Finale Report for CMRF: Dr Patrice Rosengrave

To evaluate the effect of vitamin C on physical functioning and performance, and mental health outcomes of survivors of sepsis.

I am providing some preliminary results obtained from this research project that will be part of a published manuscript relating to the randomised controlled trial (RCT) assessing the short-term effects of intravenous vitamin C administrated to patients with severe sepsis. There were delays in getting this trial started and in combination with a slow recruitment enrolment which had a flow-on effect with getting follow-up data for this research.

The final sample size for a complete follow-up data set is a total of 19 participants. Statistically, we will be unable to confirm differences in quality-of-life outcomes of those patients who received vitamin C compared to the control group. However, health-related quality of life measures of the combined data set (survivors of severe sepsis) can be compared to New Zealand population average values.

This study provides the first data set whereby survivors of sepsis from the Christchurch intensive care unit have been followed up post-hospital discharge and quality of life measures obtained. In addition, this study provides data that will inform future research proposals in this area. Recognition of residual impairments to quality of life resulting from a critical illness such as sepsis shifts values from merely a reduction in-hospital mortality to more "patient-centred outcomes.

Methods

Participants for this study had been enrolled, upon admission to the Christchurch Hospital ICU, in a double-blind, randomised controlled trial (RCT) assessing the short-term effects of intravenous vitamin C administration (See table 1 for participant enrolment characteristics). All patients over 18 years admitted to the Christchurch Public Intensive care unit (ICU) were screened for inclusion in the RCT. Inclusion criteria include receiving IV antimicrobial treatment for infection, receiving IV > 5 mcg/min adrenaline/noradrenaline, and evidence of organ dysfunction. We enrolled a total of 40 patients into the RCT. Of this cohort, 14 patients died (seven from the treatment group (received IV vitamin C while in ICU) and seven from the placebo group (received Iv 5% dextrose).

At six weeks, three months and six months post-hospital discharge, patients who consented and were alive (enrolled in the RCT) were contacted by a blinded research coordinator to conduct Health-Related Quality of Life (HRQoL) assessment using the SF-36v2®, the EQ-5D-5L®, and a cognitive assessment tool (COBRA). The EQ-5D-5L® collates responses into five domains of HRQoL (mobility, self-care, usual activities, pain or discomfort, and anxiety or depression) with a five-level score (no problems, slight problems, moderate problems, severe problems, extreme problems or unable). The SF-36v2® captures the participants' perception of their general health by scoring them into the following eight scales: physical role functioning, bodily pain, general health perceptions, vitality, social role functioning, emotional role functioning, and mental health. The eight scales can be combined into two summary measures, providing overall physical health and mental health estimates. Other data collected were perceptions of participants' current overall health; the scale graduated from 0 (the worst imaginable health state) to 100 (the best imaginable state), along with employment history pre and post-admission to the ICU. We will use general New Zealand population norms to provide a basis for meaningful comparisons of domains. The administration of all questionnaires took approximately 20 minutes to complete via phone interview.

Results

A total of 19 survivors of sepsis have completed the follow-up questionnaires (this data will be part of a flow chart for the final manuscript). In addition, all the data has been entered into a database programme (REDCAP). I am currently, with my collaborator Dr Anitra Carr, in the process of analysing data and preparing manuscripts for publication as a result of the RCT and this follow-up study.

Preliminary data (see attached graphs) suggests no significant differences in mental health performance (figure 1) quality of life measures (figure 2), comparing patients with intravenous vitamin C compared to patients who received intravenous placebo. I will use general New Zealand population norms to provide a basis for meaningful comparisons of domains for these quality-of-life measures for the complete dataset

Table 1. Randomised clinical trial participant demographic and clinical characteristics. Patients diagnosed with severe sepsis admitted to the Christchurch Intensive Care Unit. Intervention patients received vitamin C infusion of 25 mg/kg 6 hourly and the placebo patients 5% dextrose six hourly.

	Intervention (n=20)	**Placebo (n=20)**	**Total (N=40)**
Gender (male)	16 (80.0%)	11 (55.0%)	27 (67.5%)
Age in years	68.5 (63.5, 76.1)	65.7 (56.6, 71.1)	67.7 (61.1, 75.1)
Ethnicity			
Maori	2 (10.0%)	1 (5.0%)	3 (7.5%)
Pacific	1 (5.0%)	0 (0.0%)	1 (2.5%)
Asian	0 (0.0%)	1 (5.0%)	1 (2.5%)
European	16 (80.0%)	18 (90.0%)	34 (85.0%)
Unknown	1 (5.0%)	0 (0.0%)	1 (2.5%)
Source of Sepsis			
Abdominal	8 (40.0%)	6 (30.0%)	14 (35.0%)
Pulmonary	3 (15.0%)	6 (30.0%)	9 (22.5%)
Skin/soft tissue	4 (20.0%)	3 (15.0%)	7 (17.5%)
Bloodstream	3 (15.0%)	4 (20.0%)	7 (17.5%)
Urinary	0 (0.0%)	1 (5.0%)	1 (2.5%)
UTI	2 (10.0%)	0 (0.0%)	2 (5.0%)
Other	1 (5.0%)	0 (0.0%)	1 (2.5%)
Measures of Organ Failure/mortality and disease severity			
SAPS 2	49.5 (40.5, 58.8)	49.0 (42.0, 57.5)	49.5 (41.0, 58.2)
APACHE-II score	21.5 (18.0, 25.0)	21.0 (19.0, 24.0)	21.0 (18.5, 24.5)
SOFA Score	8.5 (6.8, 11.2)	9.0 (7.8, 10.0)	9.0 (7.0, 10.2)

APACHE Ⅱ = acute physiology and chronic health evaluation, SOFA = sequential organ failure assessment. SAP 2 = Simplified Acute Physiology Score,

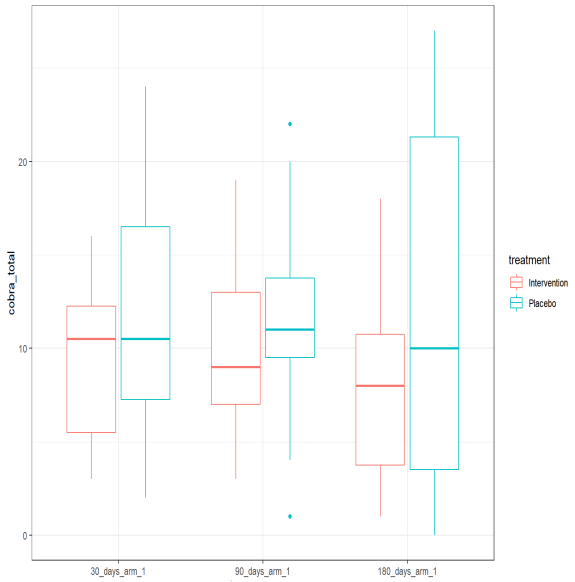

Figure 1. Boxplots comparing cognitive function between patients with sepsis who received IV vitamin C in ICU (intervention) and those that received 5% dextrose (placebo) at 30 days, 90 days and 180 days discharge from the intensive care unit at Christchurch Public Hospital. The "cognitive complaints in bipolar disorder rating assessment" (COBRA) was administered.

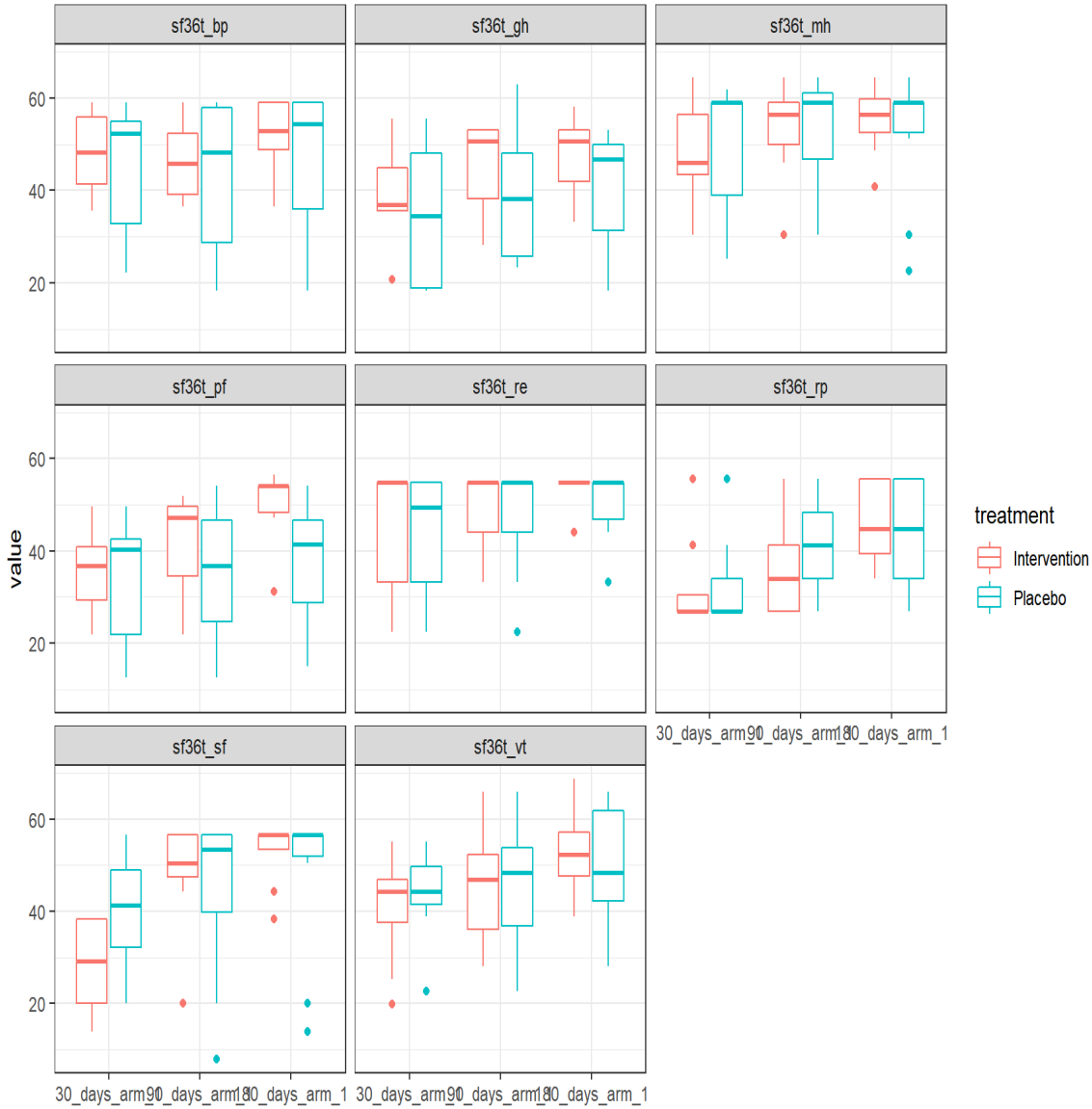

Figure 2. Boxplots showing the comparison of health-related quality of life measures between with sepsis who received IC vitamin C in ICU (intervention) and those that received IV 5% dextrose (placebo) at 30 days, 90 days and 180 days post-discharge from the intensive care unit at Christchurch public hospital. The SF 36v2 questionnaire was administered, which includes the following measures of quality of life (physical functioning (pf), role physical, bodily pain (bp), general health (gh), vitality (vt), social functioning (sf), role emotional, mental health (mh).

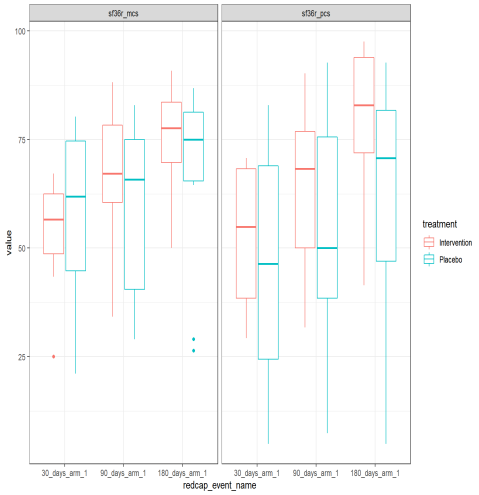

Figure 3. Boxplots showing comparisons between overall estimates of physical (pcs) and mental health (mcs) measures between patients with sepsis who received IV vitamin C in the ICU (intervention) compared to those patients that received IV 5% dextrose (placebo) at 30 days, 90 days and 180 days post-discharge from the intensive care unit at Christchurch Public Hospital