

Host response to critical illness and personalised care

Dr David Antcliffe

Clinical Senior Lecturer and Honorary Consultant in Intensive Care
Charing Cross Hospital

The problem

Sepsis **syndrome**

Systemic inflammatory response **syndrome**

Post cardiac arrest **syndrome**

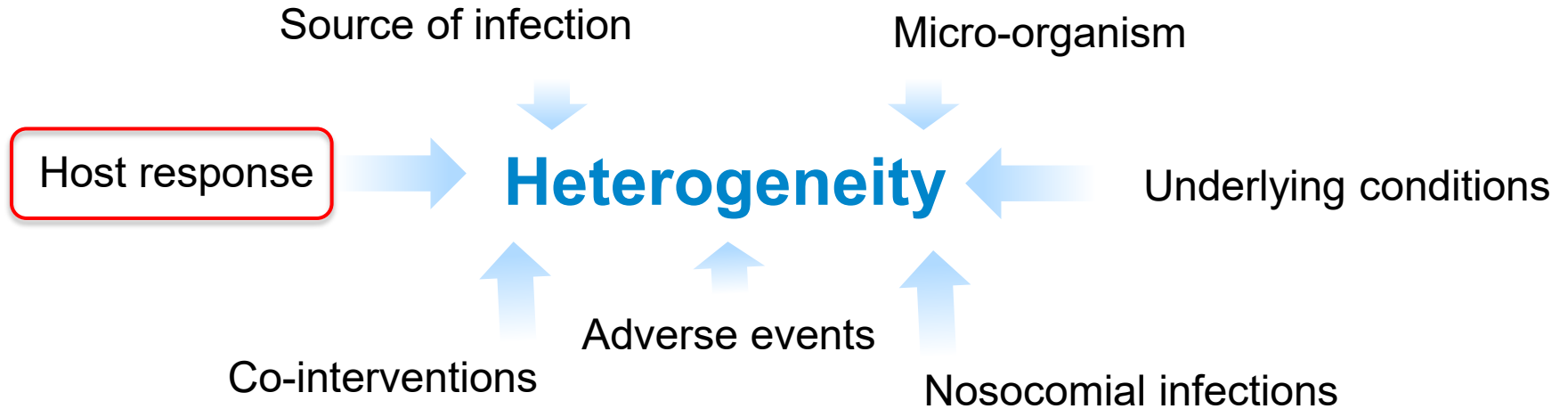
Acute respiratory distress **syndrome**

Sepsis

“Organ failure caused by a dysregulated host response to infection”

- 250 000 cases of sepsis a year in the UK
 - 46,000 deaths occur from sepsis in the UK
 - Septic shock accounts for about 20% of ICU admissions
-

Precision Medicine

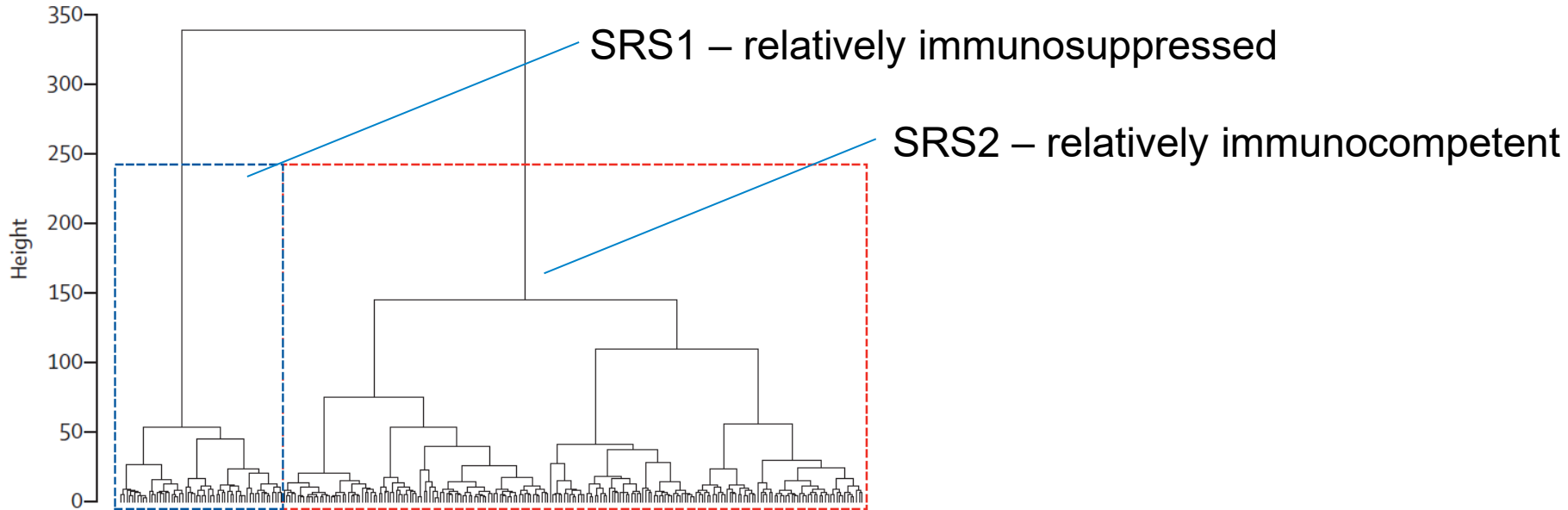


Gene Expression Signatures in Sepsis

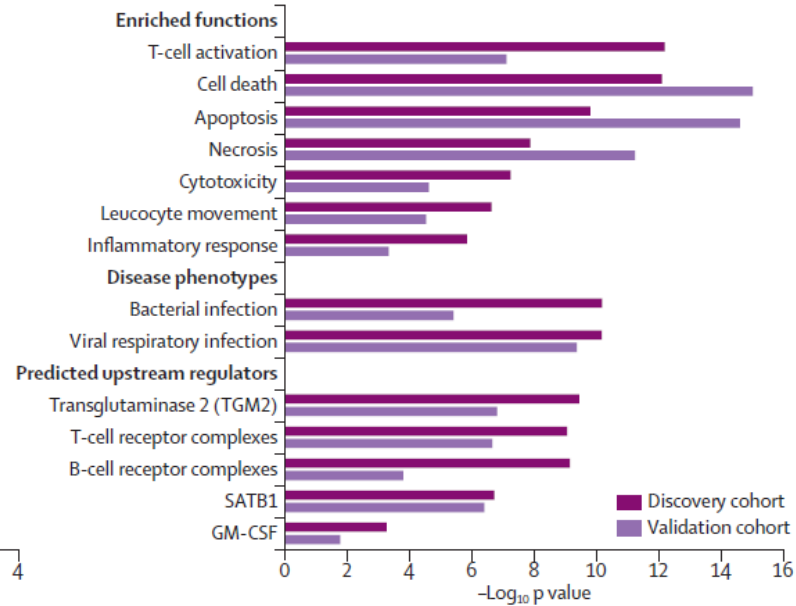
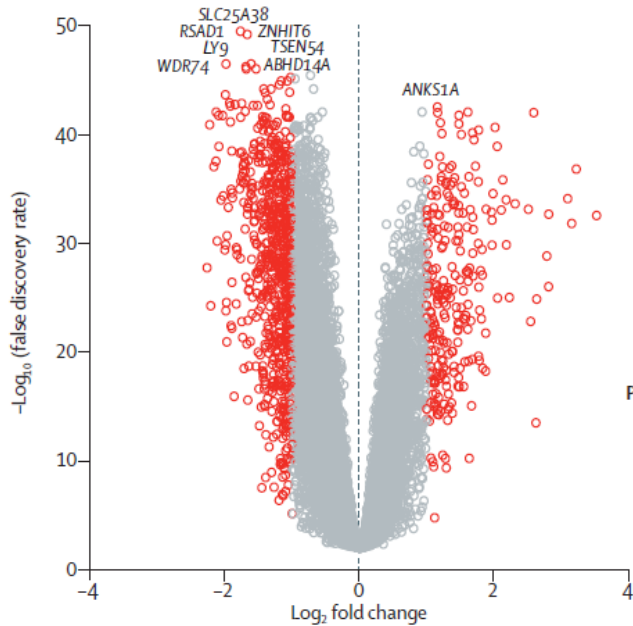
RNA Profiling– GAINs Consortium

- ICU patients with sepsis in 29 ICUs:
 - Community Acquired Pneumonia (CAP)
 - (n=263 derivation and 105 validation)
 - Faecal Peritonitis (FAP)
 - (n=64 derivation and 53 validation)

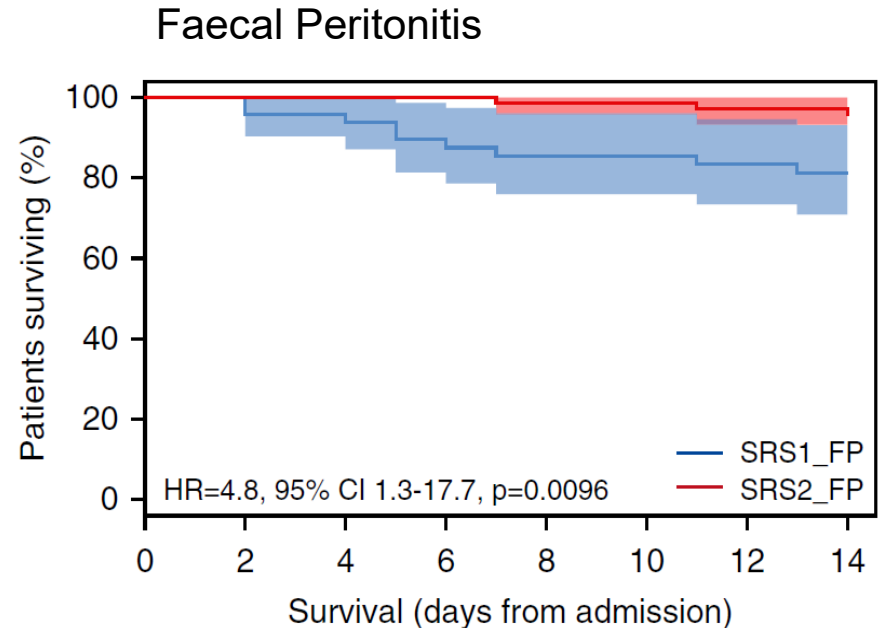
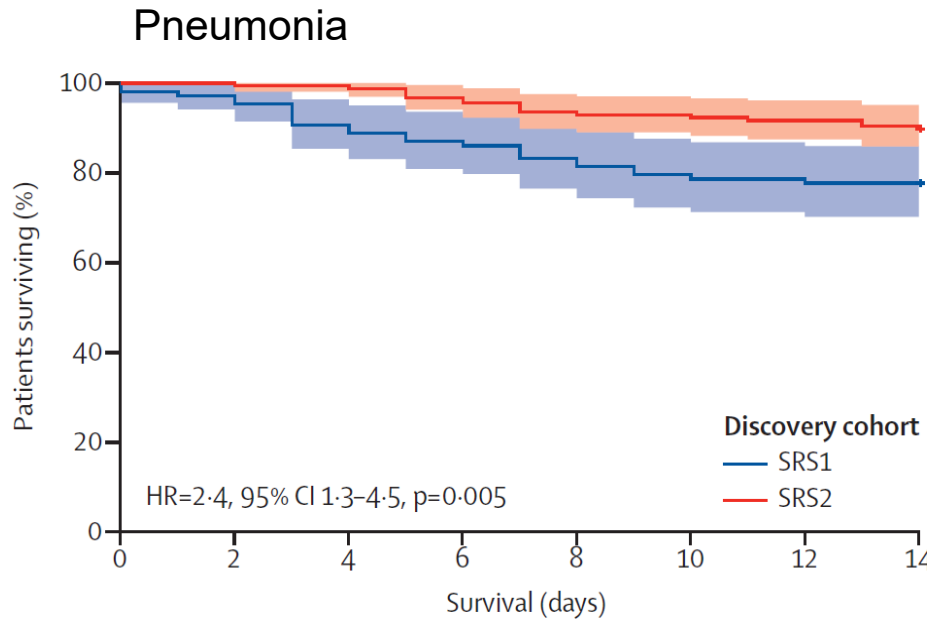
Sepsis Response Signatures – GAinS Consortium



Sepsis Response Signatures



Sepsis Response Signatures - Outcomes



Imperial College
London

Precision Medicine



SRS Signatures and Treatment in Septic Shock

Corticosteroids

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Adjunctive Glucocorticoid Therapy in Patients with Septic Shock

B. Venkatesh, S. Finfer, J. Cohen, D. Rajbhandari, Y. Arabi, R. Bellomo, L. Billot, M. Correa, P. Glass, M. Harward, C. Joyce, Q. Li, C. McArthur, A. Perner, A. Rhodes, K. Thompson, S. Webb, and J. Myburgh, for the ADRENAL Trial Investigators and the Australian–New Zealand Intensive Care Society Clinical Trials Group*

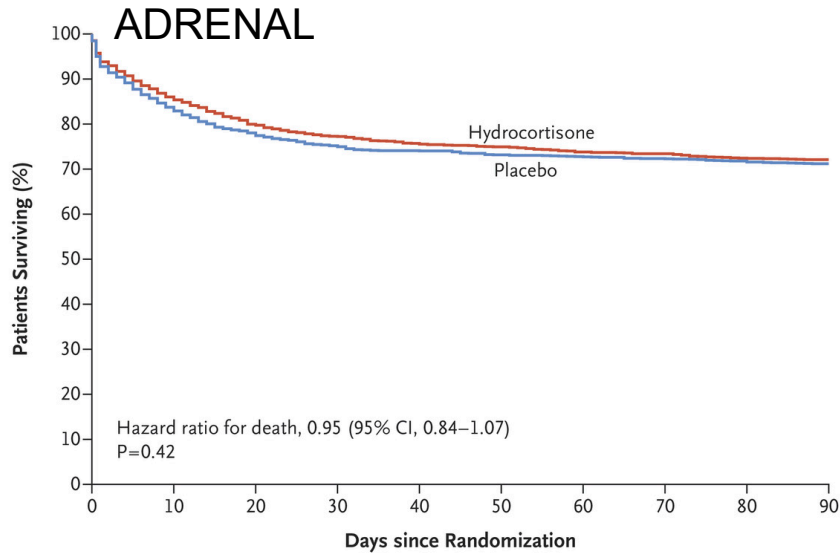
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ORIGINAL ARTICLE

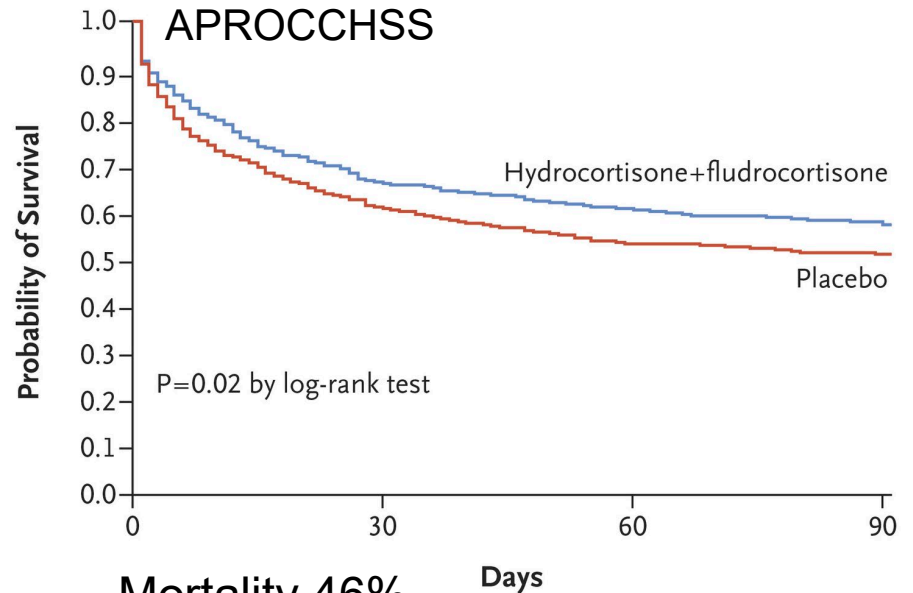
Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

D. Annane, A. Renault, C. Brun-Buisson, B. Megarbane, J.-P. Quenot, S. Siami, A. Cariou, X. Forceville, C. Schwebel, C. Martin, J.-F. Timsit, B. Misset, M. Ali Benali, G. Colin, B. Souweine, K. Asehnoune, E. Mercier, L. Chimot, C. Charpentier, B. François, T. Boulain, F. Petitpas, J.-M. Constantin, G. Dhonneur, F. Baudin, A. Combes, J. Bohé, J.-F. Loriferne, R. Amathieu, F. Cook, M. Slama, O. Leroy, G. Capellier, A. Dargent, T. Hissem, V. Maxime, and E. Bellissant, for the CRICS-TRIGGERSEP Network*

Corticosteroids



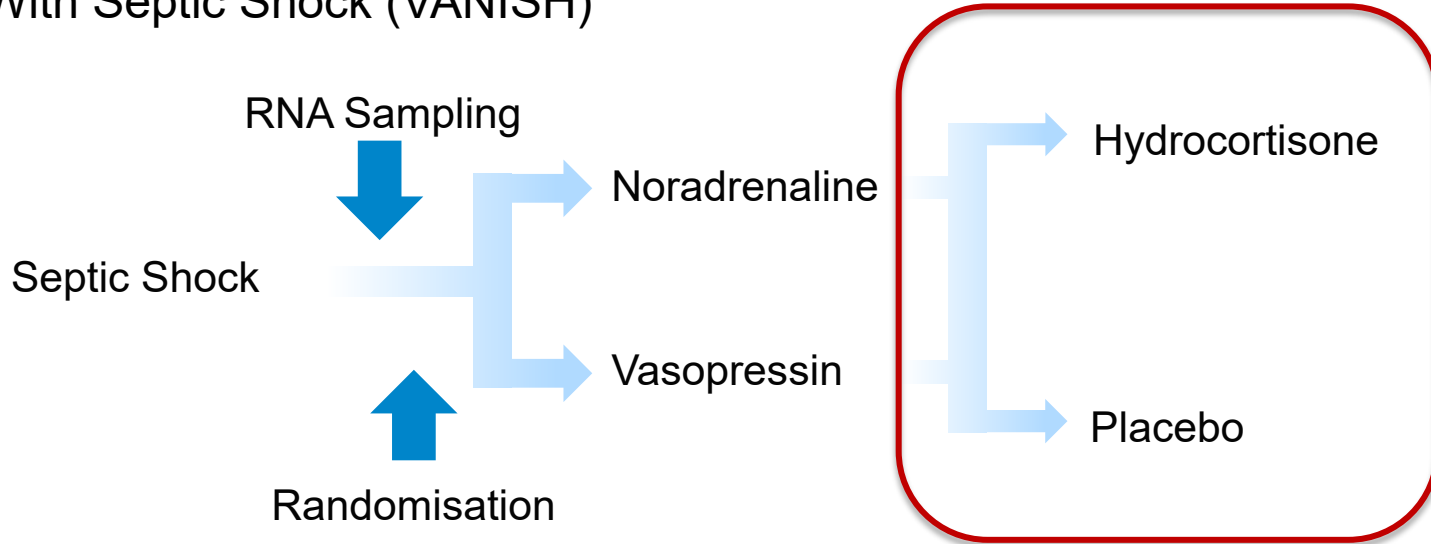
Mortality 28%



Mortality 46%

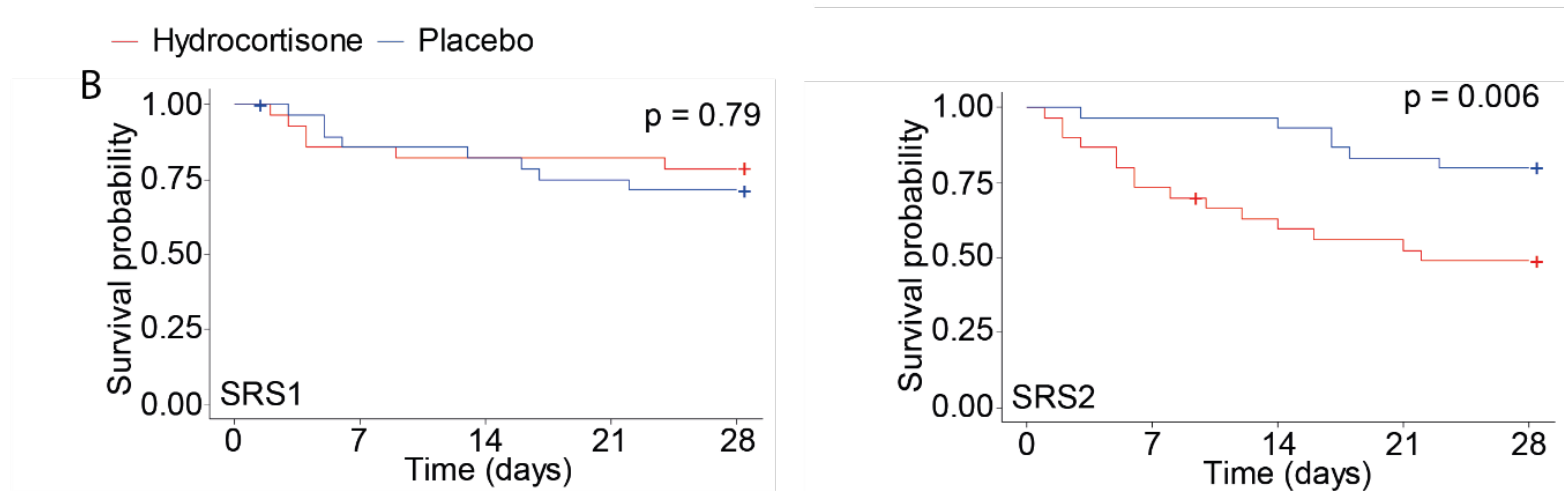
Sepsis Response Signatures and Corticosteroids

- Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock (VANISH)



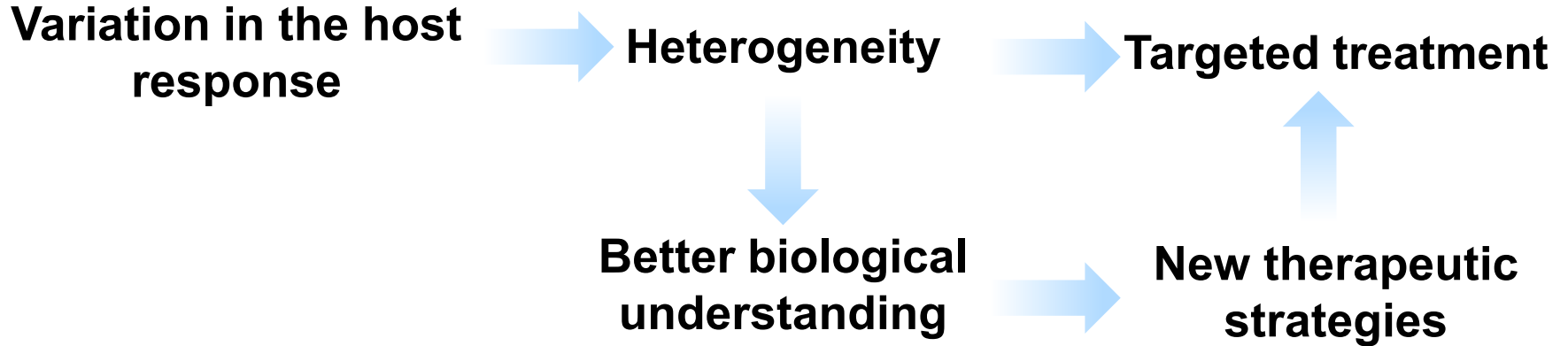
Sepsis Response Signatures and Corticosteroids

Interaction effect $p=0.02$

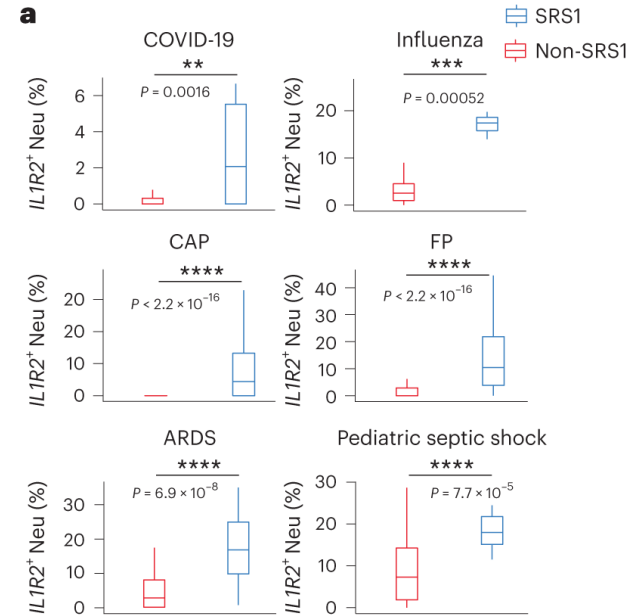
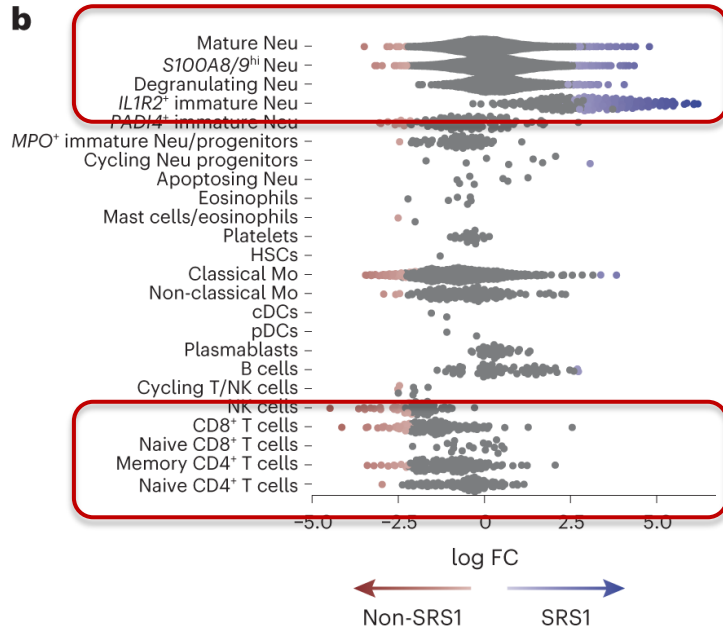


Biological Insight

Precision Medicine

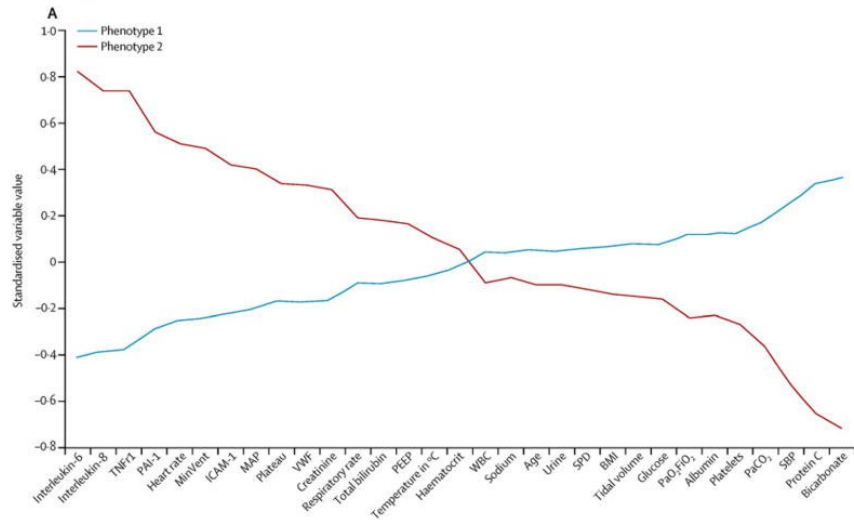
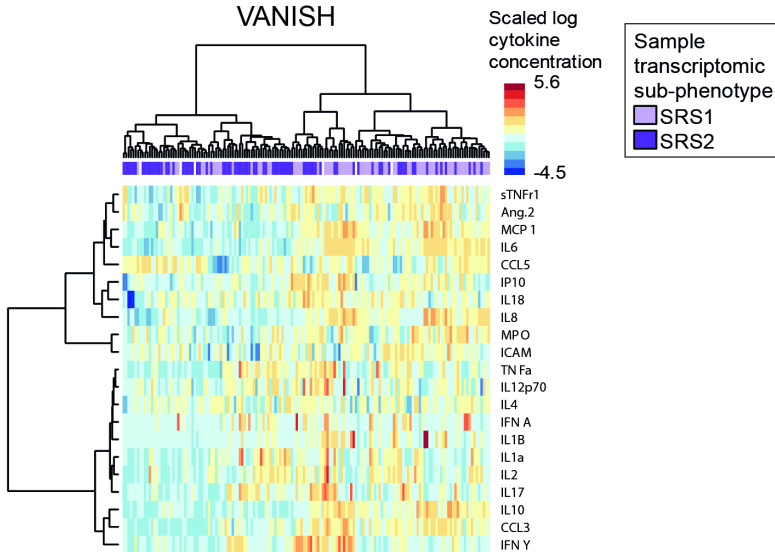


What drives gene-expression phenotypes?



Other Molecular Phenotypes

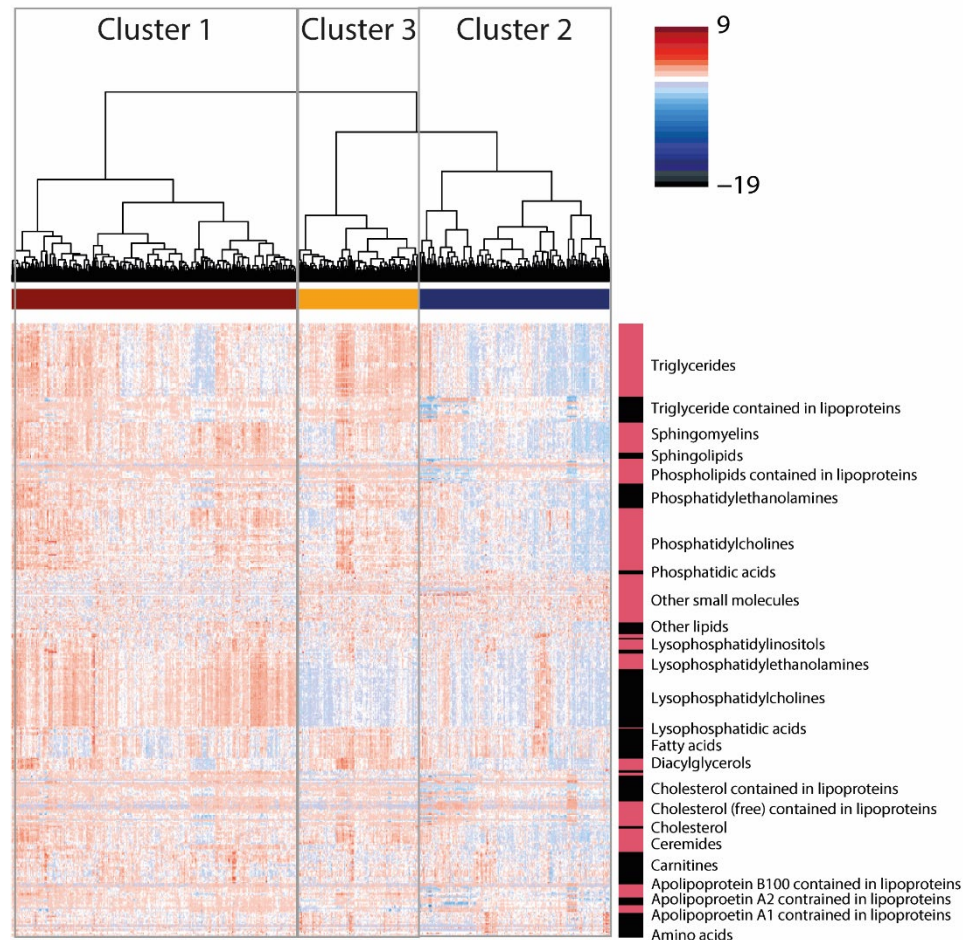
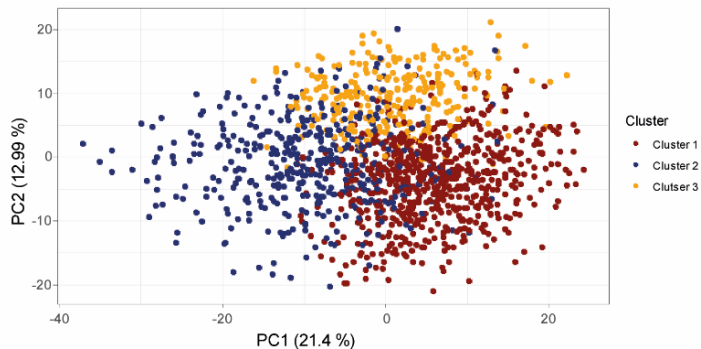
VANISH



- Ventilation strategies
- Simvastatin
- Fluid strategy
- Activated Protein C



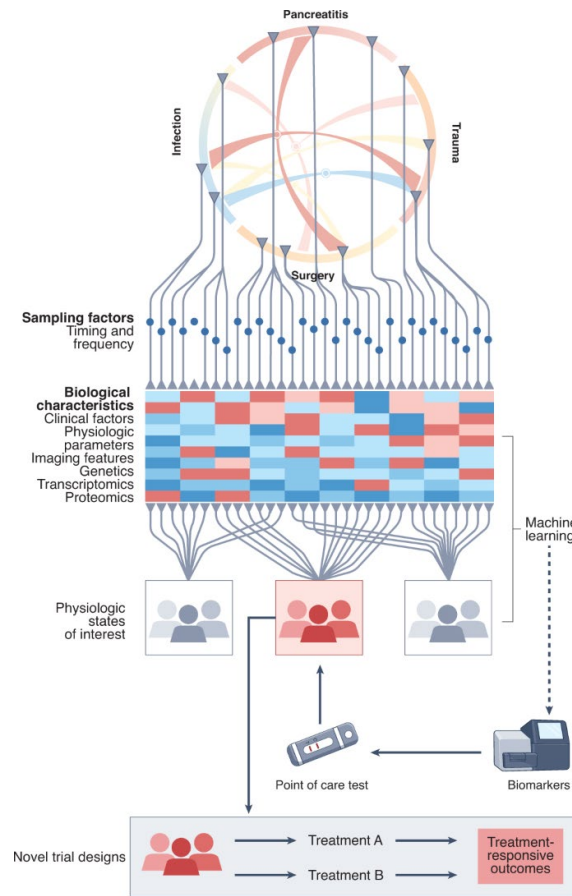
Elsa Harte



Redefining critical illness

[David M. Maslove](#) , [Benjamin Tang](#), [Manu Shankar-Hari](#), [Patrick R. Lawler](#), [Derek C. Angus](#), [J. Kenneth Baillie](#), [Rebecca M. Baron](#), [Michael Bauer](#), [Timothy G. Buchman](#), [Carolyn S. Calfee](#), [Claudia C. dos Santos](#), [Evangelos J. Giamarellos-Bourboulis](#), [Anthony C. Gordon](#), [John A. Kellum](#), [Julian C. Knight](#), [Aleksandra Leligdowicz](#), [Daniel F. McAuley](#), [Anthony S. McLean](#), [David K. Menon](#), [Nuala J. Meyer](#), [Lyle L. Moldawer](#), [Kiran Reddy](#), [John P. Reilly](#), [James A. Russell](#), ... [John C. Marshall](#) + Show authors

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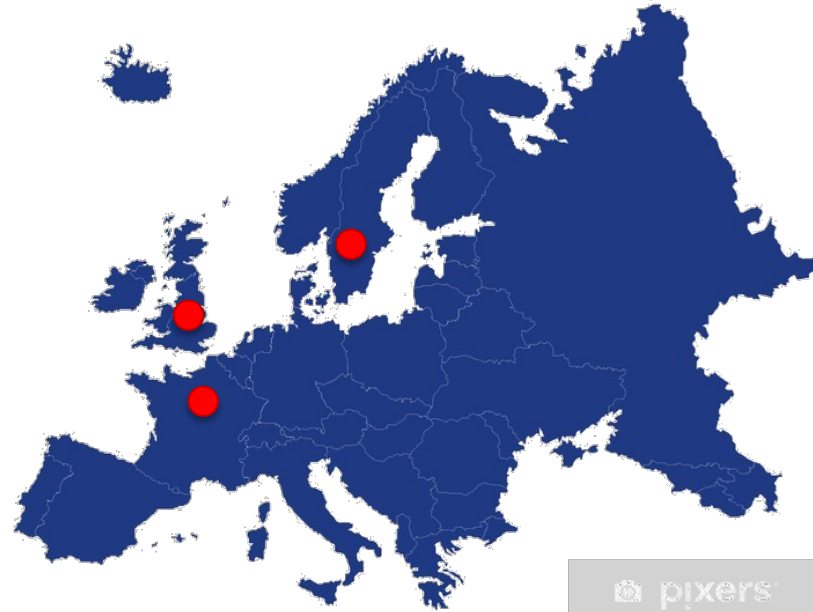


Clinical Application

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IMmune Profiling of ICU pAtients to address Chronic Critical illness and ensure healThy ageing



The Future

- Bring these processes to the bedside
- Trajectory
- Overlap of phenotypes
- Embedded into trials



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 - Dr Emma Davenport
 - Prof Charles Hinds (Barts and the London)

NIHR | National Institute
for Health Research

NIHR | Imperial Biomedical
Research Centre

 intensive care
society

Thank You
