this, PSV trials were well tolerated in the majority with active weaning in pressure support subsequently achieved. Individual screening criteria were not associated with PSV failure. Of clinical significance, failure to sustain a PSV trial could be an early indicator of prolonged mechanical ventilation and ICU mortality, and predictive characteristics of this warrant further investigation. Application of screening criteria, as reported in weaning literature, may delay initiation of weaning in some patients.

S137 FAILURE OF NICE GUIDANCE CG83 IMPLEMENTATION: NATIONAL UK SURVEY OF REHABILITATION SERVICES FOR SURVIVORS OF CRITICAL ILLNESS

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Introduction National guidelines advocating multidisciplinary rehabilitation delivered throughout the continuum of recovery following critical illness were published in 2009 (NICE CG83). However, lack of supporting evidence for these recommendations has resulted in inconsistent implementation, particularly in the post hospital discharge phase. As expected, nursing and medical staff have been surveyed for involvement in intensive care unit (ICU) follow-up with previous surveys of physiotherapy practice focussed on within-ICU rehabilitation practice. This survey aimed to characterise post critical illness follow-up and rehabilitation following hospital discharge.

Method A predominantly closed-question, physiotherapy-specific postal survey distributed to senior critical care clinicians at UK hospitals with a listed ICU, excluding specialist-only units, and coded to facilitate respondent identification.

Abstract S137 Table 1. Barriers to availability of post hospital discharge rehabilitation programmes for post critical illness patients.

Barrier	Frequency reported overall n (%)	Frequency reported as main barrier n (%)
Lack of funding	147 (90.7)	98 (63.6)
Lack of sufficient staff	127 (78.4)	17 (11.0)
Resources prioritised to other patient groups/clinical areas	70 (43.2)	4 (2.6)
Not considered required service at managerial level	66 (40.7)	22 (14.3)
Lack of available space	50 (30.9)	2 (1.3)
Insufficient patient numbers to justify	34 (21.0)	10 (6.5)
Extra-contractual (out-of-area) patient caseload	15 (9.3)	0 (0.0)
Lack of trained staff	12 (7.4)	0 (0.0)
No evidence	4 (2.5)	0 (0.0)
Not sure what to include in a programme	2 (1.2)	0 (0.0)
Other (time constraints)	1 (0.6)	1 (0.6)

For frequency of reported barriers overall, n = 162 responses. For frequency of reporting as main barrier, n = 154 responses.

Results Physiotherapists at 240 identified ICUs were sent surveys. 182 surveys were returned (75.8% response rate), including one blank survey. 36.5% were from university teaching hospitals, 63.5% from district general hospitals. Forty-eight centres reported follow-up services at 2–3months, the majority as clinics (39/48, 81.3%). Physiotherapists were involved in 43 follow-up services, albeit in a third of cases, on a referral-only basis. Critical care nursing staff were the main other clinician involved. Health-related quality of life (83.3%) and psychological status (81.3%) were the main items addressed, with exercise capacity reviewed in almost 60% of cases. Only 12/182 (6.6%) centres reported post hospital discharge rehabilitation programmes, all including an exercise component, but only four offering education topics. Substantial variation existed between programmes regarding eligibility, delivery format, structure, content and evaluation. Where rehabilitation programmes were not available, barriers to offering this service were detailed (Table 1). Lack of funding was the most frequently reported, and the main barrier listed. The majority of respondents (96/169; 56.8%) reported referral of post critical illness patients into alternative rehabilitation streams, predominantly accessing community and domiciliary in-patient or out-patient services.

Conclusion Data from this survey demonstrated a low level of available follow-up and rehabilitation services for post critical illness patients following hospital discharge. This reflects a lack of implementation of high-profile national guidelines, the main reason for which was reported to be lack of funding. Further investment in these services is required.

Mechanisms in pulmonary vascular disease

S138 BLOOD OUTGROWTH ENDOTHELIAL CELLS ISOLATED FROM PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION POSSESS LESS CAVEOLAE AND REDUCED CAVIN-2 EXPRESSION

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Pulmonary arterial hypertension (PAH) is a progressive disease characterised by a marked elevation in pulmonary arterial pressure due to increased muscularisation and obliteration of small pulmonary arteries. The majority of heritable PAH cases are due to mutations in members of the transforming growth factor- (TGF) receptor signalling pathway. Although predominantly associated with mutations in the bone morphogenetic protein type II receptor (BMPR-II) genetic variations causing disease have recently been identified in caveolin-1, the major component of caveolae generation. Caveolae are flask shaped invaginations in the plasma membrane that play an important role in many endothelial cell functions including vesicular trafficking and signalling. Correct caveolae formation in the lung has recently been shown to require serum deprivation protein response (SDPR), also known as cavin-2. Using blood outgrowth endothelial cells (BOECs) isolated from patients with PAH we sought to determine the expression of cavin-2 and caveolae formation.

Methods Blood outgrowth endothelial cells (BOECs) were isolated from control subjects and individuals with PAH, including BMPR-II mutation and idiopathic patients. Following transmission electron microscopy (TEM) the number of caveolae and depth of invaginations were assessed in ten cells from each cell line. Protein expression of caveolin-1, cavin-1 and cavin-2 were assessed by western blotting. Caveolin-1 and cavin-2 knockout

mice were assessed for right ventricular systolic pressure (RVSP) and right ventricular hypertrophy.
Results Reduced caveolae and depth of invaginations were observed in idiopathic PAH patients and individuals with a BMPR-II mutation when compared to controls. Interestingly, an individual with a BMPR-II mutation without disease had similar levels to controls. Furthermore, cavin-2 protein expression was decreased in cells from individuals with pulmonary hypertension, but other caveolae components appeared unaffected. In the absence of a disease stimulus caveolin-1 and cavin-2 knockout mice did not develop pulmonary hypertension although slightly elevated RVSP was observed.
Conclusions Our preliminary data suggests that caveolae formation is dysregulated in cells from individuals with pulmonary hypertension. In addition, reduced levels of cavin-2 could play a significant role in the decreased number of caveolae. Cavin-2 and caveolae generation could therefore be novel therapeutic targets for pulmonary hypertension.

S139 THE ROLE OF ENDOTHELIN RECEPTORS (ETRA/B) IN FIBROCYTE DIFFERENTIATION

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Introduction Scleroderma (SSc) is an autoimmune connective tissue disease of unknown aetiology. Pulmonary involvement including the development of pulmonary arterial hypertension (PAH) is characterised by vascular remodelling, collagen deposition and expression of connective tissue growth factor (CTGF). $CD14^+$ monocytes can differentiate into spindle shaped cells termed 'fibrocytes'. Fibrocytes express haematopoietic and mesenchymal markers including collagen, and amplify inflammatory/immune responses via antigen presentation and chemokine secretion. Fibrocyte differentiation is enhanced by fibrogenic cytokines including PDGF. The role fibrocytes play in promoting PAH in SSc is unknown.
Methods $CD14^+$ PBMCs were isolated from SSc and healthy donor blood. Fibrocyte differentiation in the presence of MCSF and/or ET-1 was assessed after 14 days. The effect of endothelin receptor (ETR) antagonists (selective/dual) on fibrocyte differentiation ($n = 6$) was investigated. SSc and control fibrocyte secretomes were assessed by ELISA ($n = 6$), and the effects on fibroblast-mediated gel contraction determined.
Results MCSF and ET-1 alone and in combination induced fibrocyte differentiation ($P < 0.05$). SSc fibrocytes exhibited enhanced differentiation from $CD14^+$ PBMCs than healthy control donors in response to MCSF ($P < 0.05$), ET-1 ($P < 0.05$) and in combination ($P < 0.01$). ETR antagonists BQ123 (ETR_A), BQ788 (ETR_B) and Bosentan ($ETR_{A/B}$) inhibited MCSF induced fibrocyte differentiation. CTGF secretion was elevated in SSc compared to control fibrocytes ($P < 0.05$) cultured with MCSF. Conditioned media from SSc fibrocytes promoted gel contraction by control pulmonary fibroblasts ($P < 0.05$).
Discussion $CD14^+$ SSc PBMCs readily differentiate into fibrocytes in response to ET-1 and MCSF via ETR_A and ETR_B. Our data suggests fibrocytes contribute to the development of PAH in SSc via a paracrine mechanism modulating the functional activities of resident tissue fibroblasts.

S140 BMPR-II DEFICIENCY LEADS TO AN INCREASE IN EGG DEPOSITION AND CYTOKINE RELEASE IN THE LUNGS OF MICE CHRONICALLY INFECTED WITH SCHISTOSOMIASIS

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Rationale and Objectives Schistosomiasis is the world-wide leading cause of pulmonary arterial hypertension (PAH) and is particularly prevalent in the third-world. More than 80% of patients with PAH in the western world have a mutation in bone morphogenetic protein type-II receptor (BMPR-II), which is a member of the transforming growth receptor-beta (TGF-b) superfamily and is important in cell proliferation and differentiation. The aim of the study was to determine if mice with a heterozygous null mutation in BMPR-II are more susceptible to schistosomiasis–induced PAH, compared to wild-type littermates.
Methods Wild-type and mutant C56/BL6 mice were infected percutaneously with a low dose of *S.mansoni*. Non-infected WT and MUT mice were also studied. At 17 weeks post-infection right ventricular systolic pressure (RVSP) and right ventricular (RV) hypertrophy, liver and lung egg counts and body weight were measured. Pulmonary vascular remodelling and liver histology were assessed by morphometry, following immunohistochemistry. Micro-CT was performed to determine egg deposition. A macrophage phagocytosis assay was also performed.
Measurements and Main results At 17 weeks post-infection there was no significant difference in RVSP, the degree of RV hypertrophy, mean area of liver vasculature, mean number of liver vessels or liver weight between infected BMPR-II + / + and BMPR-II +/- mice. However, there was a significant reduction in body weight, a significant increase in lung egg deposition and lung cytokine expression in the BMPR-II +/- mice compared to the wild-type mice 17 weeks post-infection. There was no significant difference in serum or liver cytokine levels. We saw a significant increase in pulmonary vessel wall thickness in both BMPR-II + / + and BMPR-II +/- mice infected mice, compared to their respective non-infected controls. There was no difference in the ability of macrophages from BMPR-II + / + and BMPR-II +/- mice to phagocytose fluorescently tagged beads.
Conclusions This study has shown that BMPR-II mutations do not predispose to schistosomiasis-induced PAH, but that there is an increased ability of the eggs to gain access into the lungs and a subsequent heightened inflammatory response. This appears not to be due to an innate difference in the liver vasculature or a defect in egg clearance by macrophages.

S141 BMP9 IS REQUIRED FOR LPS-MEDIATED NEUTROPHIL RECRUITMENT TO PAH-PATIENT DERIVED BLOOD OUTGROWTH ENDOTHELIAL CELLS WITH BMPR-II MUTATIONS

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Introduction Heterozygous mutations in the gene encoding bone morphogenetic protein (BMP) receptor II (BMPR-II) are present in >70% of patients with heritable pulmonary arterial hypertension (hPAH) and 15–26% of idiopathic PAH (iPAH)