vitro. Thus, we provide important insights into the changes occurring after prolonged *in vitro* expansion, underlining the importance of using low passage MSCs in clinical trials for ARDS. In agreement with published data, we also found that MSCs do not induce cellular proliferation in the absence of stimulation.

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S12 PLASMA SYNDECAN-1 LEVEL AS A PREDICTIVE MARKER OF VASOPLEGIA ASSOCIATED WITH SURGERY REQUIRING CARDIOPULMONARY BYPASS AND POSSIBLE INVOLVEMENT OF OXIDATIVE STRESS

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Background Vasoplegic syndrome (severe refractory hypotension) is associated with oxidative stress leading to endothelial dysfunction and complicates 10 to 40% of surgery requiring cardiopulmonary bypass (CPB). Whilst operative mortality is low, recovery is often prolonged in patients developing vasoplegia. There are, as yet, no validated biomarkers for vasoplegia that could be used to identify 'at risk' patients. We hypothesised that plasma levels of the endothelial surface layer (glycocalyx) protein, syndecan-1, shed during CPB, will be higher in patients who develop vasoplegia and that leukocyte responses to oxidative stress will be altered.

Methods Patients (n = 48) undergoing cardiac surgery requiring CPB were, prospectively, enrolled; blood collected and indices of outcome recorded. A surrogate index of vasoplegia was adopted: requirement for infusion of vasoconstrictor agents for longer than 48h. An enzyme-linked immunosorbent assay was used to measure plasma levels of syndecan-1 at four time-points: after induction of anaesthesia but before CPB (T1); within 30 min of CPB ending (T2); 2h (T3) and 24h (T4) post-CPB. Real time qPCR was used to determine, in patient leukocytes (n = 20), relative expression (to house-keeping gene18*S*) of mRNA for markers of oxidative stress; NQO1 and SOD2, cytoplasmic and mitochondrial enzymes, respectively; and for comparison, TNFα.

Results Syndecan-1 levels at T2 were significantly higher in vasoplegic patients (110.7 ng/mL, IQR 65.46–155.2) than non-vasoplegic patients (53.8 ng/mL, IQR 40.67–102.2; $p < 0.001$). ROC curve analysis showed syndecan-1 had significant ($p = 0.009$) predictive power for onset of vasoplegia, with an area under the curve of 0.766 (95% CI: 0.6019–0.9301); and a cut-off of 63.33 ng/mL (83.33% sensitivity, 69.23% specificity). Syndecan-1 levels were higher in patients whose intensive care unit length of stay (LOS) and hospital LOS were above corresponding medians for the cohort ($p = 0.0061$ and $p = 0.0148$, respectively). NQO1 relative expression was significantly higher ($p = 0.022$) in vasoplegic patients (3.779 ± 1.036) than non-vasoplegic patients (1.3 ± 0.302); whereas, neither SOD2 nor TNFα expression were significantly altered.

Conclusion Plasma syndecan-1 measured immediately post-CPB had good predictive power for patients at risk of vasoplegia. Greater relative expression of leukocyte NQO1 in vasoplegic patients indicates activation of antioxidant defence mechanisms in response to oxidative stress, which could contribute to syndecan-1 shedding.

S13 PHARMACOKINETICS AND PHARMACODYNAMICS OF ANTIMICROBIALS IN CRITICALLY ILL PATIENTS WITH LOWER RESPIRATORY TRACT INFECTIONS. ARE 'ONE SIZE FITS ALL' DOSES APPROPRIATE?

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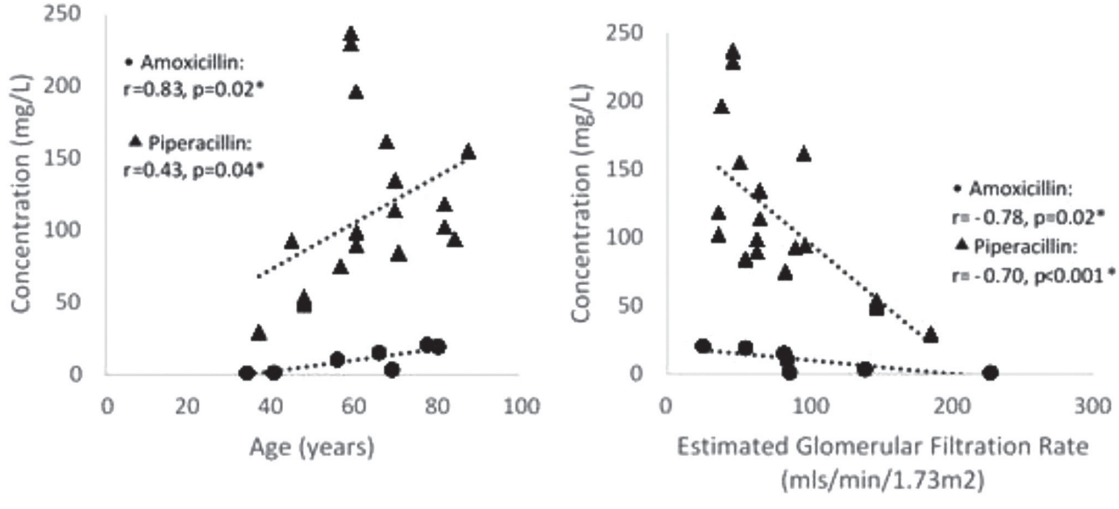
Introduction Respiratory infection is a common cause of severe sepsis.[1] Current therapeutic guidelines emphasise the importance of early initiation of antibiotic therapy, but make no



Abstract S13 Figure 1 Antimicrobial concentration measured at 50% of the dosing interval plotted against age (left) and eGFR (right). Line of best fir and associated coefficients suggest correlation with age and negative correlation with eGFR

recommendations on dose. Recent studies have suggested that some critically ill patients fail to achieve sufficient plasma antibiotic concentrations to treat infection effectively.[2]

We determined whether critically-ill patients with respiratory infection achieved pharmacokinetic/pharmacodynamic (PK/PD) targets during antibiotic treatment and investigated factors associated with failure to meet these targets.

Methods This was a subgroup, interim analysis of an ongoing study, ABDose. Participants were adults in intensive care receiving piperacillin-tazobactam or co-amoxiclav for respiratory infection. Demographics and measures of organ function were recorded. Antibiotic concentrations were measured, at steady-state, in plasma at 50% and 100% of the dosing interval. Efficacy of beta-lactam antibiotics is dependent upon time above minimum inhibitory concentration(MIC). We chose PK/PD targets of antibiotic concentration >MIC and a more conservative >4 × MIC of likely pathogen or microbiological isolate (when available). These targets have been used previously.[2] During 28-day follow up, need for additional antibiotics was recorded.

Results 24 participants (median age 61, IQR [50–70] years), received co-amoxiclav (n = 7), piperacillin-tazobactam (n = 15) or both (n = 2). At 100% of the dosing interval, 12 achieved plasma antibiotic concentrations >MIC and 8 achieved >4×MIC. Participants who did not achieve PK/PD targets were younger (48 [39–59] years vs 68 [61–80] years, p = 0.002*) and had a higher eGFR (131 ± 58 mls/min/1.73m^2 vs 64 ± 28 mls/min/1.73m^2, p = 0.004*) than those who did. Antibiotic concentrations were correlated with age and negatively correlated with eGFR (Figure 1). All participants failing to achieve antibiotic concentrations >4 × MIC at 100% of the dosing interval required further courses of antibiotics during follow-up compared to 50% of patients achieving this target (p = 0.02*).

Conclusion In critically-ill patients with respiratory infection, uniform dosing of beta-lactam antibiotics does not consistently achieve PK/PD targets required for optimal efficacy. Younger patients, with better renal function may be under-dosed. These interim findings identify a need for further work to determine whether personalised dynamic dosing regimens could improve outcomes for patients with severe respiratory infection. Population PK modelling and further covariate analysis is planned within ABDose.

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S14 PATIENTS' PERCEPTIONS OF AN EXERCISE PROGRAMME DELIVERED FOLLOWING DISCHARGE FROM HOSPITAL AFTER CRITICAL ILLNESS (THE REVIVE TRIAL)

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Introduction The REVIVE RCT investigated the effectiveness of an individually tailored (personalised) exercise programme for patients discharged from hospital after critical illness.[1] By including qualitative methods, we aimed to explore their perceptions of engaging in the 6 week programme to facilitate a better understanding of the intervention and trial outcomes.

Methods Patients allocated to the exercise group were invited to participate in semi-structured interviews following their final outcome assessment (6 months following randomisation). Interviews were conducted by a trained member of the research team not involved in the intervention. Interviews were audio recorded, transcribed verbatim and content analysis used to explore themes arising from the data.

Results Of 30 patients allocated to the exercise group 21 completed interviews. Seven core themes were identified (1) sequelae of critical illness and critical care recovery; (2) satisfaction and endorsement of the exercise programme; (3) beneficial impact of the exercise programme on physical and psychological health; (4) facilitators of beneficial impact; (5) barriers to beneficial impact; (6) challenges to continuing exercise; (7) contrasting views on outcome measures.

Patients provided insight into the physical and mental sequelae they experienced following critical illness. There was a strong sense of patients' need for the exercise programme and its importance for their recovery following discharge home. The programme was described as invaluable, and provided feelings of motivation and hope. Key facilitators of beneficial impact included supervision, tailoring of the exercises to personal needs, and the manual. Barriers to the beneficial impact of the programme included poor mental health, existing physical limitations and lack of motivation. Patients' views of the questionnaires and performance based outcome measures in the REVIVE trial varied. Many patients were unsure about what would be the best way of measuring how the programme affected their health.

Conclusion The benefits of physical rehabilitation programmes, needs to be counterbalanced against patients' mental health status post-ICU and any pre-admission limitations, if they are to be successful. Including this qualitative component improved our understanding of the mechanisms underpinning the impact of the programme and how programmes should be evolved for future trials.

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S15 CHANGES IN PERIOPERATIVE ARDS WITH TIME: A COMPARISON OF TWO TRIALS

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Introduction and objective The BALTI-Prevention Trial1 translational sub-study (recruitment completed in 2011) and VINDALOO Trial2 (recruitment completed in 2015) both used oesophagectomy as a model for investigation of the pharmacological prevention of ARDS. The VINDALOO trial showed a lower ARDS incidence independent of the agents evaluated. Our objective was to characterise this difference.

Methods Databases from both trials were available and additional information was obtained retrospectively from hospital records. Analysis was performed using appropriate statistical tests.