# Confidential donation confirmation as an alternative to confidential unit exclusion: 15 months experience of the HEMOMINAS foundation

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***Background:*** *Confidential unit exclusion remains a controversial strategy to reduce the residual risk of transfusion-transmitted infections.*

***Objective:*** *This study aimed to analyze confidential unit exclusion from its development in a large institution in light of confidential donation confirmation.*

***Methods:*** *Data of individuals who donated from October 1, 2008 to December 31, 2009 were analyzed in a case-control study. The serological results and sociodemographic characteristics of donors who did not confirm their donations were compared to those who did. Variables with p-values < 0.20 in univariate analysis were included in a logistic multivariate analysis.*

***Results:*** *In the univariate analysis there was a statically significant association between positive serological results and response to confidential donation confirmation of "No". Donation type, (first-time or return donor - OR 1.69, CI 1.37-2.09), gender (OR 1.66, CI 1.35-2.04), education level (OR 2.82, CI 2.30-3.47) and ethnic background (OR 0.67, CI 0.55-0.82) were included in the final logistic regression model. In all logistic regression models analyzed, the serological suitability and confidential donation confirmation were not found to be statistically associated. The adoption of new measures of clinical classification such as audiovisual touch-screen computer-assisted self-administered interviews might be more effective than confidential unit exclusion in the identification of donor risk behavior. The requirement that transfusion services continue to use confidential unit exclusion needs to be debated in countries where more specific and sensitive clinical and serological screening methods are available.*

***Conclusion:*** *Our findings suggest that there are not enough benefits to justify continued use of confidential donation confirmation in the analyzed institution.*

***Keywords:*** *Blood donors; Blood-borne pathogens; Blood banks; Evaluation of the efficacy-effectiveness of interventions*

## Introduction

Different strategies have been adopted in an effort to reduce the residual risk of transfusion-transmitted infections (TTI) including educating blood donation candidates, confidential unit exclusion (CUE), direct questioning about HIV risk behavior in private, serological and molecular tests, audiovisual touch-screen computer assisted self-interviewing and pathogen inactivation methods.[1-6] According to the World Health Organization (WHO), the adoption of screening strategies appropriate to the needs, infrastructure and resources of each country should contribute dramatically to improving transfusion safety. Over the last 20 years, countries that have implemented effective blood screening programs have significantly reduced the risks of TTI.[7]

The use of CUE remains a controversial strategy. There is evidence that prospective donors and even blood banking staff have difficulty understanding terminology used in the CUE leading to unnecessary disposal of blood units from low-risk donors.[8-13] A study published by the American Red Cross, based on data on more than 6,500,000 donations, estimated that CUE prevented only 0.6 of TTIs in the entire American Red Cross system per year. Among 109 donors found to be HIV-positive using nuclear acid technology (NAT), only four (3.7%) had elected under CUE to exclude their blood.[14]

In 2002, Brazil's National Health Surveillance Agency (ANVISA) mandated the implementation of CUE with the publication of resolution 343.[15] In December, 2010, resolution 57 of Anvisa made offering CUE optional. As noted by Martins et al.[16] there are few studies about this issue in Brazil.

The present study aimed to analyze CUE after its implementation in a large institution, under a new approach: the use of confidential donation confirmation (CDC). Believing that

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its purpose would be better understood, CDC was implemented in September 2008. Only blood units from donors who have confirmed by choosing the "Yes" option - that their units may be used for transfusion - are released. The vote is identified with a bar coded tag and is filled in confidentially after completing collection. The donor´s option remains secret to the professionals responsible for the pre-donation interview and blood collection, even in return donations.

We conducted a case-control study among donors of the largest collection unit of the study institution with the objective of comparing the sociodemographic characteristics and the serology results of donors who confirmed and did not confirm their donations.

## Methods

We analyzed data of individuals who donated blood from October 1, 2008 to December 31, 2009 at the main blood collection center of a regional blood bank. Using the institution's blood banking database, we created a second database specific for the study using Excel 2010® (Microsoft, USA). Variables included were: Study registry number, institutional registry number, age, gender, donation type (first-time or return), donor type (community or replacement), marital status (single, married, other), attained level of educational, ethnic background and serological status. A case group consisted of donors who had elected that their blood should not be transfused (CDC response "No"), left the CDC blank (CDC "Blank"), annulled the CDC (CDC "Null") or had not deposited the CDC (CDC "Non-complying"). The comparison (control) group consisted of donors who had affirmed in the CDC that their blood should be transfused (CDC "Yes"). Case and control groups were matched according to age. After a preliminary analysis, definitions for three variables were simplified: educational level: less than 9 years or 9 or more years of schooling; ethnical background: white or non-white; and serological status: reactive or non-reactive.

Exclusion criteria included: being considered ineligible to donate in the pre-donation screening, blood collection was abandoned because of difficult venous access or because the donor changed his mind and serology testing not being completed. The proportion of controls to cases was 2:1. The matching criteria were age, within 5 years of the corresponding case, and having donated in the same week as the case. The selection of controls was randomized. The serological data of all subjects was updated on November 30 2010 in order to check whether subjects who repeated the tests on a second sample had been allowed to donate or had become permanently ineligible.

We also verified if any of the donors from this period were subsequently included in hemovigilance procedures because of suspicion of seroconversion in accordance with current legislation.

The data was analyzed by comparing corresponding pairs. A univariate analysis was conducted first and variables found to be significant (p-value < 0.20) were incorporated in a multinomial logistic regressive model. The same logistic model was separately applied to each vote category. Analysis was performed for each voting class both separately and grouping the categories blank, null and non-complying votes in a group called "other CDC" (the blood of donors in these groups was discarded even though the donors themselves did not explicitly state that it should be).

Statistical analysis used STATA® version 10.1 statistical software (StataCorp, USA).

## Results

During the study period 345,696 units were collected by the institution. Of these, 4418 units (1.28%) were discarded because of the CDC. In the biggest facility, 89,284 CDC were analyzed with 945 corresponding to the categories "No", "Blank", "Null" and "Non-complying".

During the selection of the case group (those who had not confirmed their donation), 12 individuals were excluded because they changed their minds inside the collection room, had poor venous access, were actually stem cell donors or were clinically ineligible. In addition, 31 donations were excluded from the evaluation because the individuals had donated more than once during the study period and 16 donors were excluded as symptoms such as hypotension or fainting made collection impossible and thus serological screening was not performed. Thus the case group included 884 samples. Of these, 463 (52.38%) were CDC "No", 221 (25%) CDC "Blank", 90 (10.18%) CDC "Null", and 110 (12.44%) CDC "Non-complying". The case-control matching was analyzed and there were no statistically significant differences between the two groups.

Table 1 shows the frequency of serological deferrals for reactive results in five serology assays according to CDC category: "Yes", "No" and "Other CDC" ("Blank", "Null" and "Non-complying").

Table 1 - Serological deferral according to reactive test and CDC category

| CDC | "Yes" | "No" | "Other CDC" |
|---|---|---|---|
| Hepatitis B | 37 | 16 | 9 |
| Hepatitis C | 2 | 1 | 0 |
| Syphilis | 17 | 10 | 6 |
| HIV | 13 | 5 | 2 |
| HTLV | 2 | 0 | 1 |
| Total | 71 | 32 | 18 |

There was a statistically significant difference only for syphilis for CDC "No". Among the donors who had their blood discarded on the basis of their CDC, seven were found

to be HIV-reactive in serological screening. One of these had not performed a second assay as of November 30, 2010. Among the other six, two had non-reactive second samples and were allowed to donate; one was HIV indeterminate by ELISA 1 in the second sample with an indeterminate western blot; and the other three were HIV indeterminate by ELISA 1 with a negative western blot in the second sample. For HBV, 39 donors whose blood was discarded were reactive. For HCV, only one donor had an indeterminate result and as of November 30, 2010 had not repeated the test.

Table 2 shows the odds ratios for demographic variables and serological status according to the CDC category.

Table 2 - Demographic data and serological screening according to the CDC category

| | CDC Total discards OR (95% CI) | CDC "No" OR (95% CI) | CDC "Other CDC" OR (95% CI) |
|---|---|---|---|
| Donor type | | | |
| Community | 1.0 | 1.0 | 1.0 |
| Replacement | 1.03 (0.87-1.22) | 1.02 (0.81-1.29) | 1.05 (0.82-1.37) |
| Donation type | | | |
| Return | 1.0 | 1.0 | 1.0 |
| First-time | 1.62 (1.34-1.95) | 1.80 (1.39-2.35) | 1.43 (1.09-1.89) |
| Gender | | | |
| Female | 1.0 | 1.0 | 1.0 |
| Male | 1.80 (1.48-2.18) | 2.19 (1.66-2.88) | 1.946 (1.11-1.92) |
| Education level | | | |
| Less than 9 years schooling | 1.0 | 1.0 | 1.0 |
| 9 or more years schooling | 3.26 (2.66-4.01) | 3.21 (2.40-4.29) | 3.31 (2.48-4.43) |
| Ethnic background | | | |
| Non-white | 1.0 | 1.0 | 1.0 |
| White | 0.59 (0.49-0.71) | 0.56 (0.43-0.72) | 0.46 (0.32-0.68) |
| Marital status | | | |
| Single | 1.0 | 1.0 | 1.0 |
| Married | 0.95 (0.75-1.20) | 0.90 (0.64-1.25) | 1.00 (0.72-1.41) |
| Others | 0.97 (0.69-1.36) | 1.22 (0.78-1.90) | 0.68 (0.40-1.17) |
| Returned to Donate | | | |
| No | 1.0 | 1.0 | 1.0 |
| Yes | 0.85 (0.71-1.02) | 0.67 (0.53-0.86) | 1.11 (0.85-1.19) |
| Serological status | | | |
| Non-reactive | 1.0 | 1.0 | 1.0 |
| Reactive | 1.45 (0.99-2.13) | 1.76 (1.05-2.93) | 1.12 (0.63-2.02) |

CI = confidence interval

In the univariate analysis, donor type, community or replacement, and marital status were not statistically significant in the CDC "No" or in the CDC "Other CDC" group. The marital status category "others" has its limitations because it includes separated or divorced individuals as well as those living in a stable relation; thus, it is likely to be heterogeneous with regards to being sexually monogamous. The variables donor type, gender, education level, and ethnic background were significant for both CDC "No" and "Other CDC". The variable serological status was significant only for CDC "No".

Data from multivariate analysis for CDC "No" are shown in table 3.

After adjustment, the variable serological status became non-significant in CDC "No" as well. The other variables remained significant both for CDC "No" and "Other CDC". Considering the demographic differences found among first-time and return donors, the analysis was stratified by donation type. After stratification only the variables gender and education level remained statistically significant.

Table 3 - Multivariate analysis for CDC "No"

| Variable | OR | 95% CI | P> \|z\| |
|---|---|---|---|
| Serological status | | | |
| Non-reactive | 1.0 | | |
| Reactive | 1.34 | 0.76 - 2.35 | 0.317 |
| Donation type | | | |
| Return | 1.0 | | |
| First-time | 1.87 | 1.40 - 2.51 | 0.000 |
| Gender | | | |
| Female | 1.0 | | |
| Male | 2.09 | 1.56 - 2.81 | 0.000 |
| Education level | | | |
| Less than 9 years schooling | 1.0 | | |
| 9 or more years schooling | 2.80 | 2.08 - 3.75 | 0.000 |
| Ethnic background | | | |
| Non-white | 1.0 | | |
| White | 0.60 | 0.45 - 0.80 | 0.000 |

CI = confidence interval

Univariate analysis considering serological status as the dependent variable was performed. There was a statistically significant difference in the variable 'donation type' for both CDC "No" and "Other CDC" and in the variable related to the case control definition only for CDC "No". In the multivariate analysis of CDC "No", only donation type remained statistically significant (Table 4).

Table 4 - Multivariate analysis for CDC "No" with serological status as the dependent variable

| Variable | OR | 95% CI | P> \|z\| |
|---|---|---|---|
| Confidential Donation Confirmation | | | |
| "Yes" | 1.0 | | |
| "No" | 1.50 | 0.85 - 2.64 | 0.158 |
| Donation type | | | |
| Return | 1.0 | | |
| First-time | 6.01 | 2.85- 12.67 | 0.000 |

CI = confidence interval

In compliance with federal regulations (ANVISA board resolution 153 of 2004), 194 hemovigilance processes were initiated for donations collected at the institution's largest facility during the study period. Of these, 11 evolved with confirmed seroconversion. In all eleven, the donors had confirmed through their CDC that their blood could be used for transfusion. In only five cases the unit of blood had been discarded because of the CDC. In three of the five, seroconversion was not established; the other two were inconclusive, one because the donor had a history of having been vaccinated for Hepatitis B, and the other had an indeterminate anti-HBc in a second sample without anti-HBs titers. Among the 11 confirmed seroconversion cases, one donor reported that after collecting the second sample, he repeated the tests at the Universidade Federal de Minas Gerais where he was followed in a program for men with

partners of the same sex. This donor reported that he had had sexual relationships with other men in the past five years, a period during which he had donated blood at the institution on twelve occasions; three were after the implementation of CDC and each time he confirmed that his blood could be used for transfusion. Another donor reported he had had two casual sexual partners in the 12 months preceding the donation. There is no further documentation after the donation for one of the donors. All the others denied exposure to situations which increased the risk of TTI.

## Discussion

The findings of this study demonstrate that blood discarded with the CDC was similar to that reported in the literature for the traditional CUE option, although there is a wide range of results for different services and countries.[9-14,17,18]

In the univariate analysis of CDC "No", the variables donation type, gender, ethnic background, education level, and serological status were statistically significant factors which explain differences in relation to the group that confirmed the donation.

Even in the univariate analysis, there was no statistically significant difference for the variable serological status for the CDC "Other CDC" category ("Blank", "Null" and "Non-complying"). This suggests that units discarded on this basis did not contribute to reducing the risk of TTI. The stratified analysis demonstrated that CDC "Null" and "Non-complying" donors differ in sociodemographic characteristics to donors whose CDC was "No" or was left "blank". Our findings suggest that, for these donors, difficulty in understanding the donation confirmation process was the determining factor to discard their blood. These findings are consistent with older reports in the literature regarding CUE, which always identified low educational as a factor of donors who have difficulty in understanding the confidential exclusion procedure, as was donating for the first time.[9-14,17,18] There are reports of interventions in the procedure to increase prospective donor's understanding regarding the purpose of the CUE and the procedure itself, such as changing how the choice is presented and how the explanations were given by healthcare professionals.[10]

In the univariate analysis, considering serological status as the dependent variable, only donation type (first time or return) was statistically significant for the donors who had their blood discarded because of a CDC categorized as "Other CDC". There were significant associations of CDC "No" with donation type and with vote category; nevertheless, in the multivariate analysis, the association between serological status and vote category was not statistically significant. The only variable which was statistically significant to explain the difference between negative and positive serological donors was donation type, both for CDC "No" and those categorized as "Other CDC". Return donors are, in reality, pre-selected donors from a serological standpoint; once they are found to have reactive tests in a second sample, they are permanently barred from donating blood. It is, therefore, expected that repeat donors will have a lower serological deferral rate, and this is the reason that it is desirable to have committed repeat donors.

A previous study using the traditional CUE carried out in another facility of the same institution obtained different results concerning the serological status. This difference could be due to several factors. That analysis was only univariate, and did not adjust for other variables which in our sample proved to be significant. The other sample size was bigger; however it was obtained over 10 years, a period in which there were many changes in serological screening assays. Data from our study were obtained over a 15 month period and were thus subject to less variability in the sensitivity and specificity of the laboratory tests.

As noted by Korelitz et al.[9] studies evaluating the efficacy of CUE do not evaluate the primary objective, namely its ability to identify donation candidates at increased risk of transmitting blood-borne infections. The results can be strongly influenced by difficulties in understanding the process, leading donors with low education levels who have never donated before to exclude their blood donation, even when they have not been exposed to situations that increase the risk of TTI. The higher number of first-time donors among donors who exclude their blood may explain the greater frequency of serological ineligible donors among those who confidentially excluded units compared to those who did not. To measure the influence of the increased number of first-time donors in the group whose blood was discarded would require studies that follow donors over time comparing the incidence of seroconversion among the donors who had their blood discarded because of self-exclusion (or failure to confirm donation) with the incidence of seroconversion among those whose blood was made available for transfusion. It is appropriate to also consider if the donation index included in the study was in fact a first or return donation. Due to the recent implementation of CDC, such an analysis is not feasible.

The donation confirmation method did not prove to be more effective than CUE. Confidential exclusion, whether by CUE or CDC, is used with the goal of reducing the residual risk of TTI. Data analyzed however, did not demonstrate that discarding units of blood from donors who have not explicitly expressed that their blood should not be used for transfusions reduces the risk of transfusing units during the so-called immunologic window. The use of CUE or CDC by blood banking services which have the latest generation of serological and/or molecular screening methods does not seem to add enough benefits to justify discarding units, even from donors who say their blood should not be transfused. Discarding units of blood – in addition to raising production

costs – can increase deaths by contributing to shortages of blood components, with greater social consequences than those prevented by reducing TTI. The adoption of new clinical screening methods, such as audiovisual touch-screen computer-assisted self-administered interviews, could be more effective than confidential exclusion options in identifying donors exposed to high risk situations, by directly identifying exposure under conditions that are more private than traditional interviews. Further studies are necessary to address applicability. Countries which have limited access to laboratorial screening methods can benefit from CUE, but the obligatory nature of the exclusion or confirmation option should be reconsidered in settings that have more specific clinical screening methods and more sensitive serological methods. The findings from this study suggest that currently there are not enough benefits for the studied institution to justify the continued use of CDC after the rescission of the legal requirement of a confidential exclusion method.

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