

## Development of a Point-of-Care (POC) Theranostic Assay to Stratify Patients with Acute Respiratory Distress Syndrome (ARDS)

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### INTRODUCTION

ARDS has no effective pharmacological therapy. Recent studies have shown that patients with ARDS can be stratified into hypo- and hyper-inflammatory subphenotypes, based on clinical and biomarker profiles. In secondary analysis of prior trials, these subphenotypes have a differential response to treatments, including better survival with simvastatin in the hyper-inflammatory subphenotype. Inflammatory subphenotype stratification could therefore enable a precision medicine approach in ARDS. However, rapid stratification with a real-time or point of care (POC) test is required to achieve this. Here we describe the development and initial testing of such a theranostic test. The aim of this study was to develop a quantitative, POC immunoassay to rapidly identify hypo- and hyper-inflammatory subphenotypes in patients with ARDS and compare subphenotype allocation in patients with ARDS using laboratory-based assays and the Randox ARDS assay.

### METHODOLOGY

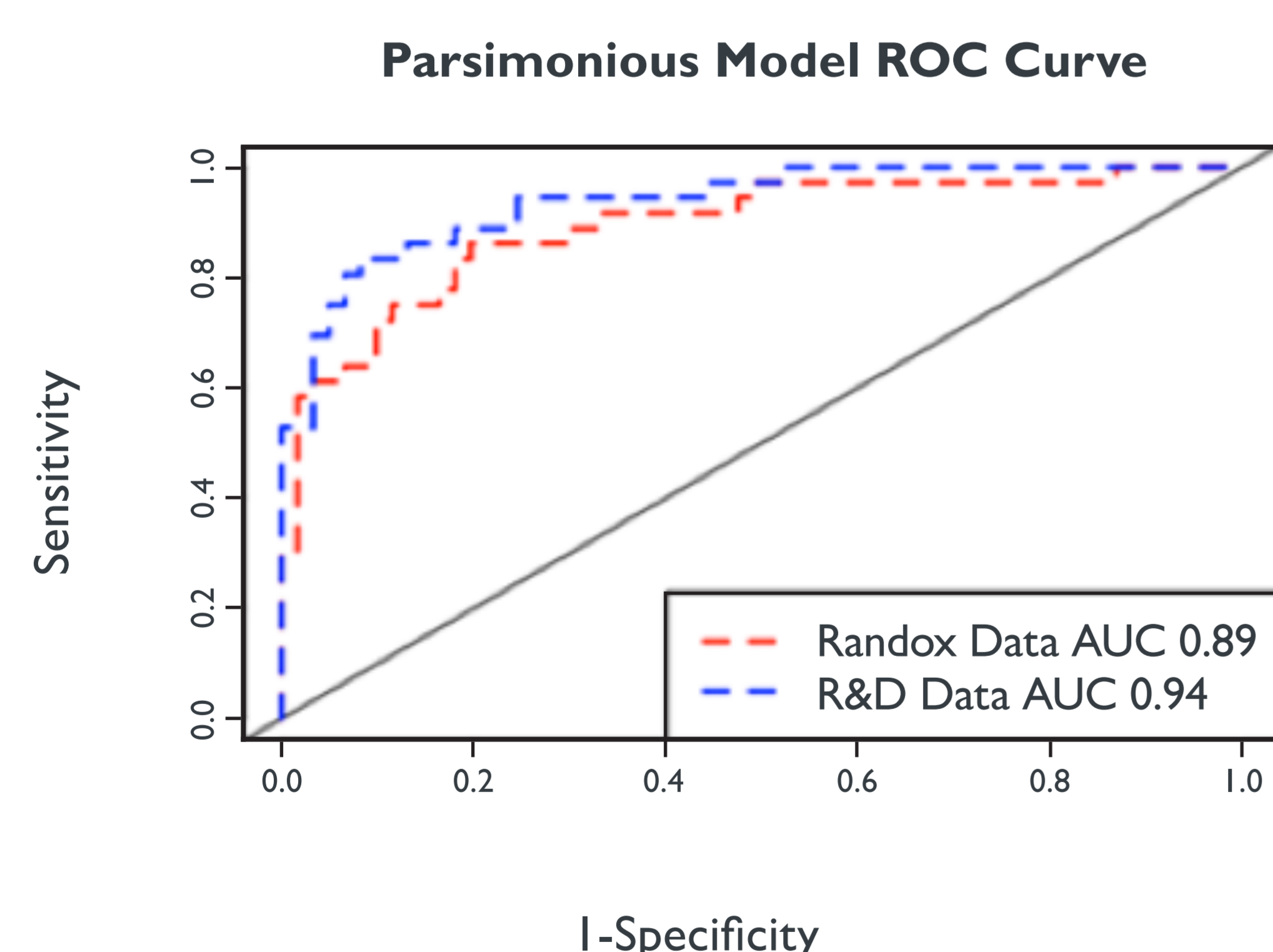
Using Randox Biochip Array Technology, a rapid quantitative plasma immunoassay for IL-6 and soluble TNFR1 (sTNFR1) was developed for use on the Randox Evidence MultiSTAT POC analyser. HARP-2 was a randomised controlled clinical trial evaluating simvastatin in 540 patients with ARDS. Patient samples (n=98) from the HARP-2 study were randomly selected and run on this ARDS assay. Subphenotype allocation as defined by a parsimonious model using IL-6, sTNFR1 and vasopressor requirement was generated using data either from IL-6 & sTNFR1 ELISAs (R&D Systems) or the Randox ARDS assay, with both compared to subphenotype allocation using latent class analysis with R&D data.

### RESULTS

A quantitative ARDS immunoassay was successfully developed for the Randox MultiSTAT POC analyser, with an assay time of 36 min compared with 6h (post-overnight capture) with the R&D Systems ELISAs. The AUC for subphenotype allocation for the Randox assay was 0.89 compared with 0.94 for the R&D Systems data (n=98; Figure 1). There was good correlation in the probabilities generated for subphenotype allocation between both assays (n=90; Pearson's correlation  $r=0.94$ ; Figure 2).

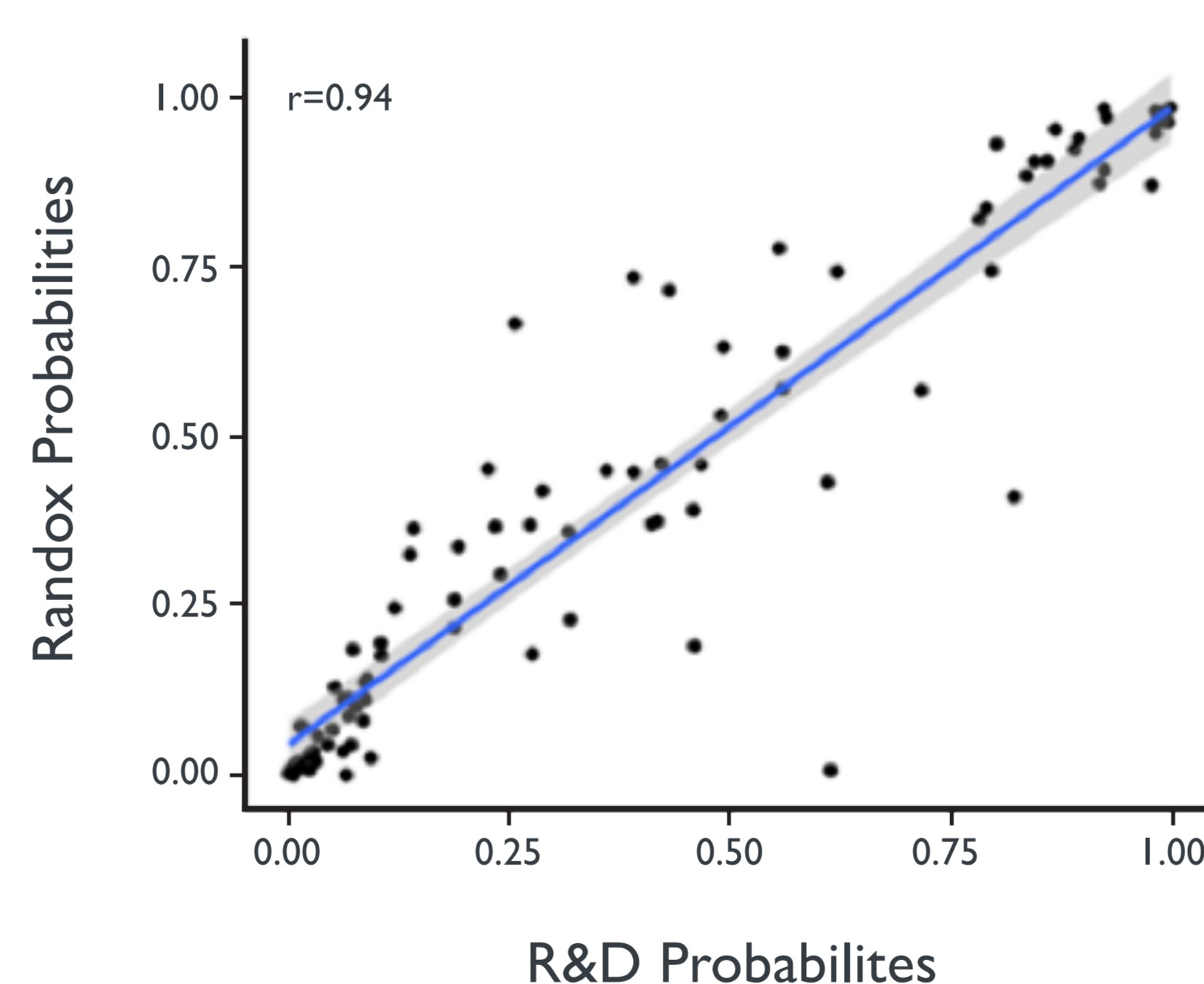
#### FIGURE 1

Area under the Curve for the Randox POC assay and R&D Systems ELISAs for subphenotype allocation using the parsimonious model, with latent class analysis derived subphenotypes as the gold-standard.



#### FIGURE 2

Correlation of the Randox POC Assay and R&D Systems ELISAs for subphenotype allocation using the parsimonious model.



### DISCUSSION

These preliminary results demonstrate that the Randox ARDS POC immunoassay performs well for subphenotype allocation in comparison to using research grade, laboratory-based assays. These findings suggest that the Randox assay can accurately phenotype patients, with the potential to deliver precision medicine to patients with ARDS. The Randox ARDS assay is now being assessed across multiple ICU sites in the UK in a prospective observational trial (PHIND Study – ClinicalTrials.gov number: NCT04009330).

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