NIHR | Southampton Biomedical Research Centre

University of Southampton | University Hospital Southampton NHS Foundation Trust

NIHR Southampton Biomedical Research Centre

RESEARCH THEMES SMART OBJECTIVES

Nutrition, Lifestyle and Metabolism (2022-2027): Scientific aims and SMART Objectives (n = 18)

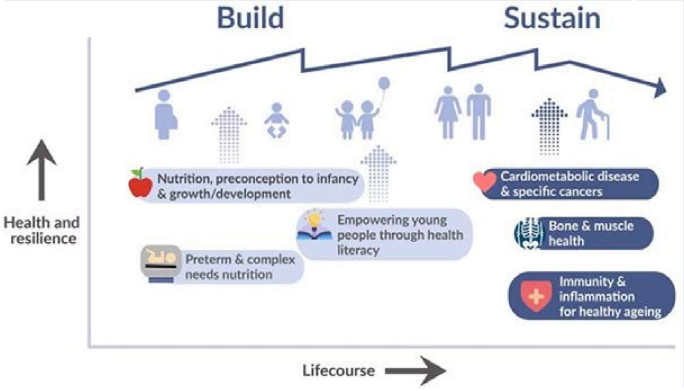
Scientific Aims

Nutrition, Lifestyle and Metabolism (NLM)
Improving health and resilience across the lifecourse, addressing patient and population needs through improving diet quality/ nutrient status, smoking/alcohol behaviours, physical activity, obesity/body composition and cardiometabolic musculoskeletal and immune health.

Research Questions?

1. How to promote healthy development of functional capacity through improving nutrition, lifestyle and metabolism before and after birth and during childhood?

2. How to sustain functional capacity and promote resilience through improving nutrition, lifestyle and metabolism in adulthood?



Short term SMART scientific objectives

(1) 1b-i: Characterise how patterns of nutrient intake influence growth and clinical outcomes

(2) 2c-i: Test effects of a novel omega-3 fatty acid source on inflammation

Medium term SMART scientific objectives

(3) 1a-ii: Characterise infant/childhood phenotypes influenced by gestational cholecalciferol supplementation

(4) 1a-iii: Develop and test food environment interventions

(5) 1b-ii: Develop validated body composition, nutritional and neurodevelopmental assessment toolkits for routine clinical application

(6) 1c-i: Develop and evaluate materials to support behaviour change and healthier choices with other themes

(7) 2b-i: Develop and evaluate stratified vitamin D treatment approaches informed by genotype/ epigenotype

(8) 2c-ii: Test whether novel nutritional strategies enhance immunity and control inflammation in older people, relating effects to gut microbiome alterations

Long term SMART scientific objectives

(9) 1a-i: Develop mother-offspring multi'omic "handprints" that predict child phenotypes

(10) 1b-iii: Improved growth and development of infants born preterm or with complex disorders

(11) 1c-ii: Develop and evaluate a 3-pillar blended online/in-person engagement programme to strengthen scientific, health and nutrition literacy

(12) 1c-iii: Develop and evaluate equitable and inclusive advanced digital learning tools and services to strengthen nutrition and health literacy for all UK students

(13) 2a-i: Complete feasibility trial of intervention to optimise identification of liver fibrosis in patients and populations at risk of liver cancer and the complications of MAFLD

(14) 2a-ii: Develop and evaluate novel noninvasive probes/risk markers, serological, tissue and metabolomic markers of cardiometabolic risk and cancer detection and monitoring

(15) 2a-iii: Use of tissue biopsies (adipose and liver) to investigate the association between tissue remodelling and cardiometabolic risk

(16) 2b-ii: Use implementation science to optimise screening for high fracture risk nationally

(17) 2b-iii: Translate our myocyte mitochondrial energy handling insights into novel nutritional interventions for sarcopenia

(18) 2c-iii: Investigate inflammatory processes in human adipose tissue and test potential nutritional strategies to control these through ex vivo studies

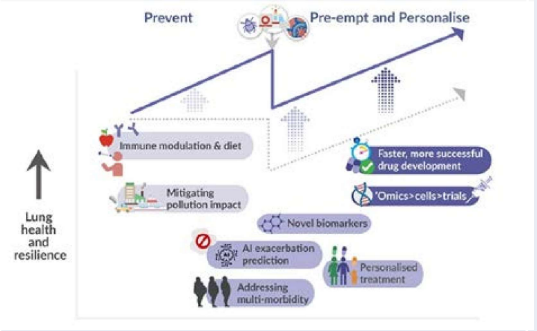
Respiratory and Allergy Theme (2022-2027): Scientific Aims and SMART Objectives (n=20)

Scientific Aims

Respiratory and Allergy (RA)
Delivering preventive interventions for allergy and respiratory disease, identifying biomarkers to provide earlier and more accurate diagnosis and personalise therapy, and utilising our ex-vivo models and innovative trial designs to accelerate identification of new therapeutic approaches.

Research Questions?

1. How can respiratory and allergic disease be prevented across the life-course?
2. How can we improve clinical outcomes through earlier diagnosis and personalised treatment?
3. How do we develop new respiratory treatments in a much shorter time frame, with higher success rates?



Short term SMART scientific objectives

(1) 1b-i: Reducing impacts of air pollution on the development and exacerbation of lung disease- i. Research database design and establishment of SOPs for integration of air pollution data sources with clinical lung health screening data

(2) 2a-i: Identifying new diagnostic markers of early respiratory disease- i) Extend the existing Paediatric PCD database to include longitudinal adult data

(3) 2a-i: Identifying new diagnostic markers of early respiratory disease- i) Proof of concept that RNAseq of nasal cells can enhance diagnostic uplift by discovering and validating splice altering variants 'missed' by genetic testing of blood DNA

(4) 2b-i: Precision medicine strategies to treat lung-disease, allergy and multimorbidity i) To optimise breathing retraining for adolescents as a personalised strategy to manage anxiety and dysfunctional breathing in asthma

(5) 2c-i: Developing Novel strategies to predict, prevent and treat acute exacerbations

(6) 3. Pipeline for accelerated drug development from new targets to proof of concept. Establishment of a cross-disciplinary advanced cell culture working group

Medium term SMART scientific objectives

(7) 1b-ii: Reducing impacts of air pollution on the development and exacerbation of lung disease- ii) Define personal-level exposure to PM concentration for high risk-individuals

(8) 2a-i: Identifying new diagnostic markers of early respiratory disease i) Extend nasal nitric oxide as a screening test for PCD into pre-school age group

(9)2c-i: Novel strategies to predict, prevent and treat acute exacerbations- testing phase.

(10) 3. Pipeline for accelerated drug development from new targets to proof of concept. – Validation of four models and progression of target identification

Long term SMART scientific objectives

(11) 1a-i: Reducing risk of developing asthma and allergy in early life. i) Feasibility and safety of rapidly dissolving tablet allergen formulation in infants to design a definitive effectiveness study.

(12) 1a-ii: Reducing risk of developing asthma and allergy in early life- ii). To develop approaches to help parents introduce allergens into infant diets earlier to prevent food allergy which will be tested in a definitive effectiveness study.

(13) 1b-iii: Reducing impacts of air pollution on the development and exacerbation of lung disease- iii) Determining the relationship between source specific longitudinal air pollution exposure and ILA progression or regression

(14) 2a-ii: Identifying new diagnostic markers of early respiratory disease ii) Develop the infrastructure to interrogate health records to screen for rare disease syndromes using PCD as an exemplar

(15) 2a-ii: Identifying new diagnostic markers of early respiratory disease ii) Identify novel genetic causes of PCD to facilitate diagnostic testing.

(16) 2a-ii: Identifying new diagnostic markers of early respiratory disease ii) Age specific versions of PICADAR as screening tools for PCD

(17) 2a-iii: Identifying new diagnostic markers of early respiratory disease - iii) To develop novel diagnostic markers of COPD and ILD

(18) 2b-ii: Precision medicine strategies to treat lung-disease, allergy and multimorbidity ii) multimodal physical and emotional support intervention to address multimorbidity in difficult-to-treat asthma.

(19) 2c-i: Novel strategies to predict, prevent and treat acute exacerbations. Testing and Scaling.

(20) 3. Pipeline for accelerated drug development from new targets to proof of concept - Progression from new targets to preclinical models and/or proposals/external funding for early phase clinical trials

Data Health and Society Theme (2022-2027): Scientific aims and SMART Objectives (n=15)

Scientific Aims	Short term SMART objectives	Medium term SMART objectives	Long term SMART objectives
Data, Health and Society (DHS) Moving beyond data science to harness computer science, artificial intelligence and exploration of societal implications to create a trusted and trustworthy learning healthcare system. **Research questions** 1. How can we build trustworthy healthcare systems that are equitable for all members of a digital society? 2. How do we improve insights from healthcare data and turn them into significant health and social care benefits? 	NONE STATED as all medium to long term	(1) 1b: Develop principles for autonomous systems using data by creating trustworthy health systems. (2) 1c-i: Integrate AI-assisted decision-making into clinical practice using visualised explanations of AI-assisted decision support to improve understanding and interpretation of models in clinical settings. (3) 1c-ii: Integrate AI-assisted decision-making into clinical practice by using data storytelling to improve communication, understanding and trust of AI-assisted decision tools. (4) 2a: Improve data sharing for shared decision-making processes by using shared framework of terms relevant to care needs, and piloting optimum digital mechanisms for reaching shared decisions and reviewing their outcomes. (5) 2c-i: Manage real time risks to data quality from integration of diverse data via automated management of algorithmic performance risk from data/concept drift and variable data quality. (6) 3b-i: Integrate data across boundaries for prevention across the lifecourse by establishing a regional near real-time maternal-child linked dataset of routine health and wider social determinants data for research.	(7) 1a-i: Co-create the data ecosystem to balance privacy and utility (ELSA). (8) 1a-ii Co-create the data ecosystem to balance privacy and utility. (9) 1a-iii: Co-create the data ecosystem to improve inclusion of underserved communities. (10) 2b: Enhance automated decision-making using early warning signals in clinical pathways by automating the identification of risks leading to poor outcome, and designing interventions to address. (11) 2c-ii: Manage real time risks to data quality from integration of diverse data by assessment of dependability risk from dynamic integration of personal data stores (PDS) within diverse care settings, applications and business processes. (12) 3a: Integrate highly complex data for clinical decision-making using high throughput genomic data with various longitudinal clinical data to provide mechanistic and diagnostic insight that informs management. (13) 3b-ii: Integrate data across boundaries for prevention across the life course via use of linked longitudinal data in pre-hospital critical care pathways for all pathology (medical and trauma) to generate targets to improve prehospital critical care pathways for all and provide evidence to drive societal change. (14) 3c-i: Create and test comparative data resources for real-world evaluation by creating a biorepository of signal and image data resources to enable comparative model generation and real-world testing of new index cases to identify individuals at risk of poor outcomes or deterioration. (15) 3c-ii: Create and test comparative data resources for real world evaluation by creating a biorepository of signal and image data resources to enable comparative model generation and real-world testing of new index cases to identify individuals at risk of poor outcomes or deterioration.

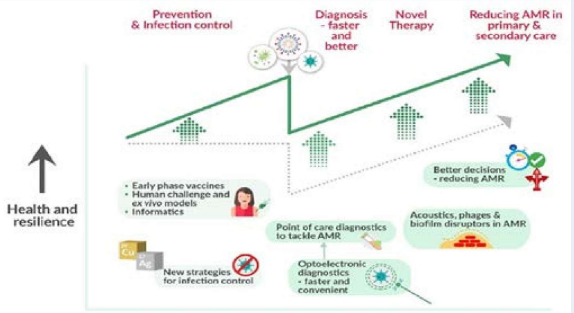
Microbiology Immunology and Infection Theme (2022-2027): Scientific aims and SMART Objectives (n=20)

Scientific Aims

Microbiology, Immunology & Infection (MII)
Delivering innovative solutions to infectious threats and help overcome antimicrobial resistance by conducting experimental evaluation of novel vaccines and other prevention strategies, as well as advanced diagnostics and therapies.

Research questions

1. Preventing/controlling infectious disease with novel immuno-prophylaxis, vaccine technologies and innovative systems.
2. Accelerating diagnosis using novel technologies and operational systems, improving patient pathways; reducing AMR.
3. Engineering solutions for difficult-to-treat/AMR infections in hospitals using novel antimicrobial strategies such as acoustics, phages, novel surfaces and biofilm-active small molecules.
4. Improving infection management in Primary Care, by enhancing responsible antibiotic usage and use of rapid diagnostics.



Short term SMART objectives

(1) 1a: Define immune markers associated with protection against with Bordetella pertussis, in a controlled human infection model.

(2) 1a: Determine whether commensal nasopharyngeal bacteria inoculated into pregnant women are transmitted to their infants (to potentially generate a `healthy` shared microbiome).

(3) 2b: Demonstrate the utility of a flow-based rapid phenotypic antimicrobial susceptibility assay for the Clinical Microbiology Laboratory.

(4) 2b/3: Obtain proof of concept for direct, non-destructive and label free pathogen identification and biofilm characterisation within ex-vivo tissue using novel Raman spectroscopy and imaging technology to test putative therapy.

(5) 4a/b: Develop a comprehensive antimicrobial stewardship package for primary care to reduce use in all age groups.

Medium term SMART objectives

(6) 1b: Conduct phase I trials of new vaccines and vaccine technologies for respiratory infection/pandemic control.

(7) 2a: Evaluate the real world performance and clinical impact of syndromic molecular point-of-care testing for gastrointestinal pathogens in secondary care.

(8) 2a: Evaluate the real world performance and clinical impact of syndromic molecular point-of-care testing for pneumonia pathogens in critically ill patients.

(9) 2b: Demonstrate utility of low-cost optoelectronic-based health diagnostics.

(10) 3: Identify adjunctive therapies to improve host control of Mycobacterium tuberculosis by integrating 3D biolectrospray model with a multiparameter microengineered readout platform.

(11) 4a/4b: Safely identify care home residents with suspected UTI who do not benefit from antibiotic treatment.

Long term SMART objectives

(12) 1a/1b: Determine whether vaccination with standard and/or novel vaccines inhibits asymptomatic infection with Bordetella pertussis in a controlled human infection model.

(13) 1a: Demonstrate that refined genetically modified bacteria, administered intranasally in young adults, boost broad protective immunity to meningococcal disease.

(14) 1b: Achieve progression to later phase clinical development of at least one vaccine or vaccine technology emerging from early phase investigation by NIHR Southampton BRC.

(15) 1c/3: Provide evidence to stratify the treatment of chronic hepatitis by ethnicity and KIR genotype.

(16) 2b: Commercialise at least one diagnostic technology developed by NIHR Southampton BRC investigators.

(17) 3: Progress commercialisation of a device for prevention and treatment of infection of venous leg ulcers using acoustic energy in water streams.

(18) 3.Conduct a proof-of-concept clinical trial of a new biofilm disrupting treatment developed by NIHR Southampton BRC and/or its collaborating partners.

(19) 4a: Implement a comprehensive antimicrobial stewardship tool for primary care to reduce antibiotic use in all age groups.

(20) 4a/4b: Improve primary care antibiotic prescribing through use of our experimental interventions.

Perioperative and Critical Care Theme (2022-2027): Scientific aims and SMART Objectives (n=8)

Scientific Aims	Short term SMART objectives	Medium term SMART objectives	Long term SMART objectives
Perioperative and Critical Care (PCC) Developing, evaluating and individualising interventions to promote, rebuild and maintain resilience across surgical and critical care pathways. **Research questions** 1. How do we improve decision-making for patients and healthcare professionals? 2. How do we promote, rebuild and maintain physical and psychological resilience by individualising interventions?	(1) 1a: Development of artificial intelligence perioperative risk models. (2) 1b: Evaluating shared decision- making. (3) 2a-i: Evaluating digital screening and prehabilitation interventions. (4) 2a-ii: Evaluating multi-modal prehabilitation-rehabilitation interventions. (5) 2a-iii: Refining exercise interventions and exploring mechanisms. (6) 2b: Defining the surgical strategy for cancer resections. (7) 2c: Individualised oxygen and fluid therapy. (8) 2d: Defining optimal timing and content of interventions at end-of-life.	(1) 1a: Development of artificial intelligence perioperative risk models. (2) 1b: Evaluating shared decision-making. (3) 2a-i: Evaluating digital screening and prehabilitation interventions. (4) 2a-ii: Evaluating multi-modal prehabilitation-rehabilitation interventions. (5) 2a-iii: Refining exercise interventions and exploring mechanisms. (7) 2c: Individualised oxygen and fluid therapy. (8) 2d: Defining optimal timing and content of interventions at end-of-life.	(1) 1a: Development of artificial intelligence perioperative risk models. (2) 1b: Evaluating shared decision- making. (3) 2a-i: Evaluating digital screening and prehabilitation interventions. (4) 2a-ii: Evaluating multi-modal prehabilitation-rehabilitation interventions. (5) 2a-iii: Refining exercise interventions and exploring mechanisms. (6) 2b: Defining the surgical strategy for cancer resections. (7) 2c: Individualised oxygen and fluid therapy. (8) 2d: Defining optimal timing and content of interventions at end-of-life.