macrophages, and whether they are required for this remodelling remains unclear. We have recently developed a mouse model (MacLow) where approximately 50% of macrophages are depleted and now aim to investigate whether MacLow mice would demonstrate a reduced pulmonary hypertension phenotype in response to hypoxia, when compared to non-macrophage ablated littermates.

Methods: Macrophage ablation was induced in CD68-rTA-eGFP/tetDTA double transgenic mice (MacLow) where macrophage-specific (CD68) induction of the cytotoxic diphtheria toxin A chain (DTA) is achieved by administration of doxycycline containing chow diet (doxy-chow). Mice were divided by sex and then fed either regular or doxy-chow for 2 weeks prior to either 2 weeks exposure to hypoxia (10% oxygen), or room air. All mice were phenotyped for PH by echocardiography followed by closed chest cardiac catheterisation. Heart and lung tissue were harvested for morphological, immunohistochemical and biochemical analyses.

Results: Doxy-chow fed mice displayed the expected 50% reduction in macrophages (liver) compared to controls. MacLow mice with the induced ablation of macrophages were not protected from hypoxia induced pulmonary hypertension although females displayed a trend for higher RVSP after hypoxia (54 mm Hg vs 29 mm Hg). Interestingly male MacLow mice with induced macrophage ablation displayed a spontaneous PAH phenotype (53 mm Hg), in normoxia, that was not further increased by hypoxia. The changes in RVSP were accompanied by appropriate changes in RVH.

Conclusion: These data suggest that macrophages play a modulating role in pulmonary vascular remodelling but further work is required to explore the mechanisms involved in this phenotype, and to fully assess the change in macrophage number within the lungs of these mice.

REFERENCES
Introduction Pulmonary embolism (PE) is a common presentation in the emergency department and in-patient setting. Measurement of D-dimer in conjunction with clinical risk assessment is used to exclude patients at low risk of PE. Some of the conditions that mimic PE, including infection and inflammation, are also associated with elevated D-dimer concentrations such that the test lacks specificity. Most infectious and inflammatory conditions result in an elevated acute-phase serum response which can be quantified using C-Reactive Protein (CRP) assay. We hypothesised, therefore, that patients with isolated PE would have a higher D-dimer: CRP ratio than patients with infectious or inflammatory mimics of PE and therefore that this ratio would be more discriminatory.

Methods We analysed data from all patients who underwent V/Q scanning to confirm or exclude PE at Royal Free Hampstead NHS Trust, London, UK, during 2010. The CRP and D-dimer results were available for all patients. The CRP and D-dimer were measured using a latex agglutination assay (D-dimer) and a nephelometric assay (CRP). The D-dimer: CRP ratio was calculated. The diagnostic test results were obtained within 11 days of the V/Q scan. ROC analysis was performed separately for patients with low and intermediate pre-test probability.

Results 362 patients were included in the analysis, 207 (57%) had low, 129 (36%) intermediate and 26 (7%) high pre-test probability. Prevalence of PE was 2% in the low probability group, 14% in the intermediate probability group and 42% in the high probability group. No patients with a D-dimer of >0.5 mg/l who were discharged without further tests had a positive D-dimer result for all patients presenting to our ambulatory PE clinic and had neither D-dimer nor CRP assay (12 (3.6%) low pre-test probability had a latex agglutination D-dimer test. If this result was =0.5 μg/ml they had further investigations, otherwise they were discharged. The diagnosis of PE was made if a VQ scan showed ventilation/perfusion mismatch or CTPA report demonstrated PE. Receiver operating characteristic curve analysis was performed separately for patients with low and intermediate probability and the optimum cut-off value to exclude PE determined. Sensitivity, specificity, negative predictive value and positive predictive value for different cut-off points were determined.

Conclusion The diagnostic accuracy of D-dimer testing may be improved in patients with a low pre-test probability by adjusting the cut-off threshold.