Impact of Infusion Rates of Fresh Frozen Plasma and Platelets During the First 180 Minutes of Resuscitation

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BACKGROUND: Whether high-ratio resuscitation (HRR) provides patients with survival advantage remains controversial. We hypothesized a direct correlation between HRR infusion rates in the first 180 minutes of resuscitation and survival.

STUDY DESIGN: This was a retrospective analysis of massively transfused trauma patients surviving more than 30 minutes and undergoing surgery at a level 1 trauma center. Mean infusion rates (MIR) of packed red blood cells (PRBC), fresh frozen plasma (FFP), and platelets (Plt) were calculated for length of intervention (emergency department [ED] time + operating room [OR] time). Patients were categorized as HRR (FFP:PRBC > 0.7, and/or Plts: PRBC > 0.7) vs low-ratio resuscitation (LRR). Student’s t-tests and chi-square tests were used to compare survivors with nonsurvivors. Cox proportional hazards regression models and Kaplan-Meier curves were generated to evaluate the association between MIR for FFP:PRBC and Plt:PRBC and 180-minute survival.

RESULTS: There were 151 patients who met criteria: 121 (80.1%) patients survived 180 minutes (MIR:PRBC 71.9 mL/min, FFP 92.0 mL/min, Plt 3.5 mL/min) vs 30 (19.9%) who did not survive (MIR:PRBC 47.3 mL/min, FFP 33.7 mL/min, Plt 1.1 mL/min), p = 0.43, p < 0.0001, and p < 0.011, respectively. A Cox regression model evaluated PRBC rate, FFP rate, and Plt rate (mL/min) as mortality predictors within 180 minutes to assess if they significantly affected survival (hazard ratios 1.01 [p = 0.054], 0.97 [p < 0.0001], and 0.75 [p = 0.01], respectively). Another model used stepwise Cox regression including PRBC rate, FFP rate, and Plt rate (hazard ratios 1.00 [p = 0.85], 0.97 [p < 0.0001], and 0.88 [p = 0.24], respectively), as well as possible confounding variables.

CONCLUSIONS: This is the first study to examine effects of MIRs on survival. Further studies on the effects of narrow time-interval analysis for blood product resuscitation are warranted. (J Am Coll Surg 2014;219:181-e188. © 2014 by the American College of Surgeons)
The timing and volume of blood product administration in patients with severe hemorrhage from trauma is therefore critical to uncovering a survival benefit associated with such strategies.

From military and civilian experience, increased awareness regarding avoidance of unnecessary crystalloids in bleeding trauma patients has emerged, with attention shifting toward target-directed use of blood and blood products for resuscitation in patients requiring massive transfusion. Damage-control resuscitation has emerged as a balanced resuscitation strategy for combating injury-associated coagulopathy in both military and civilian settings. This strategy involves the use of fresh frozen plasma (FFP) as a primary resuscitative fluid in high ratios (1:1 to 1:2) with packed red blood cells (PRBCs). The survival advantage for high-ratio resuscitation (HRR) in exsanguinating patients has also been described for platelets (Plt:PRBC). Multiple investigations have shown a survival benefit when patients have received FFP early in resuscitation, and at high ratios. The impact of volume and timing of high-ratio resuscitation with respect to its survival benefit in hemorrhaging severely injured patients has not been reported.

Despite these advances in resuscitative survival strategies, controversy remains regarding the temporal relationship between blood product administration and survival, and there have been only a handful of studies critically examining the timing of resuscitation in this population. These studies recognize that the timing of blood product administration affects outcomes. It has been noted that the apparent survival advantage among patients receiving higher ratios of FFP:PRBC may merely be due to the fact that they lived long enough to receive the higher ratio of products, therefore the concept of survival bias. Moore and colleagues recognized that the critical timeframe and focus for research on massive transfusion occurs in the first 3 hours. To date, examining volume infusion rates of FFP, Plt, and PRBCs and their effect on survival advantage in severely hemorrhaging patients undergoing damage control surgery has not been studied.

In this study, we examined mean infusion rates (MIR) of blood products in patients with severe hemorrhage undergoing damage control surgery. We hypothesized a dose-dependent direct correlation between infusion rates (for both FFP:PRBC and Plt:PRBC) early in resuscitation (in the first 180 minutes of hospital time) and survival. Furthermore, we postulated that early, time-sensitive appraisal of blood product infusion rates can reveal whether or not early HRR is actually taking place, diminishing the effects of survival bias in studies examining HRR. We believe that using MIR to examine early resuscitation may help elucidate a better understanding of the true impact of HRR on survival.

**METHODS**

Between January 2009 and January 2011, all adult trauma patients treated at the Spirit of Charity Hospital in New Orleans, LA, who underwent massive transfusion and proceeded directly to the operating room (OR) from the emergency department (ED), were selected for inclusion in this study. Adults were defined as nonpregnant, nonincarcerated patients 18 years of age or greater, without traumatic brain injury. Massive transfusion was defined as the administration of 10 or more units of PRBC during the first 24 hours of hospitalization. The Spirit of Charity Hospital is the only American College of Surgeons-verified level 1 trauma center in Louisiana.

Demographics, transfusion events, laboratory data, and mortality during the first 180 minutes of hospitalization were retrieved from the electronic medical records in collaboration with our trauma registry. A team of trauma surgeons determined and defined length of intervention as ED + OR treatment time. Quality control for data was performed by a second set of trauma surgeons who compared the times for blood product release from the blood bank with the recorded time of product arrival and administration. No data inconsistencies were noted.

Mean infusion rates (MIR, in mL/min) were calculated for PRBC, FFP, and Plts for the length of intervention by dividing the volume of each blood product given per care phase (ie, ED time or OR time) by the time spent in each care phase. No patient had exclusively ED or OR care phases, and no patient had zero blood product given in either care phase. Additionally, all patients received both PRBC and FFP in each care phase. Preliminary review demonstrated that most significant events occurred within the selected study timeframe of the first 180 minutes of hospitalization, and total length of intervention for patients included in the study was less than or equal to 180 minutes for 116 of 151 patients (76.8%). The ratios FFP:PRBC and Plts:PRBC were calculated in units.
Patients with (FFP:PRBC or Plt:PRBC) ratios greater than/equal to 0.7 (≥ about 1:1.4) were included in the “high-ratio resuscitation” (HRR) group, and patients with ratios less than 0.7 (< about 1:1.4) were included in the “low-ratio resuscitation” (LRR) group. This stratification of patients was selected based on recently published series recommending FFP:PRBC ratios of approximately 1:1.5 for significantly lower risk of mortality after massive transfusion.12,13 Patients who received PRBC but no plasma (n = 6) and/or no Plts (n = 60) had a calculated MIR of 0, and were included in the LRR group. Because the Spirit of Charity Hospital massive transfusion protocol (MTP) emphasizes initiation of MTP in the ED when significant hemorrhage is suspected, based on initial staff trauma surgeon objective evaluation (assessing physiology/mechanism of injury, known coagulopathy, or 3 of 6 hemodynamic instability criteria being met), all MTPs considered in this study were initiated within 15 minutes of arrival to the hospital.14 Although equal temporal administration of FFP and PRBC (eg, administration of 1 unit of PRBC followed immediately by 1 unit of FFP, before the next unit of PRBC) is not explicit in the MTP protocol/policy, all 10 staff trauma surgeons at our institution advocate early intraoperative temporal equity of blood product administration. Therefore, the vast majority of patients received PRBC and FFP early in the MTP.

Statistical analysis
Demographic and clinical characteristics were compared between survivors and nonsurvivors using Student’s t-tests and chi-square tests for continuous and categorical variables, respectively. Cox proportional hazards regression models and Kaplan-Meier curves were generated to evaluate the association between MIR for FFP:PRBC and Plt:PRBC and 180-minute survival. If patients survived within the first 180 minutes, with adjustment for age, sex, mechanism of injury, and initial coagulopathy or 3 of 6 of 6 hemodynamic instability criteria being met), all MTPs considered in this study were initiated within 15 minutes of arrival to the hospital.14 Although equal temporal administration of FFP and PRBC (eg, administration of 1 unit of PRBC followed immediately by 1 unit of FFP, before the next unit of PRBC) is not explicit in the MTP protocol/policy, all 10 staff trauma surgeons at our institution advocate early intraoperative temporal equity of blood product administration. Therefore, the vast majority of patients received PRBC and FFP early in the MTP.

RESULTS

A total of 151 patients met inclusion criteria, all of whom had complete medical records available to review. Of these, 120 patients (79.5%) achieved HRR of FFP:PRBC, with 104 patients surviving 180 minutes (86.7%). Thirty-one patients (20.5%) were categorized as LRR FFP:PRBC; 17 of these patients survived 180 minutes (54.8%), p < 0.001. Thirty-seven patients (24.5%) achieved HRR of Plt:PRBC, with 34 patients surviving 180 minutes (91.9%). In contrast, 114 patients (75.5%) were categorized as LRR Plt:PRBC, and 87 of these patients survived 180 minutes (76.3%), p < 0.004. In total, 124 patients (82.1%) achieved HRR of either FFP:PRBC or Plt:PRBC, and 107 of these survived 180 minutes (86.3%). Twenty-seven patients (17.9%) were categorized as LRR for FFP:PRBC and Plt:PRBC, and 14 of these patients survived 180 minutes (51.9%), p < 0.0001.

Overall 180-minute survival for the study timeframe was 80.1% (121 patients). Among the group who survived 180 minutes, the MIRs were: 71.9 mL/minute for PRBC, 92.0 mL/minute for FFP, 3.5 mL/minute for Plts. Thirty patients (19.9%) did not survive 180 minutes, and MIRs for this group were: 47.3 mL/minute for PRBC, 33.7 mL/minute for FFP, 1.1 mL/minute for Plts; p = 0.43, p < 0.0001, and p < 0.011, respectively.

Overall in-hospital mortality for all patients was 49.7% (75 deaths), with the majority of deaths (66.7%, 50 patients) occurring in the first 360 minutes, and 30 deaths (40%) occurring in the first 180 minutes. Clinical characteristics of survivors and nonsurvivors are presented in Table 1. No significant differences were noted in age, sex, mechanism of injury, and initial prothrombin time, activated partial thromboplastin time, international normalized ratio, and hemoglobin between survivors and nonsurvivors. Injury Severity Score and shock index were higher among nonsurvivors.

Table 1. Characteristics of Survivors and Nonsurvivors

<table>
<thead>
<tr>
<th>Total patients (January 2009 to January 2011) (n = 151)</th>
<th>Survivors (n = 121)</th>
<th>Nonsurvivors (n = 30)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, mean (SD)</td>
<td>31.1 (11.3)</td>
<td>34.9 (16.2)</td>
<td>0.24</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>111 (91.7)</td>
<td>27 (90.0)</td>
<td>0.76</td>
</tr>
<tr>
<td>Penetrating, n (%)</td>
<td>103 (85.1)</td>
<td>24 (80.0)</td>
<td>0.68</td>
</tr>
<tr>
<td>Admission GCS score, mean (SD)</td>
<td>11.9 (5.1)</td>
<td>6.3 (5.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ISS, mean (SD)</td>
<td>22.2 (12.1)</td>
<td>36.4 (16.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Shock Index, mean (SD)</td>
<td>1.2 (0.5)</td>
<td>1.3 (0.6)</td>
<td>0.62</td>
</tr>
<tr>
<td>SBP, mmHg, mean (SD)</td>
<td>108.7 (17.8)</td>
<td>82.1 (23.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Heart rate, bpm, mean (SD)</td>
<td>112.6 (29.6)</td>
<td>110.5 (33.0)</td>
<td>0.76</td>
</tr>
<tr>
<td>INR, mean (SD)</td>
<td>1.5 (1.4)</td>
<td>2.2 (2.7)</td>
<td>0.30</td>
</tr>
<tr>
<td>PT, s, mean (SD)</td>
<td>18.7 (24.7)</td>
<td>31.8 (50.3)</td>
<td>0.29</td>
</tr>
<tr>
<td>aPTT, s, mean (SD)</td>
<td>39.1 (32.4)</td>
<td>60.3 (55.4)</td>
<td>0.13</td>
</tr>
<tr>
<td>Hgb, g/dL, mean (SD)</td>
<td>10.5 (2.5)</td>
<td>9.9 (2.5)</td>
<td>0.30</td>
</tr>
</tbody>
</table>
| aPTT, partial thromboplastin time; bpm, beats per minute; GCS, Glasgow Coma Scale; Hgb, hemoglobin; INR, international normalized ratio; ISS, Injury Severity Score; PT, prothrombin time; SBP, systolic blood pressure.
The injury severity burden distribution between the 2 groups was evaluated by noting the presence of major injuries sustained by each patient. Major cardiac, vascular, hepatic, splenic, and pelvic injuries were considered for the purposes of better characterizing individual and group injury severity burden. Vascular injuries were the most common type of major injury in both groups. Of the 122 patients who survived 180 minutes, 67 (54.9%) sustained at least 1 major arterial or venous injury. Seventeen of the 30 (56.7%) patients who did not survive 180 minutes suffered 1 or more arterial or venous injury. The caliber and mean number of injured vessels in patients with at least 1 vascular injury were comparable in both groups (p > 0.05).

Eleven of the 122 (9.0%) patients who survived 180 minutes sustained major cardiac injuries; only 1 of the 30 (3.3%) patients who did not survive 180 minutes suffered similar major cardiac injuries. Thirty-two of the 122 (26.2%) surviving patients sustained major hepatic injuries, while 11 of the 30 (36.7%) patients not surviving 180 minutes sustained major hepatic injuries. Thirteen (10.7%) patients surviving 180 minutes sustained major splenic injury, compared with 2 of 30 (6.7%) patients not surviving 180 minutes. Lastly, although 13 of the 122 (10.7%) patients in the group surviving 180 minutes had pelvic injuries, only 1 of the 30 (3.3%) patients in the nonsurvival group was found to have major pelvic fractures/injuries.

Thirty of the 122 (24.6%) patients surviving 180 minutes had 2 major injuries concurrently, and 7 (5.7%) had 3 major injuries concurrently. Among the group not surviving 180 minutes, 7 (23.3%) had 2 major injuries, and 1 (3.3%) had 3 of the major injuries discussed.

Survival rates (180-minute survival) associated with the LRR and HRR groups for both FFP:PRBCs and Plts:PRBCs were calculated. In total, 124 patients (82.1%) achieved HRR of either FFP:PRBC or Plt:PRBC, and 107 of these survived 180 minutes (86.29%). Twenty-seven patients (17.9%) were categorized as LRR for FFP:PRBC and Plt:PRBC, and 14 of these patients survived 180 minutes (51.85%), p < 0.0001. Mean infusion rates were calculated for each blood product (PRBC, FFP, Plts) for the first 180 minutes of hospital time for each patient. Figure 1 shows the MIRs of PRBCs, FFP, and Plts for survivors and nonsurvivors in the first 180 minutes of hospitalization. Blue bar, survival, n = 121; red bar, nonsurvival, n = 30.

DISCUSSION

Our study demonstrates a survival advantage when HRR is examined during the first 180 minutes of resuscitation using infusion rates measured with narrow time intervals, rather than infusion ratios measured at larger time intervals. This may be due to the fact that mean infusion rates...
with narrow time intervals inherently demonstrate FFP:PRBC and Plt:PRBC administration in high ratios with appropriate temporal equity, not allowing for the assumption of such. The use of MIRs as a proxy for determining if appropriately early HRR is taking place has important implications for the interpretation of observational studies, which seek to inform recommendations for HRR/damage-control resuscitation in exsanguinating trauma. This is the first study to analyze the impact of MIRs on survival of massively hemorrhaging patients. We demonstrated a survival advantage in the first 180 minutes of resuscitation at high MIRs of FFP:PRBC and Plts:PRBC in patients with severe hemorrhage.

Multiple military and civilian studies have demonstrated improved survival for HRR groups relative to LRR groups using infusion ratios for both Plt:PRBC and FFP:PRBC, but few have specifically examined these ratios with respect to the timing of the resuscitation efforts. Given the increased emphasis on early achievement of high ratios of FFP:PRBC (and Plt:PRBC) for maximizing survival advantage, a powerful few studies have emerged specifically addressing the timing of transfusion products and survival. These studies have successfully raised the question of the impact of survival bias on studies examining HRR and drawing conclusions about survival advantage.

Both Snyder and colleagues in 2009, and Magnotti and associates in 2011 specifically examined the association between HRR and reduced mortality, and recognized

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard ratio</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRBC rate, mL/min</td>
<td>1.00</td>
<td>0.980, 1.017</td>
<td>0.85</td>
</tr>
<tr>
<td>FFP rate, mL/min</td>
<td>0.97</td>
<td>0.954, 0.977</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Plt rate, mL/min</td>
<td>0.88</td>
<td>0.715, 1.088</td>
<td>0.24</td>
</tr>
<tr>
<td>Age, y</td>
<td>0.99</td>
<td>0.964, 1.023</td>
<td>0.66</td>
</tr>
<tr>
<td>Sex, male</td>
<td>0.53</td>
<td>0.164, 1.731</td>
<td>0.30</td>
</tr>
<tr>
<td>Injury mechanism</td>
<td>2.81</td>
<td>1.011, 7.794</td>
<td>0.048</td>
</tr>
<tr>
<td>ED GCS</td>
<td>0.94</td>
<td>0.870, 1.024</td>
<td>0.17</td>
</tr>
<tr>
<td>Shock Index</td>
<td>1.35</td>
<td>0.623, 2.905</td>
<td>0.45</td>
</tr>
<tr>
<td>ISS</td>
<td>1.03</td>
<td>1.007, 1.062</td>
<td>0.01</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>1.00</td>
<td>0.984, 1.007</td>
<td>0.41</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>0.97</td>
<td>0.953, 0.978</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

bpm, beats per minute; ED, emergency department; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score; PRBC, packed red blood cells; Plt, platelets; SBP, systolic blood pressure.
that this association was not apparent after correcting for survival treatment selection bias. Snyder and coworkers\textsuperscript{35} noted that the apparent survival advantage seen among those receiving higher FFP:PRBC ratios may be due to the fact that these patients lived long enough to receive the higher ratio, i.e., survival bias accounted for the observed survival advantage. They concluded that after adjusting for survival bias, the association between higher ratios of FFP:PRBC at 24 hours and improved survival was not statistically significant. Magnotti and coauthors\textsuperscript{3} expounded on the temporal analysis of blood product administration and survival in their 2011 study. They noted that the study by Snyder and colleagues\textsuperscript{35} was limited by a potential ordering bias because the authors had indicated a disparity in the administration of plasma in their study: although PRBC administration commenced within minutes of admission, FFP was often not administered until 90 minutes or longer after admission. Magnotti and associates\textsuperscript{3} amended this discrepancy in their study, commencing transfusions of FFP and PRBC within minutes of a patient's arrival to the hospital. They likewise performed a survival bias analysis and observed improved survival in patients receiving higher FFP:PRBC ratios in the first 24 hours.

In 2012, Brown and coworkers\textsuperscript{36} studied a prospective cohort of 604 massively transfused blunt trauma patients, and sought to characterize mortality in the first 24 hours and control for the time-varying effects of transfusion, in order to minimize survival bias. They broke the cohort into HRR and LRR groups, and compared them at 6 hours, 12 hours, and 24 hours and found that HRR FFP:PRBC was associated with a 68% reduction in 24-hour mortality, and that HRR Plt:PRBC was associated with a 96% reduction in 24-hour mortality. Subgroup analysis revealed that a the highest-ratio resuscitation groups had a significant 24-hour survival benefit relative to the less high ratio groups at 6 hours and at 24 hours, suggesting a dose-dependent relationship between FFP administration and survival. They concluded that high FFP:PRBC and Plt:PRBC ratios are associated with a survival advantage as early as 6 hours, and through 24 hours, even when accounting for time-dependent fluctuations in components-based transfusion. This suggests that the survival benefit associated with HRR is unlikely due to survival bias, and that early attainment of HRR can significantly decrease the risk of mortality in massively transfused patients.

Given that survival bias greatly affects interpretation of outcomes in studies of HRR in trauma patients, based on variations in achievement of the high ratio (i.e., temporal differences in the administration of FFP relative to PRBC), it is of critical importance to study the effects of achievement of HRR as early as possible in the resuscitative period on survival and survival bias. Moore and colleagues\textsuperscript{30} noted that the critical timeframe for massive transfusion is the first 3 hours, and we therefore focused our study on the first 3 hours after admission for patients with severe hemorrhage. Our novel method of examining HRR vis-à-vis survival in massively transfused trauma patients was to evaluate MIRs over a much shorter timeframe (180 minutes for the length of intervention). This strategy focuses on the critical portion of massive transfusion interventions, and obviates need to look at cumulative (6- or 24-hour) ratios and then retrofit calculations for shorter time intervals. The use of mean infusion rates within such a short timeframe allows us to examine the dose-relationship of FFP in patients undergoing massive transfusion. Interestingly, FFP rate remained an excellent predictor of mortality across all 3 Cox regression models, and the hazard ratio was strikingly consistent across all 3 models. This suggests that FFP rate is a solid predictor of mortality and that the effect remains virtually unchanged even when results are adjusted for demographics and other characteristics.

This study does not eliminate survival bias, and in fact, it may be impossible to completely remove the effects of survival bias on studies examining survival based on any resuscitative or therapeutic intervention. Rather, by examining outcomes based on resuscitation over a relatively narrow but critical time interval, the effects of survival bias can be dampened. It is critical to recognize that even within narrow timeframes, some patients will receive lower amounts of blood product resuscitation because they do not survive that time interval. The results of our study should be understood with several other important limitations. First, because this is the first study to examine the impact of using MIR as a means of discerning appropriate early HRR of FFP:PRBC and Plt:PRBC, there are no volumetric standards in place with which to compare our rates, and the precise rate at which a survival benefit is recognized has not been established by a larger cohort. Larger studies will be required to further characterize the infusion rates at which a critical survival benefit is substantiated. Additionally, actual rates of blood product infusion could not be discerned in this retrospective study because that would involve real-time analysis of the entire resuscitation period. The MIRs used in this analysis are a proxy of actual rates of infusion. Because the actual order and timing of individual blood product infusions are not known, these MIR calculations are imprecise, and may be confounded by temporal inequity in administration of any of the blood products. Although the fact that all patients received both PRBC and FFP in each care
phase (ED and OR) attenuates this limitation, there were some patients who did not receive platelets in the ED care phase. Further studies with narrower time intervals will be required to better evaluate the impact of MIRs on elucidating survival benefit among trauma patients.

Other limitations of this study are those related to retrospective study design. The data used for this study may lack certain caveats of medical/surgical history and resuscitation of patients with severe hemorrhage, such as prehospital transport times and the use of crystalloid in these prehospital settings. Although this study compares our method for evaluating HRR with conventional methods, the Cox regression models performed are not duplicated with smaller time intervals (as they are with other studies evaluating survival bias), because rate data cannot be assessed as ratios at fixed intervals. Additionally, because transfusion protocols and applications vary significantly, the results from a single-center study may not be generalizable to other trauma centers, both military and civilian. Finally, the relatively small study population of 151 patients may not provide the requisite statistical power to determine an actual survival advantage.

CONCLUSIONS

Whether or not HRR of blood products provides a survival advantage to severely injured patients remains controversial. Using MIRs as a proxy for determining if appropriately early HRR is taking place has important implications for the interpretation of observational studies, which seek to inform recommendations for HRR and damage-control resuscitation in exsanguinating trauma. This is the first study to analyze the impact of MIRs on survival of massively hemorrhaging patients. We demonstrated a survival advantage in the first 180 minutes of resuscitation at high MIRs of FFP and Plts:PRBC; however, further analyses of the impacts of MIRs of crystalloid, colloid, and other blood products on trauma patient survival are warranted. A multi-institutional analysis is needed in order to validate these results.

Author Contributions

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Analysis and interpretation of data: Simms, Hennings, Hauch, Musa, Wascom, Bock-Heaney, Fontenot, Myers, Duchesne

Drafting of manuscript: Simms, Hennings, Hauch, Duchesne

Critical revision: Simms, Hennings, Hauch, Fontenot, Hunt, McSwain, Meade, Long, Bock-Heaney, Duchesne

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