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 ml/min/1.73m² vs 64 ± 28 ml/min/1.73m², $p = 0.004^*$) 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.

Abstract S15 Figure 1 ARDS incidence was higher in the BALTI-Prevention compared to the VINDALOO trial ($p = 0.004$)

Results There was a substantially higher ARDS incidence in BALTI-P compared to VINDALOO (RR 1.17 (1.08–1.28)) (Figure 1). There were more never (21 versus 7) and fewer current (12 versus 25) smokers in the VINDALOO group ($p = 0.003$). Perioperative risk scores did not differ between groups (P-POSSUM mortality $p = 0.98$, P-POSSUM morbidity $p = 0.87$, O-POSSUM $p = 0.58$), nor did use of neoadjuvant chemotherapy ($p = 1.0$). The incidence of serious complications (Clavien-Dindo score of four or more), was not different between the two groups (RR 1.15 (0.94–1.40)). Univariate analysis of the combined groups showed risk factors for ARDS not using regional anaesthesia (OR 3.2 (1.0–9.8) $p = 0.038$) and current smoking (OR 3.0 (1.1–8.3) $p = 0.038$).

Conclusion Smoking is an environmental risk factor for ARDS and changing patterns in smoking behaviour appear important in these perioperative cohorts. Other studies have demonstrated that aggregates of small but important changes in care can cumulatively make a significant difference to risk of nosocomial ARDS and our data suggests that this may have resulted in a reduction in perioperative ARDS in this group.

Our study has demonstrated that ARDS incidence post oesophagectomy has fallen. In future, trials utilising oesophagectomy as a model of ARDS should consider selection of a defined higher-risk sub-set of patients.

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S16

SIMVASTATIN IMPROVES NEUTROPHIL MIGRATION IN ELDERLY PATIENTS WITH SEPTIC PNEUMONIA AND REDUCES 6-MONTH MORTALITY AND RE-ADMISSIONS: RESULTS OF THE SNOOPI TRIAL

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Introduction and objectives Community acquired pneumonia is a leading infectious cause of death in the elderly and the

commonest source of sepsis. Neutrophil functions decline with age, and deteriorate further in sepsis.¹ Restoring neutrophil function may improve sepsis outcomes. Recent in-vitro and in-vivo studies suggest simvastatin improves aspects of neutrophil function.² Adjuvant statin therapy in severely critically ill patients has failed to improve outcomes and may be associated with increased morbidity,^{4,5} however our ASEPSIS study suggested that early intervention with statins may reduce the progression of sepsis in a ward-based cohort of milder sepsis patients.⁶ In light of this, we investigated whether oral treatment with simvastatin improved neutrophil function and clinical outcomes in elderly patients with septic pneumonia.

Methods 'SNOOPI' was a phase-4, randomised controlled trial comparing 7-days of 80mg simvastatin with placebo in patients aged 55 years or over admitted to hospital with septic pneumonia.³ The primary outcome was changes in neutrophil extracellular trap (NETs) formation by day3/4 compared with baseline. Secondary outcomes included neutrophil migration, safety and tolerability, length of stay, readmissions and mortality.

Results 61 patients were recruited acute admissions unit at the Queen Elizabeth Hospital Birmingham between 2013 and 2015, with 31 patients randomised to simvastatin and 30 to placebo. Groups were well matched for baseline characteristics, pneumonia and sepsis severity, co-morbidities and biochemical and haematological parameters.

There was no significant difference in the primary end-point of change in NETs at day3/4. Directional neutrophil migration (chemotaxis) was significantly improved in patients who received simvastatin at day 3/4 ($0.35 \pm 0.16 \mu\text{m}/\text{min}$ vs. $-0.15 \pm 0.17 \mu\text{m}/\text{min}$; $p = 0.033$). Simvastatin was well tolerated with no SUS-ARS, even with the co-prescription of macrolides. At 6-months, patients in the simvastatin group were less likely to have been admitted to hospital or died compared to those in the placebo group (OR: 0.44; 95% CI: 0.21–0.91; $p = 0.02$) (Figure 1).

Conclusions The current study suggests that early intervention with statins in septic pneumonia patients may improve patient outcomes. We propose that one of the mechanistic drivers may be the restoration of sepsis-associated dysregulated neutrophil function. Further larger studies are warranted to confirm whether early intervention with statins in patients with sepsis confer an overall survival benefit.

Abstract S16 Figure 1 Kaplan-Meier Curve showing the time (in-days) to either death or re-admission to hospital in patients' allocated to simvastatin or placebo