood policy decisions. Many of the following comments and suggestions are consistent with the recommendations of the *Panel*.

Based on an inspection of the reference sections of the all of the other articles, the three cost benefit analyses are rarely considered by other researchers. The controversial issue of placing a monetary value on human life may explain the lack of interest in these studies. However, cost benefit analysis has an advantage over other types of economic analysis because placing all costs and benefits in monetary terms necessarily requires adoption of the societal perspective. The societal perspective permits a detailed listing of all component costs and benefits, which are then easily aggregated and compared as an overall ratio. In the studies reviewed, the only true attempts at a societal perspective occur in the cost benefit analyses. For cost effectiveness and cost utility studies, several researchers report the societal perspective erroneously because they either do not provide all of the important costs or do not justify why they omitted important components, such as donor costs and consequences, and out-of-pocket expenditures for transfusion recipients.

The importance of the societal perspective has been debated, and in some settings this perspective may not be relevant. However, we believe that because the blood supply begins with members of society donating blood for the greater welfare of society, the societal perspective is relevant in blood safety and transfusion medicine interventions. In addition, as Russell and colleagues have discussed, the societal perspective is important for decision makers. In brief, the societal perspective corresponds to the public interest, and because it counts all costs and effects, provides a benchmark against which to assess the results from other perspectives.[43] Furthermore, because the societal perspective includes all costs and consequences, the researcher can restrict costs to specific perspectives, such as third party payer or blood bank, after evaluation from the societal perspective. This combination of results from different perspectives may be highly valued when blood policy decision makers must consider the costs and benefits that accrue to different groups.

A related concern is the rigor of the methods used to estimate cost parameters. Our review suggests incomplete cost estimation is common regardless of the stated analysis

perspective and many investigators fail to report the methods used to obtain cost information. The use of appropriate accounting methods and accurate reporting of cost information are as important to economic evaluation as are the clinical trial, epidemiological, and literature review methods used to estimate effectiveness parameters. For example, researchers use price or charge data instead of opportunity costs. Opportunity costs represent the value of forgone benefits because a resource is not available for its best alternative use.[44] Often price or charge may be the only practical way to estimate certain cost parameters. However, few researchers acknowledge their use of price or charge data and may not appreciate the limitations of such data. In addition, cost estimates from research and development phases of product development, particularly prospective estimates of the cost of new screening tests, are rarely justified when compared to administrative cost data subsequently obtained during routine use. Another potential costing problem is the use of previously published cost of illness estimates that may not be sufficiently up-to-date to capture current treatment costs at the time a new economic evaluation is conducted. In this case, updating a cost estimate with a Consumer Price Index value may not be sufficient to reflect the current costs of an intervention or unit of blood due to practice pattern changes.

Summary cost effectiveness ratios combine costs and effects into one measure, potentially obscuring quantitative information that may be useful to decision makers. A cost consequence analysis may be more useful; it is a disaggregated listing of all of the relevant costs and outcomes or consequences of the interventions under comparison, which then can be used to calculate composite measures such as cost per infection identified or cost per QALY saved.[45] Presentation of separate incremental costs and incremental effectiveness results is valuable. Many studies provide incremental cost results, but too few studies provide incremental effectiveness results. Moreover, frequently the separate cost and consequence results do not correspond to the cost effectiveness ratios. The best example of a cost consequence table from blood policy evaluation comes from Sonnenberg and colleagues' autologous blood donation study[38] in which

separate results can easily be combined to reproduce the cost effectiveness ratio from the base case analysis. Furthermore, a recent editorial in *JAMA* recommends researchers present incremental cost and effectiveness results graphically.[46] We concur and use this approach to compare the autologous blood donation evaluations in Figure 1.2. When multiple interventions are plotted graphically, important information is gained on the relative impact of each intervention.

Study framing is important—the nature of the question and researcher assumptions have a large influence on the results. Typically, only one study addresses a given intervention and a decision maker is unable to observe the impact of author assumptions on the cost effectiveness result. A decision maker faced with multiple studies and conflicting results is placed in the position of trying to evaluate two potentially conflicting issues: which studies include populations that closely correspond to those of the decision maker (generalizability) and which studies appear to have the highest quality (validity). The completeness of the reporting in each evaluation is the best source of the comparative quality for the decision maker. We can directly observe the impact of framing because a sufficient number of studies have compared the use of autologous blood to allogeneic blood. The inclusion of immunomodulatory effects of allogeneic blood and the resulting risk of bacterial contamination greatly changes the cost effectiveness results. Without bacterial infection risk, autologous blood donation appears prohibitively expensive, whereas, with bacterial infection captured, autologous blood donation may even be cost saving compared to allogeneic blood.

Transparency is lacking for many of the models used in blood safety and transfusion interventions. It is difficult to assess model validity or identify methodological inconsistencies because relatively little information is provided on the structure of each model, leaving researchers open to the criticism that models are biased or do not capture important aspects of a given problem. Critics of economic evaluation often suggest one of the weakest aspects of these

methods is the use of mathematical models to represent reality. However, there is no alternative to modeling. Randomized trials or observational studies of health interventions are often infeasible because of the cost of conducting these studies for rare events. In addition, if previous clinical trials of an intervention have demonstrated health benefits it may be unethical to randomize. Critics point to the fact that models are under researcher control and subject to inherent biases. While it is not possible to counter this argument, one of the best ways to insulate against it is for researchers to provide a complete description of the model structure, function, and source of parameter estimates.

In regard to uncertainty in economic evaluations, two important points standout. First, sensitivity analyses, if even reported, are often 1-way analyses compared to the incremental cost effectiveness ratio (costs and effects not separately evaluated by sensitivity analysis). The overall reporting of sensitivity analysis results could be improved by the use of graphical presentation, such as tornado plots of the results. These plots of all 1-way analyses convey a large amount of information regarding which model parameters have the greatest impact on the cost effectiveness results. In addition, a tornado plot can include threshold values for each parameter that indicate, after holding all other values constant, what the value of the parameter is such that the comparison interventions have equivalent cost effectiveness. These threshold values can then be compared to real data, such as the prevalence of disease, helping to inform decision making. Of all 19 articles reviewed, only Lopez-Plaza and colleagues' work provides graphical sensitivity analysis results.[34] At a glance, the two sensitivity analysis figures from this paper identify, for the reader or decision maker, which parameters have the greatest influence on the cost effectiveness results. More advanced sensitivity analyses, such as multi-way or probabilistic analyses, will capture important correlation, but graphical presentation of 1-way analyses succinctly summarizes a large amount of potentially useful information.

Second, in cost utility analyses, the utility values or preference weights for each health state of a given disease are very rarely determined from experimentally elicited preferences. Frequently, the values used are author-modified (expert opinion) preferences weights estimated from select populations. As long as the weights used by different researchers are similar, the influence on decision making would be minimal. However, theoretically, preferences weights should be estimated in a combination of persons having a condition and at risk of developing the condition. It is unlikely that results would dramatically change because researcher-modified utilities are typically close to more formally estimated values. However, it is important to recognize that researcher-modified utilities may have the highest level of uncertainty of any of the parameters in a cost utility evaluation. Therefore, it is always appropriate to include a range of values for each health state utility, the impact of which can be explored through sensitivity analysis.

Our review of blood safety policy economic evaluation studies has limitations. First, our focus on studies conducted for the U.S. setting excludes many evaluations that have been conducted for other settings. Any inference as to the quality of studies from other settings is inappropriate. In countries such as the U.K., Canada, and Australia, where economic evaluations are explicitly included in health care decision making, studies may have higher quality. In these countries and others, guidelines have been established to increase the comparability of studies by requiring common methods and to improve the consistency of reporting.[44,47-49]

To compare the quality of the studies we selected two sets of review questions, one from the *U.S Preventative Services Task Force* and the other from Sculpher and colleagues. Neither of the question sets are validated instruments. Rather we used these questions to create our own set of assessment and abstraction forms. The *Task Force* questions were developed to specifically consider the quality of evidence for preventative health care services. Because blood supply safety requirements are based on the prevention of events, we believe the *Task Force* questions

provide an appropriate point of view. Likewise, the questions developed by Sculpher and colleagues are intended to specifically consider the mathematical models used in economic evaluation. Both question sets may be insensitive to important components of quality in economic evaluation. However, we believe the chosen question sets are good guides for assessing economic evaluation studies and, at minimum, have face validity.

Our relative ratings of study quality are not anchored to outside standards. Such standards have not been universally accepted and may be dubious because in different clinical disciplines the most important contributors to quality and usefulness of economic evaluations are not the same. While we wouldn't expect the ratings to change for the studies we included in this review, it is possible that as a group the studies could be defined as having higher or lower quality than is stated here if compared to economic evaluation assessments from other disciplines.

Nonetheless, this review of economic evaluation studies in blood supply safety and transfusion medicine highlights the magnitude of economic evaluation results for this discipline, and provides specific details on methods and reporting of such studies. We believe four key improvements can improve the relevance of economic evaluation literature in blood safety and transfusion medicine. Researchers should provide more explicit detail on cost parameters in each study and the methods used to obtain them because this can enhance confidence in the cost data. The societal perspective is important for evaluating blood safety initiatives because it captures all important costs and consequences that accrue to different groups. At minimum, 1-way sensitivity analysis should be conducted on all parameters in each evaluation. Finally, researchers should place greater reliance on graphical presentation of overall results and sensitivity analysis results[50] because a large amount of information can be conveyed in relatively simple figures, thus leaving more room to discuss the impact of important analysis assumptions on the results and applicability of the results to other settings.

Table 1.1 Details of safety policies adopted for the U.S. blood supply, adapted from[51]

Intervention	Reason for Adoption	Year of National Implementation
Pre-donation donor deferral	Exclusion of higher risk donors based on behaviors and health conditions	Initiated in 1983 for AIDS, criteria revised and expanded annually
Syphilis	Considered a large health concern at time of adoption—today mainly a risk behavior surrogate	Mid-1940s
HBsAg	Identification of agent believed responsible for transfusion-transmitted hepatitis	1971
Anti-HBc	Surrogate test for non-A, non-B hepatitis	1991
ALT	Surrogate test for non-A, non-B hepatitis	Introduced 1986 (not required but frequently performed)
Anti-HCV	Identification of agent responsible for transfusion-transmitted non-A, non-B hepatitis	1990
Anti-HTLV-I	Identification of agent responsible for transfusion-transmitted adult T-cell leukemia and unresolved suspected connection with AIDS	1988
Anti-HIV (non-specific)	Identification of agent responsible for transfusion-transmitted AIDS	1985
Anti-HIV-1 and Anti-HIV-2	Further understanding of agent(s) responsible for transfusion-transmitted AIDS	1992
HIV p24 antigen	Reduce window period HIV transmission	1996 (Discontinued after NAT implementation)
Anti-HTLV-II	Further understanding of agent(s) responsible for transfusion-transmitted adult T-cell leukemia	1998
Nucleic Acid Testing (NAT) for HCV RNA and HIV RNA	Further reduce window period HCV and HIV transmission	1999 (implemented as an investigation new drug) FDA approval 2002

Overall study and reporting quality[14]

Framing
1. Are the interventions and populations compared appropriate?
2. Is the study conducted from the societal perspective? If not, what perspective?
3. Is the time horizon clinically appropriate and relevant to the study question?

Effects
4. Are all important drivers of effectiveness included?
5. Are key harms included?
6. Is the best available evidence used to estimate effectiveness?
7. Are long-term outcomes used?
8. Do effect measures capture preferences or utilities?

Costs
9. Are all appropriate downstream medical costs included?
10. Are charges converted to costs appropriately?
11. Are the best available data used to estimate costs?

Results
12. Are incremental cost effectiveness ratios presented?
13. Are appropriate sensitivity analyses performed?

Model quality[15]

1. Type of model?
2. Are underlying assumptions clearly specified?
3. Does the model include the relevant disease / health outcomes states for the question of interest?
4. Is time horizon for model appropriate?
5. Are the sources of parameter values for the model clearly stated and justifiable?
6. Are the parameters values appropriately handled (rates properly converted to probabilities, uncertainty about deterministic and stochastic values, etc.)?
7. Model validation / methodological inconsistencies?
8. Comparison to other models and studies?
9. Overall impression of the modeling and reporting (could the model and results be reproduced from the report?).

Figure 1.1 Economic evaluation assessment framework. Each question is answered and an overall quality rating: high, fair, or poor is determined relative to all other studies located for the systematic review.

Table 1.2 Quality assessment of published economic evaluations of donated blood and transfusion medicine interventions from the United States 1982-2003.

Type of Analysis	Quality Rating			Total Number of Studies Identified
	High	Fair	Poor	
Cost Benefit	1	2	-	3
Cost Effectiveness (e.g. per infection averted)	1	3	2	6
Cost Utility (per QALYs)	4	5	1	10

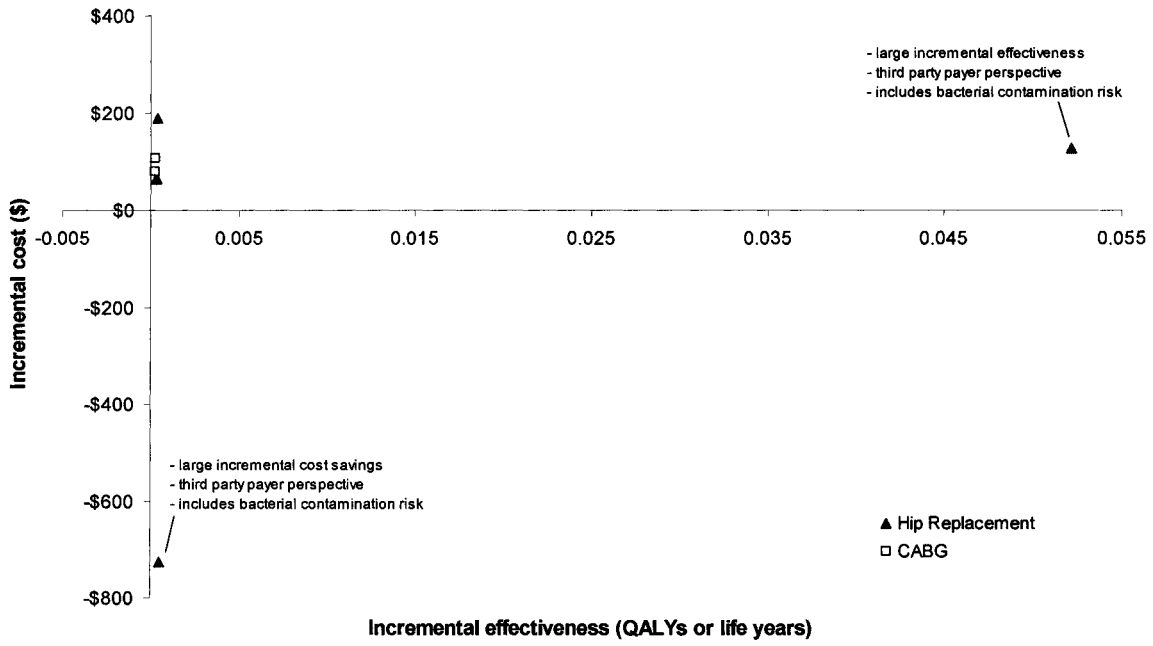

Figure 1.2 Economic evaluation results for autologous blood donation in elective medical procedures: incremental costs plotted against incremental effectiveness from four separate studies that reported incremental estimates

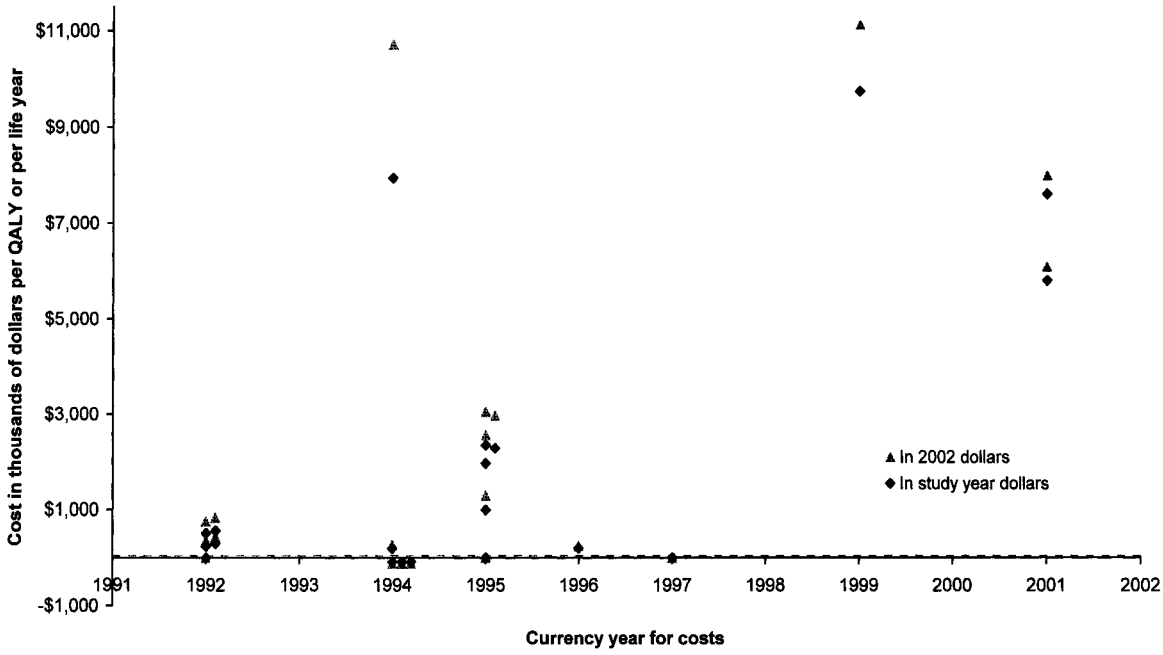

Figure 1.3 Comparison between the cost effectiveness results and currency year for blood policy evaluations focused on reducing HIV, HCV, and HBV risks in donated blood

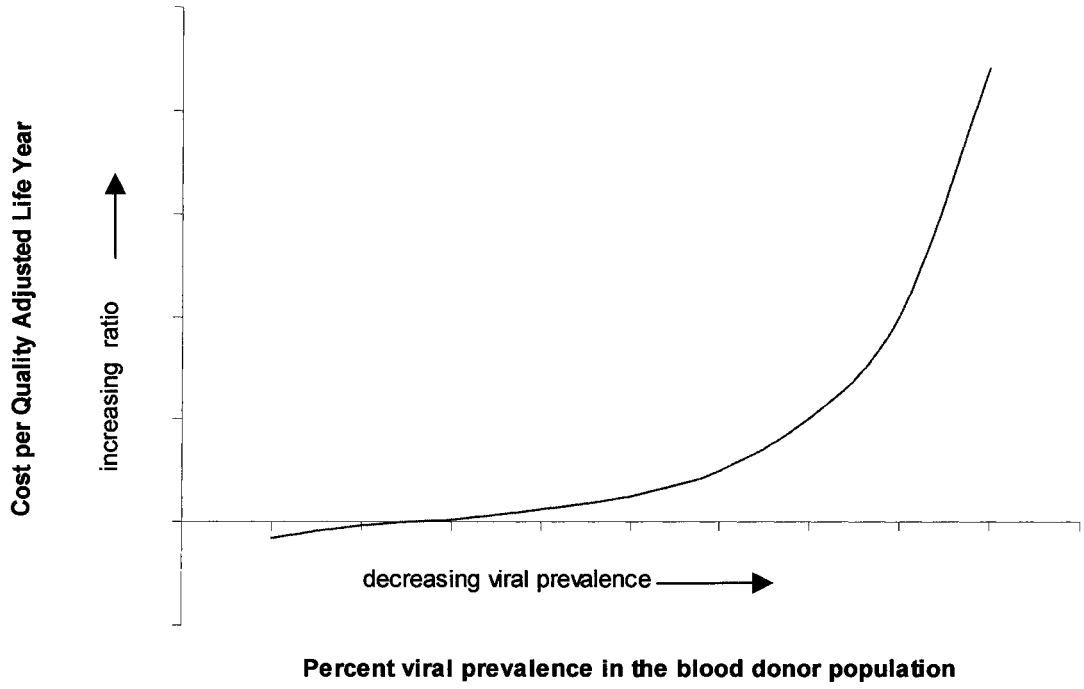

Figure 1.4 Hypothetical relationship between cost effectiveness and viral prevalence

Table 1.3 Cost benefit evaluations of blood safety interventions.

Intervention & reference	Comparator	Effectiveness data time period (publication years)	Cost data and time period (publication years)	Results	Strengths	Limitations	Overall quality assessment
ALT in donated blood Hornbrook, 1982	Current blood supply screens (in 1982)	1977-1982	1980-1982	In 1982 $ Benefits: $898-$31,629 per 1000 blood units Costs: $3151-$4003 per 1000 blood units B:C ratio (scenario dependent) -$2,253 to +$27,626	Sensitivity analysis provided in the form of scenarios Question modeled as a detailed flow chart of the blood testing process Hepatitis outcomes also presented in a natural history chart	Assumes ALT test results is predictive of hepatitis outcomes Donor opportunity costs are not included in the study	Fair
HIV antibody in donated blood Eisenstaedt, 1988	No HIV screening	1979-1987	1982-1987	In 1986 $ Benefits: $43,490 per 1000 donors Costs: $36,234 per 1000 donors B:C 1.2:1 Net benefit: $0.73 per donor Cost per life year extended $10,885	Includes lost earnings for HIV infected transfusion recipients Sensitivity analysis conducted in terms of elasticites (%change in factor per %change B:C)	Test sensitivity and specificity estimates not based on strong evidence Donor opportunity costs are not included in the study Only considers red blood cell preparations and not other cellular components	High
HIV-1 antibody in donated blood Gelles, 1993	Current non-specific Anti-HIV screen	1988-1989	1987-1989	In 1989 $ Costs: $90,749-$322,083 per AIDS case prevented Benefits: Value of a human life $1.6 million to $ 8.5 million	Detailed description of assumptions and calculations Corrected for likelihood of infected blood resulting in infection in recipient Included HIV consequences for positive donors	Calculations based on many assumptions without strong justification or supporting evidence in some cases Benefits estimate from another source (not determined in this study)	Fair

Table 1.4 Cost effectiveness evaluations of blood safety interventions

Intervention and reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
HIV antibody screening (5 alternates to current screening strategy) Schwartz, 1990	1. No screening 2. Current HIV screening strategy in 1990 (EIA, if positive 2 repeat EIAs, if 1+ positive, Western blot)	Mix of blood bank (direct testing costs and effects)	1985-1989 and primary (Red Cross) data	1988 and author estimates	Markov process	In 1988 $ 1. $16,850 to $62,000 per HIV infected unit compared to no screening 2. Dominant to $2.18 per HIV infected unit compared to current screening Results vary by strategy based on prevalence in donor population High: 2.9 per 10,000 Low: 1.6 per 10,000	Comparison of multiple screening strategies Model includes several important determinants of supply Model provides multiple outputs (infected units, donor false positives, wasted units, etc.) Good sensitivity analysis	Charges or prices used in analysis to represent some costs Other costing methods not specified Model function is not transparent	High
HIV antigen screening Mendelson, 1990	Anti-HIV screening	Not stated, assume blood bank (direct test cost only)	1987-1989 and primary (Red Cross) data	1989	Probability equations	In 1989$ $18-24 million per HIV case prevented in persons living 4 years or more after transfusion	Sensitivity analysis based on window period length	Insufficient consideration of costs – only direct test cost considered Analysis perspective not stated Comparator not explicitly modeled Health outcomes not considered The validity of one the of probability equations has been questioned	Poor

Table 1.4 (Continued)

Intervention and reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
HIV antibody screening (in separate populations based on HIV prevalence) McCarthy, 1993	No screening	Third party payer	1988-1991	1990	Markov cycle tree (Decision tree with Markov process for CD4 count and disease prognosis)	In 1990$ First time blood donors with no reported risk factors: Males, $290,000 per Life Year Females, $1,277,400 per Life Year	Good explanation of data sources Includes nearly all important cost and outcomes for the donors Good sensitivity analysis – HIV prevalence drives all results	Framing not specific to blood donation testing Does not consider the costs and outcomes in transfusion recipients No screening strategy is unrealistic for blood donation setting – although this may be relevant in some of the other populations considered	Fair (from the view point of blood screening)
Serologic test for syphilis as a surrogate for window period viral infections Herrera, 1997	Correspond-ing viral screens	Blood bank (direct test cost only)	1992-1994 and primary (Red Cross) data	1991-1996 and investigator estimates of test cost	Simple cost and effects ratio	Currency year not specified: $16 million per HIV infection averted $5.8 million per HBV infection averted $18.8 million per HCV infect. averted $7 million per HTLV-I infect. averted	Explicitly assumes that syphilis test is a surrogate for other infectious disease as opposed to a comparator of no screening at all	Not formally modeled and no sensitivity analysis Included test costs only Did not consider health outcomes Test sensitivities based on a select group of ARC centers (18 of 45) with high viral prevalence	Poor

Table 1.5 Cost Utility Evaluations of Blood Safety Interventions

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
ALT screening after implement-ation of Anti-HCV Busch, 1995	ALT screening alone Anti-HCV screening alone	Blood bank and health care provider	1978 (utilities) to 1993 and primary (REDS) data	1993-1994 and investigator estimates of test cost	Decision analysis with Markov process disease prognosis	In 1994 $ ALT added to Anti-HCV: $7.93 million per QALY Anti-HCV added to ALT: -$87,900 per QALY Each screen alone is also cost saving	Compares three strategies to determine incremental benefit of each one Shows that ALT and Anti-HCV screening alone provide similar cost effectiveness results	Researcher estimated utilities Insufficient evidence to support cost estimates Prices not costs used Too few specifics on model with references to previous publications Separate results for incremental costs and incremental effects not presented	Fair
HBV core Antigen as a surrogate for HIV window period infections Busch, 1997	Current screens including Anti-HIV-1 and p24 Ag testing	Third party payer	1978 (utilities) to 1995 and primary (REDS) data	1993-1995 and investigator estimates of test cost	Decision analysis with Markov process disease prognosis	In 1995$ $0.99 to $2.35 million per QALY	Explicitly assumes that Anti-HBc is a surrogate for HIV as opposed to a comparator of no screening at all	Researcher estimated utilities Insufficient evidence to support cost estimates Prices not costs used Too few specifics on model with references to previous publications No sensitivity analyses reported	Poor

Table 1.5 (Continued)

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
1. HIV p24 Antigen 2. HIV RNA screening AuBuchon, 1997	Anti-HIV screening	Third party payer	1978-1995 and primary (REDS) data	1993 and investigator estimates of test cost	Decision analysis with Markov process disease prognosis	In 1995$ p24 Antigen: $2.28 million per QALY HIV RNA: $1.97 million per QALY	Provides incremental estimates for all HIV blood screens	Researcher estimated utilities Insufficient evidence to support cost estimates Prices not costs used Too few specifics on model with references to previous publications	High
Nucleic Acid Testing for HIV, HCV, (and HBV) by minipool Jackson, 2003	Current screens for all three viruses	Third party payer (authors claim societal)	<1993-2000	<1993-2001	Decision analysis with Markov process disease prognosis	In 2001$ HIV/HCV NAT: $5.8 million per QALY HIV/HCV/HBV NAT: $7.6 million per QALY	Provides good details on model structure Probabilistic sensitivity analysis on some parameters Compared several different scenarios including discontinuation of some current screens Based on previous Birkmeyer model (1993) with updated HCV chronicity and HIV treatment information Cost and consequence details provided	Not true societal perspective Insufficient details on costing—specifically for stated societal perspective Not clear that viral treatment regimens and costs represent current practice in 2001	Fair

Table 1.6 Cost Effectiveness and Cost Utility Evaluations of Transfusion Medicine Interventions

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
Prospective autologous blood donation (For 4 surgical procedures) Etchason, 1995	Standard allogeneic blood	Third party payer (authors claim societal)	1978 (utilities) 1989-1993	1980-1993 and primary (hospital and case series) data	Decision analysis	In 1992$ Procedure and disease dependent: Autologous blood provides about 2 to 4 hours of quality adjusted life per person $235,000 to $23 million per QALY	Compared more than one treatment scenario Highlights the cost of discarded autologous blood Authors conducted both a blood donation cost study and transfusion complications cost study	Structure of model not provided Range of values for sensitivity analysis not provided Authors claim societal perspective but only health care payer costs considered Utility values based on old study and researcher opinion – these values seem high Equivalent risk of bacterial contamination for autologous and allogeneic blood	Fair
Autologous blood donation for total hip or knee replacement Birkmeyer, 1993	Allogeneic blood for total hip or knee replacement	Hospital	1978 (utilities) 1987-1992	1982-1991	Decision analysis with Markov process disease prognosis	In 1992$ Procedure dependent Autologous blood provides about ¾ hour to 4.5 hours of quality adjusted life per person $40,000 to $1.15 million per QALY	Model structure and details provided Good discussion of sensitivity analysis	Use of cost to charge ratios for costing has been criticized by others Insufficient details on costs Utility values based on old study and researcher opinion	High

Table 1.6 (Continued)

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
Autologous blood for elective hip replacement Sonnenberg, 1999	Allogeneic blood for elective hip replacement	Third party payer	1979-1997	1993-1996 plus primary (case series) data	Markov cohort simulation	In 1997$ Base case: $2470 per QALY	Very thorough and detailed justification for all model parameter values Authors conducted cost studies Includes bacterial contamination risks	Focuses on elective hip replacement population with minimal discussion of other procedures Cost of outdated autologous units and subsequent destruction based on Etchason and not updated or re-evaluated	High
Autologous blood for hip replacement Healy, 1994	Allogeneic blood for hip replacement	Third party payer	1989-1993 plus primary data	1989-1993 plus primary data	Decision analysis	In 1992$ Base case: autologous blood is dominant; 0.18 days greater LE and $725 cost savings per patient	Includes bacterial contamination risks Good discussion of limitations particularly in regard to other patients and settings	Cost data appears to be prices or charges as opposed to costs Insufficient justification for costs used Stated societal perspective but is third party payer No window period for acquisition of viral infection– costs start accumulating immediately No accounting for cost of wasted autologous blood Bacterial infection data based on increased hospital stays and not culture positive verification	Fair

Table 1.6 (Continued)

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
Autologous blood for elective CABG Birkmeyer, 1994	Allogeneic blood for elective CABG	Hospital	1976-1991	1989 and primary (hospital) data	Decision analysis with Markov process disease prognosis	In 1992$ Base case: $508,000 per QALY	Model structure and details provided Good discussion of sensitivity analysis	Use of cost to charge ratios for costing has been criticized by others Insufficient details on costs Utility values based on old study and researcher opinion Perspective unclear – mix of blood bank and health care provider	Fair
Solvent detergent treated frozen plasma AuBuchon, 1994 Jackson, 1999 update	Standard preparation method of plasma at the time of study	Hospital	1978-1993 and primary (case series) data	1989-1994 and investigator estimates of test cost	Decision analysis with Markov process disease prognosis	In 1992$ Solvent detergent treated plasma provides 35 minutes of quality adjusted life per transfusion Base case: $289,000 per QALY Scenarios: $55,300 to $422,300 per QALY	Update demonstrates the importance of high-quality parameter estimates for any modeling effort	Too few details on model structure and components with reference to previous publications No table providing data sources, point estimates, or ranges Insufficient justification for costs used	High

Table 1.6 (Continued)

Intervention & reference	Comparator	Perspective	Effectiveness data time period (publication years)	Cost data time period (publication years)	Model type	Results	Strengths	Limitations	Overall quality assessment
Single donor platelets by platelet-pheresis Lopez-Plaza, 1999	Random donor platelets from whole blood pools	Hospital	1993-1996 and primary (case series) data	1993-1997 and primary data	Decision analysis	In 1996$ Procedure/ disease dependent: $168,700 to $519,800 per QALY	Tornado type sensitivity analysis figures provided Compared impact of platelets in different patient populations undergoing different medical procedures	Clinical efficacy of each preparation assumed to be the same Decision tree format for disease prognosis may not appropriately reflect reality Utility values based on research consensus	Fair
Mechanical barriers to prevent mistransfusion AuBuchon, 1996	Current transfusion practices	Hospital	1959-1992 and primary (hospital) data	1991 and primary (hospital) data)	Decision analysis	In 1994 $ Base case $197,000 per Life year	Carefully detailed what would and would not be prevented with mechanical barriers	Estimated some costs as ½ transfusion charges	Fair

Notes to Chapter

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Chapter 2: Community Blood Supply Model

Abstract

Efforts to improve the safety of the United States blood supply have been very successful. Through a combination of pre-donation donor screening and donated blood screening, the blood supply is safer than it has ever been. However, as a result of these safety measures, one of the greatest threats to the blood supply may be an insufficient supply. The trade-off between the safety and the sufficiency of the blood supply has not received enough attention. We developed a new mathematical model that incorporates the determinants of a safe and sufficient supply of blood in order to investigate blood policy decisions. The focus of the model is the production of whole blood for provision to health care providers. The model is a cohort simulation, where the population of presenting donors is stratified into eight sex- and age-specific groups because the probability of pre-donation donor deferral and post-donation screening test deferral varies based on these demographic characteristics. All parameters for the model are estimated from Blood Centers of Pacific (BCP), San Francisco, California, data for the year 2000. In addition to modeling donor and donation outcomes, we estimated cost parameters from BCP expenditure data from the year 2000. We sought to establish face validity for the model by demonstrating that the simulation model closely mimics the outcomes and costs observed by blood bank administrators. The model can be used to evaluate the impact of pre-donation donor deferrals, such as the expanded European travel deferral for variant Creutzfeldt-Jakob disease (vCJD), or the model can be used to evaluate the impact of new donation screening strategies, such as the impending nucleic acid test for West Nile Virus.

Introduction

Following the terrorist attacks on September 11, 2001, the U.S. public overwhelmingly responded to calls for blood donation, ensuring that a more than sufficient supply was available to address any immediate medical emergencies. However, two days later concerns about the availability of blood and blood components turned into concerns about excess collections, outdates, and potential shortages in the weeks ahead because many donors scheduled to give blood in the coming weeks had responded to the crisis.[1]

The blood supply plays a critical role in the American health care system. Each year, clinicians transfuse 3.5 million Americans, requiring a supply of 14 million donated units. While blood and blood products can save lives, they carry the risk of infectious disease transmission, such as HIV and hepatitis,[2] as well as emerging pathogens. Donor deferral and screening mitigate these risks; blood supplies of the U.S. and other developed countries are now so safe that prospective follow-up studies of transfusion recipients are unable to document transmission events, let alone yield risk estimates.[3] Moreover, the greatest increase in safety may result from pre-donation deferral based on self-reported behaviors. With the combination of pre-donation deferrals and the currently mandated screening tests, the estimated residual risk per million donations is 0.82 for HIV, 4.3 for HCV, and 4.5 for HBV.[4]

Recent blood donation or blood donor models examine specific issues regarding donation, such as predicting donor return behavior using various regression methods.[5-8] These regression models provide useful information on the likelihood of, and time period for donor return. Other blood donation models reported in the literature focus on work flow and blood donation processing,[9] and the use of previously frozen blood to alleviate acute shortages.[10] In addition, several post-transfusion health outcomes and economic evaluation models have been developed to explore the impact of new blood screening or prevention strategies.[11-15] These models provide valuable insight into the consequences of mistransfusion or transfusion of blood

and blood products containing infectious agents. However, none of these models were developed to describe the factors that influence the available quantity of blood. All of these models assume that a sufficient supply of blood will be available, and none incorporate epidemiological differences between donors, donor deferrals, or the economics of blood supply production.

Maintaining a supply of blood from voluntary donors is dependent on a sufficient number of individuals who are willing to present for donation. Presenting for donation does not mean a donor is eligible to donate, or that an eligible donor will provide blood that can be released for transfusion. Both pre-donation donor evaluation and post-donation blood unit screening are critical processes contributing to the safety of the blood supply. Yet, the impact of pre-donation evaluation on the available supply of blood has not received sufficient attention. Presenting donors are deferred for multiple reasons related to personal safety for the donor and threats to safety for the blood supply. Regardless of the reason, these pre-donation deferrals lead to a diminished eligible donor pool. The smaller the eligible donor pool, the smaller the number of available blood units. Maintaining a sufficient supply of blood requires constant consideration of the trade-off between maximizing blood unit availability and ensuring the safety of blood units that are made available.

A complete picture of the contributors to a safe and sufficient supply of blood needs to consider all the determinants that influence the quantity of blood available. We sought to develop a new mathematical model of the blood supply. The model tracks the 'natural history' of the blood supply beginning with the experience of persons presenting for donation and ending with screened blood units that can be released for use. In addition, we include activity costs because economic factors are important in producing a supply. We call this model the community blood supply model and it is intended to mimic the important determinates of a safe and sufficient supply of blood.

Methods

Model Overview

The model is a cohort simulation. The time horizon for the model is one year. The focus of the model is allogeneic whole blood donation. The year is divided into six, two-month intervals approximately corresponding to the maximum number of times an individual can donate whole blood in one year (once every 56 days). We specifically structured the model in this way to permit consideration of seasonal factors related to blood donation. All persons over the age of 18 years are potentially eligible to donate and persons 16 or 17 years of age are potentially eligible to donate with parental consent. The population of presenting blood donors is stratified into eight sex- and age-defined groups (16-24 year old males, 16-24 year old females, 25-39 year old males, 25-39 year old females, 40-54 year old males, 40-54 year old females, 55+ year old males, and 55+ year old females) based on observed epidemiological differences related to age and gender.

The core structure of the model is provided in Figure 2.1 using a decision tree framework. Within each demographic group, persons who present for donation are either first time or repeat donors. Each presenting donor is classified into one of four categories prior to donation; eligible to donate, short term temporary deferral, long term temporary deferral, or permanent deferral. There are multiple potential reasons for each type of pre-donation deferral. We defined short term temporary deferrals as deferrals between 1 day and 2 months in length, long term temporary deferrals as deferrals between 2 months to 1 year in length, and permanent deferrals as 3-year Malaria-related deferrals, 5-year cancer-related deferrals, and true permanent deferrals. All pre-donation deferrals are based on self-reported exposures or behaviors during the pre-donation interview, medical evaluation, previous screening results, or historical deferral. After assessing donor eligibility, each eligible donor is either able or unable to donate (e.g., if the phlebotomist cannot locate a vein for blood collection or if the donor faints before completion of the donation process). Following collection of a unit of blood, the unit is sent to the laboratory for

screening. A positive test on any of the blood screens for syphilis, HIV, HTLV, HCV, or HBV leads to interdiction of the blood unit and deferral of the blood donor. Regulations require that the quantity of blood collected must be within 10 percent of the prescribed collection volume in order for the unit to be useable.[16,17] Although under and over collections are subjected to the same blood screens as fully donated units so that results can be provided to donors, these units are removed from the supply because they do not meet quality assurance requirements. A unit that screens negative for all blood screens and meets quality requirements is cleared for release. Persons who donate a unit of blood that screens negative are eligible to present for donation as early as 56 days later, corresponding to a date beginning at some time in the next cycle of the model.

Data Sources and Analysis - Outcomes

Institutional review board approval of the study design and use of data was obtained from the University of Washington, Human Subject Division, and the University of California, San Francisco, Committee on Human Research.

All donor and donation data comes from encounter information collected by Blood Centers of the Pacific (BCP), San Francisco, CA. BCP is a subsidiary of Blood Systems Inc., which is composed of individual centers operating in 14 U.S. states, with two large centralized laboratories for donation testing. BCP serves the northern California counties of Marin, Napa, San Francisco, Shasta and Solano. BCP is also a participant in the Retrovirus Epidemiology Donor Study (REDS) along with four other blood centers in the United States. Donor and donation information has been collected for REDS since 1991. A dataset containing 10 years of BCP-specific REDS data (1991-2000) was provided for this study. REDS data includes allogeneic, autologous, directed, and pheresis donation records.

Allogeneic donation constitutes 78% of all donations and 91% of all whole blood donations to BCP. Persons who donate blood components through pheresis or those who present

for directed donation or autologous blood collection might not be comparable to voluntary allogeneic blood donors, and their reasons for donation are not the same. In addition, donor eligibility rules for these types of donation are not the same as for allogeneic donation.

Figures 2.2 through 2.5 show the differences in the frequency of disease marker positive donations based on the type of donation. These plots provide a graphical summary of screening test information for the year 2000. Each figure consists of four separate panels. Within each panel on the horizontal axis, the days throughout the year are plotted as a continuous measure from 1 (January 1, 2000) to 365 (December 31, 2000) and the eight age- and sex-specific demographic groups are plotted on the vertical axis. Each dot represents one blood collection on a specific day in the year. Days with no blood collection are evident, such as day 359, Christmas Day; day 328, Thanksgiving Day; and day 248, Labor Day. Within each demographic group, the data have been jittered vertically so that an indication of the number of persons from that group who presented on the same day can be discerned. Plotting the data in this way provides an indication of the number of collections within each demographic group over the course of the year. The text at the top of each panel represents conditioning variables, meaning the data plotted within each panel is restricted to persons who meet the three conditions indicated at the top of the panel. Therefore, these plots stratify donation records into donation type, first time versus repeat donor status, and overall disease marker screening result. The upper panels in all four figures correspond to first time donors and the lower panels correspond to repeat donors. The left panels correspond to donations that screened negative on all tests and the right panels correspond to donations that screened positive on one or more screens. When considered together the four pages of figures demonstrate sub-group differences across demographic groups for allogeneic whole blood, autologous, directed, and pheresis donations. Pheresis donors are a select group of donors who have previously donated whole blood. Nearly all pheresis donations come from older repeat donors and are negative for all disease markers. Figure 2.2 also suggests that pheresis donors are

more likely to be male. Directed donation does not appear to notably vary by sex or age, except that directed donation from 16-24 year old donors is less common. Repeat directed donors very infrequently test disease marker positive. A strong age trend is evident for autologous "donors" with many older persons having blood stored for later medical procedures. Also, the frequency of disease marker positive tests from autologous donors appears higher when compared to each other type of donation.

Because we were interested in developing a model to assess the impact of blood safety policies on voluntary donors and availability of a sufficient supply of blood, we restricted the dataset to allogeneic whole blood donation records. Pre-donation donor deferrals, meaning those resulting from interview responses or medical evaluation, were not available in the REDS dataset. BCP maintains its own database of donor deferrals and provided us with a deferral dataset for the year 2000. Both the REDS data and the donor deferral data were provided with common encrypted donor identifications numbers. We merged REDS data and year 2000 BCP donor deferral data using four variables: encrypted donor identification number, donor birth date, visit date to donation clinic, and gender. The combined data provides the total population of persons presenting for whole blood donation in the year 2000.

We used the 9 years of previous donation records for BCP from the REDS dataset to confirm repeat donation status for any person deferred during the pre-donation assessment in the year 2000. If first time versus repeat donor information was missing and we could not verify previous donation using the REDS data, we classified a donor as a first time donor. Also, we classified presenting donors who were temporarily deferred prior to donation as first time donors until they were able to donate a sufficient quantity of blood because these blood sample provide the first opportunity for disease marker screening.

The donation cycle is a useful framework for analyzing blood donation records. James and Matthews describe the cycle as a series of four steps: initiating a donation attempt, a

mandatory deferral period, an elective interval, and subsequent donation attempt.[8] We believe 'initiating a donation attempt' is more clearly described as 'presenting for donation'. The mandatory deferral period results from either a successful blood donation, the presence of a deferrable characteristic prior to donation, or a positive test result after donation. The elective period is the time after a mandatory deferral where a donor is again 'at risk' for donating. A donor who presents again for donation completes the last cycle and begins a new cycle. With donation records linked by unique donor identification numbers, this framework allows for use of time-to-event analysis techniques in evaluating blood donation patterns. We generalized this framework to a cross-sectional format in order to determine donation and deferral frequencies within demographic groups as opposed to individual donor experiences.

After combining the REDS and donor deferral datasets, we obtained a total of 113,739 presenting donor records for allogeneic donors in 2000. This number includes donors who presented for donation more than once in a single 2-month period. Records for donors with multiple visits within a given cycle were collapsed to a single record based on the following hierarchy; a successful donation took precedence over all other records, a permanent pre-donation deferral record took precedence over a long- or short term deferral, and a long term deferral took precedence over a short term deferral. For example, only the record corresponding to a successful donation remained in the analysis file if the donor presented multiple times within a given 2-month period. Likewise, if a donor had multiple reasons for deferral in a 2-month period with no successful donation, the donor record corresponds to the reason resulting in the longest deferral. In this way, for each 2-month cycle, a given donor's record corresponds to the most important donation event, with successful donation considered the most important event.

Donor return information for 919 short term temporary deferrals was lost by collapsing the donor records into single records for each 2-month interval. The 2-month time interval corresponding to the mandatory 56-day deferral is the most appropriate interval to use for

assessing the sufficiency of the blood supply because this time interval establishes the theoretical limit for the maximum amount of whole blood that could be donated by an individual in one year. The total number of whole blood donor records obtained was 112,820 in the year 2000.

Missing information

After using the entire REDS dataset to inform missing values in the deferral dataset, the data sources for the project were largely complete with little remaining missing information. We did not impute information for missing values. Information was missing for 162 records. For example, the number of unknown values for sex was 148 (140 missing, 8 not reported) out of 112,820 records, or 0.13% missing information for sex. Missing sex information was mostly restricted to the 55 years and older age group, accounting for 84.5% of the missing sex values. Within the 55 years and older age group the percent missing sex information is only 0.52%. In addition, the number of missing values for age or birth date was 14. These 162 records with missing information were excluded from the dataset, leaving 112,658 records with complete information on all variables used to estimate parameters for the model. The large sample size coupled with relatively few missing values (well under 10% missing) justified our exclusion of these records.[18]

Data Sources and Analysis – Costs

Year 2000 expenses for BCP were provided in a separate dataset and were used to calculate the total and per blood unit costs for activities required to produce a supply of blood. We used process costing to estimate the average unit cost of producing whole blood from the societal perspective for Northern California. Process costing uses average cost estimates from specific categories to estimate unit costs applicable to large numbers of similar items.[19] Our overall cost object was the number of transfusable units of whole blood cleared for release to medical providers in the year 2000. We calculated the total cost of blood supply production

assuming a steady state so that it was unnecessary to consider beginning or ending inventories, using methods similar to previous blood unit costing studies.[20,21]

We identified seven cost categories at BCP: (1) donor recruiting and selection, (2) donation collection, (3) processing and screening, (4) unit distribution, (5) research and development, (6) blood and blood component purchases, and (7) general and administration. Direct blood supply production costs consist of categories (1) through (4): donor recruiting and selection, donation collection, donation processing and screening, and donation distribution. Data were not available for costs incurred by blood donors, so we estimated per donor and total costs using the human capital method.[22,23]

The cost data available to us did not differentiate between fixed and variable costs. We separated blood bank cost data into direct costs and cost requiring allocation, such as general and administration costs. The costs we could trace to specific aspects of blood supply production were classified as direct costs and tabulated in the appropriate category. To estimate costs that we could not trace directly, we created cost pools for each activity. We used stand-alone allocation so that each of the six other blood bank cost categories were allocated proportionate general and administrative costs based on the total costs incurred within each of these individual categories. To determine unit costs we used appropriate allocation bases that reflect the total number of donors or donations in each step of blood supply production. We traced screening costs based on laboratory charges submitted to BCP from the centralized Blood Systems laboratories. This ensures that costs from different blood banks within Blood Systems are assigned costs related to the total units submitted for screening and not transfusable units produced.

The sum of direct and allocated costs represents the total production cost from the blood bank perspective. We did not allocate research and development to the four supply production categories because research and development activities are funded through separate mechanisms of support. We did not allocate blood and blood component purchases from outside sources to the

four supply production categories because these purchases are funded through payments from health care providers that directly cover the cost of blood from other U.S. blood suppliers.

To estimate a donor's cost to donate, we used the human capital method in preference to other methods, such as friction-cost.[24] Using this method, we determined unit cost values and then back calculated to obtain total cost estimates for all donors. Activity times in the donation process come directly from encounter data at BCP (unpublished data provided by Dr. Nora Hirschler, CEO and Medical Director BCP, January 2003). The mean donation time was approximately 47 minutes. Donor registration and evaluation take approximately 15 minutes, with donation and recovery averaging 32 minutes. As BCP does not collect data on travel time to and from donation clinics, we assumed the average travel time to and from a donation clinic of 30 minutes total (15 minutes each way). This assumption was applied to travel to both mobile and fixed donation clinics. We defined two categories of donor cost: (1) donor presentation, including travel, registration and pre-donation evaluation, and (2) donation and recovery. Based on the April 2000 National Compensation Survey, the mean hourly wage rate is $22.06 for the San Francisco – Oakland – San Jose Area.[25] This estimate includes straight time, incentives, and hazard pay, but does not include benefits, overtime or vacation.

Analysis Software

All REDS and deferral dataset management and analysis was performed using Stata 7.0, (Stata, College Station, TX). We used S-Plus 2000 (Insightful, Seattle, WA) to produce stratified figures (i.e., Trellis Plots). We used a computer spreadsheet program (Excel, Microsoft, Redmond, WA) to calculate total and unit costs. The community blood supply model is an Excel workbook model. Simulation modeling is conducted using @Risk 3.5 (Palisade, Newfield, NY.) For each Monte Carlo simulation we ran 1000 iterations to estimate 95% confidence ranges for uncertainty in outcomes and costs.

Results – Descriptive Epidemiology of Blood Donation to Blood Centers of the Pacific

The demographic characteristics of persons presenting for allogeneic whole blood donation to BCP are provided in Table 2.1. Females present as first time donors more frequently than males, whereas for repeat donors, males present more frequently than females. Presenting donors are well represented across all ages, with first time donation more common in ages younger than 40. Persons younger than 40 years are 69% of all first time donors. The frequency of presenting repeat donors increases with age, and persons between the ages of 40 and 54 are the most common repeat presenters, comprising 40% of all repeat donors.

The frequency of first time versus repeat donors for both sexes and each age group are provided in Table 2.2. Both age group percentages and within age group percentages for first time compared to repeat donors are provided. Figure 2.6 provides a graphic display of much of the same donor presentation frequencies. Similar to Figures 2.2 through 2.5, the day of donor presentation, on the horizontal axis, is a continuous measure from 1 to 365 over the course of year 2000, and is plotted against the donor demographic group. Likewise, within each demographic group, donor presentation events are jittered vertically in order to display the number of donors who presented within that demographic group on each day of the year. The upper panel of the figure provides the pattern of presentation for first time donors and the lower panel provides the same information for repeat donors. For males and females between the ages of 16-24, a seasonal pattern is evident. For this age group, donor presentation is less likely during the summer when school is not in session and school-based blood drives are not conducted. This seasonal pattern is observed for both first time and repeat donors. For all other age groups, a seasonal component is not evident based on frequencies alone. The relative number of persons who present for donation within each demographic group is also evident in the figure. For 16-24 year old males and females, the first time and repeat donor number are not markedly different. However, for all other

sex and age groups, repeat donors are more common than first time donors, with fewer first time donors evident in persons age 55 years or older.

The observed presenting donor eligibility and pre-donation deferral frequencies are provided in Figure 2.7 using the same format as in previous plots. In this figure, the numbers of eligible and deferred donors within in each demographic group are plotted against the visit day. The plots show within each demographic group more donors are classified as eligible to donate than deferred for any reason. In addition, for all demographic groups short term temporary deferrals are the next most common event. However within, short term deferrals (the second column of panels) it is evident that for all age groups women are more likely to receive short term temporary deferrals than men regardless of first time or repeat donor status. Low hematocrit is the main reason women are more likely to receive short term temporary deferrals.

Tables 2.3 and 2.4 provide the overall probabilities of each pre-donation classification for the entire year. Detailed tables (Tables 2.5 through 2.10) describe the most common reasons for deferral within each demographic group based on pre-donation classification group.

We also estimated the probability that donors who attempt to donate are unable to do so. Attempted donation is terminated when a donor faints or if the phlebotomist is unable to obtain venous access. These persons are temporarily deferred because they are otherwise eligible to donate but unsuccessful in the attempt. We wanted to separate these temporary deferrals from other temporary deferrals based on behavioral or physical characteristics present at the time a person presents for donation. For all demographic groups, unsuccessful donation is uncommon accounting for less than one percent in any groups (data not shown).

In the blood screening component of the community blood supply model we use all screening results to determine the number of donated blood units that screen positive for any disease marker, except alanine aminotransferase (ALT). ALT screening is non-specific, and an elevated ALT result alone is rarely sufficient to lead to unit deferral without suspected or

confirmed infection. A single positive test on any other screen leads to unit interdiction. Whereas, negative screens for all tests allow the blood bank to clear the donated unit for release to health care providers.

The results of blood screening by demographic group are provided in Table 2.11. The occurrence of multiple positive screens is uncommon. It is most likely for HBV with both HBsAg and anti-HBc positivity. The total number of disease marker positive units was 1,061. Co-infections are rare. Out of 1,061 disease marker positive units, 44 were positive for 2 infectious agents, and 1 was positive for 3 infectious agents.

Figure 2.5, presented previously, is a plot of screening results for allogeneic whole blood for each donation day in year 2000 within each demographic group. Each panel represents an exclusive subset of the individuals who were able to donate a sufficient quantity of blood for screening. Disease marker positive blood donations are more common in the 25-39 and 40-54 year old demographic groups. A difference in disease marker positivity is not evident between genders within each age group. This lack of gender difference within each age group is also evident in repeat donors. However, as expected, the plots demonstrate that disease marker positivity is more common in first time donors than repeat donors – the count of positive blood units is greater in first time donors even though the total number of first time donors is lower in age groups greater than 16-24 and approximately equivalent to the number of repeat donors in the 16-24 age group.

Incomplete collection is determined by weight or volume of each collection, and represents an important step in blood supply production because a large number of blood units are prevented from entering the blood supply. These units are ineligible for release because the concentration of preservatives and anti-coagulants in the pre-loaded collection bags does not meet quality assurance requirements. Typically, the problem is under collection and not over collection. We assumed a 2 percent under collection probability for donations to BCP from all

demographic groups (personal communication, Dr. Bill Reed, Assistant Medical Director BCP, February 2003). For the donor, incomplete collection is treated in the same way as other whole blood donation and leads to a 56-day temporary donor deferral.

Results - Parameter Estimates for the Model

Outcome Parameters

Transition probabilities for the model are based on conditional probabilities estimated from BCP data. Within each demographic group and 2-month cycle of the model nine 'health outcome' probabilities are estimated:

1. Probability of being a first time donor (as opposed to repeat donor)
2. Probability a first time donor meets eligibility requirements
3. Probability a first time donor is able to donate
4. Probability a first time donor's blood unit screens negative for all disease markers
5. Probability a first time donor's blood unit meets quality assurance requirements
6. Probability a repeat donor meets eligibility requirements
7. Probability a repeat donor is able to donate
8. Probability a repeat donor's blood unit screens negative for all disease markers
9. Probability a repeat donor's blood unit meets quality assurance requirements

The nine cycle-specific probabilities lead to 54 probabilities for each demographic group over the course of the year and 432 'health outcome' probabilities in the core community blood supply model. In the Monte Carlo simulation of the model, the outcomes parameters are all assumed to follow beta–binomial distributions. Uncertainty is based on single sample binomial probabilities. These distributions are defined by two parameters, the count for the occurrence of event X, known as α, and the count for the occurrence of not X, known as β. By using the beta distribution, the probabilities are bound by the interval 0 – 1. The formulas for the beta distribution are:[26]

Mean = $\alpha / (\alpha + \beta)$

Standard Deviation = $\sqrt{\alpha \beta / (\alpha + \beta)^2 (\alpha + \beta + 1)}$

Cost Parameters

We assumed that the societal cost of whole blood production consists of direct blood bank costs and donor's cost to donate. Table 2.12 provides the cost contributor categories we used and summarizes the total and unit cost estimates. The cost parameters we estimated for the model are listed below. Parameters 1 through 5 are estimated from the BCP data.

1. Donor recruiting and selection cost
2. Donation collection cost
3. Partial collection cost (assumed to be ½ of collection cost for person's who are unable to donate due to fainting or inability to locate a vein for donation)
4. Processing and screening cost
5. Unit distribution cost
6. Blood unit interdiction and destruction (assumed to be $10 per unit)
7. Donor cost 1 (travel time and eligibility assessment – incurred at time of selection)
8. Donor cost 2 (time required to give blood – incurred at time of collection)

Because no estimate of uncertainty around the cost data was available, we used the following formula to estimate standard errors for cost parameters, assuming minimum and maximum values corresponding to +/- 10% of each estimated unit cost:

$se \approx (\text{upper value-lower value})/2 \times 1.96$.[26]

For the Monte Carlo simulation, we assumed normal distributions for all cost parameters because unlike the provision of other health care services the cost distributions are not skewed: Blood supply production costs are incurred for every donor and donation.

Overall Model

Outcomes results for each cycle of the model are aggregated within each demographic group and then summarized for the entire cohort (Table 2.13.) In the Monte Carlo simulation of the model, outcome parameter values are randomly drawn from each corresponding beta distribution, and the cost parameter estimates are randomly drawn from the prescribed normal distributions and applied equivalently to all donors or donations for each iteration of the simulation.

Discussion

Donor Epidemiology and Outcomes

Compared to first time donors, repeat donors are more likely to be white. This is consistent with overall trends reported by REDS, of which BCP is a part.[27] The population of persons who present for donation are similar to the population structure of the counties in which BCP donors reside. Both the racial and age distributions of the presenting donor population are consistent with State of California estimates for the counties in which BCP operates.[28]

Our ability to use the previous 9 years of REDS data to inform first time and repeat donor status only applies to persons who resided in the BCP donation catchment area during the 1991-2000 time period. Persons who previously donated in other locales or immigrated into the BCP catchment in the year 2000 and presented for donation may be misclassified as first time donors. However, it is unlikely persons would be misclassified as a repeat donor if they are true first time donors.

The deferral and disease marker screening results based on age and sex observed in the data are consistent with previously published studies.[27,29-31] Although the available literature on pre-donation deferrals is sparse and reflects deferral criteria from over 10 years ago, Linden and colleagues estimated pre-donation deferrals for Connecticut. Their results also indicate pre-donation deferrals are more common for women than men.[32] Halperin and colleagues considered the impact these deferrals have on donor return behavior and found that donors receiving short term temporary deferrals for conditions, such as low hematocrit, colds, or elevated temperatures, were 29% less likely to present for donation again, compared to donors who did not receive the temporary deferrals.[33] More importantly, the cumulative impact on the blood supply is that temporary deferrals lead to unit yields of 1.03 units/year/donor compared to 1.43 units/year/donor in non-deferred donors over a 4.25 year period of observation. These observations substantiate the importance that pre-donation deferrals ultimately have on the supply of blood available.

A fundamental question for blood banks is what is the actual size of the population of adults who are eligible to donate? In a recent editorial, Jones highlighted the need to understand the population of persons who meet eligibility criteria even if they are not donors.[34] This population establishes the true potential supply of blood that could be available. Previous studies that sought to define this population are becoming dated. In 1988, Linden and colleagues estimated that 57% of women and 70% of men from Connecticut would be eligible to donate based on interview and medical deferral criteria at the time.[32] These results appear to have established the often stated figure that 60% of the U.S. adult population is eligible to donate. However, at this time it is unclear what the true size of the donor pool is.

A further issue is the importance of under collection. Although the issue is well known in blood banking, quantitative estimates of the importance are lacking. One older study suggests that, on average, under collections account for as much as 2.5 to 3.5% of units donated.[35] However, AuBuchon indicated that under collections in high school blood drives may be as high as 6%.[36] The potential impact is not trivial. Under collections at high school blood drives may set a precedent in the minds of young donors, thus establishing a barrier to repeat donation. The model allows for different under collection probabilities for the eight demographic groups (data for each demographic group not available from BCP at this time). Overall, if under collections continue to be as common at other blood centers as they are at BCP, then as many as 280,000 donated blood units out of approximately 14,000,000 collected in the U.S. every year are lost regardless of disease marker screening results.

Cost Estimates

BCP expenditure data included detailed cost categories. However, the categories did not differentiate between the types of donors: allogeneic, autologous, directed, or donations: whole blood and pheresis. We determined unit cost estimates for all of these types of donors and donations combined. While there is no reason to expect cost differences based on the type of

donor, we believe whole blood and pheresis donations may not have the same costs. We suspect whole blood would be less expensive to collect than pheresis donations because of the greater reliance on technology for pheresis donations. It is possible our cost estimates for whole blood donations are higher than they would be if we could separate whole blood and pheresis costs. However, the number of whole blood donations in the year 2000 was much larger than pheresis donations (122,452 whole blood donations from all types of donors and 18,127 total plateletpheresis and plasmapheresis donations), so the magnitude of any potential cost difference between whole blood and pheresis collection is not expected to overwhelm our cost estimates.

We did not determine the cost of component production or the cost of outdates. The purpose of the costing study was to assess the cost of producing a supply of blood. The processing cost implicitly includes component preparation costs, which may elevate the apparent cost of obtaining one unit of whole blood from a donor. The data provided by BCP listed multiple cost contributors within each of the four supply production categories. However, the available cost data at BCP did not provide specific items for the costs incurred in the production of each component. The issue of blood component production costs is very complex. Costing these products requires the consideration of what are called joint costs. Joint production costs are costs incurred in a single production process that results in two or more distinct outputs. Jacobs and colleagues have addressed this issue for the blood supply.[37] To fully measure the cost of each type of blood component at BCP would require a study specifically designed to measure how much time and resources are consumed in the production of each component. Such a project would be extremely valuable, but was beyond the scope of the costing activity required for the development of the community blood supply model.

Model Results and Validity

For any mathematical model, it is important to measure how well the model can predict the set of outcomes intended to be captured by the model.[38] At the general level, the model should

make sense to persons familiar with the problem the model addresses. We believe our model captures the important steps in the production of a supply of whole blood.

However, further model validation is important for establishing the usefulness of a model.[39,40] Russell re-iterates much of the work of Eddy regarding effectiveness or outcomes validity, and also extends this formal approach to cost parameters in models. Our model uses the observed proportion of presenting donors in each demographic group to establish the initial age and sex structure of the cohort. Therefore, when the initial presenting donor population is set to 112,658, the number of presenting donors in our dataset, the model should track the experience of these presenting donors. If the model captures reality, the same mean number of presenting donors should be obtained from the model as observed in the data set. Table 2.14 compares the number of events observed in the data sources and the number of events predicted by the model. When the initial cohort is set to 112,658, our model produces a summary output for 112,658 presenting donors, and counts of other important outcomes closely correspond to those observed in the data.

Likewise, the number of donations cleared for release predicted by the model should correspond to the number that BCP reports were actually cleared for release in the year 2000. In this case, the model predicts 96,814 blood samples were submitted for screening. This number includes both complete collections and under collections.

In our model we count any disease marker positive result as sufficient to defer a donor and blood unit. In reality, confirmation testing is used and can re-instate a donor if confirmation testing is negative, allowing the opportunity to donate again at a later time. Although the unit subjected to confirmatory testing is deferred regardless of the result. There were a total of 153 confirmed negative blood units, so the bias is inconsequential.

Our use of the 2-month interval in the model also means that we undercount the number of units donated by the most dedicated donors. If donors repeat donation after the 56-day

mandatory deferral, but before the start of the next 2-month period, these donations are not included in our model. The total number of donations after the mandatory 56 days, but before the start of the next cycle was 378. When both the confirmed negative units and units lost due to the cycle are combined with the model results, we can account for 97,345 blood units. This number is difficult to verify. Two different sets of administrative records from BCP indicate 99,449 and 96,307 allogeneic whole blood donations, respectively, in the year 2000. Our result falls between these two values, and while this does not provide validation for our model, it does suggest the model is reasonably consistent with administrative records.

With regard to cost parameters for the model, there is no way to verify the cost estimates by comparison to other BCP data. Previous efforts to estimate the cost of blood donation are available in the literature. The studies by Guest and colleagues, and Tretiak and colleagues provide societal cost estimates for the United Kingdom and Canada, respectively. The unit cost estimates include different parameters such as the cost to administer blood, but the direct blood bank costs are the same order of magnitude when transfusion costs are excluded (£58 and CAN$210). U.S. costs have been estimated for other economic evaluation studies, but never from a societal perspective. The cost of a blood unit ranges from as low as $67 to as high as $398.[14,41-45] All of these studies assessed cost from the hospital perspective (purchasing and transfusing blood), not the blood bank perspective. Some of these cost estimates include the cost of unintended consequences of transfusion-transmitted infections. BCP expenses do not capture transfusion-transmitted infection costs, and the hospital perspective used for all transfusion costing studies does not address the same issues as the blood bank perspective. The focus of the hospital perspective is the delivery of transfusion in the hospital, and typically uses health care provider's acquisition cost for obtaining blood from blood banks as opposed to cost of producing the supply of blood.

As estimated from the expenditure data, observed and modeled direct blood bank unit costs of whole blood are nearly $190 and $198, respectively. Once again, the observed cost includes units that may not meet quality requirements. The modeled cost is higher, but consistent with the observed unit cost. The unit costs to acquire useable units of blood may seem elevated, yet BCP total cost of services for the year 2000 was $29,085,000, with $24,058,000 attributable to all whole blood. The total cost estimated from the model for allogeneic whole blood donation is $18,570,000, leaving approximately $5,500,000 attributable to 10,000 autologous and directed whole blood collections, and nearly 25,000 blood imports from other U.S. blood banks.

The model was developed using outcome and cost data specific to Blood Centers of the Pacific. The generalizability of the model will need further investigation. The prevalence of pre-donation deferrals and the likelihood of disease marker positive tests may not be the same in other U.S. regions. In addition, BCP operating costs likely do not apply to other settings. Wage rate and real estate costs in the San Francisco Bay Area are high compared to other parts of the country. Also, California requires a licensed nurse to be present at all donation locations. In addition, BCP is a net importer of blood from other regions in the U.S. The cost of recruiting and maintaining donors is expected to be higher for BCP than other locations because it cannot provide a sufficient supply of blood to health care providers using local donors. Thus, imports from other U.S. locales ensure that San Francisco and nearby communities have a sufficient supply of blood for health care procedures. With expanded data sources, the model parameters can be updated to address issues at specific locales or increase generalizability to other settings.

We believe this model can be used to evaluate new donor and donation deferral requirements. Our model can explicitly tally eligible donors, deferred donors, units produced, units deferred, and the costs incurred under different strategies. The model permits the consideration of both the lost supply and cost incurred in maintaining the supply at current levels. Recently adopted policies, such as the expanded European travel deferrals for variant Creutzfeldt-

Jakob disease or new screening requirements, such as screening for West Nile Virus can be evaluated using this model. In particular, this model provides the opportunity to more rigorously consider the impact of pre-donation deferrals than previously existed.

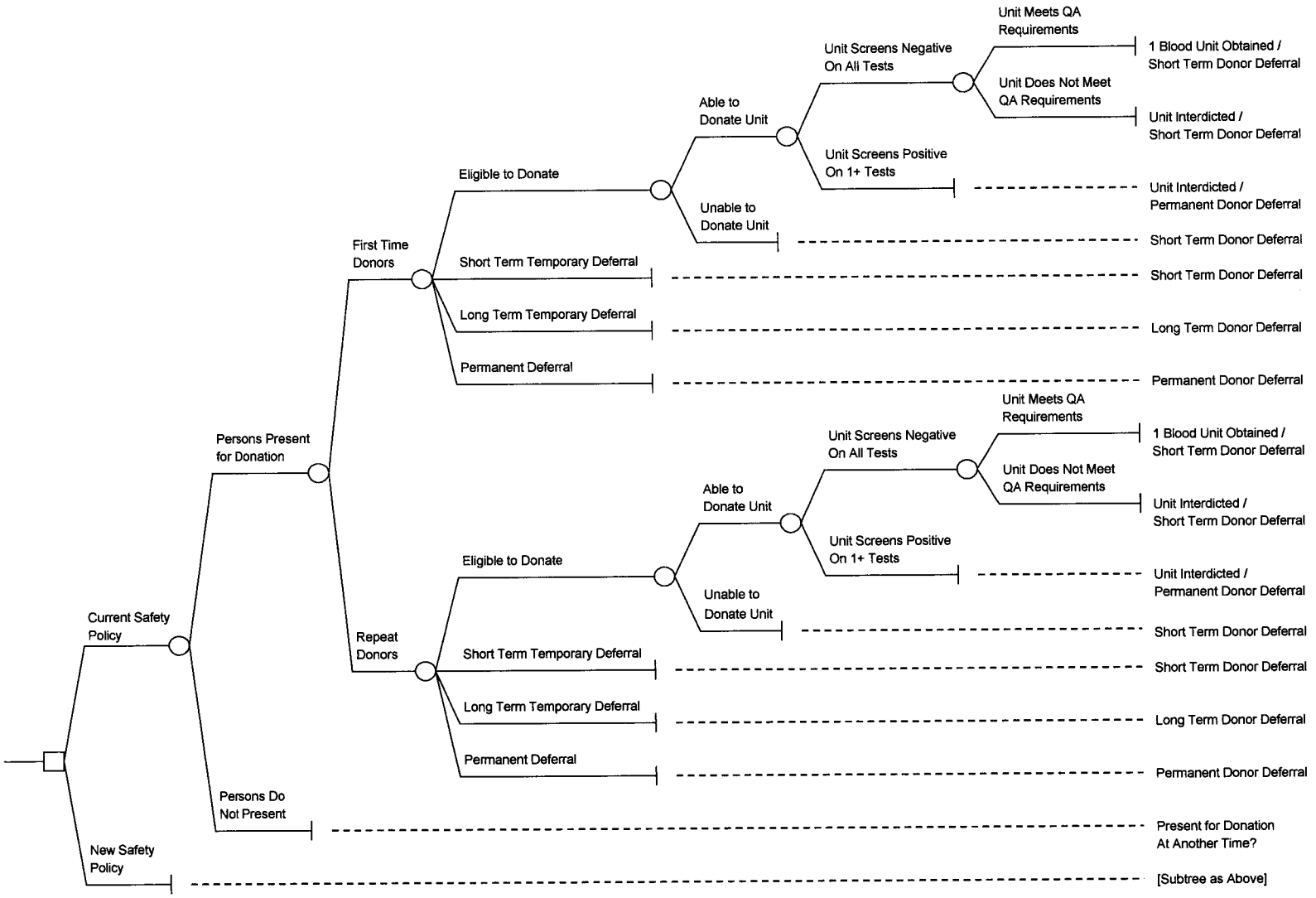

Figure 2.1 Core structure of the community blood supply model displayed using a decision tree framework

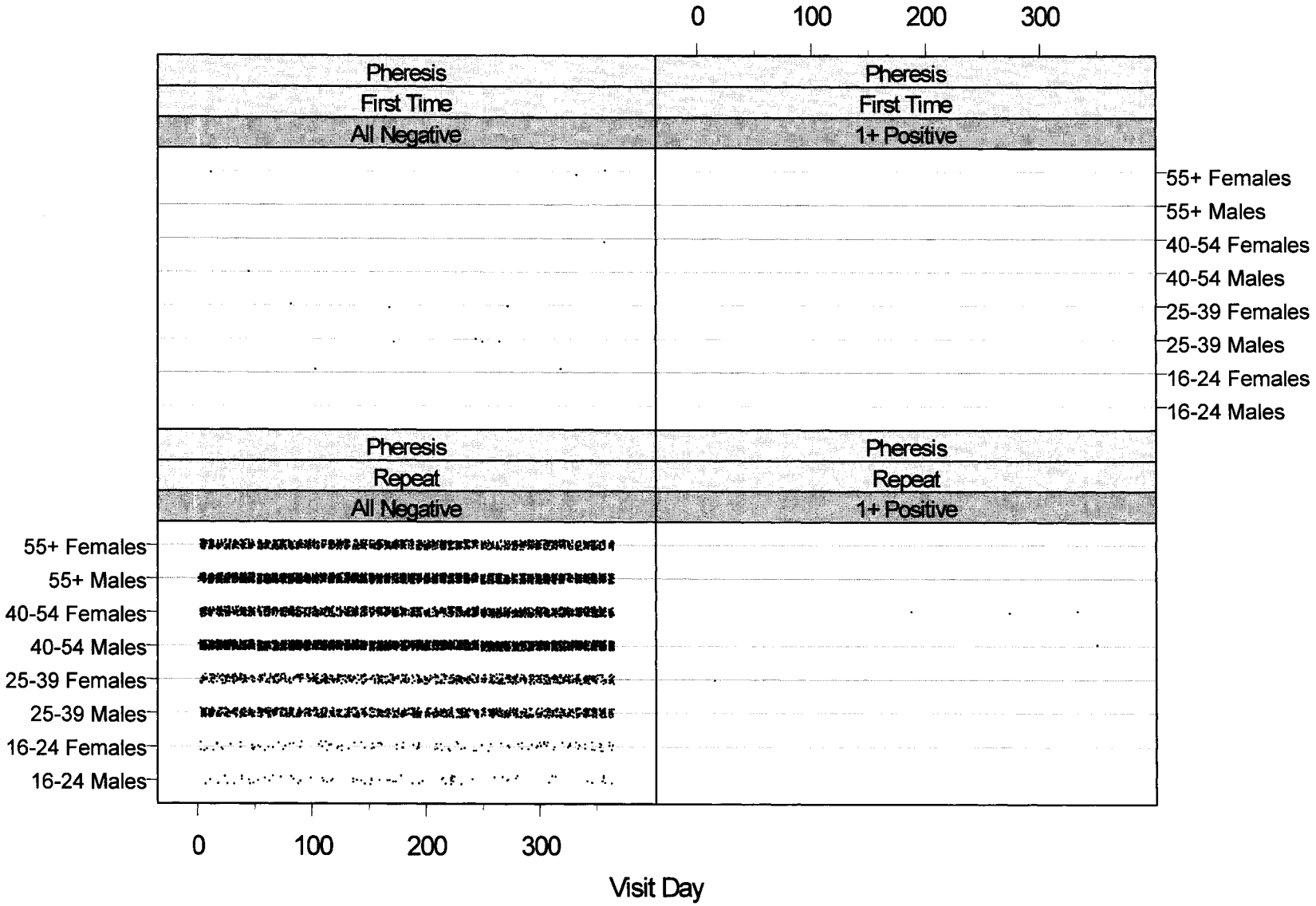

Figure 2.2 Pheresis donation screening results in the year 2000

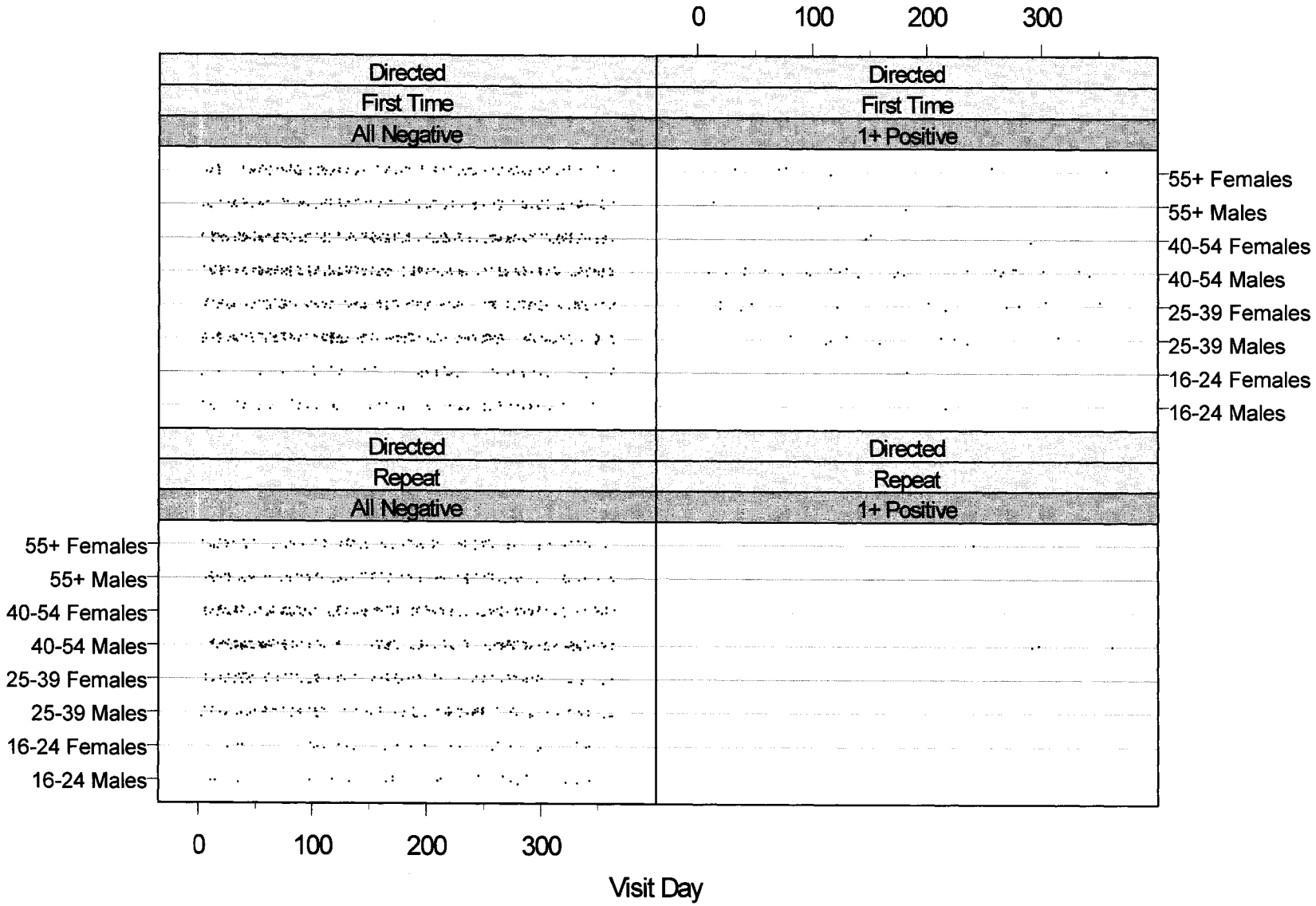

Figure 2.3 Directed donation whole blood screening results in the year 2000

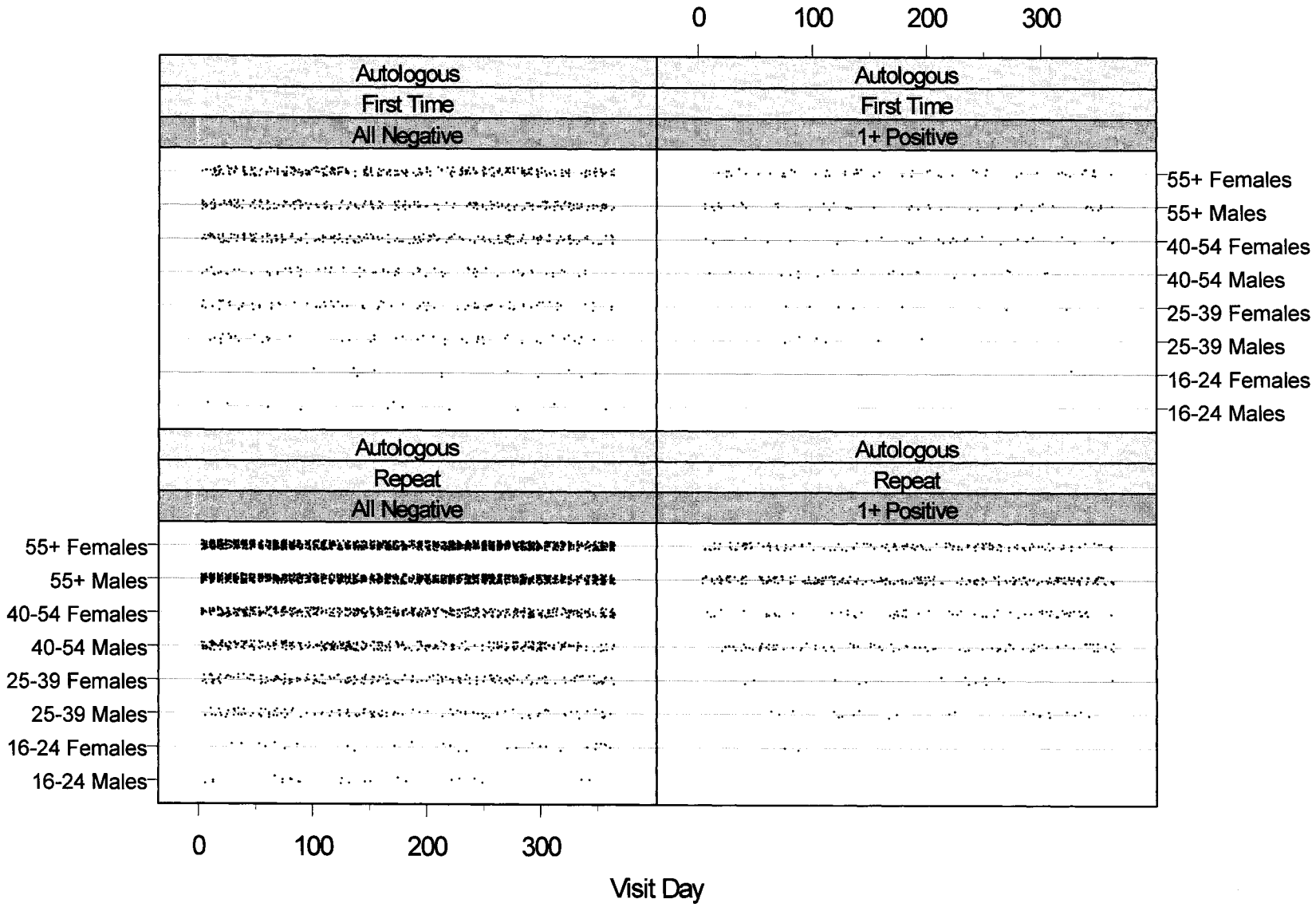

Figure 2.4 Autologous whole blood screening results in the year 2000

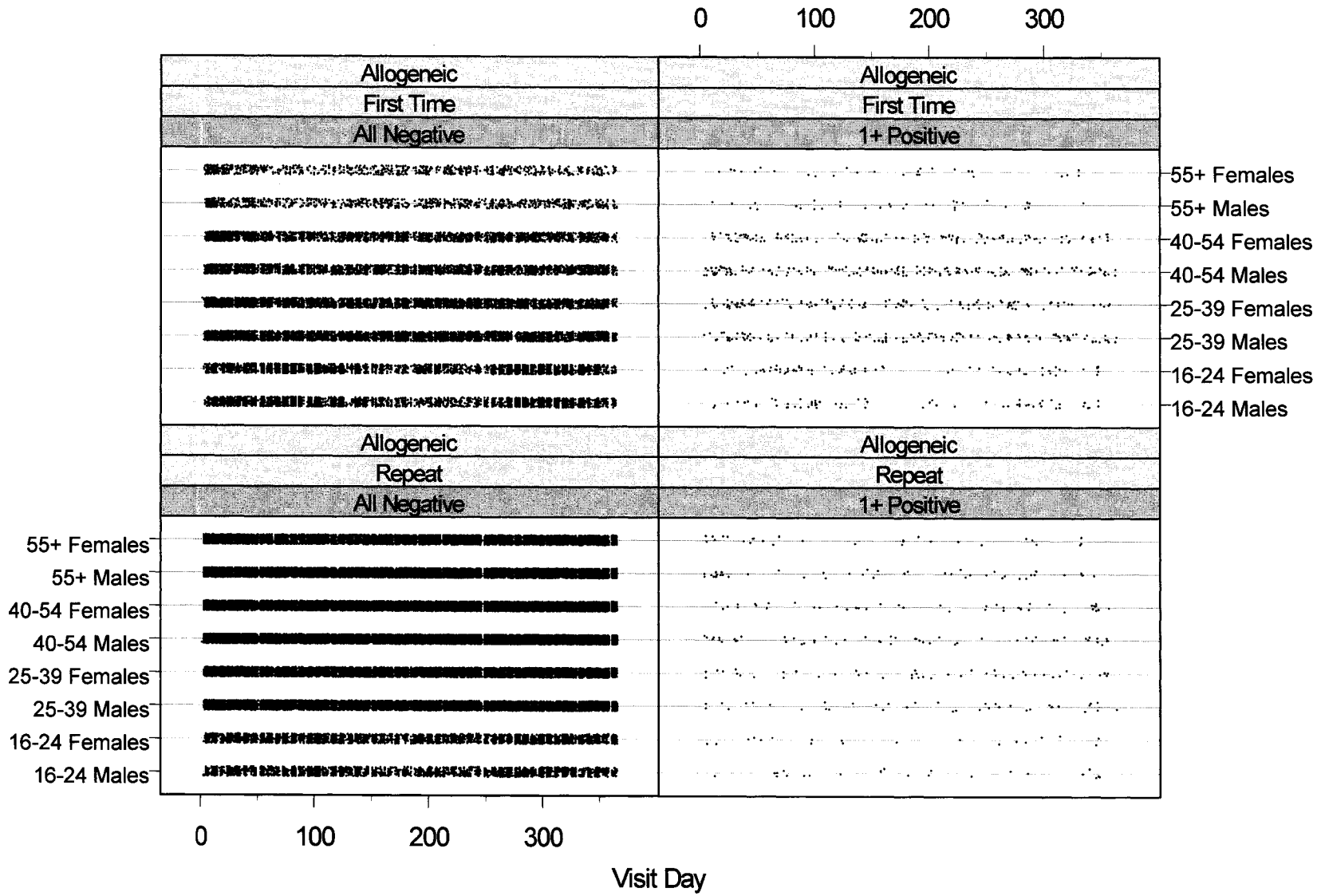

Figure 2.5 Allogeneic whole blood screening results in the year 2000

Table 2.1 Characteristics of persons presenting for voluntary whole blood donation at Blood Centers of the Pacific in 2000.

Characteristic	Overall Number (%)	First Time Donors Number (%)	Repeat Donors Number (%)
Sex			
Male	56,904 (50.5)	14,340 (45.8)	42,564 (52.3)
Female	55,754 (49.5)	16,981 (54.2)	38,773 (47.7)
Age Group			
16-24 years	18,146 (16.1)	10,540 (33.6)	7,606 (9.3)
25-39 years	31,211 (27.7)	11,144 (35.4)	20,067 (24.7)
40-54 years	39,733 (35.3)	7,240 (23.0)	32,493 (40.0)
55+ years	23,562 (20.9)	2,392 (8.0)	21,170 (26.0)
Race/Ethnicity			
White	89,852 (79.8)	21,132 (67.5)	68,720 (84.5)
Black	3,920 (3.5)	1,725 (5.5)	2,195 (2.7)
Asian/Pacific Island	9,334 (8.3)	4,219 (13.5)	5,115 (6.3)
Native American	795 (0.7)	266 (0.8)	529 (0.6)
Other/Unknown	8,381 (7.4)	3,689 (11.8)	4,692 (5.8)
Missing	376 (0.3)	290 (0.9)	657 (0.1)

Table 2.2 Summary first time and repeat presenting donor frequencies by age and sex

Age Group	Males						Females						Overall					
	First Time	*(col. %)*	Repeat	*(col. %)*	Total	*(col. %)*	First Time	*(col. %)*	Repeat	*(col. %)*	Total	*(col. %)*	First Time	*(col. %)*	Repeat	*(col. %)*	Total	*(col. %)*
16-24	4,442	*31.0*	3,027	*7.1*	7,468	*13.1*	6,099	*35.9*	4,579	*11.8*	10,678	*19.1*	10,540	*33.6*	7,606	*9.3*	18,146	*16.1*
(row % by sex)	59.5		40.5				57.1		42.9				58.1		41.9			
25-39	5,226	*36.4*	9,615	*22.6*	14,838	*26.1*	5,922	*34.9*	10,452	*26.9*	16,373	*29.4*	11,144	*35.4*	20,067	*24.7*	31,211	*27.7*
(row % by sex)	35.2		64.8				36.2		63.8				35.7		64.3			
40-54	3,414	*23.8*	17,343	*40.7*	20,756	*36.5*	3,826	*22.5*	15,151	*39.1*	18,977	*34.0*	7,240	*23.0*	32,493	*40.0*	39,733	*35.3*
(row % by sex)	16.4		83.6				20.2		79.8				18.2		81.8			
55+	1,258	*8.8*	12,579	*29.6*	13,837	*24.3*	1,134	*6.7*	8,591	*22.2*	9,725	*17.5*	2,392	*8.0*	21,170	*26.0*	23,562	*20.9*
(row % by sex)	9.1		91.0				11.7		88.3				10.2		89.8			
Total	14,340		42,564		56,904		16,981		38,773		55,754		31,231		81,337		112,658	
(row % by sex)	25.2		74.8				30.5		69.5				27.8		72.2			

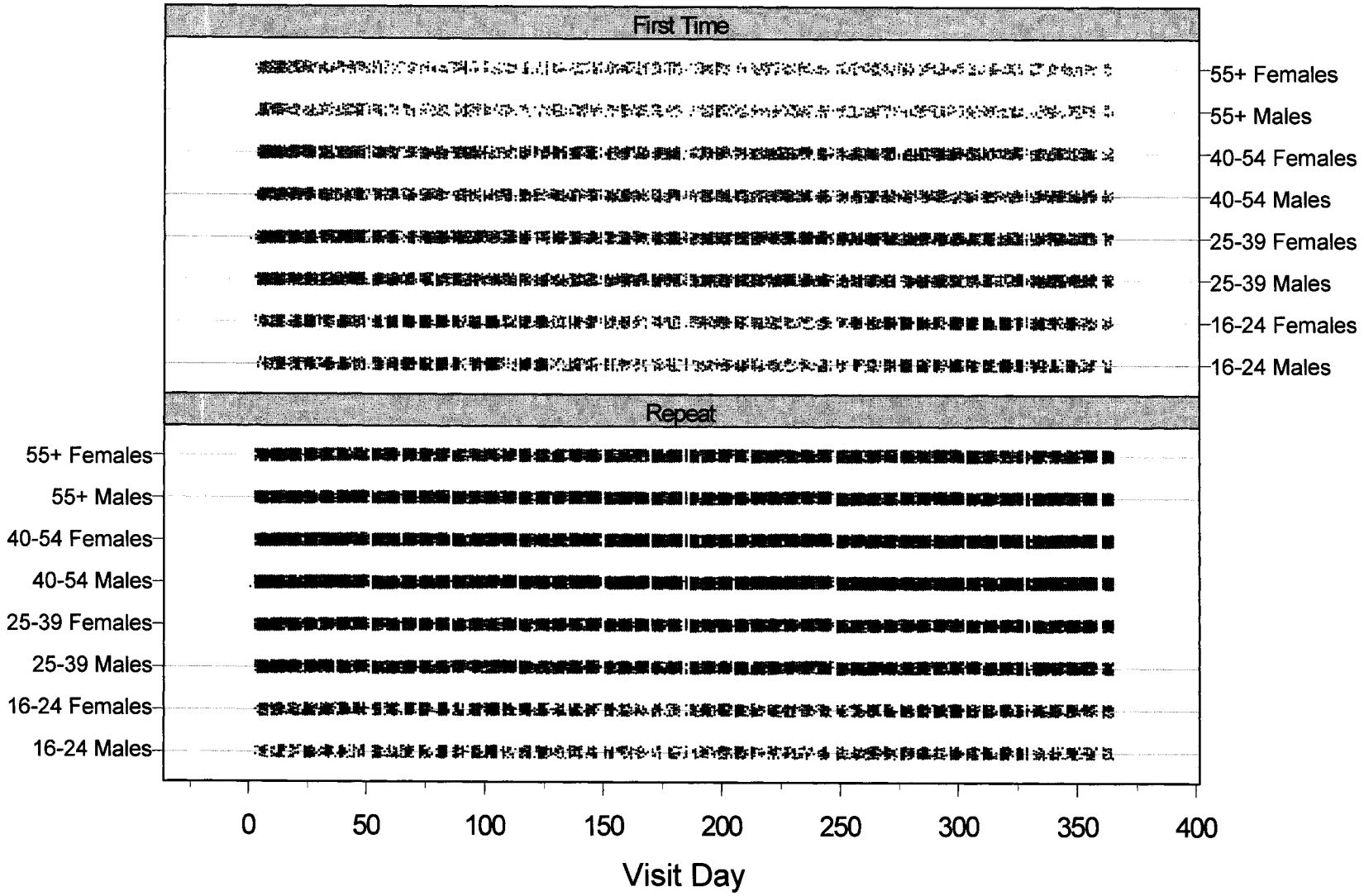

Figure 2.6 First time and repeat donor presentation

Table 2.3 Summary pre-donation classification probabilities in first time donors

Demographic Group	Eligible		Short Term		Long Term		Permanent	
	Number	Probability	Number	Probability	Number	Probability	Number	Probability
Males Age 16-24	3,774	0.8429	332	0.0747	305	0.0687	61	0.0086
Females Age 16-24	4,301	0.7052	1,295	0.2123	433	0.0710	70	0.0050
Males Age 25-39	4,382	0.8385	266	0.0509	321	0.0614	257	0.0122
Females Age 25-39	4,196	0.7085	1,188	0.2001	377	0.0637	161	0.0120
Males Age 40-54	2,888	0.8459	224	0.0656	151	0.0442	151	0.0055
Females Age 40-54	2,718	0.7104	837	0.2188	157	0.0410	114	0.0073
Males Age 55+	942	0.7488	112	0.0890	72	0.0572	132	0.0061
Females Age 55+	799	0.7046	216	0.1905	62	0.0547	57	0.0095

Table 2.4 Summary pre-donation classification probabilities in repeat donors

Demographic Group	Eligible		Short Term		Long Term		Permanent	
	Number	Probability	Number	Probability	Number	Probability	Number	Probability
Males Age 16-24	2,783	0.9194	114	0.0378	104	0.0343	26	0.0137
Females Age 16-24	3,629	0.7925	781	0.1706	146	0.0319	23	0.0115
Males Age 25-39	9,068	0.9431	225	0.0234	204	0.0212	118	0.0492
Females Age 25-39	8,499	0.8113	1,543	0.1706	285	0.0273	125	0.0272
Males Age 40-54	16,568	0.9553	456	0.0263	224	0.0129	95	0.0442
Females Age 40-54	12,838	0.8473	1,982	0.1476	220	0.0145	111	0.0298
Males Age 55+	11,939	0.9491	423	0.0336	140	0.0111	77	0.1049
Females Age 55+	7,525	0.8759	864	0.1006	120	0.0140	82	0.0503

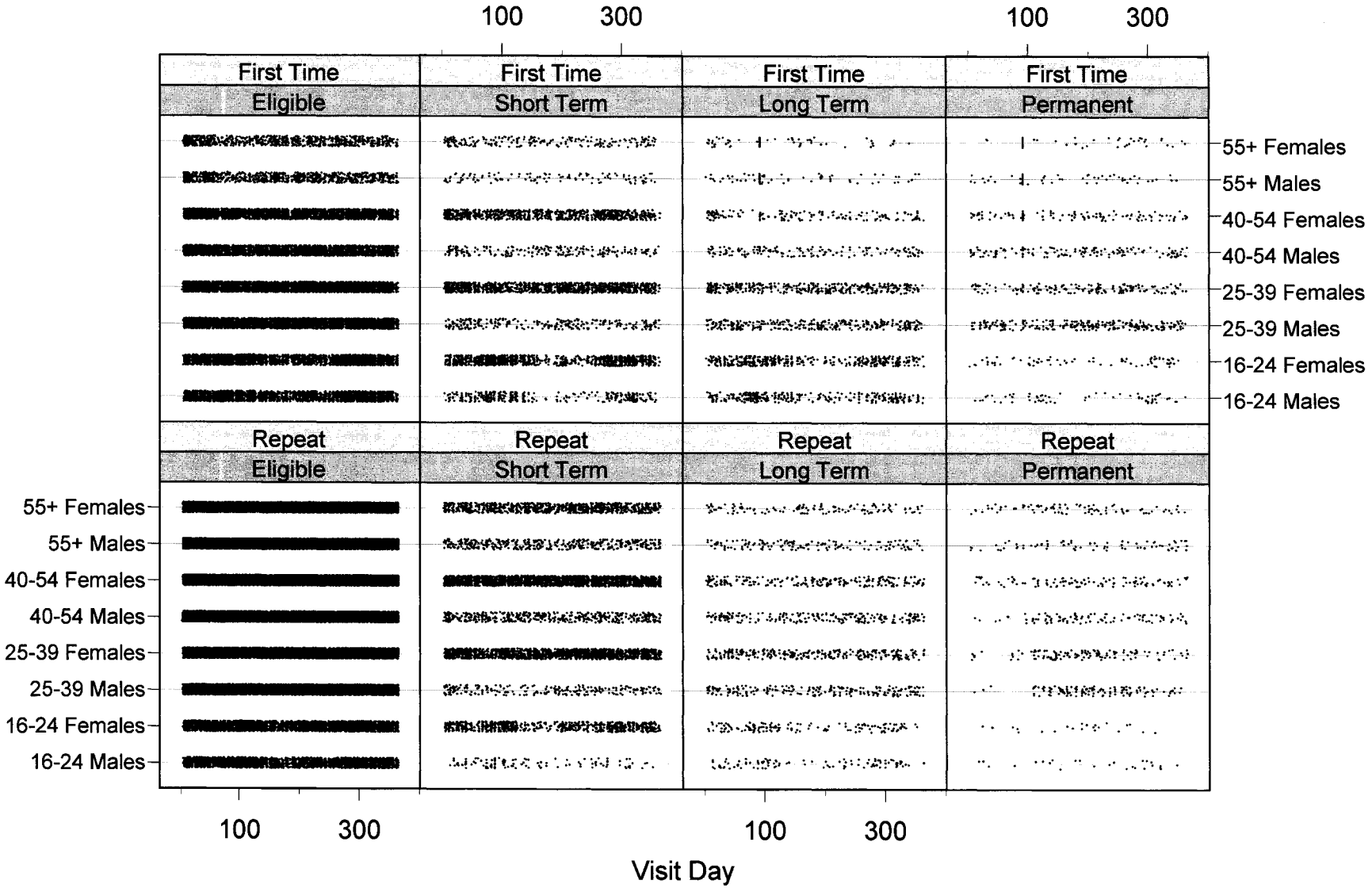

Figure 2.7 Pre-donation donor eligibility classification

Table 2.5 Reasons for permanent pre-donation deferral of males by age group

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	4,442	61	18 (29.5)	From Malaria endemic area	3,027	26	18 (69.2)	Previous UK travel / CJD risk
			15 (24.6)	Previous UK travel / CJD Risk			2 (7.7)	From Malaria endemic area
			13 (21.3)	HIV / AIDS related			2 (7.7)	Injection drug use
			15 (24.6)	All others			4 (15.4)	All others
25-39	5,226	257	81 (31.5)	Previous UK travel / CJD risk	9,615	118	97 (82.2)	Previous UK travel /CJD risk
			76 (29.7)	From Malaria endemic area			4 (3.4)	Hepatitis history
			37 (14.4)	HIV/AIDS related			3 (2.5)	From Malaria endemic area
			29 (11.3)	Hepatitis history			3 (2.5)	Injection drug use
			14 (5.5)	Injection drug use			11 (9.4)	All others
			20 (7.6)	All others				
40-54	3,414	151	38 (25.2)	Previous UK travel / CJD risk	17,343	95	66 (69.5)	Previous UK travel / CJD risk
			25 (16.6)	HIV / AIDS related			8 (8.4)	Anti-HBc positive
			22 (14.6)	Hepatitis history			3 (3.2)	Therapeutic donor /
			21 (13.9)	Injection drug use				Other blood disease
			17 (11.3)	Therapeutic donor /			3 (3.2)	Cancer related
				Other blood disease			3 (3.2)	HIV / AIDS related
			28 (18.4)	All others			12 (12.5)	All others
55+	1,258	132	87 (65.9)	Cancer related	12,579	77	23 (29.9)	Previous UK travel /CJD risk
			14 (10.6)	Hepatitis history			18 (23.4)	Cancer related
			10 (7.6)	Unspecified historical deferral			11 (14.3)	Anti-HBc positive
			5 (3.8)	Previous UK travel / CJD risk			5 (6.5)	Unspecified historic deferral
			16 (12.1)	All others			5 (6.5)	Heart / Lung / Liver / Kidney
							15 (19.4)	All others

Table 2.6 Reasons for permanent pre-donation deferral of females by age group.

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	6,099	70	29 (41.4)	From Malaria endemic area	4,579	23	14 (56.2)	Previous UK travel / CJD risk
			21 (30.0)	Previous UK travel / CJD Risk			5 (21.7)	HTLV Positive
			9 (12.9)	Hepatitis history			2 (8.7)	Injection drug use
			4 (5.7)	HIV / AIDS related			3 (13.4)	All others
			7(10.0)	All others				
25-39	5,922	161	71 (44.1)	Previous UK travel / CJD Risk	10,452	125	99 (79.2)	UK travel / CJD risk
			27 (16.8)	From Malaria endemic area			5 (4.0)	Cancer related
			19 (11.8)	Hepatitis history			4 (3.2)	HIV / AIDS related
			13 (8.1)	HIV / AIDS related			4 (3.2)	Anti-HBc positive
			12 (7.5)	Cancer related			13 (10.4)	All others
			19 (11.7)	All others				
40-54	3,826	114	29 (25.4)	Cancer related	15,151	111	47 (42.3)	Previous UK travel / CJD risk
			23 (20.2)	Previous UK travel / CJD risk			15 (13.5)	Anti-HBc Positive
			20 (17.5)	Hepatitis history			15 (13.5)	Cancer related
			13 (11.4)	Injection drug use			6 (5.4)	HIV / AIDS related
			11 (9.7)	HIV / AIDS related			28 (25.3)	All others
			18 (15.8)	All others				
55+	1,134	57	31 (54.4)	Cancer related	8,591	82	19 (23.2)	Cancer related
			4 (7.0)	Previous UK travel / CJD risk			17 (20.7)	Anti-HBc Positive
			3 (5.3)	Hepatitis history			15 (18.3)	Previous UK travel / CJD risk
			3 (5.3)	Anti-HBc positive			9 (11.0)	Unspecified historical deferral
			16 (28.0)	All others			22 (26.8)	All others

Table 2.7 Reasons for pre-donation long term temporary deferral of males by age group

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	4,442	305	142 (46.6)	Tattoo / Other needle exposure	3,027	104	48 (46.2)	Tattoo / Other needle exposure
			122 (40.0)	Travel to Malaria endemic area			43 (41.4)	Travel to Malaria endemic area
			24 (7.9)	Prison inmate			5 (4.8)	Prison inmate
			17(5.5)	All others			8 (7.6)	All others
25-39	5,226	321	220 (68.5)	Travel to Malaria endemic area	9,615	204	154 (75.5)	Travel to Malaria endemic area
			75 (23.4)	Tattoo / Other needle exposure			33 (16.2)	Tattoo / Other needle exposure
			11 (3.4)	Prison inmate			5 (2.4)	Unspecified hepatitis exposure
			7 (2.2)	Transfusion recipient			4 (2.0)	Transfusion recipient
			8 (2.5)	All others			8 (3.9)	All others
40-54	3,414	151	107 (70.9)	Travel to Malaria endemic area	17,343	224	170 (75.9)	Travel to Malaria endemic area
			19 (12.6)	Tattoo / Other needle exposure			20 (8.9)	Tattoo / Other needle exposure
			10 (6.6)	Unspecified hepatitis exposure			12 (5.4)	Transfusion recipient
			7 (4.6)	Heart condition			8 (3.6)	Unspecified hepatitis exposure
			8 (5.3)	All others			14 (6.2)	All others
55+	1,258	72	44 (61.1)	Travel to Malaria endemic area	12,579	140	105 (75.0)	Travel to Malaria endemic area
			22 (30.6)	Heart condition			19 (13.6)	Heart condition
			2 (2.8)	Tattoo / Other needle exposure			7 (5.0)	Transfusion recipient
			4 (5.5)	All others			5 (3.6)	Tattoo / Other needle exposure
							4 (2.8)	All others

Table 2.8 Reasons for pre-donation long term temporary deferral of females by age group

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	6,099	433	221 (51.0)	Tattoo / Other needle exposure	4,579	146	80 (54.8)	Tattoo / Other needle exposure
			162 (37.4)	Travel to Malaria endemic area			54 (38.3)	Travel to Malaria endemic area
			14 (3.2)	Unspecified hepatitis exposure			6 (4.1)	Prison inmate
			12 (2.8)	Prison inmate			2 (1.4)	Syphilis-related (temporary)
			11 (2.5)	High risk sexual partner			2 (1.4)	All others
			13 (3.1)	All others				
25-39	5,922	377	210 (55.7)	Tattoo / Other needle exposure	10,452	285	178 (62.5)	Tattoo / Other needle exposure
			130 (34.5)	Travel to Malaria endemic area			83 (29.1)	Travel to Malaria endemic area
			10 (2.7)	High risk sexual partner			11 (3.9)	High risk sexual partner
			10 (2.7)	Unspecified hepatitis exposure			5 (1.8)	Unspecified hepatitis exposure
			17 (4.4)	All others			8 (2.7)	All others
40-54	3,826	157	100 (63.7)	Travel to Malaria endemic area	15,151	220	152 (69.1)	Travel to Malaria endemic area
			33 (21.0)	Tattoo / Other needle exposure			38 (17.3)	Tattoo / Other needle exposure
			8 (5.1)	Unspecified hepatitis exposure			9 (4.1)	Unspecified hepatitis exposure
			6 (3.8)	High risk sexual partner			7 (3.2)	Heart condition
			10 (6.4)	All others			14 (6.3)	All others
55+	1,134	62	31 (50.0)	Travel to Malaria endemic area	8,591	120	85 (70.8)	Travel to Malaria endemic area
			18 (29.0)	Tattoo / Other needle exposure			18 (15.0)	Tattoo / Other needle exposure
			7 (11.3)	Heart condition			7 (5.8)	Heart condition
			6 (9.7)	All others			10 (8.4)	All others

Table 2.9 Reasons for pre-donation short term temporary deferral for males by age group

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	4,442	332	90 (27.0)	Couldn't wait / Second thoughts	3,027	114	22 (19.3)	Couldn't wait / Second thoughts
			58 (17.4)	Cold / Sore throat			21 (18.4)	Blood pressure or pulse related
			51 (15.4)	Blood pressure or pulse related			17 (14.9)	Cold / Sore throat
			38 (11.4)	Prescription medication			11 (9.6)	Temperature above 99.5
			95 (28.8)	All others			43 (37.8)	All others
25-39	5,226	266	80 (30.1)	Couldn't wait / Second thoughts	9,615	225	46 (20.4)	Couldn't wait / Second thoughts
			58 (21.8)	Blood pressure or pulse related			44 (19.6)	Blood pressure or pulse related
			38 (14.3)	Prescription medication			31 (13.8)	Prescription medication
			31 (11.6)	Cold / Sore throat			31 (13.8)	Low hematocrit
			27 (10.2)	Under physician care			26 (11.6)	Cold / Sore throat
			32 (12.0)	All others			47 (20.8)	All others
40-54	3,414	224	83 (37.1)	Blood pressure or pulse related	17,343	456	142 (31.1)	Blood pressure or pulse related
			52 (23.2)	Couldn't wait / Second thoughts			80 (17.5)	Low hematocrit
			24 (10.7)	Prescription medication			80 (17.5)	Couldn't wait / Second thoughts
			20 (8.9)	Low hematocrit			51 (11.2)	Under physician care
			17 (7.6)	Under physician care			41 (9.0)	Cold / Sore throat
			28 (12.5)	All others			62 (13.7)	All others
55+	1,258	112	36 (32.1)	Blood pressure or pulse related	12,579	423	143 (33.8)	Blood pressure or pulse related
			27 (24.1)	Couldn't wait / Second thoughts			94 (22.2)	Low hematocrit
			15 (13.4)	Under physician care			59 (14.0)	Under physician care
			12 (10.7)	Low hematocrit			53 (12.5)	Couldn't wait / Second thoughts
			12 (10.7)	Prescription medication			25 (5.9)	Cold / Sore throat
			10 (9.0)	All others			49 (11.6)	All others

Table 2.10 Reasons for pre-donation short term temporary for females by age group

Age Group	First Time Donors				Repeat Donors			
	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason	Presenting Donors	Total Number of Deferrals	Frequency by Reason (%)	Deferral Reason
16-24	6,099	1,295	661 (51.0)	Low hematocrit	4,579	781	576 (73.7)	Low hematocrit
			170 (13.1)	Couldn't wait / Second thoughts			59 (7.6	Blood pressure or pulse related
			129 (10.0)	Blood pressure or pulse related			45 (5.8)	Couldn't wait / Second thoughts
			66 (5.1)	Temperature above 99.5			22 (2.8)	Cold / Sore throat
			64 (4.9)	Underweight			21 (2.7)	Temperature above 99.5
			64 (4.9)	Cold / Sore throat			58 (7.4)	All others
			141 (11.0)	All others				
25-39	5,922	1,188	750 (63.1)	Low hematocrit	10,452	1,543	1216 (78.8)	Low hematocrit
			114 (9.6)	Couldn't wait / Second thoughts			81 (5.3)	Blood pressure or pulse related
			93 (7.8)	Blood pressure or pulse related			75 (4.9)	Couldn't wait / Second thoughts
			64 (5.4)	Temperature above 99.5			56 (3.6)	Temperature above 99.5
			45 (3.8)	Under physician care			38 (2.4)	Under physician care
			122 (10.3)	All others			77 (5.0)	All others
40-54	3,826	837	555 (66.3)	Low hematocrit	15,151	1,982	1588 (80.1)	Low hematocrit
			87 (10.4)	Blood pressure or pulse related			109 (5.5)	Blood pressure or pulse related
			70 (8.4)	Couldn't wait / Second thoughts			89 (4.5)	Couldn't wait / Second thoughts
			38 (4.5)	Under physician			58 (2.9)	Under physician care
			29 (3.5)	Cold / Sore throat			51 (2.6)	Temperature above 99.5
			58 (6.9)	All others			87 (4.4)	All others
55+	1,134	216	123 (56.9)	Low hematocrit	8,591	864	663 (76.7)	Low hematocrit
			28 (13.0)	Blood pressure or pulse related			57 (6.6)	Blood pressure or pulse related
			24 (11.1)	Couldn't wait / Second thoughts			49 (5.7)	Under physician care
			15 (6.9)	Under physician care			47 (5.4)	Couldn't wait / Second thoughts
			9 (4.2)	Cold / Sore throat			16 (1.9)	Prescription medication
			17 (7.9)	All others			16 (1.9)	Cold / Sore throat
							16 (1.9)	All others

Table 2.11 Summary post-donation blood unit screening probabilities based on donor demographic characteristics

Demographic Group	First Time				Repeat			
	1+ Positive	All Negative	Positivity Probability	Binomial 95% CI*	1+ Positive	All Negative	Positivity Probability	Binomial 95% CI*
Males Age 16-24	66	3,678	0.0176	0.0136 – 0.0224	23	2,760	0.0083	0.0052 – 0.0124
Females Age 16-24	76	4,225	0.0177	0.0139 – 0.0221	19	3,610	0.0052	0.0032 – 0.0082
Males Age 25-39	142	4,420	0.0324	0.0274 – 0.0380	37	9,031	0.0041	0.0029 – 0.0056
Females Age 25-39	130	4,066	0.0310	0.0259 – 0.0367	45	8,499	0.0053	0.0039 – 0.0071
Males Age 40-54	167	2,721	0.0578	0.0496 – 0.0670	52	16,516	0.0031	0.0023 – 0.0041
Females Age 40-54	129	2,859	0.0475	0.0398 – 0.0561	43	12,795	0.0033	0.0024 – 0.0045
Males Age 55+	34	908	0.0361	0.0251– 0.0501	43	11,896	0.0036	0.0026 – 0.0048
Females Age 55+	27	772	0.0338	0.0224 – 0.0488	28	7,497	0.0037	0.0025 – 0.0054

* 95 Percent Confidence Interval

Table 2.12 Blood Centers of the Pacific whole blood production costs; total costs, allocation base and unit costs by activity; 2000 U.S. dollars

Activity	Total Cost ($)	Allocation Base	Unit Cost ($)
Blood Bank Cost			
Donor Recruitment and Selection	1,588,500	112,658 Presenting Donors	14.10
Donation Collection	10,601,700	96,819 Attempted Donations	109.50
Donation Screening and Processing	4,929,700	96,660 Successful Donations	51.00
Donation Distribution	1,436,400	95,559 Units Screened Negative	15.00
Total Blood Bank Cost	18,556,000		189.60
Donor Cost			
Travel Time, Interview, and Medical Evaluation	1,858,900	112,658 Presenting Donors	16.50
Donation and Recovery Time	1,135,800	96,660 Successful Donations	11.75
Total Cost Incurred by Donors	2,994,700		28.25
Societal Cost	21,551,000		217.85

Table 2.13 Model results by demographic group

Demographic Group	Presenting Donors	Short Term Deferrals	Long Term Deferrals	Permanent Deferrals	Successful Donation Attempts	Total Unsuccessful Attempts	Disease Marker Positive Units	Under Collected Units	Total Units Cleared for Release
Females 16-24	10,676	2,012	575	94	7,927	68	96	117	7,715
Males 16-24	7,467	440	405	87	6,525	9	89	129	6,308
Females 25-39	16,378	2,691	660	286	12,698	43	175	250	12,272
Males 25-39	14,842	489	525	375	13,450	3	179	171	13,099
Females 40-54	18,976	2,802	376	225	15,555	18	172	308	15,076
Males 40-54	20,758	674	374	246	19,457	8	219	385	18,857
Females 55+	9,724	1,070	181	139	8,323	11	55	165	8,102
Males 55+	13,837	534	212	209	12,879	2	77	256	12,546
Total	112,658	10,712	3,308	1,661	96,814	162	1,062	1,781	93,975

Table 2.14 Comparison between number of events observed in data sources and number predicted by the baseline model.

Outcome	Number Observed in Data	Number Predicted by Model	Difference	Percent Difference
Presenting blood donors	112,658	112,658	0	0
Able to donate	159	163	+4	+2.5
Short term deferrals	10,711	10,711	0	0
Long term deferrals	3,309	3,309	0	0
Permanent deferrals	1,660	1,661	+1	+0.06
First time donor collections screened	23,970	23,968	-2	-0.008
Repeat donor collections screened	72,849	72,846	-3	-0.004
Units screening 1+ positive	1,061	1,058	-3	-0.3

Notes to Chapter

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Chapter 3: Assessment of European Travel Deferral for Variant Creutzfeldt-Jakob Disease

Abstract

Recently, the United States Food and Drug Administration adopted additional blood donor deferral criteria for persons who have spent time in European countries in order to protect the blood supply from the risk of variant Creutzfeldt-Jakob disease (vCJD). Animal models suggest that vCJD can be transmitted via blood transfusion. However, human-to-human transmission via blood or blood products has not been demonstrated. The new deferral criteria will decrease the number of eligible donors, but the impact in terms of the number of blood units available or the cost of maintaining the blood supply has not been investigated empirically. In combination with the results from a recent blood donor survey of European travel, we used a cohort simulation model of blood supply production to investigate the influence of the expanded vCJD deferral criteria. The cohort simulation begins with the population of persons who present for donation and ends with units of blood cleared for release or further processing into components. We modeled the impact for a community blood supply program using data from this program (Blood Centers of the Pacific, San Francisco, CA). Expanded European travel deferral will lead to the permanent deferral of 3,271 donors (95% Confidence Range, 2,600 – 3,973 donors) reducing the supply of blood by 3,141 units out of an approximate 94,000 unit annual supply produced by the blood bank. The cost of producing each unit of blood increases by $0.53 per unit from the blood bank perspective and by $1.22 per unit from the societal perspective. The model predicts that 2.8% of blood units that would have been available before the policy will be lost from the supply unless recruitment efforts are enhanced to bring in new donors or increase the frequency of repeat donation. The projected impact on the U.S. blood supply is a loss of 392,000 units based on a theoretical threat to safety. Under conservative assumptions, the additional cost to replace this amount of blood from the blood bank perspective would be over $7.4 million, and from the societal perspective would be over $17.0 million.

Introduction

In January 2002, the United States Food and Drug Administration, Center for Biologics Evaluation and Research, adopted expanded blood donor deferral recommendations related to Creutzfeldt-Jakob Disease (CJD) and variant Creutzfeldt-Jakob Disease (vCJD).[1] These recommendations are intended to further reduce the potential risk of these transmissible spongiform encephalopathies (TSE) in human blood and blood products by deferring donors for multiple reasons including the extent of time spent in Europe. The focus of this policy is vCJD, which is the human form of bovine spongiform encephalopathy. Busch and colleagues have recently reviewed the rationale for TSE donor deferrals and other emerging threats to the safety of the blood supply.[2] Specific to European travel, the deferral recommendations call for the permanent deferral of persons who meet any of the criteria summarized in Table 3.1.

Based on the precautionary principle,[3] a theoretical improvement in safety is cited to justify the implementation of the policy even with the acknowledgement that the deferrals could lead to a reduced supply of blood.[4,5] Before policy implementation, many blood collection programs predicted that the overall impact of expanded European travel deferral could be as high as a 10 percent donor loss.[6] Researchers have investigated the influence of vCJD-related donor deferral in Canada and Australia.[7-9] However, to our knowledge, a formal evaluation of the influence of the expanded policy for the United States has not been conducted, and no one has explicitly considered the influence these requirements will have on both the quantity of blood available and the additional cost of maintaining a supply at the current level. We sought to quantify the effect of these deferrals on donors, donations, and the cost of producing a supply of blood using a community blood supply policy evaluation model and a recently completed blood donor survey.

Methods

Community Blood Supply Model

Model structure and data sources have been discussed previously (chapter 2). Figure 3.1 provides the core structure of the model using a decision tree framework. In brief, the model includes donor demographics, the patterns and reasons for donor deferral, and the costs incurred in producing a supply of blood. The model is a cohort simulation. The time horizon for the model is one year. The focus of the model is allogeneic whole blood donation. The donation year is divided into six two-month intervals approximately corresponding to the maximum number of times an individual can donate whole blood in one year (once every 56 days). We specifically structured the blood supply model to include seasonal factors related to blood donation, patterns of donor return over a year-long period, and culling of the donor pool as a policy is implemented. The cohort of presenting blood donors is stratified into eight age and sex defined demographic groups (16-24 year old males, 16-24 year old females, 25-39 year old males, 25-39 year old females, 40-54 year old males, 40-54 year old females, 55+ year old males, and 55+ year old females) because the probability of donor deferral, both before and after donation, varies by age and gender.

Within each demographic group, persons who present for donation are either first time or repeat donors. Each presenting donor is classified in one of four categories before donation; eligible to donate, short term temporary deferral, long term temporary deferral, or permanent deferral. There are multiple reasons for each type of pre-donation deferral. We defined short term temporary deferrals as deferrals between 1 day and 2 months in length, long term temporary deferrals as deferrals between 2 months to 1 year in length, and permanent deferrals as 3-year Malaria-related deferrals, 5-year cancer-related deferrals, and true permanent deferrals. All pre-donation deferrals are based on self-reported exposures or behaviors during the pre-donation interview, medical evaluation, or previous reasons for deferral. After establishing donor

eligibility, each eligible donor is either able to donate or unable to donate if the phlebotomist is unable to locate a vein for blood collection or if the donor faints before completion of the donation process. Following collection, blood samples are sent to the laboratory for screening. A positive disease marker test on any of the blood screens for syphilis, HIV, HTLV, HCV, or HBV leads to interdiction of the blood unit and deferral of the donor. We did not consider elevated alanine aminotransferase (ALT) test results as sufficient to lead to unit interdiction. During collection, two tubes of blood are filled before the plastic unit bag. The unit may not be useable if the volume of blood collected does not meet required collection volume. For the unit to be useable, regulations require the quantity of blood collected be within 10 percent of the prescribed collection volume.[10,11] If outside the allowed collection volume, although sample tubes have been sent to the laboratory for screening, the unit of blood does not meet quality assurance requirements, and is ineligible for release or further processing. The unit of blood is deferred. Disease marker positive screening results for under or over collections still lead to deferral of the donor.

The cohort simulation is a series of linked Excel workbooks (Microsoft, Redmond, WA). Sensitivity analysis is conducted with the assumption of beta – binomial distributions for the outcome probability parameters of the model[12] and normal distributions for the cost parameters of the model. We estimated cost parameters directly from Blood Centers of the Pacific expenditure data and assumed variability around the cost parameters of 10 percent of each point estimate. The model runs as a Monte Carlo simulation using @Risk 3.5 (Palisade, Newfield, NY).

Donor Survey

Murphy and colleagues recently completed analysis of a blood donor survey that sought to estimate the proportion of persons deferred as result of the expanded European travel deferral policy (Murphy, Submitted). We used data from this survey to update the pre-donation deferral probabilities in the community blood supply model. The total number of persons who completed

all portions of the survey was 6,855. The number of persons meeting one or more of the deferral definitions, total number of respondents, and probability of deferral within each age and gender group based on donation history in the last 12 months are presented in Tables 3.2 and 3.3. These data suggest differences in European travel deferral by sex and age. Males 30-39 years of age report more deferrable travel or employment and therefore are more likely to be permanently deferred from donating blood. Within each age group, differences in the probability of vCJD deferral, based on gender, are generally not large for persons reporting no donations in the last 12 months. However, in each age group reporting at least one donation within the last 12 months, males are more likely to report deferrable geographic exposure than females.

In the community blood supply model, we separately track both first time and repeat blood donors within each demographic group. Although the blood donor survey reported by Murphy and colleagues did not explicitly ask donors about their first time or repeat status, the questionnaire did include the frequency of donation in the last year. We used survey responses to classify donors as first time donors if they reported no donation in the 12-month period before the survey and as repeat donors if they reported one or more whole blood or pheresis donations in the last 12-month period. Also, the age groups used in the donor survey do not correspond exactly to the age groups in the community blood supply model. The community blood supply model uses 15-year age ranges and the donor survey provided age checkboxes with 10-year ranges. However, the age groups map sufficiently close to permit the use of the travel survey results in assessing the impact on the blood supply using the model.

Within each demographic group of the community blood supply model, all persons classified as first time donors regardless of 2-month interval will be exposed to the European travel deferral policy for the first time. We used the sex- and age-specific probabilities from the donor survey to model first time donor deferral as a result of the expanded policy. The percent

deferral within each 2-month period is the same as that estimated by the donor survey because first time donors by definition will be newly exposed to the policy.

For repeat donors, modeling the impact is not as straightforward. For example, in the second 2-month interval of the modeled donation year, presenting repeat donors consist of a mixture of persons who presented in the first interval and persons who presented at some time before the modeled year. We determined the pattern of repeat donor presentation over the course of the six cycles in the modeled year by linking successive donations through unique blood donor identification numbers. We determined eight separate patterns of donor return corresponding to the eight demographic groups represented in the model. Each repeat donor can present again in any of the subsequent donation intervals in the model and all possible patterns of donor return are observed in the data. Some donors return every 2 months and others have longer inter-donation intervals. The repeat donor return matrices provide the number of returning donors from all of the previous cycles in the year. With the assumption that once a donor is permanently deferred as a result of the policy, and therefore does not present for donation again, only those donors who have not presented for donation in a previous cycle of the modeled year can be newly deferred because of the policy. As the policy is implemented, the number of repeat donors susceptible to the policy decreases in each subsequent cycle. Each of the donor return matrices is linked directly with the community blood supply model and is used to determine updated permanent deferral probabilities for each cycle within each demographic group.

The combination of the estimated deferral proportion from persons who completed the donor survey coupled with the repeat donor return pattern allowed us to estimate the influence of the European travel deferral policy in terms of donors deferred, available blood units, and cost of producing blood units with and without the expanded policy. Deferral probabilities were assumed to follow the same beta–binomial distributions as the other outcome parameters. One-way and Monte Carlo simulation sensitivity analyses were conducted. The analysis was conducted from

the blood bank and societal perspectives. The comparator is all of the donor deferrals and blood screens prior to the implementation of expanded European travel deferral policy.

Results

By simulating the Blood Centers of the Pacific donor cohort using the community blood supply model, we assessed the influence of the expanded European travel deferrals due to possible vCJD exposure. Table 3.4 details the consequences of the expanded policy. Based on year 2000 donations records, before the implementation of the policy, the community blood supply model predicts the overall number of blood units cleared for release is 93,975 out of 112,658 presenting donor encounters. This represents an 83.4% yield of blood units cleared for release from persons willing to present for blood donation. Obtaining this supply of blood costs the blood bank approximately $18,570,000, resulting in a unit cost of $197.65 per disease marker negative blood unit obtained. If the opportunity cost incurred by donors is included, the societal cost is $21,570,000 resulting in a unit cost of just over $229.50. The implementation of the expanded European travel deferrals leads to a decrease in the available supply of blood. In the first year of implementation of the policy, 3,271 BCP donors (95% Confidence Range, 2,660 – 3,973) will be deferred leading to a total available supply of 90,834 units, or a net loss of 3,141 units that would have been cleared for release to health care providers. This represents an 80.6% blood unit yield from persons willing to present for blood donation. Obtaining this supply of blood costs the blood bank approximately $18,000,000 resulting in a unit cost of nearly $198.20 per blood unit. The incremental impact of the expanded policy is to reduce the available supply of blood by 2.8%. Because vCJD-related travel deferral occurs before donation, the costs incurred in obtaining and screening blood are decreased with the implementation of the expanded policy and therefore the total costs are decreased compared to before the policy assuming the same number of donors present for donation. However, because there are fewer blood units available, the unit cost of obtaining each unit increases by over $0.50. If the opportunity cost incurred by donors is

included the total societal cost is $20,960,000, resulting in a unit cost of $230.75. The societal unit cost increases by $1.22 per unit whereas the blood bank cost increases by $0.53 per unit because blood bank costs are incurred throughout the blood donation process and are highest during collection and screening, whereas a greater proportion of donor opportunity costs are incurred in presenting for blood donation before the collection of blood.

Table 3.5 details the effects of the expanded vCJD policy within each demographic group. The net loss of blood units varies by demographic group, with the greatest net loss of 5.3% from males 25-39 years of age, and the smallest net loss of 1.2% from female donors age 55 years or older. The net loss of blood units cleared for release within each demographic group results from two factors: (1) the combined influence of the donor survey results for first time and repeat donors, and (2) the pattern of repeat donor return within each demographic group.

Sensitivity Analysis

In one-way sensitivity analysis, where a single parameter value is varied over a pre-specified distributional range, as expected, the probability of European travel deferral has the most impact on the number of available units. The model is most sensitive to the impact of deferring 25-39 year old females who are first time donors and 25-39 year old males who are first time donors. In order, the next most sensitive parameters are the deferral probability in 40-54 year old male repeat donors, 25-39 repeat male donors, 40-54 year old male first time donors, and 40-54 year old female first time donors. After all of the 16 estimated travel deferral probabilities, the model is most sensitive to under collected units and the ability to collect blood from specific demographic groups (Figure 3.2).

For total and unit costs, whether from the blood bank or societal perspective, the model is most sensitive to the cost of collecting a unit of blood, followed by the cost of processing and screening. From the blood bank perspective, the next most sensitive parameter is the cost of

recruiting and pre-donation assessment, whereas from the societal perspective the next most sensitive parameter is the donor's cost to present for donation (Figure 3.2).

We used Monte Carlo simulation to estimate the overall influence of uncertainty on the available supply and cost of producing blood units. Table 3.4 also provides confidence range values for the influence of the travel deferral policy. The 95% confidence range for the number of units available after implementation of the policy ranges between 90,343 and 91,292, with 2,660 to 3,973 donors deferred as result of the expanded policy. The blood bank unit cost ranges from $180 to $218, and the societal unit cost ranges from $212 and $249 per disease marker negative blood unit obtained.

Discussion

Before implementation of the expanded policy for vCJD deferrals, vCJD deferrals for 6-month or greater stays in the U.K. between 1980 and 1996 were already implemented (November 1999). The results reported here are in addition to the deferrals previously resulting from the old UK-specific policy.

Three other policy analysis studies have discussed vCJD deferrals. Wilson and colleagues detailed the major decisions made by the Canadian Blood System related to vCJD risk in blood donation.[3,8] Specific analysis estimating the loss to the blood supply was not performed. Correll and colleagues evaluated the influence of vCJD deferrals on the available supply of blood in Australia.[7] This analysis considered the impact of the previously adopted deferral based on 6-month or greater stays in the U.K. between 1980 and 1996. The researchers estimated 5.3% of all Australian donations would be excluded. Out of 946,000 donations in Australia in 1998, 51,100 would be excluded from the blood supply. Researchers did not include the cost of producing the supply, nor did they discuss the impact of the loss of over 50,000 units of blood.

Given the new unit cost for each blood unit following the implementation of the expanded policy, the number of donors deferred, the cost to BCP to provide the same quantity of

blood, and conservatively assuming no changes in the characteristics of persons who present for donation, the incremental cost of maintaining the same supply is an increase of $49,800. While this incremental cost may seem relatively small, it only applies to BCP and assumes replacing lost donors is as simple as persuading more donors with the same characteristics to present for donation so that marginal costs do not increase. However, it is unlikely BCP can solely increase donor recruitment to recover the lost supply of blood because BCP is a net importer of blood; it is unable to supply a sufficient quantity of blood to the local health care providers using local donations. Each year, BCP imports blood by purchasing it from other blood banks. In 2000, BCP spent nearly $3.3 million on purchases of (approximately 25,000) units of whole blood, red cells, and blood components. The loss of nearly 3,200 units of whole blood due to the European travel deferral will most likely require additional blood purchases if the same supply quantity is to be maintained. With other blood banks implementing the expanded policy, the loss of eligible donors at these blood banks, coupled with loss of donors from BCP, means the cost of maintaining the same supply will increase for all blood banks. The true marginal or incremental cost will be dependent on the demographic structure and deferral characteristics of local donor populations. If we assume BCP will have to pay premium prices for additional units because blood purchases will come from other blood banks faced with decreased blood supplies as a result of the expanded travel deferral, we can estimate more realistic costs for the expanded policy. To do so we added 10% to the blood bank unit cost and societal unit cost to reflect a price premium for the 3,141 lost units of blood. In this "worst case" scenario, returning the blood supply to the same level as before the expanded policy will result in an additional cost of $685,000 from the blood bank perspective and $798,000 from the societal perspective (Table 3.6). Whereas, in the "best case" scenario, in which BCP can easily obtain more presenting donors with the same characteristics as current BCP donors at no additional the cost, the replacement cost is approximately $50,000 to the blood bank and $114,000 to society.

Our analysis of the impact of vCJD-related travel deferrals on the cost and supply of blood has several limitations. First, the travel survey used to estimate the impact of the policy on donors does not have the same age groups as the blood supply model. The differences in survey age groups and model age groups may lead to imprecise estimation of the impact of travel deferrals. In addition, the donor survey did not specifically inquire about first time and repeat donor status. We used questions from the donor survey on whole blood and pheresis donations in the last 12-month period to classify persons as either first time or repeat donors. Thus, we misclassified some repeat donors who had not donated in the last 12-month period as first time donors. However, based on the available information, it is unlikely we misclassified persons in the other direction (i.e., first time donors classified as repeat donors). Nonetheless, the misclassification of first time versus repeat status may bias the results, particularly in the age groups with marked differences in deferral proportions between first time and repeat donors.

The community blood supply model is not able to address questions regarding the appropriate use of blood and blood products. Both blood loss reduction and the appropriate utilization of blood products have received greater attention as the available supply of blood has not kept pace with the demand for blood.[13] The loss of blood units from pre-donation deferrals may be counter-balanced with further efforts to improve blood utilization or through the use of blood substitutes.

The community blood supply model was designed to address factors that influence the available supply of blood. The model does not consider the separation of whole blood into components. Component preparation increases the cost of producing blood and blood products. However, components also improve the utilization of blood because multiple, specific therapeutic products can be manufactured from whole blood. The focus of the current study was the influence of a pre-donation deferral on the acquisition of a supply of blood. Future analyses can more explicitly detail the impact of component production.

Furthermore, the model cannot address the impact of donor self-deferral for persons who are aware of the expanded European travel policy and choose not to present for donation. If the donor survey captures information on self-deferral, then the model will implicitly include donor self-deferral. The importance of self-deferral as a consequence of the vCJD or other policies is unclear and may require surveying of the general population using established surveys, such as the National Health and Nutrition Examination Survey, to fully appreciate.

The community blood supply model predicts that a measurable decrease in the available supply will result from the expanded vCJD policy. However, the model does not confirm a purported consequence as high as 10% donor loss.[6] In fact, over the course of the modeled year, the percent donor loss decreases due to the culling of eligible donors as the policy becomes established. For repeat donors, the model suggests that many of the individuals likely to be deferred will be deferred within a one-year time period. For first time donors, the impact is constant and represents a continued diminution of the overall population of eligible donors, based on the theoretical risk of vCJD transmission in human transfusion.

We can use the results for BCP to estimate the national impact of the expanded vCJD deferral policy if we make several assumptions: (1) the donor population, demographic characteristics, and probability of disease marker positive donations are the same for rest of the country; (2) the cost parameters for the BCP can be applied to the rest of the country; (3) marginal costs do not increase; and (4) a sufficient number of virtually identical additional donors could be persuaded to donate to maintain the same quantity of supply. In reality, these assumptions are probably not justifiable, but with them we can approximate the overall influence of the expanded policy. With approximately 14,000,000 whole blood donations annually in the U.S., the number of donations lost as result of the expanded policy would be 392,000. The incremental cost of replacing these lost donations from the blood bank perspective would be $7,420,000, and from the societal perspective would be $17,080,000. This loss of available blood

units, and additional cost required to replace the lost units, was not sufficiently considered before the implementation of the expanded policy. The theoretical risk of vCJD transmission in blood and blood products has lead policy makers to exercise extreme caution. However, if blood supply shortages increase in frequency or become prolonged, an insufficient supply of blood will be a greater threat to morbidity and mortality than the risk of vCJD. Moreover, if the costs associated with increased morbidity and mortality could be incorporated into the social cost of blood, the unintended consequences of the European travel deferral policy could be far beyond anyone's reckoning to date.

Table 3.1 Permanent donor deferrals for expanded European travel due to vCJD risk

Cumulative time in UK ≥ 3 months between 1980 and 1996
Cumulative time in Europe ≥ 5 years between 1980 and present
Military posting in Belgium, the Netherlands and/or Germany ≥ 6 months between 1980 and 1990
Military posting in Spain, Portugal, Turkey, Italy, and/or Greece ≥ 6 months between 1980 and 1996
Received a transfusion in UK since 1980

Figure 3.1 Core structure of the community blood supply model for the expanded European travel deferral policy evaluation

Table 3.2 Self-reported vCJD-related European travel deferral probabilities for males

Age Group	No Donations in Last 12 months				1 or More Donations in Last 12 months			
	Deferred (n)	Total (N)	Percent	Binomial 95% Confidence Interval	Deferred (n)	Total (N)	Percent	Binomial 95% Confidence Interval
16-29	4	179	2.23	0.61 – 5.62	17	520	3.27	1.92 – 5.18
30-39	6	77	7.79	0.29 –1.62	37	511	7.24	5.15 – 9.84
40-49	2	57	3.51	0.43 – 12.11	31	640	4.84	3.31 – 6.81
50+	3	71	4.23	0.88 – 11.86	33	1,177	2.73	1.94 – 3.92
All Males	15	384	3.91	2.20 – 6.36	118	2,848	4.14	3.44 – 4.94

Table 3.3 Self-reported vCJD-related European travel deferral probabilities for females

Age Group	No Donations in Last 12 months				1 or More Donations in Last 12 months			
	Deferred (n)	Total (N)	Percent	Binomial 95% Confidence Interval	Deferred (n)	Total (N)	Percent	Binomial 95% Confidence Interval
16-29	8	259	3.09	1.34 – 5.99	19	692	2.75	1.66 – 4.25
30-39	8	113	7.08	3.11 – 13.47	18	524	3.44	2.05 – 5.37
40-49	6	102	5.88	2.19 –12.37	24	857	2.80	1.80 – 4.14
50+	3	105	2.86	0.59 – 8.12	18	973	1.85	1.10 – 2.91
All Females	25	577	4.33	2.82 – 6.33	79	3,046	2.59	2.06 – 3.22

Table 3.4 Costs (year 2000 U.S. dollars) and consequences of the expanded European travel deferral policy

Outcome	Before Expanded Policy	After Expanded Policy	95% Confidence Range After Expanded Policy
Total Whole Blood Units Available	93,975	90,834	90,343 – 91,292
CJD deferrals due to expanded policy:			
First time donors		1,558	1,222 – 1,986
Repeat donors		1,713	1,438 – 1,987
Total		3,271	2,660 – 3,973
Total Blood Bank Cost	$18,574,000	$18,001,000	$16,384,000 – $19,768,000
Bank Unit Cost	$197.65	$198.18	$180.01 – $217.55
Total Societal Cost	$21,570,500	$20,960.000	$19,236,000 – $22,701,000
Societal Unit Cost	$229.53	$230.75	$211.89 – $249.27

Table 3.5 Results of expanded European travel deferral policy by demographic group.

Demographic Group	Presenting Donors*	Units Cleared Before Expanded Policy*	Percent Yield Before (%)	Units Cleared After Expanded Policy*	Percent Yield After (%)	Net Loss of Cleared Units (%)
16-24 Females	10,676	7,715	72.26	7,429	69.59	2.68
16-24 Males	7,467	6,308	84.48	6,155	82.43	2.05
25-39 Females	16,378	12,276	74.95	11,653	71.15	3.80
25-39 Males	14,842	13,099	88.26	12,312	82.95	5.30
40-54 Females	18,976	15,076	79.45	14,628	77.09	2.36
40-54 Males	20,759	18,857	90.84	18,306	88.18	2.65
55+ Females	9,724	8,102	83.32	7,989	82.16	1.16
55+ Males	13,836	12,546	90.67	12,366	89.37	1.30
Overall	112,658	93,975	83.42	90,834	80.63	2.79

* Sub-group and overall totals are not equal due to rounding

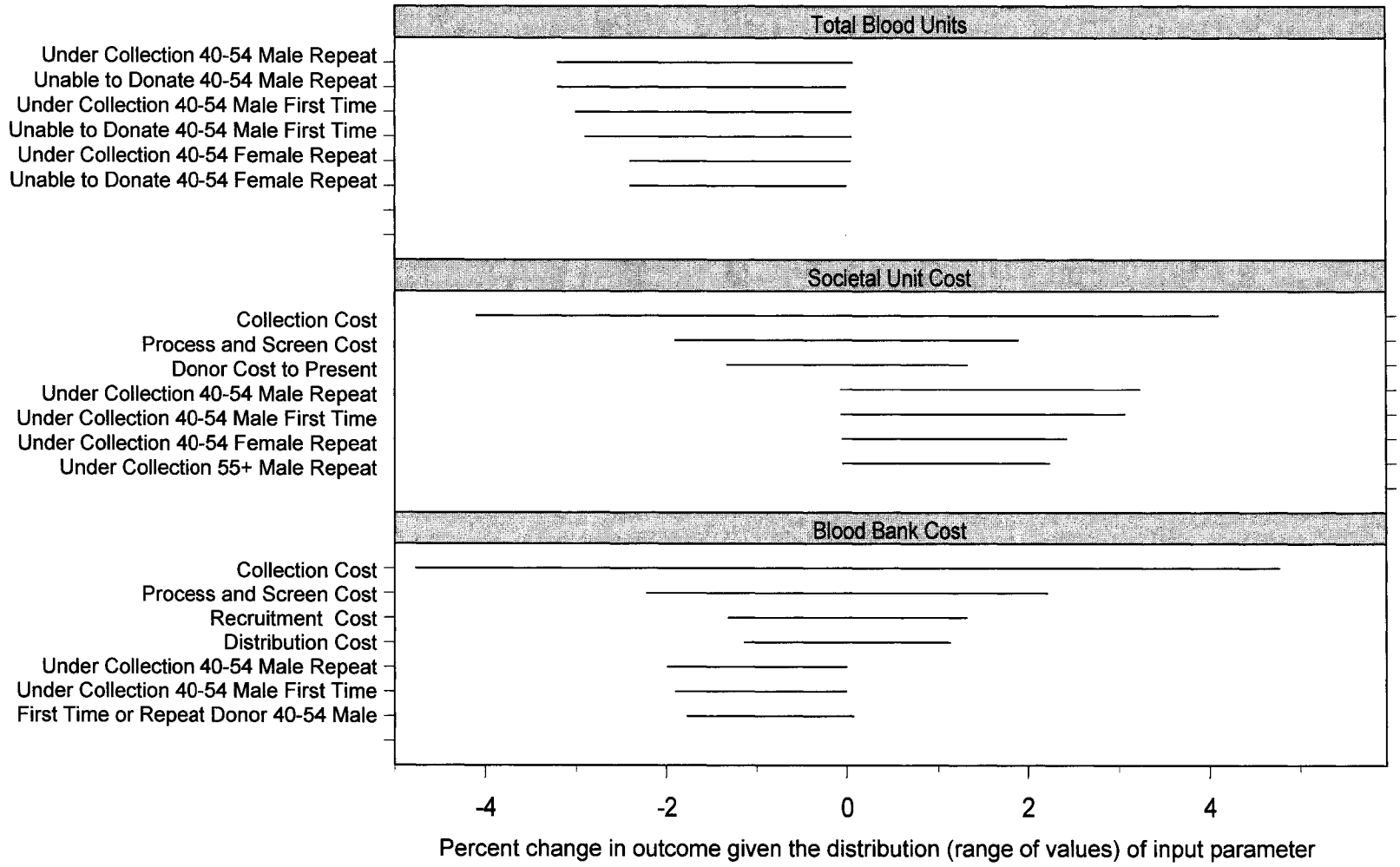

Figure 3.2 One-way sensitivity analysis results

Table 3.6 Estimated cost for Blood Centers of the Pacific and the community to replace 3,141 blood units lost due to European travel deferral policy

Outcome After Expanded Policy	Estimated Costs Assuming BCP Can Replace Units Based on Model Costs ($)	Estimated Costs Assuming Outside Blood Purchases at Premium Pricing ($)
Blood Bank Unit Cost to Obtain Replacement Units	198	218
Additional Blood Bank Cost	50,000	685,000
Total Blood Bank Cost for 93,975 Unit Supply	18,624,000	18,686,0000
Blood Bank Unit Cost to Obtain Replacement Units	231	254
Additional Societal Cost	114,000	798,000
Total Societal Cost for 93,975 Unit Supply	21,199,000	21,758,000

Notes to Chapter

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Vita

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