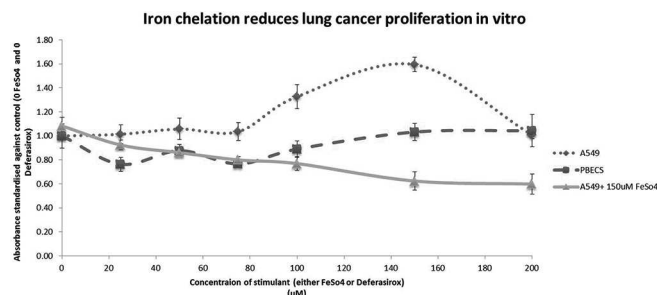


and cellular proliferation decreased below levels seen in unstimulated cells. Deferasirox was also seen to effect unstimulated cancer cells, reducing their proliferation by 50% ( $P = 0.02$  and  $0.03$  respectively).

**Conclusion** Iron exposure was shown to have a significant effect on cellular proliferation within lung cancer cell lines, although the underlying mechanism is not yet fully understood. This iron mediated cellular proliferation could be reversed using the chelator deferasirox. Down-regulated expression of *IREB2* may cause the cancer cell lines to exhibit similar behaviour to the PBECS when stimulated with iron. These findings show that iron may provide a potential new target and deferasirox a potential new therapeutic agent for lung cancer.



**Abstract S131 Figure 1.** The dotted line shows that the increasing concentration of  $\text{FeSO}_4$  has a statistically significant effect at 100 M ( $M = 1.33$ ,  $SD = 0.19$ ,  $P = 0.04$ ), however, 150 M shows an even more significant increase in proliferation ( $M = 1.59$ ,  $SD = 0.12$ ,  $P = 0.002$ ). A dose of 200 M of  $\text{FeSO}_4$  shows a return to base line and no significant difference in cellular proliferation. The solid line shows that deferasirox causes a decrease in proliferation when applied to cells after incubation with 150 M of  $\text{FeSO}_4$ . This is statistically significant at 50 ( $M = 0.86$ ,  $SD = 0.03$ ,  $P = 0.04$ ), 150 ( $M = 0.62$ ,  $SD = 0.08$ ,  $P = 0.01$ ) and 200 M ( $M = 0.60$ ,  $SD = 0.08$ ,  $P = 0.0004$ ) of deferasirox and the greater the dose of deferasirox, the greater the decrease in proliferation. The dashed line indicates the effects of  $\text{FeSO}_4$  incubation on PBECS. There is no statistical significance seen in proliferation rates for any concentration of  $\text{FeSO}_4$ .

### S132 LINEAGE TRACING IN HUMANS REVEALS STOCHASTIC HOMEOSTASIS OF AIRWAY EPITHELIUM RESULTING FROM NEUTRAL COMPETITION OF BASAL CELL PROGENITORS

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In recent years, the development of lineage tracing approaches has provided quantitative new insights into tissue homeostasis in mice. However, the relevance of these discoveries to human epithelial homeostasis and alterations in disease is not

known. We demonstrate that the statistical analysis of pathologically neutral somatic mitochondrial mutations that are accumulated over time can provide access to clonal fate behaviour at single cell resolution in human, providing a direct means to explore mechanisms of cell fate and tissue maintenance. Employing this approach, we define the progenitor cell population and the cellular hierarchy of the major human airways. By applying a novel quantitative approach to lineage tracing data, we conclude that, in normal homeostasis, the lining of human lung epithelium is maintained by an equipotent progenitor cell population of basal cells, in which the chance loss of cells due to commitment is perfectly compensated by the duplication of neighbouring cells, leading to neutral drift dynamics of the clone population. Further, we show that in airways of smokers, this process is accelerated leading to intensified clonal consolidation and a fertile background for tumorigenesis. This study provides the benchmark for the use of somatic mutations to quantitatively explore patterns of homeostatic growth in human tissues, and a platform to explore factors leading to homeostatic dysregulation and disease.

## Outcomes post critical care

### S133 OBSERVATIONAL COHORT STUDY OF OUTCOME OF PATIENTS REFERRED TO A REGIONAL WEANING CENTRE

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10.1136/thoraxjnl-2013-204457.140

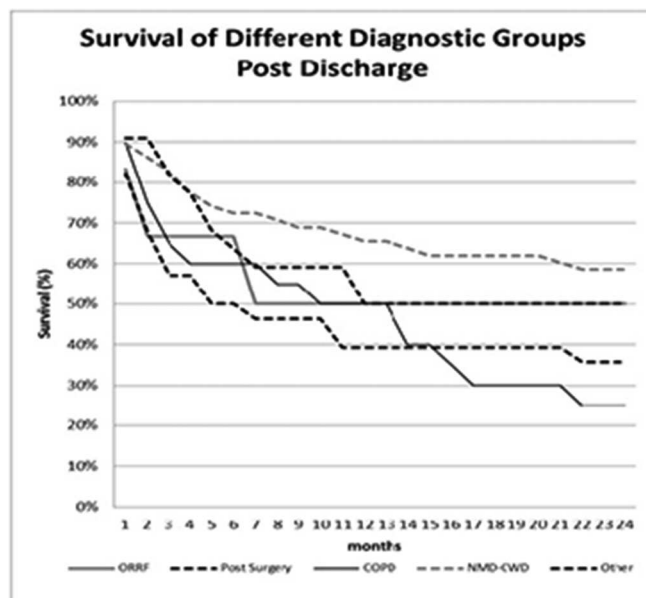
**Introduction** Data on outcome of the patients referred to weaning and rehabilitation centres are limited. In this observational cohort study, we report the outcomes of patients referred to a specialist complex home ventilation, weaning and rehabilitation centre.

**Methods** Data from the LFRU database from February 2005 to February 2011 were analysed. The primary diagnosis causing prolonged mechanical ventilation (MV) were classified into five groups: (1) neuromuscular and chest wall disease (NMD-CWD); (2) chronic obstructive pulmonary disease (COPD); (3) post-surgical patients; (4) obesity related respiratory failure (ORRF); and (5) other causes. The principal outcomes measured were weaning success, hospital mortality, 1-year and 2-year survival following discharge.

**Results** A total of 369 patients were referred over the 6 year period. Of these, 194 (52.6%) were admitted. The commonest outcome was total liberation from all forms of MV (45%). The remainder were shown to (1) require nocturnal non-invasive ventilation (NIV) (22%); (2) require nocturnal and intermittent daytime NIV (1%); (3) require long-term tracheostomy ventilation (24%); and (4) died in hospital (8%). Post-surgical and COPD patients had the highest rate of total liberation from mechanical ventilation at 60% and 54%, respectively. The median time from admission to tracheostomy decannulation was 18 days (9–33). NMD-CWD patients had the lowest hospital mortality (7%), whereas COPD patients had the highest hospital mortality (29%). The overall survival at 12 and 24 months was 60% and 50%, respectively. 25% of the COPD patients were alive and 59% of the NMD-CWD patients were alive at 24 months (Figure 1).

**Conclusions** The majority of patients with weaning failure were successfully liberated from mechanical ventilation. The weaning

time was less than 3 weeks and only one-fifth of patients required nocturnal non-invasive ventilation. NMD-CWD patients were most likely to survive hospital but almost one-third of COPD patients died during the weaning process. COPD patients had the worst outcome at 2-years, whereas over half of the NMD-CWD patients were alive at 2-years. These data strongly support the Department of Health's plan to develop 'Complex Home Ventilation, Weaning and Rehabilitation Centres' as part of the investment in specialist respiratory services to enhance patient outcome.



Abstract S133 Figure 1

**S134** ACTIVITY MONITORING IN INTENSIVE CARE UNIT SURVIVORS: ASSESSING DAILY PHYSICAL ACTIVITY WITH OBJECTIVE OUTCOME MEASURES

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10.1136/thoraxjnl-2013-204457.141

**Introduction and Objectives** Intensive care unit (ICU) survivors commonly report long-term functional disability and reduced daily physical activity (PA). This adversely impacts on their health-related quality of life (HRQL). We aimed to investigate the relationship between subjective and objective measures of PA in this patient group.

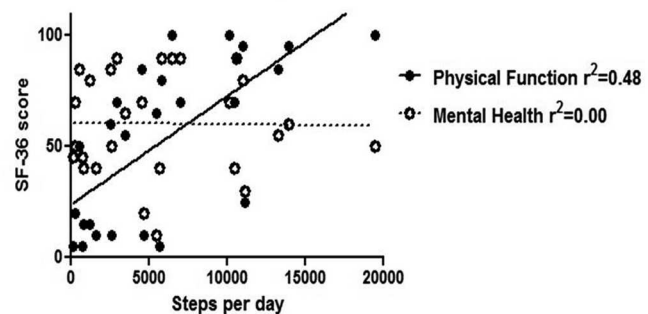
**Methods** Subjects were ICU survivors drawn from the 63 participants of the Musculoskeletal Ultrasound Study in Critical Care: Longitudinal Evaluation (MUSCLE) study. All were over 16 years, invasively ventilated for > 48 hours with an ICU length of stay >7days. Objective (SenseWear Pro accelerometers, Body-Media Inc, Pittsburgh, US) and self-reported subjective PA levels (HRQL SF-36 questionnaire, QualityMetric Inc, Lincoln, US) were measured.

**Results** At 18 months 20 pts had died; 17 were lost to follow-up, and 1 withdrew. 27 patients were studied (14 female) with a mean age  $\pm$  SEM of  $56.6 \pm 3.6$  years and a post-ICU discharge

time of  $576 \pm 190$ d. SF-36 scores were lower than normal range scores. Age-adjusted (AA) mean steps/day correlated with norm-based physical component summary (PCS) SF-36 scores (Pearson's  $r = +0.58$ ;  $p < 0.01$ ), but there was no correlation with the mental component summary scores (Fig. 1). AA daily step variation showed positive associations with absolute levels of AA daily steps ( $r = +0.85$ ;  $p < 0.01$ ), SF-36 physical function (PF) scores ( $r = +0.62$ ;  $p < 0.01$ ), and prior working status ( $r = +0.69$ ;  $p < 0.01$ ); and a negative association with chronic disease ( $r = -0.54$ ;  $p < 0.01$ ). Levels of AA daily steps contributed more to AA daily step variation than SF scores ( $r^2 = 0.72$ , 0.38 respectively). Receiver Operator Characteristic analysis indicated that AA daily steps and PF scores are good (but non-significant) predictors for working post-ICU (0.88, 0.86 respectively;  $p > 0.05$ ).

**Conclusion** This is the first report on the use of activity monitors in ICU survivors, and indicates that subjective and objective measures of PA are correlated. Such complementary data can be used to investigate functional disability in critical illness survivors. Both methods of assessing PA identified strong associations with health and socio-economic factors. Variation in step count, and specifically lack of variation in step count, may be more attributable to absolute step count than self-reported PF or chronic disease. Objective PA measures may offer advantages for monitoring post-ICU patients compared with subjective methods.

**Correlations between Activity and SF-36 forms**



Abstract S134 Figure 1. Correlations between Physical Function and Mental Component Summary SF-36 Scores against Physical Activity.

**S135** LONG-TERM OUTCOMES IN PATIENTS REFERRED TO A SPECIALISED WEANING CENTRE; THE IMPACT OF REFERRAL SOURCE, NON-INVASIVE VENTILATION AND DIAGNOSIS

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**Introduction** The expansion of specialised weaning centres serving networks of external ICUs has been recommended by the NHS commissioning board. However, data are limited for this proposed model of care. Papworth Hospital provides a multi-disciplinary weaning service in-line with these recommendations.

**Methods** We analysed the records of patients transferred to our service for weaning from invasive ventilation (IMV) between 1992–2011 inclusive. Patients were categorised according to diagnosis (neuromuscular, COPD, post-surgical, non-COPD respiratory, chest-wall disorders and others).

## Correction

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D Mifsud Bonnici, T Sanctuary, B Creagh-Brown, *et al.* S133: Observational cohort study of outcome of patients referred to a regional weaning centre. *Thorax* 2013;63(Suppl 3):A68. doi: 10.1136/thoraxjnl-2013-204457.140

The results section of this abstract should read:

**Results** A total of 369 patients were referred over the 6 year period. Of these, 194 (52.6%) were admitted. The largest outcome group was total liberation from all forms of MV (45%). The remainder were shown to (1) require nocturnal non-invasive ventilation (NIV) (21%); (2) require nocturnal and intermittent daytime NIV (1%); (3) require long-term tracheostomy ventilation (19%); and (4) died in hospital (15%). Post-surgical and COPD patients had the highest rate of total liberation from mechanical ventilation at 60% and 54%, respectively. The median time from admission to tracheostomy decannulation was 18 days (9–33). NMD-CWD patients had the lowest hospital mortality (7%), whereas COPD patients had the highest hospital mortality (29%). The overall survival at 12 and 24 months was 55% and 47%, respectively. 25% of the COPD patients were alive and 59% of the NMD-CWD patients were alive at 24 months (Figure 1).

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