ADAPT-Sepsis Trial

BiomArker-guided Duration of Antibiotic treatment in hospitalised PaTients with **Sepsis**

Trial Details

Funder	National Institute of Health Research (NIHR), Health Technology Assessment (HTA).
Chief Investigator	Professor Paul Dark, Honorary NHS Consultant in Critical Care Medicine, Salford Royal NHS Foundation Trust; Chair of Critical Care Medicine, University of Manchester
Sponsor	University of Manchester, Oxford Road, Manchester, M13 9PL
Clinical Trials Unit	Warwick Clinical Trials Unit, University of Warwick, Gibbet Hill Campus, Coventry, CV4 7AL Trial Co-ordinator – Nicola McGowan
NHS Contractor	Salford Royal NHS Foundation Trust, Stott Lane, Salford, M6 8HD Co-ordinator – Nessa Nevels
E-mail Contact	adaptsepsistrial@warwick.ac.uk

ADAPT- Sepsis Trial Summary

Aim: To deliver a UK-wide multi-centre randomised controlled trial to determine whether treatment protocols based on monitoring daily CRP (C-reactive protein) or PCT (procalcitonin) safely allow a reduction in duration of antibiotic therapy in hospitalised adult patients with suspected sepsis.

Design: Multicentre three-arm randomised controlled trial with internal pilot.

Setting: 30 UK (including England, Scotland, Wales & Northern Ireland) Acute NHS hospitals.

Target population: Hospitalised adults who have been commenced on intravenous antibiotics for sepsis.

Inclusion criteria: (a) At least 18 years old; (b) receiving intravenous antibiotics for sepsis; (c) no more than 24 hours of systemic antibiotic treatment for present sepsis episode; (d) likely to require intravenous antibiotics for at least 72 hours and (e) requirement for critical care.

Main exclusions: (a) prolonged antimicrobial therapy mandated; (b) severely immunocompromised; (c) All treatment for suspected sepsis likely to be stopped within 24 hours of its initiation because of futility. (d) any patient given, or anticipated to receive an IL-6 receptor inhibitor drug (e.g. tocilizumab or sarilumab) during their acute hospital admission.

Health Technology: 3 protocols for guiding antibiotic discontinuation will be compared: (a) standard care; (b) standard care + daily CRP monitoring; (c) standard care + daily PCT monitoring. Standard care will be based on routine sepsis management with associated NHS antibiotic stewardship guidance. We have developed biomarker protocols, based on daily assays, adopting the best evidence from the international guidance for CRP and including NICE guidance for PCT to guide antibiotic discontinuation.

Measurement of costs and outcomes: Outcomes will be assessed to 28 days. The primary outcomes are total duration of antibiotics and safety outcome of all-cause mortality. Secondary outcomes include: escalation of care/re-admission; infection re-lapse/recurrence; dose of antibiotics; length and level of critical care stay and length of hospital stay. 90-day all-cause mortality rates will also be collected. An assessment of in-trial cost effectiveness will be performed.

Sample size: A total sample size of 2760 would be able to detect both a mean of 1-day reduction in antibiotic duration (using a mean antibiotic duration of 7 days, a pooled standard deviation of 6 days, 90% power, a significance level of 5%, with a 5% withdrawals rate) and a non-inferiority safety margin of 5.4 % (using a 1-sided significance level of 2.5%, 90% power and 5% withdrawal rate) assuming 28-day mortality is 15%.

Project timetable: Commencing May 1st 2017: Set up (6/12), recruitment (30/12), follow up, analysis and reporting (12/12).