Estimation of the prevalence and rate of acute transfusion reactions occurring in Windhoek, Namibia

Benjamin P.L. Meza
Britta Lohrke
Robert Wilkinson
John P. Pitman
Ray W. Shiraishi
Naomi Bock
David W. Lowrance
Matthew J. Kuehnert
Mary Mataranyika
Sridhar V. Basavaraju

Blood Transfusion
7.1 Abstract

Background
In sub-Saharan Africa, acute transfusion reactions are likely common but transfusion reaction surveillance systems have not been widely established. In 2008, The Blood Transfusion Service of Namibia implemented a national acute transfusion reaction surveillance system, but substantial under-reporting was suspected. We estimated the actual prevalence and rate of acute transfusion reactions occurring in Windhoek, Namibia.

Methods
The percentage of transfusion events resulting in a reported acute transfusion reaction was calculated. Actual percentage and rates of acute transfusion reactions per 1,000 transfused units were estimated by reviewing patient records from six hospitals, which transfuse >99% of all blood in Windhoek. Patient records for 1,162 transfusion events occurring between January 1–December 31 2011 were randomly selected. Clinical and demographic information were abstracted and Centers for Disease Control and Prevention National Healthcare Safety Network criteria were applied to categorize acute transfusion reactions. [1]

Results
From January 1–December 31, 2011, 3,697 transfusion events occurred (involving 10,338 blood units) in the selected hospitals. Eight (0.2%) acute transfusion reactions were reported to the surveillance system. Of the 1,162 transfusion events selected, medical records for 785 transfusion events were analyzed, and 28 acute transfusion reactions were detected, of which only one was also reported to the surveillance system. An estimated 3.4% (95% confidence interval [CI]: 2.3-4.4) of transfusion events occurring in Windhoek resulted in an acute transfusion reaction, with an estimated rate of 11.5 (95%CI: 7.6-14.5) acute transfusion reactions per 1,000 transfused units.

Conclusion
The estimated actual rate of acute transfusion reactions is higher than the rate reported to the national hemovigilance system. Improved surveillance and interventions to reduce transfusion-related morbidity and mortality are required in Namibia.

7.2 Introduction

Since the 1980’s, programs and policies related to blood transfusion safety in sub-Saharan Africa have focused on reducing the risk of transfusion-transmitted HIV infection. [2-4] While much has been done to quantify the risk of HIV transmission through blood transfusion [5-9]
and to identify risk-reduction strategies, [10-14] there is limited information related to other adverse transfusion outcomes in sub-Saharan Africa, including acute transfusion reactions such as sepsis due to bacterial contamination of the donor unit and hemolysis secondary to transfusion with ABO incompatible blood products. However, based on data from industrialized countries, [15-18] previously published reports describing unsafe transfusion practices, [5, 19-21] and some limited studies from the region that have evaluated adverse transfusion-related outcomes, [22, 23] acute transfusion reactions in sub-Saharan Africa are likely more common than they are clinically recognized.

Surveillance systems designed to monitor and detect serious transfusion reactions are now in place for most industrialized countries as part of national hemovigilance systems, although the methodology and extent of implementation differ. [15,16,24] With the exception of South Africa, such systems have historically been absent in sub-Saharan Africa. [25] In Namibia, a country of 2.1 million people in south-western Africa, The Blood Transfusion Service of Namibia (NAMBTS) is the only organization authorized to collect, process, and distribute blood and blood components intended for transfusion. From 2000-2007, suspected transfusion reactions in the country were reported to NAMBTS using a non-standardized process which did not include clinical investigation or a comprehensive laboratory follow-up for reported events. As a result, reporting clinicians received limited feedback from the blood service and the system was under-utilized. In 2008, NAMBTS implemented a national hemovigilance system which included a systematic method of reporting, along with comprehensive clinical and laboratory investigations of all reported acute transfusion reactions in the country. This system is intended to provide timely, comprehensive feedback to support the implementation of corrective measures to reduce transfusion-associated morbidity and mortality.

In 2010, NAMBTS conducted a national audit of transfusion practices in all 46 transfusion facilities and found a lack of standardized transfusion practice between facilities and health care practitioners (personal communication: B. Lohrke 25 July 2012). Using the results of the audit, NAMBTS revised its training curriculum and launched the “BeST: Better and Safer Transfusions” training program based on an Australian model. [26] The NAMBTS “BeST” program is designed to strengthen training related to clinical transfusion practices, patient monitoring, and reporting of acute transfusion reactions. Under the revised reporting process, all healthcare workers who order or perform transfusions are asked to voluntarily report all acute transfusion reactions to NAMBTS. As a first step, the blood bank technologist and the on-call NAMBTS medical officer are notified via telephone by the reporting facility. The medical officer provides clinical guidance and specific instructions related to sample collection. This phone call is followed by submission of a standard, paper-based transfusion reaction report, along with patient samples and the remaining unused contents of the blood unit to NAMBTS via courier.

Between 2000-2007, reports of acute transfusion reactions increased from three to 10 per year (personal communication B. Lohrke 25 July 2012). Following the launch of the nation-
al hemovigilance system in 2008, the number of reports continued to increase, but despite comprehensive training and outreach activities, only 20 reactions (0.1%) were reported out of approximately 20,000 units transfused nationally in 2010. Few published studies have estimated the prevalence or rate of acute transfusion reactions in sub-Saharan Africa. [22,27,28] But this likely represents under-recognition and reporting as acute transfusion reactions have been reported to occur in approximately 1-3% of all transfusions in other countries. [29] In order to enhance monitoring of blood transfusions, facilitate the implementation of corrective measures to protect transfusion recipients, and reduce the future occurrence of adverse events, quantifying the burden of acute transfusion reactions and determining the associated morbidity and mortality are important objectives for blood services in the region. This study was conducted to estimate the prevalence and rate of acute transfusion reactions occurring in Windhoek, Namibia, and by using retrospective medical record review, to compare the estimated prevalence of adverse events with the prevalence reported to the NAMBTS hemovigilance system. The probable diagnoses and severity of acute transfusion reactions occurring in Windhoek are also described.

7.3 Materials and Methods

Approval and informed consent
All data collection followed approval from the Namibia Ministry of Health and Social Services (MOHSS). Because the study involved the evaluation of a routine surveillance program, it was considered exempt from review by an Institutional Review Board by the office of the Associate Director for Science of the U.S. Centers for Disease Control and Prevention (CDC), Division of Global HIV/AIDS in Atlanta, Georgia.

Study sites and design
Due to logistical and resource constraints, the study was limited to six transfusion facilities in Windhoek, the capital of Namibia. These facilities collectively transfuse >99% of all blood in Windhoek. In 2010, 8,580 (36%) of the 23,744 blood units transfused in Namibia were transfused in the six selected facilities. Except in rare cases where whole blood may be clinically indicated (e.g., neonatal exchange transfusion), all transfusions in Namibia are conducted using blood components. Since most patients are transfused more than one unit of blood in a 24 hour period, for the present study, “transfusion events,” rather than individual units, were reviewed in the medical record for evidence of an acute transfusion reaction. A transfusion event was defined as a single episode encompassing the duration of transfusion and the 24 hour period following cessation of transfusion in which a patient received any combination of components and/or number of units for one clinical indication.

Calculation of prevalence of acute transfusion reactions as reported to the surveillance system
To determine the percentage of transfusion events resulting in acute transfusion reactions that were reported to the surveillance system, case reports submitted to NAMBTS by the six selected Windhoek facilities between January 1, 2011 and December 31, 2011 were reviewed. These documents contained clinical, laboratory, and radiographic data, and results of the NAMBTS investigation. The likely diagnosis determined by the NAMBTS investigators was recorded for each report. The denominator for the calculation of the percentage of reported transfusion events resulting in acute transfusion reactions was the total number of transfusion events occurring in the six selected Windhoek hospitals in 2011.

Estimation of the percentage and rate of acute transfusion reactions

Given the suspected under-reporting of adverse transfusion events, we estimated an actual percentage and rate of acute transfusion reactions occurring in the Windhoek facilities. This estimated percentage was based on a review of patient records and compared with the percentage reported to the surveillance system. Determination of the sample size of medical records needed for review for the Windhoek study sites was based on a published estimated acute transfusion reaction rate of 1%. [29] A sample size of 1,162 was selected for this study as it would produce a two-sided 95% exact confidence interval (95% CI) with a total width of 1% when the detected percentage is 1%. [30] The observed sample size of 785 would have yielded a 95% CI with a total width of 1.5% for an estimated acute transfusion reaction rate of 1%. A roster of patient medical records representing 1,162 randomly selected transfusion events was generated through a SQL query of the electronic NAMBTS database. Transfusion events were eligible if they occurred between January 1 and December 31, 2011, and if specific identifier information (e.g., patient name, date of transfusion) was available to facilitate location of the medical record in the facilities. The selected transfusion events were intended to be representative of Windhoek for the specified timeframe.

Data collection

Patient records were retrospectively evaluated during February-April 2012 for evidence of an acute transfusion reaction occurring during or within 24 hours of the final unit in the transfusion event. Data collection from the medical record abstraction was performed using the Census and Survey Processing System (CSPro) (U.S. Census Bureau, Washington, DC). Patient demographic information, physician and/or nurse documentation, laboratory data, and radiographic findings were reviewed for each medical record. Pertinent demographic and clinical information related to each transfusion event were entered into the CSPro tool which was programmed to assign a likely acute transfusion reaction diagnosis, severity score, and imputability score for each transfusion event. Imputability is defined as the likelihood that the reaction was associated with the transfusion event. [1] These scores were based on criteria described in the CDC National Healthcare Safety Network Hemovigilance Module (NHSN). [1] If the physician’s or nurse’s documentation, laboratory, or radiographic findings did not
suggest an acute transfusion reaction, the CSPro program assigned a diagnosis of ‘none.’ For transfusion events assigned to the ‘none’ category, severity and imputability scores were not calculated.

If the documentation in the medical record suggested an acute transfusion reaction had occurred, a diagnosis, based on NHSN criteria, [1] was generated by the pre-programmed CS-Pro algorithm. Diagnoses included: allergic, acute hemolytic, febrile non-hemolytic, hypotensive, sepsis due to bacterial contamination of the donor unit, transfusion associated circulatory overload, transfusion associated dyspnea, and transfusion-related acute lung injury. [1] If documentation indicated that an acute transfusion reaction had occurred, but sufficient data were not available for the algorithm to assign a specific diagnosis, a designation of “transfusion reaction, not otherwise specified” was assigned. Based on available documentation for each transfusion event for which an acute transfusion reaction had occurred, severity scores were calculated as mild, moderate, life-threatening, or death. Imputability scores were designated as: possible, probable, or definite. Only two investigators (S.V. Basavaraju and B. Lohrke) could override the CSPro algorithms and assign new diagnoses, severity, or imputability scores. All acute transfusion reactions detected through the review of patient medical records were further evaluated to determine if they were previously reported by hospital staff to the surveillance system. All acute transfusion reactions detected through the record review, which were either designated as life threatening or death, were subsequently referred for investigation by NAMBTS. The results of subsequent investigations are not presented here.

Statistical analysis
The percentages of transfusion events resulting in an acute transfusion reaction as reported to the surveillance system, and as determined by the chart abstraction, were calculated and compared using a one proportion Z-test. The percentages of transfusion events resulting in a reported or an unreported acute transfusion reaction was estimated using the total sampled transfusion events as the denominator. The reported rate of acute transfusion reactions per 1,000 units was calculated using the total units transfused during 2011 at the selected facilities as the denominator. The estimated rate of acute transfusion reactions per 1,000 units was calculated using data collected from the medical record abstraction.

Estimated rates of acute transfusion reactions per 1,000 units of each component type were also calculated using data collected from the medical record abstraction. For these estimates, a fraction of each acute transfusion reaction detected in the study sample was attributed to each component in proportion to the number of component units transfused during the respective transfusion event (e.g., 0.75 acute transfusion reactions were attributed to packed red blood cells (PRBC) if three PRBC units and one platelet unit were transfused during the transfusion event). Relative standard error (RSE) was calculated for rates of acute transfusion reactions for each component type. The estimated percentage and rates were weighted to account for variation in non-response between facilities. The weight adjustments
were defined as \( \frac{1}{\text{total response rate}} \) at each facility. Application of sample weights allowed for adjustment of prevalence and rate estimates to reduce bias resulting from non-response. Confidence intervals were adjusted using a finite population correction factor. All data analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, NC). Weighted analyses were performed using SAS survey procedures.

7.4 Results

Between January 1, 2011 and December 31, 2011, 3,697 transfusion events, which included 10,373 blood units, (7,777 adult and pediatric PRBC, 1,894 adult and pediatric fresh frozen plasma (FFP), 686 adult and pediatric platelets, and 16 whole blood units) occurred in the six Windhoek hospitals. NAMBTS received reports of eight acute transfusion reactions from these facilities during this period. Of these 3,697 transfusion events, 3,461 (94%) events had sufficient patient information in the NAMBTS database to facilitate location of the patient medical records (Figure 1). From these 3,461 transfusion events, 1,162 events were selected via simple random sampling. Patient medical records for 311 events were either missing or otherwise inaccessible in the facilities and were excluded. After reviewing the patient medical records for the remaining 851 transfusion events, 12 transfusion events occurred within 24 hours of a second randomly sampled event for the same patient and were collectively analyzed as six transfusion events. After reviewing the patient medical records for the remaining 845 transfusion events, another 58 events were excluded because the medical record contained evidence that the transfusion was cancelled or had no documentation that the transfusion had occurred. Two transfusion events selected for review occurred during 2010 or 2012 and were excluded, leaving 785 transfusion events for data analysis (Figure 1). This total included 2,284 blood units (1,688 adult and pediatric PRBC, 446 adult and pediatric FFP, 148 adult and pediatric platelets, and two whole blood units).

Four of the eight acute transfusion reactions reported to the surveillance system in 2011 were mild; two were moderate severity; and one resulted in death (Table 1).

The severity score for the remaining reported acute transfusion reaction was not documented in the surveillance report. Of the 785 transfusion events documented in patient medical records which were retrospectively reviewed, 28 medical records contained evidence that an acute transfusion reaction had occurred during or after the associated transfusion event. Of the 28 acute transfusion reactions detected through the chart review, only one, an allergic reaction, had also been reported to the surveillance system. Twenty of the 28 acute transfusion reactions were classified as mild severity; four were moderate severity; two were life threatening; and two resulted in death (Table 2).
Table 1: Diagnoses and severity scores of acute transfusion reactions reported to the national acute transfusion reaction surveillance system: Windhoek, Namibia - 2011

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severity</th>
<th>Mild</th>
<th>Moderate</th>
<th>Life-threatening</th>
<th>Death</th>
<th>Not Documented</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Allergic</td>
<td></td>
<td>1</td>
<td>1§</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Febrile non-hemolytic</td>
<td></td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Hypotensive</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis due to bacterial contamination of the donor unit</td>
<td></td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Transfusion-associated circulatory overload</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Transfusion-associated dyspnea</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Transfusion reaction not otherwise specified</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>4</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
</tbody>
</table>

§ Reaction was also detected by reviewing a selected sample of transfusion events. No cases of transfusion-related acute lung injury were reported to the surveillance system or detected reviewing a selected sample of transfusion events.

Documentation was not sufficient to assign a specific diagnosis for seven acute transfusion reactions, resulting in a classification of “transfusion reaction not otherwise specified.” Based on physician and nursing documentation of clinical signs and symptoms, one of the life threatening acute transfusion reactions identified through the medical record review was classified by the CSPro algorithm as sepsis due to bacterial contamination of the donor unit. One of the two deaths identified through the medical record review was designated by the CSPro algorithm as an acute hemolytic reaction. For both of these transfusion events, the clinical signs and symptoms were documented while monitoring the patient during and immediately following the transfusion event.

However, our findings suggest that the clinical staff did not recognize the signs and symptoms could have resulted from an acute transfusion reaction and neither of these suspected reactions were reported to the surveillance system. For these events, laboratory data, required by NHSN criteria to assign an imputability score of ‘definite’ were not available. However, the
Table 2: Diagnoses and severity scores of acute transfusion reactions as determined by reviewing a selected sample of transfusion events: Windhoek, Namibia - 2011

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Severity</th>
<th>Imputability</th>
<th>Mild</th>
<th>Moderate</th>
<th>Life-Threatening</th>
<th>Death</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute hemolytic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Probable¶</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Allergic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Febrile non-hemolytic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>4</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>5</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Hypotensive</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Sepsis due to bacterial contamination of the donor unit</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Transfusion-associated dyspnea</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Possible¶</td>
<td></td>
<td></td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>3</td>
</tr>
<tr>
<td>Transfusion reaction not otherwise specified</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>Definite</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Probable</td>
<td></td>
<td></td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Possible</td>
<td></td>
<td></td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>20</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>28</td>
</tr>
</tbody>
</table>
Laboratory data were unavailable. Clinical scenario, signs, and symptoms were highly consistent with these diagnoses, resulting in the imputability designations. No cases of transfusion-related acute lung injury were detected reviewing a selected sample of transfusion events. The Total column designates the total number of reactions detected in each diagnostic category. Imputability scores were based on criteria described in the CDC National Healthcare Safety Network Haemovigilance Module and were designated as: Possible, Probable, or Definite. In this table, for each diagnosis, only imputability categories for detected acute transfusion reactions are listed in the Imputability column. For example, no acute haemolytic reactions with “Possible” or “Definite” imputability designations were detected in this study. Hence, “Possible” and “Definite” are not included in the Imputability column for acute haemolytic reactions.

**Clinical details were strongly suggestive of these diagnoses resulting in the imputability designations of possible (sepsis due to bacterial contamination of the donor unit) and probable (acute hemolytic).**

**FIGURE 1: FLOW DIAGRAM OF TRANSFUSION EVENTS REVIEWED FOR EVIDENCE OF AN ACUTE TRANSFUSION REACTION (WINDHOEK, NAMIBIA, JANUARY 1 - DECEMBER 31, 2011)**
Based on reports received by the surveillance system (eight acute transfusion reactions in 3,697 transfusion events), the percentage of total transfusion events in Windhoek resulting in an acute transfusion reaction was observed to be 0.2% (Table 3). The estimated percentage of reported and non-reported acute transfusion reactions calculated from the medical record review was 3.4% (95% confidence interval (CI): 2.3-4.4). This estimate was significantly higher than the percentage determined by reports to the surveillance system (p < 0.01).

The rate of acute transfusion reactions per 1,000 blood units transfused was 0.8 when calculated using the eight transfusion reactions reported to the surveillance system (10,338 blood units transfused). This number increased to 11.5 (95% CI: 8.0-15.0) acute transfusion reactions per 1,000 blood units transfused when calculated using the number of reactions identified through the medical chart review. The adjusted estimated rates of acute transfusion reactions by component type transfused were: 12.9 (95% CI: 8.7-17.2) per 1,000 adult and pediatric PRBC units; 4.9 (95% CI: 1.4-8.4) per 1,000 adult and pediatric fresh frozen plasma units, and; 15.0 (95% CI: 1.0-29.0) per 1,000 adult and pediatric platelet units. No acute transfusion reactions were detected for the two whole blood units transfused in the study sample.

7.5 Discussion

The findings of this study reinforce previously published observations that morbidity and mortality related to acute transfusion reactions are a substantial public health problem in sub-Saharan Africa. [22] This study found that a significantly greater percentage of transfusion events occurring in Windhoek resulted in an acute transfusion reaction than were reported to the surveillance system in 2011. Four severe transfusion reactions, including two deaths, were not reported to the surveillance system. While laboratory data were not available to designate “definite” imputability based on NHSN criteria, two of these severe reactions were highly consistent with sepsis due to bacterial contamination of the donor unit and acute hemolytic reactions, respectively. The occurrence of these unreported severe transfusion reactions is concerning, but suggests that implementation of targeted interventions to improve bedside monitoring of patient signs and symptoms around the time of transfusion and facilitate reporting of suspected reactions to the surveillance system, could effectively reduce transfusion-related morbidity and mortality in Namibia. Consistent with previous observations, we found a higher rate of acute transfusion reactions occurring among platelet transfusions, followed by PRBCs and FFP, respectively. [15]

Some studies, restricted to one or few hospitals, have described prevalence and rates of acute transfusion reactions elsewhere in sub-Saharan Africa, with some reporting regional, not facility-based, estimates. [22,27,28,32] Due to differences in methodology, these reports describe widely varying rates and percentages of transfusions resulting in acute transfusion reactions. [22,27,28,32] The transfusion reaction rate reported here is generally comparable
with another rate reported elsewhere in sub-Saharan Africa. [28] Compared to industrialized countries, the rates and percentages described here are higher. [16,17,33-36] While this may reflect safer transfusion practices in industrialized countries, some of the differences may be attributable to varying representativeness, [35] reporting practices, [36,37] classification schemes, [16,17] and disease definitions adopted by individual transfusion reaction surveillance systems. [33] Furthermore, this study design may have resulted in higher percentages and rates than those described in other countries. Reviewing medical records for clinical evidence of acute transfusion reactions as described in this study constitutes ‘active’ surveillance and may result in higher estimated rates and percentages of acute transfusion reactions than the ‘passive’ surveillance method used by the NAMBTS hemovigilance system, which relies on healthcare worker reporting. [38]

The discrepancy between the reported and estimated percentages of acute transfusion reactions occurring in Windhoek may have two possible explanations: 1) A lack of transfusion reaction-related knowledge among healthcare workers or, 2) Infrastructure-related challenges. Since the launch of the national transfusion reaction surveillance system in Namibia, extensive training and outreach activities have been conducted by NAMBTS. However, given frequent staff turnover and movement of healthcare workers within and between facilities, many individuals involved in ordering or performing transfusions may not have yet participated in these training activities, resulting in reduced awareness related to appropriate patient monitoring, and transfusion reaction recognition and reporting. As NAMBTS continues outreach and training activities and enhances awareness among healthcare workers, acute transfusion reaction reporting should improve. In neighboring South Africa, a steady increase in reporting has been observed as the blood service has increased education and awareness activities among healthcare workers. [39] Addressing infrastructure-related barriers to reporting will likely pose a continued challenge in Namibia and other parts of sub-Saharan Africa. Limited telecommunication capacity, [40] challenges related to specimen transport [41] and few available transfusion medicine specialists [42] may preclude adequate reporting and investigation of acute transfusion reactions in these resource-limited settings. In Namibia, a national electronic medical record system is planned and once implemented, could be linked with NAMBTS to ease reporting challenges. While electronic systems may improve transfusion reaction reporting, [36] similar systems may be difficult to implement in other more resource-limited settings of sub-Saharan Africa.

Targeted interventions to address non-infectious causes of adverse transfusion reactions may provide an additional safety benefit to transfusion recipients in Namibia and similar settings. Nearly one-third of the acute transfusion reactions identified through the chart review were febrile non-hemolytic reactions with five respiratory-related transfusion reactions and three allergic reactions. Leukoreduction with filtration has been previously demonstrated to reduce the incidence of febrile, non-hemolytic reactions in industrialized countries. [43] However, this procedure is not routinely performed by NAMBTS due to cost considerations (personal
Furthermore, prevention of anaphylactic or other allergic acute transfusion reactions has been suggested by transfusing IgA-deficient plasma. [44] This intervention is unlikely to be feasible due to testing capacity or cost considerations in sub-Saharan Africa. Some interventions however, may be implemented at low or limited cost. Transfusion-associated circulatory overload may be prevented by diuretic therapy and slowing the transfusion rate for patients previously experiencing this reaction. [44] The occurrence of respiratory complications including transfusion-related acute lung injury may be prevented by preparing FFP solely from male or nulliparous female donors. [44] Given the relatively low use of FFP in Namibia, this intervention is unlikely to raise costs associated with component preparation or targeted donor recruitment.

A substantial burden of bacterial contamination of donor blood units has been reported in sub-Saharan Africa. [23] Consistent with this observation, our study detected at least one likely instance of sepsis due to bacterial contamination of the donor blood unit. These findings suggest that implementation of targeted interventions to decrease bacterial contamination of donated blood units in sub-Saharan Africa may reduce transfusion-related morbidity and mortality. Many interventions, previously demonstrated to be effective in industrialized countries, could be implemented in the region at low or minimal cost. Some of these, including deferral of donors with signs of illness or who have recently undergone medical or dental procedures and limitation of storage time prior to initiating transfusions, have already been instituted in Namibia. [35] Furthermore, NAMBTS has implemented diversion pouches to reduce bacterial entry into donor units. [45] An additional effective low-cost intervention which could be broadly implemented is a timed, double-swab disinfection protocol of the skin prior to collection, which is currently planned in Namibia in response to the findings of this study. [45] Consistent with observations in industrialized countries, our study also found high rates of transfusion reactions for platelets. [15] Given existing challenges with storage and transportation, other blood services in the region may consider the need for additional infrastructure improvements prior to implementation of platelet production.

This study is subject to the following limitations. Only transfusion events occurring in Windhoek were included in the study sample. The findings may not be generalizable to all of Namibia or to other countries in sub-Saharan Africa. Documentation in the medical records may have been incomplete and laboratory and radiographic data were frequently unavailable. This may have resulted in underestimation or misclassification of acute transfusion reactions detected. Several medical records were not located in two facilities. As a result, patient demographic information, blood component types and number of units, and clinical signs and symptoms related to transfusion events contained within these records are unknown. Despite some statistical adjustments, non-response bias cannot be excluded. Likely due to the relatively small numbers of FFP and platelet units included in the study sample, the

---

20 NAMBTS currently performs buffy coat depletion on PRBC units prior to storage.
RSE for estimates of acute transfusion reactions per 1,000 units transfused for each of these component types exceeded 30%. While there is no set cutoff, estimates with RSE greater than 30% may be statistically unreliable and should be interpreted with caution. [46]

While blood services have made substantial progress toward improving the safety and adequacy of blood supplies in many sub-Saharan African countries, [47] several challenges related to improving transfusion safety remain, especially to address adverse outcomes with non-infectious and infectious etiologies. These findings highlight an important gap in current investments in blood safety in sub-Saharan Africa, particularly in the area of patient safety during and following transfusions. Future studies in the region should reassess the burden of acute transfusion reactions after implementing targeted interventions. National health authorities and external donors should consider expanding current blood safety projects to emphasize transfusion safety and surveillance for adverse transfusion reactions, as well as the prevention of transfusion-transmissible infections.

Disclaimer
The findings and conclusions in this article are those of the authors and do not necessarily represent the views of the U.S. Centers for Disease Control and Prevention. The use of trade names is for identification purposes only and does not constitute endorsement by the U.S. Centers for Disease Control and Prevention or the Department of Health and Human Services.

Acknowledgements
The authors thank Fernando Carlosama for CSPro programming assistance and Justina Ang’huwo, Salmi Imbondi, and Deon Van Zyl for assistance with medical record abstraction.

7.6 References

services in a Kenyan hospital. AIDS 1993; 7: 995-999.