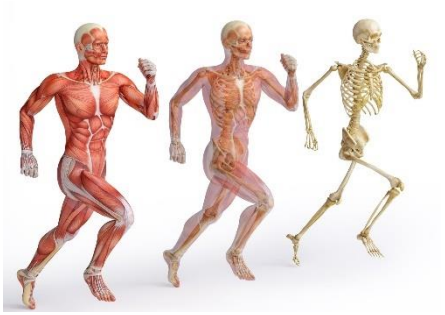
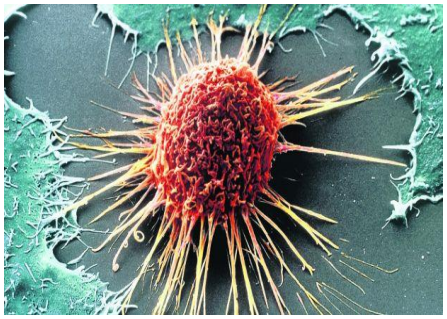
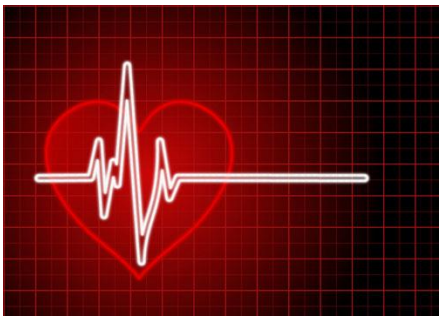
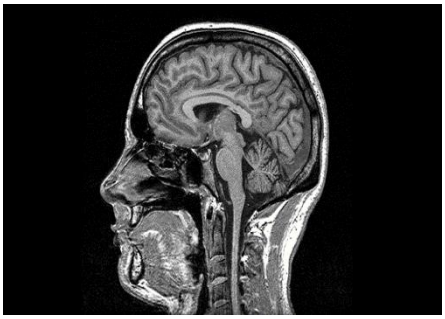
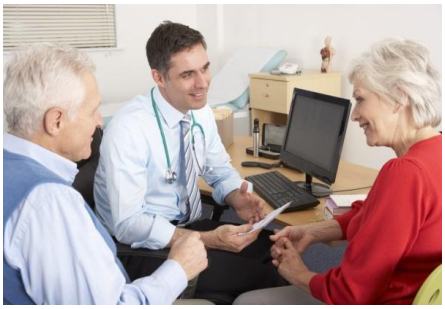
University of East Anglia | NORWICH MEDICAL SCHOOL

Medical Research Directory for MBBS Intercalating courses, Academic SFP and ACF

2025/26



CONTENTS

GASTROENTEROLOGY, GUT BIOLOGY AND MICROBIOLOGY Page 3

SURGERY Page 16

NUTRITION Page 20

DIABETES AND ENDOCRINOLOGY Page 26

MUSCULOSKELETAL BIOLOGY AND HUMAN PHYSIOLOGY Page 28

ONCOLOGY AND HAEMATOLOGY Page 34

CARDIOVASCULAR RESEARCH Page 42

RESPIRATORY MEDICINE Page 48

RHINOLOGY AND THE EYE Page 55

MENTAL HEALTH AND DEMENTIA Page 60

POPULATION HEALTH, PRIMARY CARE AND HEALTH CARE DELIVERY including PALLIATIVE CARE Page 62

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Gastroenterology, Gut Biology & Microbiology

Gastroenterology, Gut Biology & Microbiology

Gastroenterology research in Norwich offers a broad portfolio of research covering clinical research with patients, laboratory and epidemiological research. Norwich Medical School is one of the UK's major centres for gastrointestinal research; senior academics in the School and the consultants at NNUH work in close collaboration with other Institutes based at Norwich Research Park, including the Genome Analysis Centre, the John Innes Centre and the Quadram Institute (QI). Clinical gastroenterology research is concentrated at the Quadram, which houses the NNUH Endoscopy Facility and provides research facilities for academic scientists working on the biology of the gastrointestinal tract, alongside clinicians and clinician-scientists in NNUH Gastroenterology. We also have strong contacts with major epidemiological databases in the UK and USA to study dietary risk factors for gastrointestinal disease. This gives an excellent teaching environment for research training.

Current Research Opportunities

- Epidemiology of gastrointestinal malignancy – *Dr Leo Alexandre*
- The aetiology of inflammatory bowel diseases – *Dr Simon Chan*
- Primary sclerosing cholangitis of the liver – *Dr Simon Rushbrook*
- Gastrointestinal pharmacology, therapeutics and education – *Dr Ian Beales*
- Autophagy and Crohn's disease – *Prof Tom Wileman and Prof Ulrike Mayer*
- Gut microbes in health and disease – *Prof Simon Carding*
- Gut bacteria in Crohn's disease – *Dr Stephanie Schuller*
- Generation of organoids from stem cells to study innate immune responses in the GI tract – *Dr Penny Powell*
- Mucus-associated gut microbiota in health and disease – *Prof. Nathalie Juge* (*QI)*
- Discovering novel antibiotics to combat resistance **–** *Prof Arasu Ganesan*
- Understanding the survival strategies of foodborne Listeria – *Dr Matthew Gilmour*
- Pathogen variation – *Prof Rob Kingsley*
- Manipulation of the human gut microbiome for health benefits – *Prof Arjan Narbad*
- Microbiome and the gut-liver axis during chronic liver disease; from mechanisms to therapy – *Dr Naiara Beraza*
- Microbiome and Human Health - *Dr. Lizbeth Sayavedra*
- Unravelling host-guest metabolic pathways in colorectal cancer: a live-cell NMR investigation – *Dr Serena Monaco (QI)*

Medical Microbiology

- Antimicrobial resistance – Prof *Mark Webber*
- Metagenomics – Dr Falk Hildebrand
- Evolution and spread of antibiotic resistance – *Dr Benjamin Evans*
- Bacteriophages for the biocontrol of pathogenic bacteria - *Dr Evelien Adriaenssens*
- Emerging infectious disease – *Prof Paul Hunter*

Tropical Medicine

- Parasite virulence – *Dr Kevin Tyler*
- Antimicrobials – *Prof Dietmar Steverding*

Epidemiology of gastrointestinal malignancy

Patients with oesophageal cancer typically present with advanced disease and overall survival is amongst the poorest of all malignancies. Barrett's oesophagus is the only known precursor lesion to oesophageal adenocarcinoma (the predominant histological subtype in the West). The focus of our research is on understanding the epidemiology of pre-malignant and malignant upper gastrointestinal disease with the aim of developing interventions to improve prognosis. Key areas include:

- Post-endoscopy upper gastrointestinal cancer
- Chemoprevention of Barrett's related neoplasia
- Barrett's oesophagus surveillance and endotherapy
- Iron deficiency and GI malignancy

Key methods include epidemiological analysis of routinely collected hospital and primary care data, pharmaco-epidemiology and systematic review methodology. Research students, SFPs and Academic Clinical Fellows joining the group will receive training and supervision in the application of methods appropriate to the project, including the use of statistical software. Collaborative working across specialties and sites is expected. Students and trainees will be supported to present and publish their research and develop their clinical academic careers.

Contact: leo.alexandre@uea.ac.uk or view his online research profile

The aetiology of inflammatory bowel diseases

The two main forms of inflammatory bowel disease (IBD) are Crohn's disease and ulcerative colitis, chronic inflammatory disorders that affect the gastrointestinal tract. The prevalence of IBD is increasing substantially with peak incidence occurring in 20 – 40 year olds. This results in substantial morbidity with patients affected by abdominal pains, blood in the stools, diarrhoea, weight loss and potentially the need for surgery. At present the exact mechanisms leading to the development of IBD are unknown. Our research is focused on identifying risk factors, understanding how these lead to the development of IBD with the aim of developing interventions to prevent and treat these diseases.

Key research areas include:

- Identifying environmental and lifestyle exposures that are involved in the aetiology of Crohn's disease and ulcerative colitis
- Molecular characterising of IBD risk factors to understand the mechanisms leading to IBD development and progression
- Investigation of innate immunological pathways involved in the pathogenesis of IBD

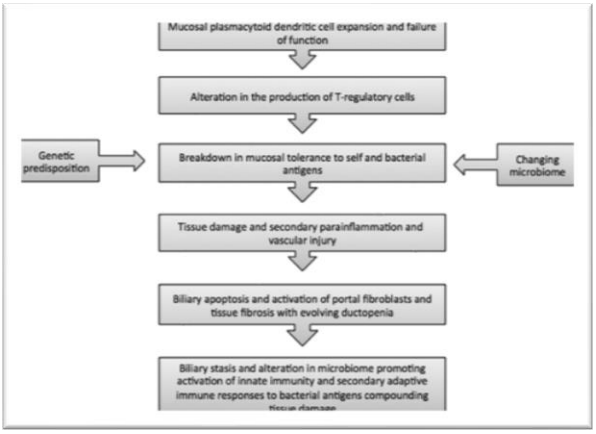
We have access to national and international datasets from large prospective cohort studies for epidemiology studies to further define and understand lifestyle and environmental exposures in the development of IBD. Molecular characterisation of risk factors and investigation of innate immunological pathways for IBD utilises tissue and blood samples from IBD patients and is done in collaboration with colleagues at UEA and the Quadrum Institute. Research students, SFPs and ACF joining the group will receive supervision and training in the methodology appropriate for their research project. We are happy to informally discuss research projects.

Contact: simon.chan@uea.ac.uk or view a list of his publications

Primary sclerosing cholangitis of the liver

Primary sclerosing cholangitis (PSC) is one of the archetypal autoimmune liver diseases characterised by biliary inflammation and fibrosis that can lead to both cirrhosis and cholangiocarcinoma. A major focus of our work is to develop a greater understanding of how these genetic loci are associated with the development of PSC by studying the immune system in both the liver and bowel of patients with PSC.

At present PSC is the 5th commonest indication for liver transplantation in the UK. Although the exact pathogenesis remains unclear, PSC is thought to have both environmental and genetic causes, with 16 genetic loci currently identified and further genetic loci undergoing evaluation in an international GWAS meta-analysis of which I am a collaborator.



Current projects include studies of the role played by genetic variation in PSC and analysis of dendritic cell and T-cell subsets in the pathogenesis of the disease.

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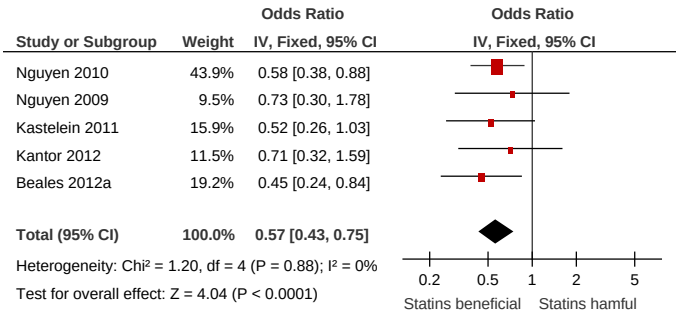
Gastrointestinal pharmacology, therapeutics and education

Dr Beales has a wide portfolio of research interests spanning clinical gastroenterology to education and training. In general, this focuses on mechanisms of disease processes and in particular the interactions of drugs on the luminal gastrointestinal tract. The current research portfolio includes participation in several international multicentre trials of novel biological and small-molecule inhibitor agents as well as locally delivered hypothesis-driven studies examining the mechanisms of drug and hormone effects particularly in Barrett's oesophagus and inflammatory bowel disease.



A variety of experimental approaches have been utilised including laboratory cell line studies, immunohistochemistry (collaborating with colleagues in histopathology), case-control methodology, systematic literature review and meta-analysis and interventional studies.

Recent important work has included the seminal original paper describing the mechanisms of the anti-cancer effects of statins in oesophageal adenocarcinoma, subsequently followed with several case-control studies and a systematic review confirming the clinical benefits. A detailed series of studies has illustrated the mechanisms linking acid-reflux, obesity and oesophageal cancer: showing how leptin combined with acid to promote oesophageal adenocarcinoma and how adiponectin may have inhibitor actions. Further studies to unravel these effects are ongoing.

Other studies have explored the safety of cyclo-oxygenase inhibitors in patients with inflammatory bowel disease, in particular showing the safety and efficacy of COX-2 inhibitors as well as the use of novel therapies to treat iron deficiency anaemia and microscopic colitis. Educational projects have examined timing of endoscopy during the day on colonoscopy performance, predictors of publication of abstracts presented at conferences and attitudes to the use of probiotics.

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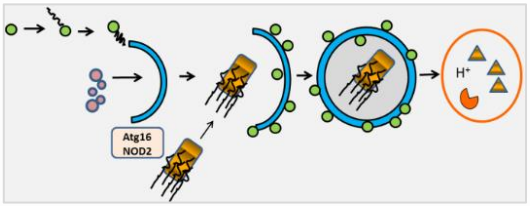
Autophagy and Crohn's disease



Autophagy is a membrane trafficking pathway that generates autophagosomes which deliver cytosol to lysosomes for degradation. Autophagy provides a powerful means of removing intracellular pathogens and is an important arm of innate immunity to infection. Recent genome wide association screens have identified autophagy gene Atg16L1 as a risk allele for Crohn's disease, an inflammatory disease of the bowel. Susceptibility to Crohn's disease is also linked to mutations in NOD2, a microbial sensor that activates autophagy during infections. We are using mouse models to investigate whether the inflammation seen in Crohn's disease is caused by defects in the control of microorganisms by autophagy in gut epithelial cells.

Contact: t.wileman@uea.ac.uk

Gut microbes in health and disease

A major research focus of the group is to understand how microbes (bacteria and viruses) resident in the lower human GI-tract (the microbiome) interact with their host to maintain lifelong health, and how microbial dysbiosis can lead to chronic diseases affecting not only the GI-tract but elsewhere in the body, including the brain. Current projects in the group include:

- The Gut-Brain axis: Identify factors produced by gut microbes that impact on specialised intestinal epithelial cells of the enteric endocrine and nervous systems that can alter signalling in the CNS.
- The role extracellular (outer membrane) microvesicles produced by gut bacteria play in mediating crosstalk between the intestinal microbiota and host cells.
- The role that the intestinal virome and prokaryotic and eukaryotic viruses play in regulating bacterial populations and in promoting dysbiosis and chronic inflammation.
- Development of novel bacteria-based therapies (e.g. probiotics, bacterial products and microbiota transplants) to treat and prevent intestinal inflammation.
- Role of the microbiota in the pathogenesis of myalgic encephalomyelitis/chronic fatigue syndrome.

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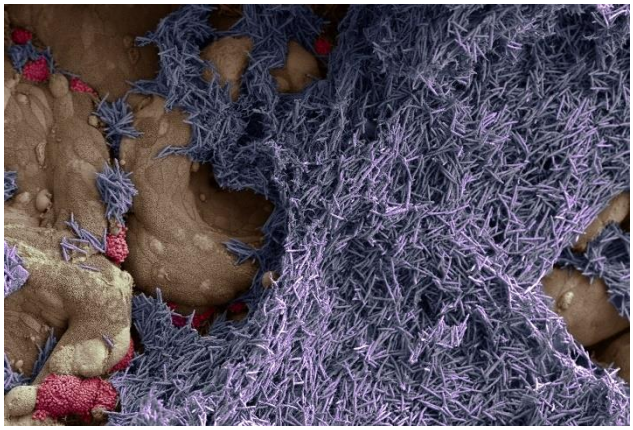
Gut bacteria in Crohn's disease

Crohn's disease (CD) is a major chronic inflammatory disorder of the intestine and has been associated with changes in gut bacteria (microbiome). In particular, CD patients show a decrease in beneficial Firmicutes and Bacteroidetes phyla while Gamma proteobacteria including adherent-invasive *E. coli* (AIEC) are enriched. However, it is not known if the microbial imbalance is a cause or consequence of CD. To this aim, we are using advanced human intestinal models including stem cell-derived organoids and low-oxygen microbiome culture systems to decipher host-microbe interactions in CD and contribute to the development of efficient therapies restoring microbiome homeostasis in CD.



Contact: s.schuller@uea.ac.uk

Generation of organoids from stem cells to study innate immune responses in the GI tract

We are interested in the innate immune response in gut following viral infection which may explain the pathogenesis of human diseases.

Innate immune responses to infection include apoptosis, autophagy and inflammation. When cells are infected with viruses these pathways are activated, the major pathway being production of interferon and interferon-stimulated genes (ISGs) triggered by dsRNA produced during viral replication. We are investigating this in primary cell cultures and gut organoids developed from small intestinal stem cells. In addition, we have used viruses to deliver exogenous genes to organoids to study innate immune pathways. The project will mainly involve bioimaging with confocal microscopy.

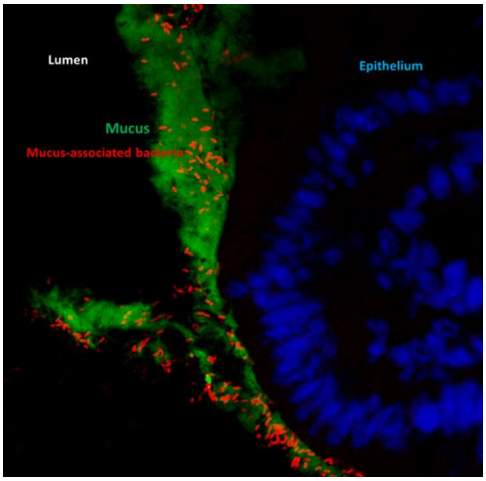
Contact: p.powell@uea.ac.uk

Mucus-associated gut microbiota in health and disease

The mucus-associated microbiota plays a predominant role in human health. We are studying how bacteria interact with mucins and their associated glycans at the mucosal surface, how mucus-associated bacteria communicate with the host and respond to changes in the physiological status of the host. Importantly, several conditions, such as irritable bowel syndrome (IBS), inflammatory bowel disease (IBD), colorectal cancer (CRC) or infections are associated with alterations in mucus-associated bacteria and mucin glycosylation, so the mechanistic knowledge we are gaining from our research can be of use for designing new biomarkers of disease and developing microbial and nutritional strategies to restore health. The Juge Group is based at the **Quadram Institute Bioscience (QIB)** within the Gut Microbes and Health (GMH) Institute strategic programme (ISP).

Current projects in the Juge group investigate:

- The changes in mucin glycosylation and mucus-associated bacteria in health (across lifetime) and disease (IBS, IBD and CRC)
- The molecular mechanisms of adaptation of gut bacteria to the mucus niche
- The modulation of gut barrier function by mucus-colonising bacteria using gut organoid-on-chip systems
- The role of mucus-colonising bacteria in protecting from pathogen infection at the mucosal interface
- The mechanisms underpinning the communication between mucus-colonising bacteria and the host immune system
- The role of mucin glycosylation and mucus associated bacteria in the gut-brain axis.
- The development of novel biomarkers of disease and of glycan-based approaches targeted to the mucus-associated bacteria to restore human health.



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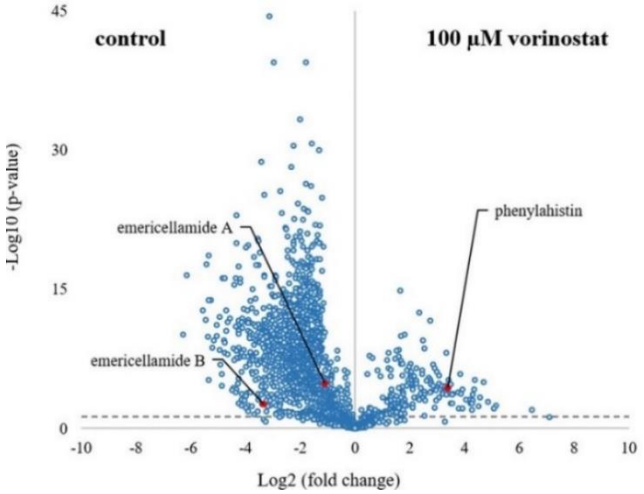
Discovering novel antibiotics to combat resistance



Due to the alarming increase in antimicrobial resistance, new antibiotics with novel mechanisms of action are desperately needed. Historically, the major source of antibiotics are soil microorganisms but in recent years the pipeline of such drugs has dried up. Does this mean that there are no new antibiotics left to be discovered? The answer is definitely not! Whole genome sequencing of microorganisms, including common ones that are intensively studied, has identified a vast number of biosynthetic gene clusters (BGCs) that encode for secondary metabolite production. However, the majority are silent, or are expressed at very low levels, under laboratory culture conditions. Our group is interested in unlocking these gene clusters, isolating novel natural products and testing them as antibiotics. An example of our research can be found in this recent publication: Epigenetic modulation of secondary metabolite profiles in *Aspergillus calidoustus* and *Aspergillus westerdijkiae* through histone deacetylase (HDAC) inhibition by vorinostat. Our projects are multidisciplinary and involve a combination of bioinformatics, genomics, microbiology, epigenetics, natural products, chemistry and biology. We use a variety of approaches to the discovery of novel metabolites ranging from the isolation of new species to optimisation of nutritional components in fermentation media to the use of human anticancer drugs in fungi and you will develop these skills as part of your research project.

Figure (right): Fermentation of an *Aspergillus* species in the presence of the histone deacetylase (HDAC) inhibitor vorinostat, clinically approved for the treatment of T-cell lymphoma, induces production of the anticancer compound phenylahistin.

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Understanding the survival strategies of foodborne *Listeria*

Listeria is a foodborne pathogen that attacks the most vulnerable, often with devastating consequences. Outbreaks of invasive listeriosis are increasing, caused by the large range of food types that can become contaminated with this resilient microbe. A recent *Listeria* outbreak was cause for national investigation after the death of multiple patients occurred when contaminated sandwiches were served in hospital.

Listeria is unusual in that it is particularly hard to eradicate from food production environments although the basis for this is not currently well understood. Our research group seeks to understand the survival strategies used by *Listeria* to persist through the rigorous application of biocides. As a zoonotic pathogen, we are also interested in the overall One Health aspect of *Listeria* and want to better understand the true level of exposure faced by humans. This will include study on the metagenomes of clinical samples such as stools which are not routinely examined for this pathogen.

While studying the adaptive processes or pathobiology of *Listeria*, students will have access to broad training opportunities in 'wet lab' microbiology approaches such as biofilm models, while also using advanced technologies such as genomics and bioinformatics.

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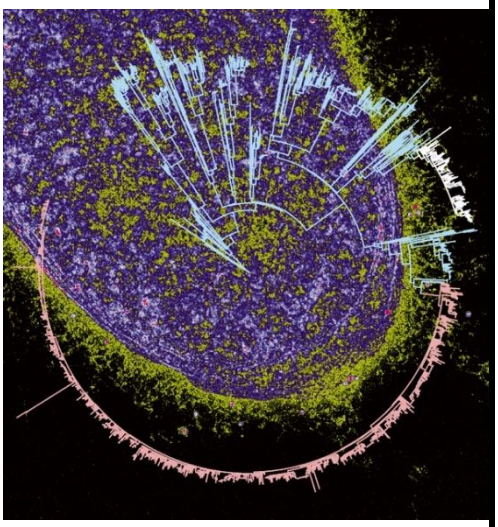
Pathogen variation



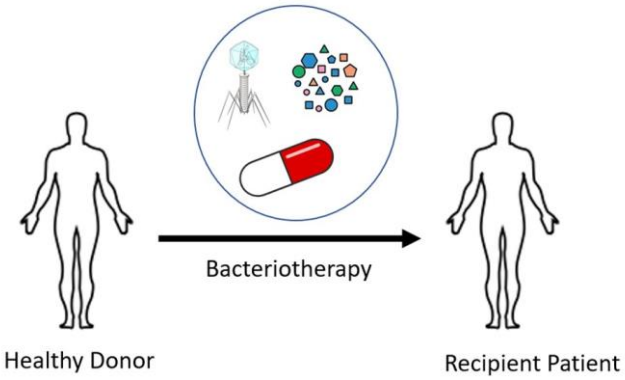
The Kingsley group combines bioinformatics, genomics, molecular microbiology and models of infection to investigate the evolution of interactions between pathogens, the environment and the host. We investigate the genomic diversity of bacterial pathogens to understand function and evolutionary history of genes important to disease, transmission, drug resistance and phage sensitivity. These data are used to infer the spread of infectious diseases and important evolutionary events pathogens. We test our inference using classical molecular genetics, microbiology and models of such as horizontal genes transfer in the emergence of new bacterial infection. Our work has shed light on how new pathogens emerge and evolve, and how epidemics spread. These studies are important because they provide the knowledge base for rational design of interventions aimed at preventing the spread of pathogens, improving surveillance and risk assessment, and guiding medical, agriculture and the food industry policy and practice.

Projects in the lab generally include training in bioinformatic analysis of bacterial and bacteriophage genomes, molecular microbiology, tissue culture and in vitro phenotyping assays. Although we are primarily engaged in fundamental research, we have strong links with industry to provide immediate impact and translate our research where appropriate.

Contact: rob.kingsley@quadram.ac.uk or view my online research profile

Manipulation of the human gut microbiome for health benefits

Our research is focussed on development of novel microbiome-based therapeutics to for modulation of the human microbiome for treatment and prevention of specific disorders. These include the application of phage endolysins, antimicrobial peptides and Faecal Microbiota Transplant (FMT) to overcome dysbiosis of patient microbiome. We are currently building MHRA licenced facility for producing materials for FMT for use in clinical trials. Specific areas of research include.



- Competitive exclusion of Clostridial gut pathogens
- New prebiotics for alteration of the gut microbiome
- Discovery of novel bacteriophages and phage endolysins for biocontrol of pathobionts in the GI tract
- Identification and characterisation of antimicrobial peptides by the gut bacteria
- Faecal Microbiota transplantation in patients with Autism, Parkinson's disease and those with recurrent CDI. Development of defined microbial consortia and microbial product.
- Understanding the mechanism of interaction between sulphate reducing bacteria and Parkinson's disease, colorectal cancers and GI inflammation.
- Development of biomarkers of Parkinson disease and colon cancers.

Contact:arjan.narbad@quadram.ac.uk or view my online research profile.

Microbiome and the gut-liver axis during chronic liver disease; from mechanisms to therapy

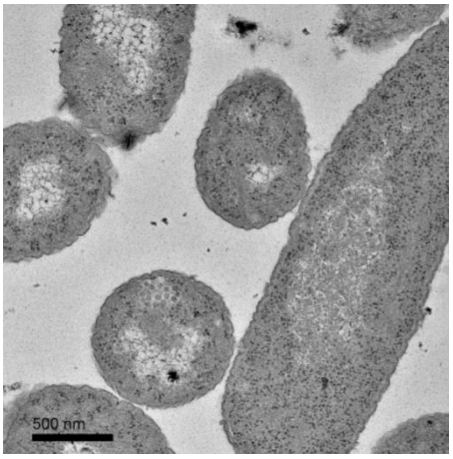
The Beraza Lab is located at the Quadram Institute and focuses on defining the mechanisms mediating host-microbiome interactions in the gut-liver axis during health and disease.

Chronic liver disease associates with changes in the microbiome composition and loss of intestine barrier function that allows the translocation of bacteria into to the liver where they aggravate disease progression. Still, the mechanisms mediating the loss of barrier integrity of the causal role of the microbiome in mediating disease progression remain largely undefined. Our research is currently focused on understanding how microbes and the host (gut-liver axis) interact during disease. Our lab is also testing different strategies to treat liver disease via the modulation of the microbiome.

The multidisciplinary research conducted in our group combines the use of basic molecular biology with high throughput analysis techniques such as next generation sequencing and metabolomics including HPLC-Mass spectrophotometry as well as other cutting-edge methodologies including bioenergetic metabolism analysis by Seahorse technology. We perform a wide variety of imaging techniques including histopathological analysis, immunohistochemistry and immunofluorescence, as well as the characterisation of the different immune cell populations by conventional and spectral flow cytometry and cell sorting. Our pre-clinical research uses established *in vivo* experimental models in combination with *in vitro* models, mainly using primary cells. As part of the translational nature of our work, we also perform analysis of human tissue samples.

Contact: naiara.beraza@quadram.ac.uk

Microbiome and Human Health



As an independent research fellow at the Quadram Institute Bioscience, I study how gut microbes influence human health through sulfur and nitrogen metabolism, particularly in the context of malnutrition—from protein deficiency to obesity. My research focuses on key anaerobic bacteria such as Bilophila wadsworthia and Desulfovibrio spp., and how their metabolic activities, including hydrogen sulfide and trimethylamine (TMA) production, impact the host. We use molecular biology, colon models, microscopy, and microbial genomics to understand these diet–microbe–host interactions. Students with an interest in microbiome science, host–microbe interactions, and microbial metabolism are welcome. Active projects available this year are:

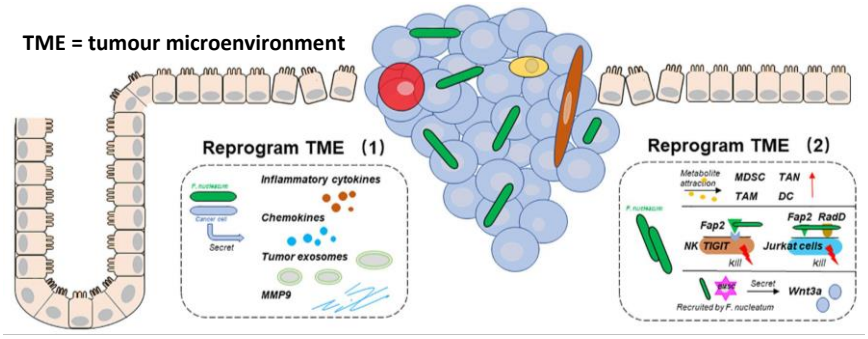
- **Uncovering the Role of Bilophila wadsworthia in Trimethylamine (TMA) Metabolism**
  This project explores how the gut bacterium Bilophila wadsworthia influences TMA production, a compound linked to cardiovascular disease, using lab-based models and molecular tools.

- **Strain Wars in the Gut: Visualising Competition and Nitrogen Fixation in Action**
  This project will model how gut bacterial strains compete for nutrients, focusing on their ability to fix nitrogen. Students will use live-cell microscopy and flow cytometry to track strain dynamics and host attachment under different nutrient conditions.

Contact: lizbeth.sayavedra@quadram.ac.uk

Unravelling host-guest metabolic pathways in colorectal cancer: a live-cell NMR investigation

The gut microbiota inhabiting the human gut has a profound impact on health and disease. While metagenomics approaches are instrumental in linking gut microbiome profiles or species to diseases, little is known about the mechanisms and potential causes of such associations.



S. Wang *et al*. *Frontiers in cell and developmental biology* 9 (2021): 710165

Fusobacterium nucleatum is an oral symbiont, found to be highly over-represented in the gut of patients with colorectal cancer (CRC). F. nucleatum is very efficient at converting cysteine into H2S, which is also found at high concentration in CRC. The mechanisms underpinning this observation are yet to be unravelled.

We use Nuclear Magnetic Resonance (NMR) to elucidate the molecular mechanisms by which F. nucleatum strains convert cysteine into H2S. The investigation will focus on metabolomics and enzymology approaches, to be performed in real-time on live bacterial cultures. NMR is a powerful, non-destructive, tool to study dynamic processes. As NMR requires minimal sample preparation, it enables monitoring of biosynthetic reactions in conditions close to physiological, providing us with a holistic and untargeted picture at the molecular level.

Contact: Serena.Monaco@quadram.ac.uk

Medical Microbiology

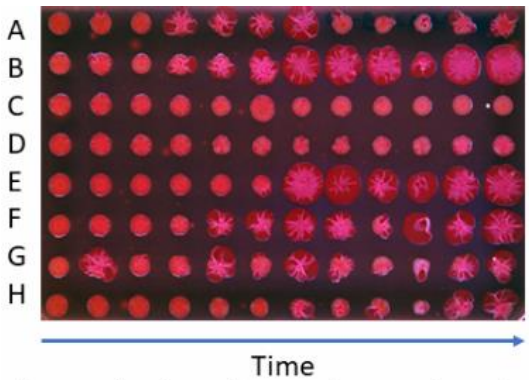


Figure showing diverse changes in colony morphology from populations (A-H) of *Salmonella* over time. Each lineage was exposed to different antimicrobial stresses showing the diversity of responses to difference conditions

Antimicrobial resistance

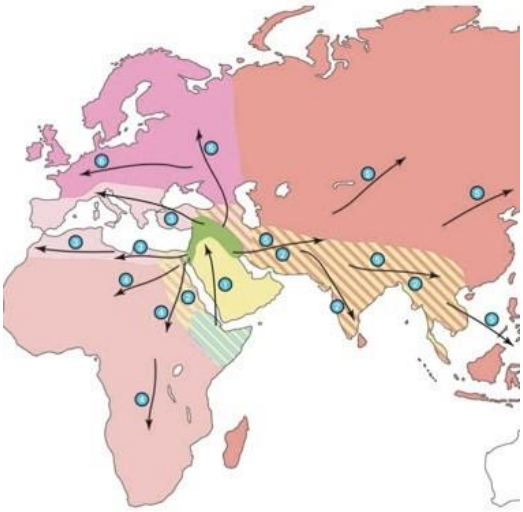
Bacterial resistance to antimicrobials is becoming a global crisis with pathogens now commonly being isolated that are resistant to the first-choice antibiotics we use to treat infections. Antibiotics are crucial to treat infections but are also needed to provide prophylaxis allowing invasive surgeries and immunocompromising therapies such as common cancer treatments. Loss of the utility of antibiotics affects almost all medicine. We investigate how bacteria are able to become resistant to antibiotics (and antiseptics and disinfectants used in infection control) and under which conditions exposure to antibiotics does and does not result in resistance emerging. We study both real world populations of isolates and mutants selected in controlled laboratory experiments to understand resistance. We aim to develop

improved strategies to use current drugs in a way that won't select resistant mutants and to help design new treatments to treat resistant bacteria.

Contact: mark.webber@quadram.ac.uk

Metagenomics

The Hildebrand group uses metagenomics to research the diversity, community interactions, and evolution of microbes in communities using custom software solutions. The group has a joint appointment between the Quadram Institute Bioscience and Earlham Institute to bridge data and life science, developing software such as LotuS2 and MG-TK and pushing the limits of high-resolution metagenomics.



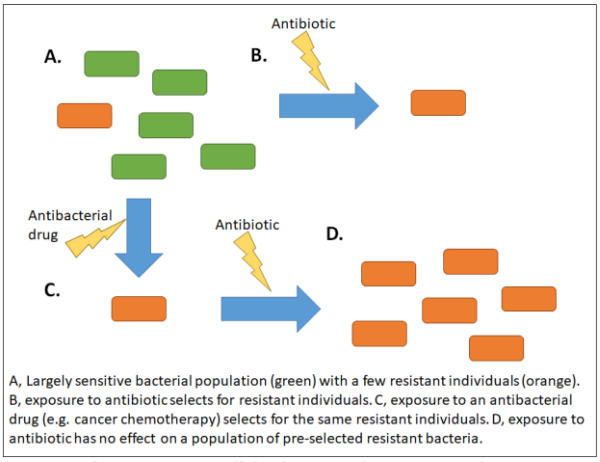
Specific research topics in the group are:

- Inheritance of a healthy gut microbiome in families, defining of "what" a healthy microbiome actually is
- Microbiome alterations in health and disease, specifically investigating microbiomes in Inflammatory bowels disease and Parkinson's Disease
- Evolvability of gut microbes and individual specific adaptations, through development of new bioinformatic algorithms and wetlab techniques

Contact: Falk.Hildebrand@quadram.ac.uk

The evolution and spread of antibiotic resistance

Bacteria can become resistant to antibiotics through a number of different mechanisms. These include intrinsic mechanism that all members of the bacterial species possess and that they switch on or 'ramp up' when exposed to antibiotics, and mechanisms that the bacteria acquire from external sources that can then be exchanged between bacteria.



A, Largely sensitive bacterial population (green) with a few resistant individuals (orange). B, exposure to antibiotic selects for resistant individuals. C, exposure to an antibacterial drug (e.g. cancer chemotherapy) selects for the same resistant individuals. D, exposure to antibiotic has no effect on a population of pre-selected resistant bacteria.

My work centres on understanding which mechanisms bacteria are using to become resistant to antibiotics, and how these are evolving and being transferred in bacterial populations. An example of current work is investigating the effect of non-antibiotic drugs, such as cancer chemotherapies, on promoting antibiotic resistance. Many drugs used in healthcare coincidently have antibacterial properties, and therefore bacteria develop resistance against these. However, in doing so, some bacteria can become more resistant to antibiotics at the same time, even without having been exposed to any antibiotics. This 'cross-resistance', where exposure to one drug (e.g. a cancer chemotherapy) causes resistance to a different drug (e.g. an antibiotic) is not well understood despite its potential to have a major impact on the evolution and spread of antibiotic resistance. By understanding how different drugs cause cross-resistance to antibiotics we will gain a more holistic view of antibiotic resistance that can be exploited in the design and development of new drugs, and in the management and use of existing drugs.

Contact: benjamin.evans@uea.ac.uk

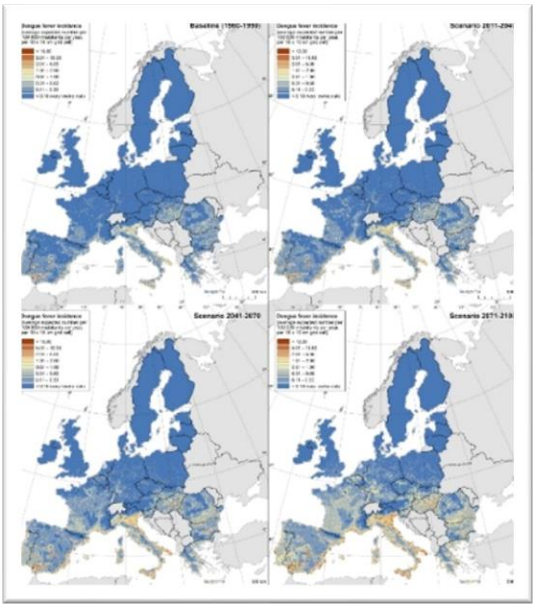
Bacteriophages for the biocontrol of pathogenic bacteria

Antimicrobial resistance is on the rise globally, resulting in treatment failures and increased mortality. In the Adriaenssens group, based in the Quadram Institute on Norwich Research Park, we investigate the use of bacteriophages, viruses of bacteria, as alternative ways to killing bacteria. We use a range of microbiology, molecular biology and bioinformatics approaches to investigate the how bacteriophages interact with their hosts and the broader microbiome. Our long-term aim is to develop bacteriophage-based therapies for the treatment of pathogens.

Projects can be lab-focused, including the discovery and characterisation of novel bacteriophages or genomics-focused, such as phage genome annotation and prophage prediction.

Contact: evelien.adriaenssens@quadram.ac.uk or view my online profile.

Emerging infectious disease



The epidemiology of emerging infectious disease especially regarding outbreaks and epidemics linked to environmental factors.

Research in the Hunter group has been focussed on the spread of infection by drinking water and insect vectors, the role of recreational water contact and food, climate conflict and other causes of rapid change. But a broader interest in zoonotic diseases, disease reservoirs and transmission pathways has developed during recent years working with SGOs like WHO and NGOs including MSF. Currently conducting case-control and other epidemiological studies in the UK, Europe and the developing world. Particular interest in risk assessment and risk communication.

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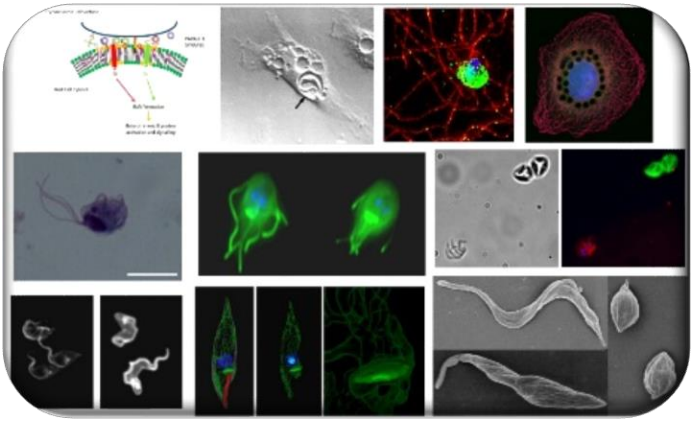
Tropical Medicine

Parasite virulence



Infectious disease remains the major cause of illness and mortality, especially of infants, worldwide but disproportionately affects those in tropical regions in the developing world. At UEA we are particularly interested in interventions to diagnose and prevent waterborne and vector borne diseases which are often most prevalent in the tropical areas, but which continue to represent a threat to the UK population. Protozoan parasites cause many of the most widespread infections; most are benign, but many are deadly.

Virulence factors determine what makes one infection deadly, while another is asymptomatic, as well as the extent and type of symptoms and pathology observed. We are interested in determining which parasite proteins are virulence factors and how we can exploit their identification for diagnosis of virulent strains, therapy and prevention. Current projects are directed towards understanding which virulence factors are associated with host range for cryptosporidiosis and trichomoniasis, with cell invasion for leishmaniasis and with enteric pathology for giardiasis. Opportunities exist for students to identify virulence factors from genomic analyses, to culture and transfect parasites and host cells and to evaluate the function of the proteins they identify and their role in pathogenesis.

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Antimicrobials

My research aims to identify synthetic and natural compounds with anti-microbial activity against neglected tropical diseases (e.g. human African trypanosomiasis or sleeping sickness) and fungal infections (e.g. candidiasis).

My work focusses on the anti-microbial activity of compounds that inhibit cysteine proteases, proteasomes or topoisomerase. We test antimicrobial activity using bloodstream forms of Trypanosoma brucei, the causative agent of human African sleeping sickness, and Candida albicans, a causative agent of superficial fungal infection of the mucosa and skin. Compounds are tested in cell culture and the effect of the compounds on parasite and fungal cells are monitored by cell counting and/or spectrophotometrically by measuring absorbance. The effect of inhibitors on the targeted enzyme is determined by activity assays using substrate specific for the enzyme.

Contact: d.steverding@uea.ac.uk

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Surgery

The surgical departments at the Norfolk and Norwich University Hospital house some of the largest subspeciality departments in the country. They have a reputation both nationally and internationally for excellent surgical outcomes as well as opportunities for research and academia. The vascular and endovascular surgical department is one of the largest in the UK and the gastrointestinal surgical department is a leader within minimally invasive surgical techniques.

Current Research Opportunities

- Upper gastrointestinal surgery – *Mr Bhaskar Kumar, NNUH*
- Vascular and Endovascular Surgery – *Mr Philip Stather, NNU*
- Breast Surgery – *Mr Mina Youssef, NNUH*

Upper gastrointestinal surgery

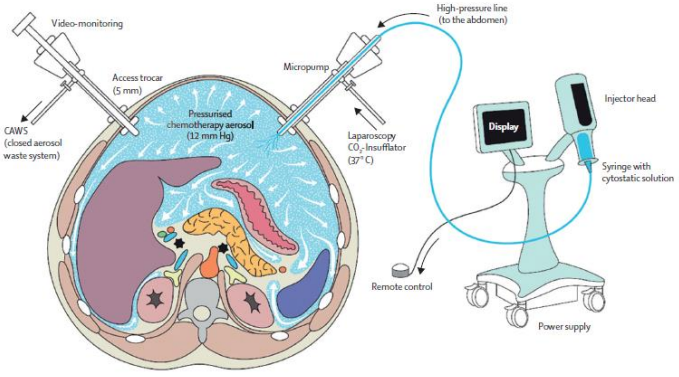
Upper gastrointestinal surgery at Norwich is a fast developing and exciting field. We currently have a growing portfolio of collaborations both national and international. We are a leading international center of excellence for minimally invasive oesophagogastric surgery. Research options are varied and include areas pertaining to cancer biology, the oesophagogastric and biliary microbiome, preoperative glycaemic control and surgical risk, Barrett's oesophagus and randomised controlled trials in biliary surgery. We have an established Academic Clinical Fellow programme and a new Academic Foundation research position in 2021. Our areas of research would suit anyone who has an interest in not only pursuing a career in surgery but also applicable to gastroenterology, microbiology, pathology, oncology and diabetes medicine.

Preoperative cardiopulmonary fitness may protect against the risk of postoperative complications after major surgery. We are currently running a multi-centred observational study across 15 UK hospitals investigating the association between preoperative cardiopulmonary fitness and the risk of postoperative mortality after oesophagectomy.

Poor preoperative glycaemic control has been shown to be independently associated with adverse postoperative outcomes. In the largest study of its kind, we are using both genetic and blood biochemistry information from the UK Biobank to investigate the association between hyperglycaemia and postoperative complications.

There is increasing evidence that the biliary microbiome may play a role in gallstone formation. Advances in sequencing and bioinformatics have made shotgun metagenomics the most detailed approach to understanding the microbiome of the biliary tract. In collaboration with the Quadram Institute of Bioscience we are using shotgun metagenomics sequencing, phylogenetic profiling and microbial genome analyses to elucidate the role of the biliary microbiome in gallstone formation and disease.

Peritoneal metastasis develops in more than 50 % of gastric cancer patients. Median survival without treatment is 3-7 months. Delivering chemotherapy directly into the peritoneum is an approach with improved tissue concentrations and reduced toxicity compared to systemic treatment. Pressurised Intraperitoneal Aerosol Chemotherapy (PIPAC) has been shown to be an effective mode for intraperitoneal drug delivery. We are generating data to justify and inform a large definitive trial to determine if PIPAC should be offered as a treatment option for patients with an otherwise dismal prognosis.



Contact: bhaskar.kumar@nnuh.nhs.uk

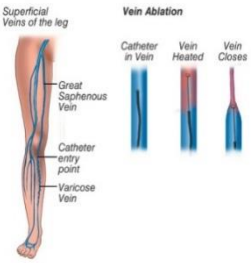
Vascular and Endovascular Surgery

The vascular surgery department undertakes a broad range of clinical research covering abdominal aortic aneurysms, carotid disease, peripheral arterial disease, varicose veins and fistulas. The department is currently setting up clinical trials into both arterial and venous disease, and has a strong background in publishing meta-analyses and systematic reviews, as well as original work. We started accepting MRes students in 2021 with both students gaining a distinction, and have a further student for 2022.

Varicose veins affect up to 50% of the population, with venous ulcers costing the NHS £2.1 billion per year. Ideal treatment includes surgery to occlude the incompetent vein but also the application of compression therapy to aid ulcer healing. The department has expertise in running trials into compression therapy and aims to determine which type of compression is the most cost effective.

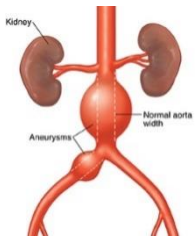
Patients with abdominal aortic aneurysms often enter surveillance programmes until they reach an appropriate size for surgical repair. Evidence suggests that as little as 20% of patients who enter surveillance actually have surgery, due to age, frailty and mortality. We are currently looking at the impact of diabetes and its control on aneurysm growth rates, and peri- and post-operative outcomes. Having built an aneurysm database of over 1,800 patients we aim to use this for further studies around complex aneurysm repair.

Peripheral arterial disease affects 5-10% of people over the age of 65. The mainstay of treatment is exercise therapy, however there is also evidence regarding the use of alternative therapies such as heat and electrical stimulation. The vascular department is evaluating multiple mechanisms of improving the collateral circulation, thus improving walking distance and decreasing the need for surgical intervention. Prof Stather has also developed an app to deliver remote exercise therapy which is undergoing further evaluation.



Prof Stather is also developing a basic science programme along with Dr Stephen Robinson and Prof Sam Fountain looking at biomarkers of peripheral arterial disease and the effect of angioplasty.

We welcome all students into the department, ensuring that you feel part of the team and become actively involved in the departmental research. By engaging early you can start to gain some understanding of what an MRes will require, and some of the skills required to do this by working on ongoing studies.

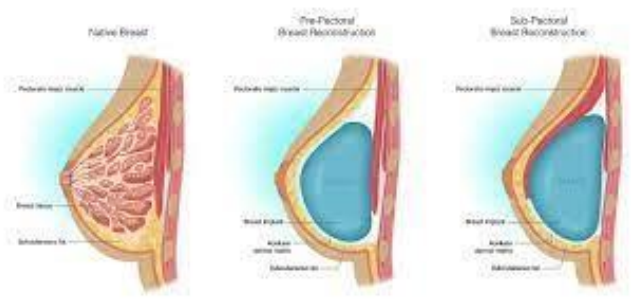


Contact: Philip.stather@nnuh.nhs.uk **or** Wissam.al-jundi@nnuh.nhs.uk

Breast Surgery

Breast surgery at Norwich is a fast developing and exciting field. Our department is collaborating nationally and internationally in many projects.

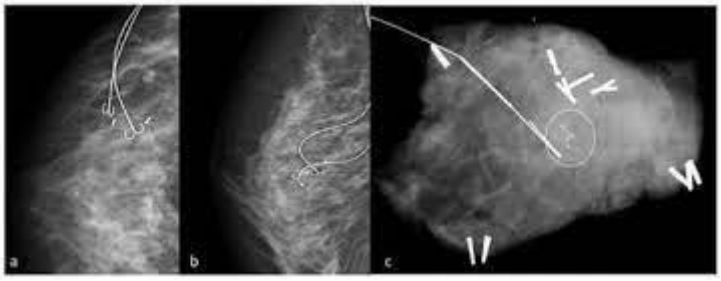
Our unit is a busy oncoplastic breast surgery unit with more than 700 cancers treated per year. We have published many results from our unit, and we continue to report our outcomes.



Our main areas of research include the impact of genomic tests (e.g. Oncotype DX) on the treatment decision making. This is an exciting field with large potential implications.

New methods of localisation for non-palpable breast cancer are constantly emerging. Evaluating and assessing these methods is a research priority as with any innovation in surgery. There is a potential research project in this area of breast surgery.

Assessing Patients Reported Outcome Measures (PROMS) is a major part of oncoplastic and reconstructive breast surgery. The impact breast reconstruction (partial or total) on the quality of life and the long-term outcomes is another developing area of research within our high volume oncoplastic unit. The increasing use of ADM (Acellular dermal matrix), implants and innovative devices constantly require evaluation.



We welcome all students into our department. There is an exciting research opportunity in this rapidly changing and innovative branch of surgery.

Please contact mina.youssef@nnuh.nhs.uk

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Nutrition

Nutrition

Our mission is to conduct world-leading nutrition research which spans from fundamental mechanistic studies to large pragmatic trials in healthy participants and 'at risk' groups. Our research will help deliver the government Ageing Grand Challenge goal of increasing healthy life expectancy by five years by 2035.

We investigate the impact of key dietary components and dietary patterns on health and risk of major age-related chronic diseases, in particular cardio-metabolic health, musculoskeletal health, cognitive health and dementia, micronutrient status and prostate cancer.

Key Research Interests include:

- Flavonoids and their metabolites, and cardio-metabolic and cognitive health
- n-3 fatty acids, metabolism and cognition
- Gut-liver-brain axis and the role of the microbiota
- Micronutrient status, health and malnutrition e.g. iron and vitamin D
- Dietary fibres and glucose metabolism
- Nutrient-gene interactions and personalised nutrition

Current Research Opportunities

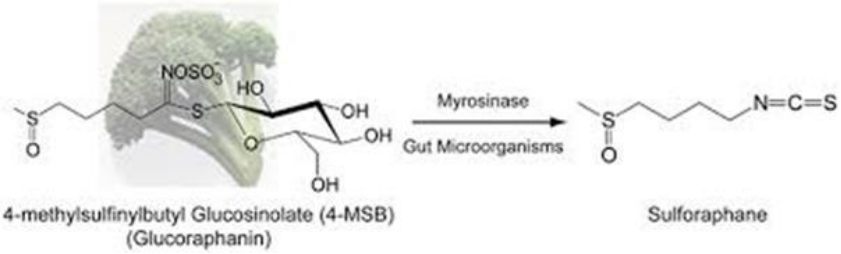
- Anti-cancer effect of isothiocyanates – *Dr Yongping Bao*
- Nutrition and Dementia – *Prof Anne Marie Minihane*
- Regulation of the RNA methylome by dietary vitamin B12 – *Dr Alper Akay*

Public Health Nutrition

- Nutritional epidemiology, nutrition in musculoskeletal aging, identifying malnutrition – *Prof Ailsa Welch*
- Dehydration in older adults – *Dr Lee Hooper*
- Public Health Paediatrics – *Dr Emma Webb*
- Nutrition and Food Systems – *Dr Maria Traka*
- Obesity and Primary Care – *Dr Helen Parretti*

Anti-cancer effect of isothiocyanates (ITCs)

The main focus of Dr Bao's team is to determine doses of Isothiocyanates (ITCs) that are optimal for health, and to investigate interactions with other nutrients in the modulation of key genes that affect cell proliferation, migration and invasion. The work will contribute to the advancement of knowledge regarding the benefits and risks of dietary bioactives.



4-methylsulfinylbutyl Glucosinolate (4-MSB) (Glucoraphanin)

Sulforaphane

ITCs derived from glucosinolates, from cruciferous vegetables, possess chemo-preventive properties. ITCs have been shown to exert antioxidant effects by the induction of the NF-E2-related factor-2 (Nrf2) transcription factor, which activates the transcription of various antioxidant genes upon binding to the antioxidant response element (ARE) in their promoters. The Nrf2-ARE pathway is typically induced in response to oxidative stress, against which it initiates a major cellular defence mechanism. This protection is very important in preventing cancer. However, the overexpression of Nrf2 in cells that are already cancerous has the potential to promote their chemo resistance.

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Nutrition and dementia

Nutrition is a significant determinant of cognitive development and decline throughout the life-course. A number of dietary components, including marine n-3 fatty acids (and in particular DHA), and select plant bioactives, have emerged as having the potential to improve cognitive performance and reduce the risk and prevalence of dementia.

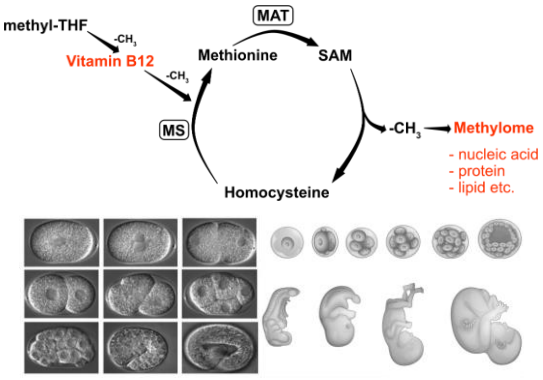
In the Nutrition group, one of our main area of research focus is investigating the independent and interactive impact of these dietary components and *APOE* genotype on cognition, brain volumes and blood flow, and circulating markers of cognitive health. An *APOE4* genotype status, which occurs in 25% of the population, is the most prevalent genetic risk factor for Alzheimer's Disease.

The majority of the work uses human randomised controlled trials (RCTs), which are complemented by cell and rodent studies and molecular biology approaches to inform the RCTs and investigate the mechanisms underlying gene*diet*health associations. It is hoped our work will contribute to the identification of strategies to promote 'healthy' brain ageing, in particular in at-risk *APOE4* individuals.

Contact: a.minihane@uea.ac.uk

Regulation of the RNA methylome by dietary vitamin B12

The RNA (epi)Genetics group's research focuses on how RNA modifications, RNA processing and non-coding RNAs regulate gene expression during development and disease. Our group combines biochemical approaches with genetics to reveal essential RNA-mediated cell processes. We use Oxford Nanopore Sequencing to study isoform-level gene expression and RNA modifications, mass-spectrometry to quantify modified RNAs, genetics for mutational analysis and microbiology to change animals' diets.



An important area of research in our group is understanding how the one-carbon pathway regulates cellular and developmental methylome. We use dietary restriction of vitamin B12 and genetic mutants to reveal how the one-carbon pathway affects RNA methylations. Microorganisms are the sole producers of vitamin B12. Animals and humans take up vitamin B12 through their diet or through bacteria in ruminants such as cattle. Vitamin B12 deficiency remains a global health issue and can lead to multiple developmental disorders and diseases.

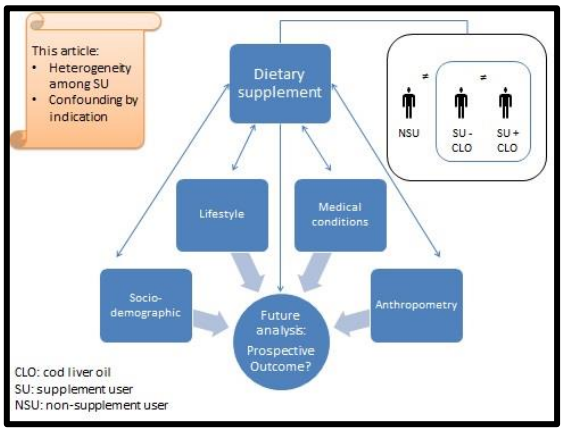
This research area offers projects on how dietary vitamin B12 restriction can affect gene regulation. These projects will allow opportunities to use genetic and biochemical methods, including mutagenesis, RNA sequencing, qRT-PCR and others.

Contact: a.akay@uea.ac.uk or view our group profile online.

Public Health Nutrition

Nutritional epidemiology

Ailsa's research focuses on nutritional epidemiology to understand the relationship between diet and ageing, with a particular focus on nutrition, muscle loss, osteoporosis and fracture risk; this research feeds into prevention for public health.



Ailsa also researches the impact of and developing nutritional public health interventions. The research will be based on using datasets with detailed information on diet and disease risk factors (for instance the EPIC-Norfolk cohort study). It could also involve evaluating local public health interventions with the Norfolk County Council, with some contact with participants.

Contact: a.welch@uea.ac.uk

Dehydration in older adults

Lee Hooper carries out innovative research on low-intake dehydration in older adults living in the community and in residential care homes.

Student research projects may include:

- data collection for and/or analysis of primary research with older adults assessing the diagnostic accuracy of signs of early dehydration,
- carrying out systematic reviews in the area of low-intake dehydration in older adults, or
- analysis of systematic review data on dietary fats and health outcomes.

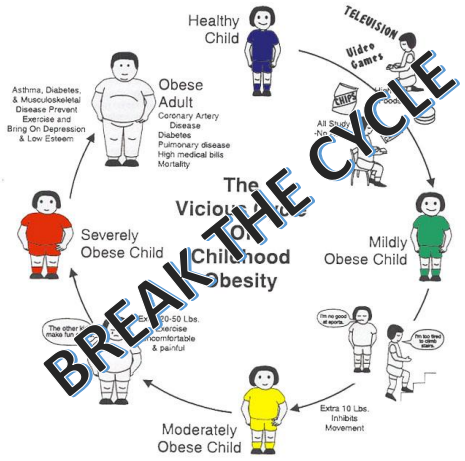
Research with Lee's team offers an introduction to low-intake dehydration in the elderly, a chance to experience research in a care home setting, and training in systematic review and/or diagnostic accuracy methodology. Students may choose to participate in an ongoing systematic review or secondary data analysis.

View the Hydrate Group website
View our recent publications

Contact: l.hooper@uea.ac.uk

Public Health Paediatrics

Malnutrition is classified by the WHO as the biggest worldwide threat to public health. Malnutrition is not only found in conjunction with low BMI but also in individuals with obesity, reducing the effectiveness of intervention programmes as well as having lifelong impacts on health and cognition. Accurate assessment of energy and micronutrient intake is therefore critical to the clinical management of patients living with obesity as well as being an important outcome measure for clinical research. Previous studies have validated 3-day food diaries and 24-hour recall for assessment of nutrition intake. Systematic reviews of these methods conclude that measuring dietary intake using these methods in children living with obesity remains problematic due to misreporting, difficulties in establishing portion size and reliance on recording dietary data via proxy reporters. Food frequency questionnaires (FFQs) capture an individuals food consumption by recording the frequency food items on a predefined food list are consumed. They are quick to complete, inexpensive and have previously been suggested to be the most reliable and valid assessment method for capturing nutritional intake in children. Currently, there is no FFQ available in the UK that is validated for assessing calorie and/or micronutrient intake in children living with obesity.



This study aims to assess the validity of an existing web-based FFQ integrated with the UK food composition database that provides robust data on micronutrient intakes while also being easy to use. The participant would gain experience in; the clinical management of children and young people living with obesity, recruitment to clinical studies, sample analysis, data processing and analysis. They would be based both at NNUH and QIB. They would have the opportunity to present their work at conferences and writing it up for publication.

Contact: EMMA.WEBB@nnuh.nhs.uk

Nutrition and Food Systems

The Traka group, located at Quadram Institute, is the leading national provider of new and continuously updated data, knowledge and tools relating to food composition, intake and food systems for use by different end-users including academia, industry, healthcare, government, consumers. Our group compiles and publishes data on the composition of foods eaten in the UK (McCance & Widdowson's 'The Composition of Foods'). We also work closely with QIB, NRP and external scientists to support the development of higher-resolution nutrition data, new dietary assessment tools, and the integration of food and microbiome data. Our current research includes investigating micronutrient deficiencies by assessing bioavailable iron and zinc in current diets, and evaluating nutritional quality and gut microbiome effects of fermented foods. Previous studies included micronutrient assessment of common plant-based products on the market and an intervention study to explore the relationship between diets rich in plant bioactives and the gut microbiome. We can offer data-driven projects around the above areas, and in areas bridging nutrition and sustainability to support food choices when transitioning to net zero.

We are also particularly interested to work with a student to assess the validity of an existing web-based food frequency questionnaire that provides robust data on micronutrient intakes while also being easy to use. This work will be in collaboration with Dr Emma Webb at the NNUH, who is leading the childhood obesity clinic. The student would

gain experience in the clinical management of children and young people living with obesity, recruitment to clinical studies, sample analysis, data processing and analysis. They would be based both at NNUH and QIB. They would have the opportunity to present their work at conferences and writing it up for publication.

Contact: maria.traka@quadram.ac.uk

Obesity and primary care

Obesity is a chronic condition affecting 25% of adults in England, which is associated with many other health conditions such as type 2 diabetes, cardiovascular disease, MASLD, cancer and depression. Alongside the cost to individuals, the estimated cost of obesity to the NHS exceeds £6 billion per annum with an economic cost to the UK in excess of £27 billion per annum. Therefore, managing obesity is one of our most significant current healthcare challenges and government strategies including the NHS Long Term Plan 2019, have highlighted obesity as a major priority.


Photo credit: ECPO Image

The causes of obesity are complex and include, for example genetic factors (40-70% BMI is determined by genetics), environmental, physiological, socioeconomic (prevalence of obesity is twice as high in people in the most deprived decile compared with the least deprived decile), and psychological factors.

To date most obesity interventions have been based on a reduction in dietary intake and promotion of healthy eating and physical activity. However, for severe or complex obesity the most clinically and cost-effective treatment is bariatric surgery, which typically leads to weight loss of 20-30%. Yet, bariatric surgery may not be clinically appropriate for some patients, others may not wish to have a surgical procedure and obesity services provision is highly variable across the UK. Until recently few medications have been available for obesity and those available only led to modest additional weight loss. The recent NICE approval of Glucagon-like Peptide-1 (GLP1) receptor agonists, such as Liraglutide and Semaglutide for the treatment of obesity has the potential to transform the management of obesity.

Dr Parretti conducts a range of research in adult obesity using methodologies such as clinical trials, routine datasets (e.g. CPRD), systematic reviews and qualitative research. She has an interest in the clinical management of adult obesity (including in patients with other health conditions), care pathways for people living with obesity (in particular, the long-term follow-up of people who have had bariatric surgery), and experiences of healthcare.

Contact: h.parretti@uea.ac.uk

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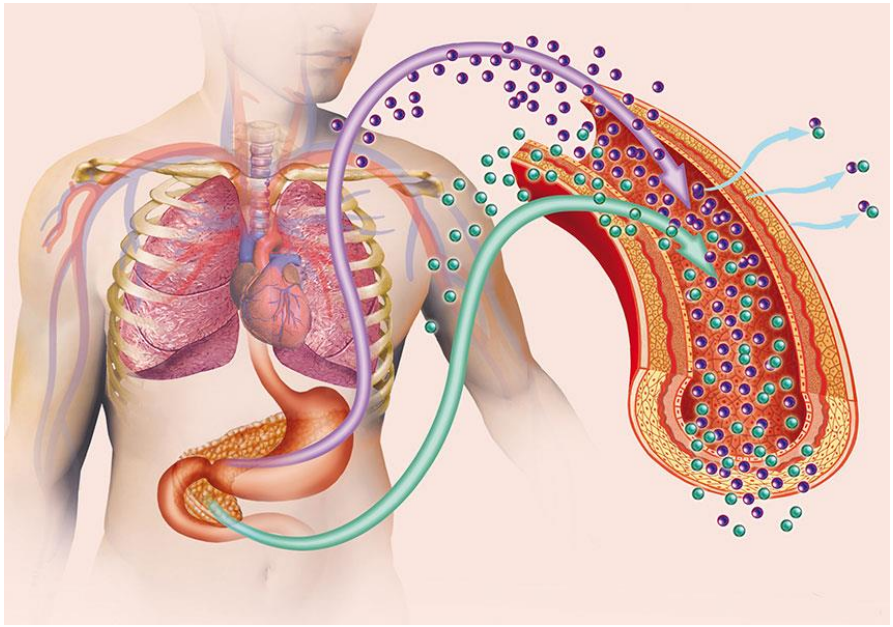
Diabetes and Endocrinology

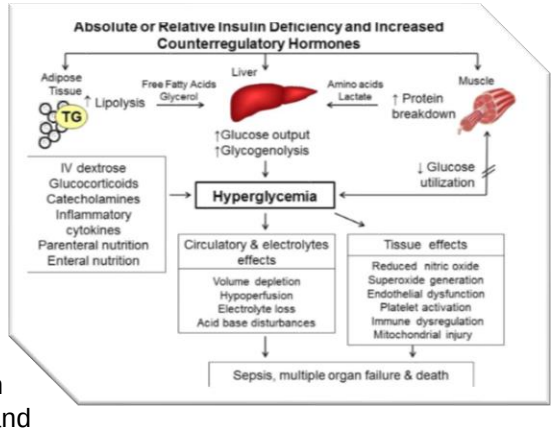


Diabetes and Endocrinology

Diabetes and endocrinology research opportunities include diabetes related foot disease and the experience, and management of, patients with diabetes within hospitals. Other researchers have developed in vitro model systems and three-dimensional models to understand the role played by inflammation in the development of a number of pathological conditions.

Diabetic foot

Dr Dhatariya leads one of the largest diabetic foot clinics in the East of England seeing over 6000 patients per year. Over the last 5 years he and his podiatry team supervised over a dozen student projects on several aspects of diabetes related foot disease. Diabetes related foot disease remains the most frequent 'diabetes specific' reason for an acute hospital admission, and £1 in every £150 spent in the NHS in the UK is spent on the 'diabetic foot'.

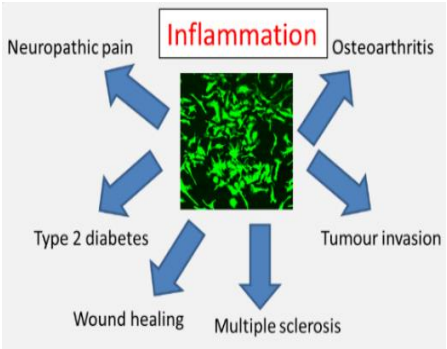


His second major interest is hospital inpatients with diabetes. Across the UK, over 20% of all inpatient beds are occupied by someone with diabetes. They are not in hospital *because* of their diabetes, they just happen to have it in addition to whatever else is wrong with them. Having diabetes as an inpatient is associated with an increased length of hospital stay, lots more complications of their underlying condition, and eventually a greater expense to the NHS. Dr Dhatariya has been an author on many of the national guidelines on the management of inpatients with diabetes, and led the recently published world's largest survey on the management of diabetic ketoacidosis. He also has a special focus on patients with diabetes undergoing surgery.

Contact: ketan.dhatariya@nnuh.nhs.uk

Inflammation and disease

We are interested in understanding the role played by inflammation in the development of a number of pathological conditions. We have developed complex in vitro model systems that allow us to mimic the in vivo environment as closely as possible. Some examples include the use of 3-dimensional systems to study the invasion of monocytes, macrophages, adipocytes, endothelial cells and tumour cells through complex 3-D collagen matrices and micro-mass cultures made from cartilage and chondrocytes. We assess inflammatory responses by exploring cell migration and the expression of metalloproteinases (MMPs, ADAMs and ADAMTS enzymes), as well as the connective tissue (CCN) family of growth factors implicated in osteoarthritis and fibrosis. We interact closely with several clinicians including Dr Jeremy Turner, Dr Martin Lee and Professor Simon Donell.



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Musculoskeletal Biology and Human Physiology

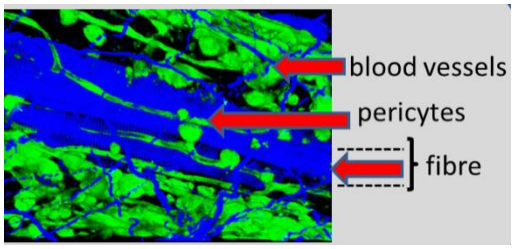
Musculoskeletal Biology and Human Physiology

In this area, there are opportunities to access the state-of-the-art technologies of the Bioanalytical Facility at BCRE, devoted to the study of disease metabolomics. Other research groups apply biochemistry and molecular biology to understand skeletal muscle regeneration, the fabrication of synthetic biomaterials to enhance surgical treatment of tendon injury plus molecular investigation of bone tumours.

Current Research Opportunities

- Stem cells for skeletal muscle repair – *Prof Ulrike Mayer* and *Prof Ernst Poschl*
- 3D modelling of joints using clinical imaging data – *Prof Tom Turmezei*
- Bone and soft tissue tumours, gene silencing, metastasis – *Dr Darrell Green*
- Autoimmunity and inflammatory bone loss disorders – *Prof Nicole Horwood*
- Musculoskeletal and nutrition research – *Dr Inez Schoenmakers*
- Ageing and Geriatric Medicine Research – *Dr Martyn Patel*
- Integrative Human Physiology – Dr Alex Carswell and Dr Josh Arnold

Stem cells for skeletal muscle repair



We are using genetically modified mice in combination with histology, fluorescence activated cell sorting (FACS), molecular biology methods and biochemical techniques as research tools to address our research question. We aim at understanding the function of these two types of stem cells by defining the differences in their specific phenotypes, expression patterns and differentiation capacities. These results will help to understand the regenerative processes in muscle in more detail during normal repair as well as in various muscle diseases.

Skeletal muscle is a terminally differentiated tissue, but has the remarkable capability of continuous and accurate repair after injury due to exercise, trauma or disease. Muscle regeneration is mainly dependent on highly specialised muscle stem cells called satellite cells. These stem cells are specified during development and are crucial for us to gain muscle mass in postnatal life. Satellite cells become dormant later in life until muscle damage occurs and regeneration is needed. More recently, blood vessel-associated stem cells, called pericytes, have been proposed to represent another source of stem cells for skeletal muscle regeneration. Our research aims to determine the signals that are required for differentiation of these stem cells into muscle cells. This knowledge will be important for developing strategies to combat muscle wasting diseases, such as during Duchenne muscular dystrophy, or muscle loss associated with ageing.

Contact: u.mayer@uea.ac.uk **or** e.poschl@uea.ac.uk

3D modelling of joints using clinical imaging data

- We use novel 3D surface modelling and image analysis techniques to analyse clinical computed tomography (CT) and magnetic resonance (MR) imaging in patients with osteoarthritis (OA). Our approach has been developed in collaboration with the University of Cambridge Department of Engineering
- These methods provide improved insight into the pathogenesis of OA as well as better assessment of disease progression and response to treatment.
- OA is a very common condition with a huge unmet need, so this work has the potential to make significant impact.
- Projects are available working with both CT and MR imaging data, including from the large prospective multicentre APPROACH (EU) and MOST (US) studies.
- Projects would involve using advanced imaging analysis software. Full training will be given, the software is user-friendly and support will always be available. However, a degree of pre-existing computer literacy would be helpful.
- The project could include training in basic programming in R and MATLAB for image data processing if this was an area of interest for the candidate.

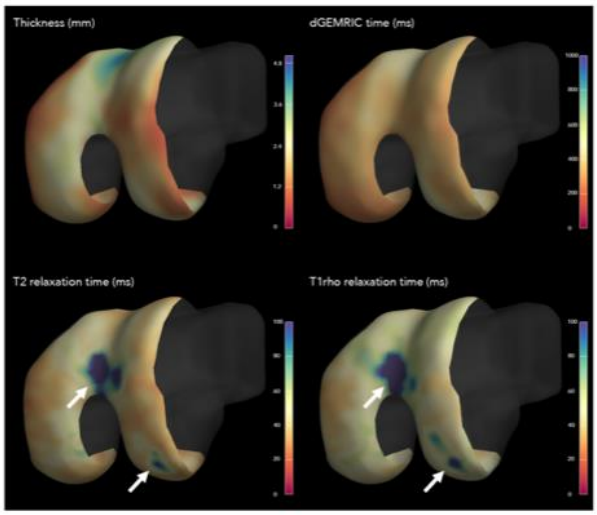
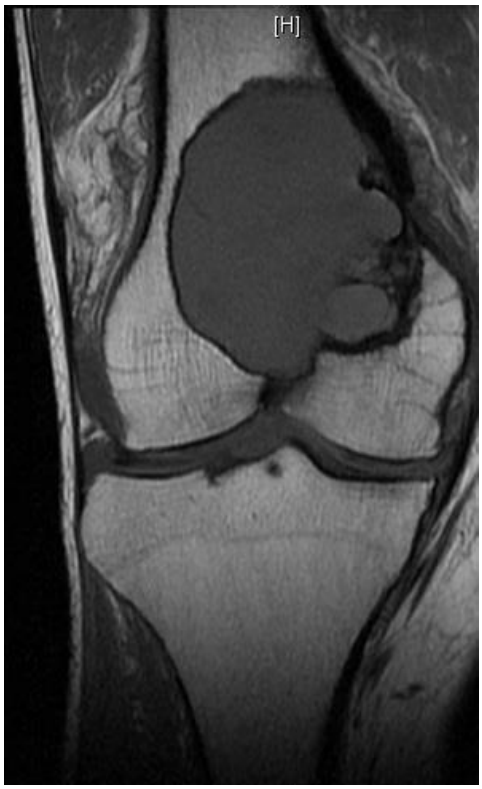


Illustration of 3D Cartilage Surface Mapping at the knee joint (distal femur). This analysis pipeline allows assessment of both cartilage morphology and composition. In this patient, areas of abnormal cartilage composition are evident at the femoral trochlea and lateral femoral condyle (arrows).

Contact: tom.turmezei@nnuh.nhs.uk

Bone and soft tissue tumours, gene silencing, metastasis



Sarcomas are cancers of the flesh and bones (e.g. muscle, fat, bone). These cancers are rare but disproportionately affect children 10-fold more than adults. According to Public Health England, sarcomas represent the 3rd most common childhood cancer. Almost half of all sarcomas are primary bone cancer affecting ~550 individuals annually in the UK and ~4,000 individuals annually in each of the USA and Europe. Five-year survival is poor at 50%. One in four patients present with detectable lung metastasis. Half of patients with apparent localised disease relapse. Treatment and survival have remained stagnant for almost 45 years.

Tumorigenesis and metastasis are independent biological events with the latter being the leading cause of cancer-related death. This multistage process requires metastatic cells to leave the primary tumour, survive in the circulation, extravasate at distant sites and restart tumourigenesis. Metastasis involves contribution from tumour cells, the tumour microenvironment and the immune system. Metastasis research is hampered by the difficulty in obtaining metastatic samples because of a lack of surgical intervention at later disease stages. Circulating tumour cells (CTCs) provide an alternative less invasive approach where samples may be accessed throughout disease course and reveal mechanisms of spread with the potential to identify novel therapeutic strategies. Our research group investigates the molecular and cellular principles of primary bone cancer metastasis. We have been at the forefront of developing and applying novel molecular techniques to study small RNAs that regulate protein-coding genes during metastasis.

Research opportunities include:

- Discovery of novel small RNAs and long non-coding RNAs in metastatic cancer
- Single cell analysis of circulating tumour cells
- Development of RNA-based therapeutics

Contact: d.green@uea.ac.uk

Autoimmunity and inflammatory bone loss disorders

Prof Nikki Horwood has recently joined UEA Medical School as a research supervisor for the MRes course. Prof Horwood is a molecular and cellular biologist who specialises in the loss or gain of bone mass during disease.

She studies the prevalence of immune cells and their soluble mediators as major regulatory factors in skeletal biology, which has become increasingly evident in the last 20 years. Osteoimmunology seeks to define the roles and interactions of immune cells with skeletal cells to understand their relative contributions to musculoskeletal diseases. She was appointed at UEA after nearly two decades at the Kennedy Institute of Rheumatology (Imperial College London and University of Oxford). Bone loss is a problem in many inflammatory diseases and there are limited therapeutic options to replace bone once it has been lost. Her research focuses on the underlying cellular causes of bone loss and identification of potential therapeutic options.

Current Research Questions:

- Determining the role of natural killer cells in the initiation of autoimmunity.

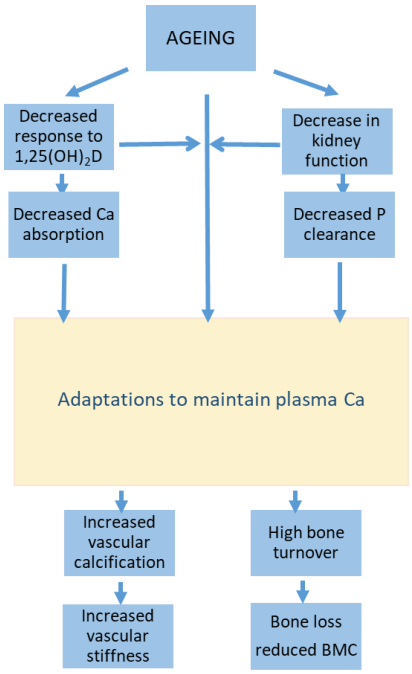
- How inflammation can cause both bone destruction and bone formation in ankylosing spondylitis?
- How the tissue repair cycle is initiated and what happens if it fails to switch off? What are the roles of different macrophage subsets in bone turnover?
- What factors control bone marrow cell fate and their correlation to disease susceptibility in the aged?
- Are there ways to reprogram bone forming osteoblasts to produce more bone?
- Altering the bone microenvironment in bone marrow cancers to reduce disease burden and preserve bone architecture.
- How to separate the anti-inflammatory properties of glucocorticoids from their adverse effects on bone destruction?
- Ways to speed fracture repair in healthy and osteoporotic bone.

These areas will be suitable to all students interested in pursuing an academic career, especially in specialities like endocrinology, rheumatology, metabolic medicine and orthopaedics. She is very happy to meet and discuss specific projects with potential MRes intercalation candidates.

Contact: n.horwood@uea.ac.uk

Musculoskeletal and nutrition research

Inez Schoenmakers's research is focussed on the investigation of calcium, phosphate and vitamin D metabolism, particularly in relation to bone health. This research aims to investigate the metabolic processes that underpin the development and maintenance of a healthy bone phenotype and how these are modulated by pregnancy, ageing, kidney function, nutrition and ethnicity.
A major part of my current research investigates the renal-bone axis in the ageing population and how this relates to the development of frailty. We investigate how this relates to micro-nutrient deficiencies.
My research offers opportunities to engage with pre-clinical research, lab-based projects, data analyses and systematic reviews and meta-analyses.



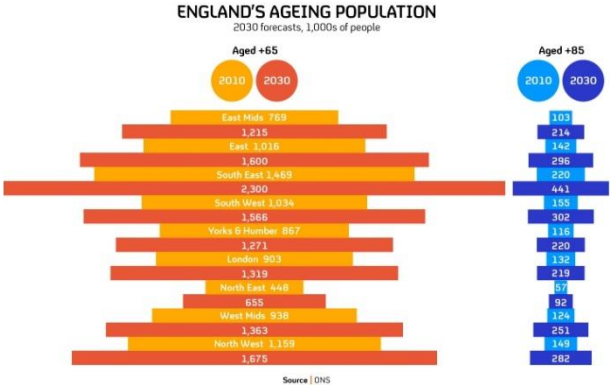
Research opportunities include:

- Does high vitamin D intake cause falls? A systematic review and meta-analyses.
- Acute illness, inflammation and coagulation: the role of vitamin D and its binding protein
- The renal-bone axis in the very old: the 85+ study
- Mediterranean diet for early CKD: what is the evidence?
- Ethnic differences in the renal-bone axis

Contact: I.Schoenmakers@uea.ac.uk

Ageing and Geriatric Medicine Research

The ageing population of the UK is often described as the single greatest challenge the NHS faces. The benefits of better medical care in childhood and midlife have led to an ongoing expansion of the elderly demographic, i.e. the percentage of the population that are living past retirement age. This expansion of the ageing population is at present time associated with a non-linear expansion of health care need for the same age group. Often there are problems with more than one long term condition (multi-morbidity) and for a percentage of older people chronic ill health can lead to frailty syndromes, and consequently an even higher need for utilisation of health and social care resources.



Designing societal reforms and health care systems that can work to improve quality of life and reduce the impact of co-morbidity in later life is one key way to address this.

The NIHR defines its top Ageing research areas of focus as:

- Healthy ageing and frailty
- Organising and delivering interventions for health promotion
- Ageing process and early markers of ill health
- Modelling links between disease and functioning
- Education and lifelong learning
- Environmental conditions for ageing well
- Effectiveness of clinical and social care.

The Older Peoples Medicine department at NNUH has a long history of supporting research in the above areas of research focus, and collaborating with UEA colleagues. We are happy to support research in any of the areas as listed above.

Martyn Patel is part of the OPM department at NNUH, and has been the CRN East of England Lead for Ageing Research since 2014. He supports research in all the above areas, and has a particular research interest in Medicines Optimisation, Dementia Care and Multimorbidity / Frailty. Dr Patel's online research profile, including publication and project details, can be viewed online.

Martyn holds one of the first of eight new Clinical Associate Professor posts, appointed to the Norwich Medical School in October 2022, and is using that time to work on projects with a focus on reducing readmissions to NHS settings for frail older adults.

Martyn is a co-applicant on the NIHR funded CHARMER study, (Comprehensive Geriatrician Led Medication Review). A five year (2020-2025), England-wide research project to develop and test a hospital deprescribing behaviour change intervention.

Martyn has successfully supervised UEA MBBS projects, MRES and PHD students as well as Academic Specialty Foundation Program doctors in the past in the areas. This has been across the areas of Dementia Care, Medicines Optimisation and Frailty Care, but all other areas are encouraged too!

Contact: martyn.patel@nnuh.nhs.uk

Integrative Human Physiology

Dr Alex Carswell and Dr Josh Arnold's research examines the influence of exercise and environmental stressors on physical function, physical performance, and human health. With an aim to better understand underlying physiological mechanisms and their translational applications, Alex and Josh have worked closely with industry and commercial partners, and a network of collaborators at other educational institutions, the NHS, Ministry of Defence, and Norwich Clinical Trials Unit to complete multidisciplinary research in healthy human volunteers.

For a summary of their research publications, please see Alex and Josh's Pure profile pages:

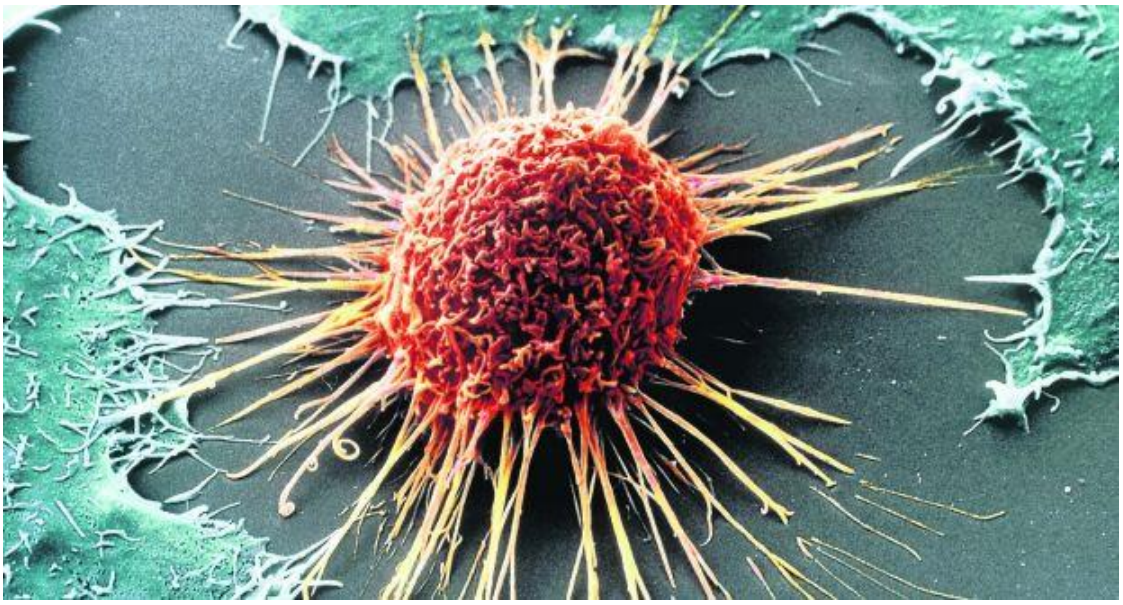
- Alex Carswell
- Josh Arnold

The research themes below are open for discussion. Alex and Josh are very happy to meet informally to discuss ideas and projects available for supervision.

- Nutritional interventions for athletes and occupational roles
- Impact of chronic arduous training on human health and function
- Responses to environmental stress (hypoxia and thermal) and their translation to clinical scenarios

Contact: physiology@uea.ac.uk

Oncology and Haematology



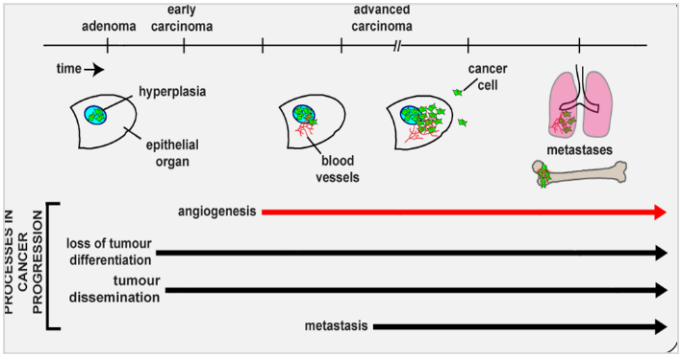
Oncology and Haematology

Current Research Opportunities

- Angiogenesis and solid cancers – *Dr Stephen Robinson*
- Prostate cancer biology, prognostic tests, and bioinformatics – *Prof Colin Cooper and Dr Dan Brewer*
- Single-cell genomics in haematopoiesis and cancer evolution – *Dr Iain Macaulay, Earlham Institute*
- Leukaemia and the bone marrow microenvironment – *Dr Stuart Rushworth and Prof Kristian Bowles*
- Oncology and radiation oncology research – *Dr Pinelopi Gkogkou, NNUH*
- Targeting RNA splicing in human diseases – *Dr Alper Akay*
- Urology – *Mr Vivekanandan Kumar, NNUH*
- Hematopoietic and vascular system development - *Dr Gi Fay (Geoffrey) Mok, BIO*
- Skin Cancer Epidemiology – *Dr Zoe Venables*

Angiogenesis and solid cancers

The recruitment of a blood supply is critical for solid cancers to grow beyond a very small size. Once this vasculature is established (by a process called angiogenesis) tumours become much more aggressive, they begin to invade nearby tissues, and they may eventually spread to distal sites throughout the body (metastasise). Thus, angiogenesis presents itself as a key target for cancer therapeutic delvelopment.



To date, the drugs that have been developed as anti-angiogenic agents are showing only limited effect in the clinic. The Robinson group works on understanding how cells of the blood vasculature respond to angiogenic signals derived from the cancer, in an effort to develop better anti-angiogenic therapies. Current goals are:

- To understand how movement of the vasculature toward a growing tumour is orchestrated; who are the essential molecular players that might serve as drug targets?
- To determine the short- and long-term impacts of current angiogenic interventions that are designed to ameliorate cancer growth and spread; are they good targets?
- To develop better anti-angiogenic strategies.

Contact: stephen.robinson@uea.ac.uk

Prostate cancer biology, prognostic tests, and bioinformatics

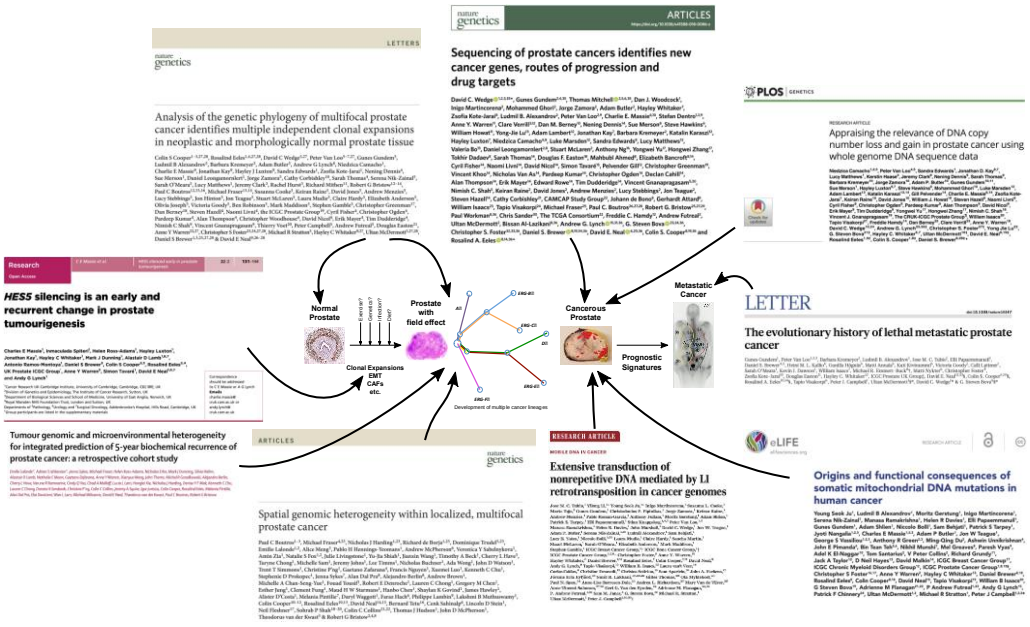
A critical problem in the management of prostate cancer is the inability to reliably distinguish aggressive from non-aggressive disease at the time of diagnosis. This leads to significant overtreatment of the disease, with many men with indolent disease undergoing unnecessary radical treatment (surgery, radiotherapy) and becoming impotent. The current

work of the Cancer Genetics team, led by Prof Cooper and Prof Brewer, is focused on identifying and implementing biomarkers to address this problem and to study the molecular evolution of prostate cancer.

We do this by generating large datasets using novel approaches in the laboratory, mainly in the 'omics space, and by applying cutting-edge data analysis techniques. Our work has strong components of both experimental work and bioinformatic analysis. We have established a diagnostic laboratory and are translating our discoveries into clinically validated tests.

Research areas for potential projects include:

- Identification and implementation of biomarkers to predict disease aggressiveness at diagnosis from urine.
- Investigating the role of bacteria in prostate cancer.
- Identifying and exploring disease subtypes in prostate cancer by analysing large expression datasets.
- To explore the impact and role of 'normal' tissue in the prostate on the development and progression of prostate cancer.



Contact: d.brewer@uea.ac.uk or colin.cooper@uea.ac.uk

See our group webpage for more information on research activities.

Single-cell genomics in haematopoiesis and cancer evolution

The Macaulay group works on the development and application of tools which enable the analysis of genomes, epigenomes and transcriptomes from individual cells. This allows us to study cellular heterogeneity in living systems, and in cancer, to investigate the evolutionary processes underlying tumour development and metastasis. Our lab is equipped with single-cell platforms (including a 10X Genomics Chromium), dedicated fluorescence activated cell sorting (FACS) and a recently acquired laser capture microdissection platform, which we will use to perform spatially resolved microbiopsies from tissue sections. Earlham Institute has excellent facilities for next generation sequencing (NGS) and computational analysis of NGS data.

Current projects in the lab include:

- Single-cell analysis of normal and ageing haematopoiesis, with a focus on megakaryocyte lineage commitment
- Lineage tracing of blood stem cells using viral barcodes and single-cell transcriptomics
- Exploration of alternative splicing and fusion transcripts in single cells using combined long-read (Pacific Biosciences) and short-read (Illumina) sequencing
- Development of single-cell multi-omic approaches to explore genomic and transcriptomic heterogeneity in cancer (CRUK funded project in collaboration with ICR London and San Raffaele Scientific Institute, Milan).

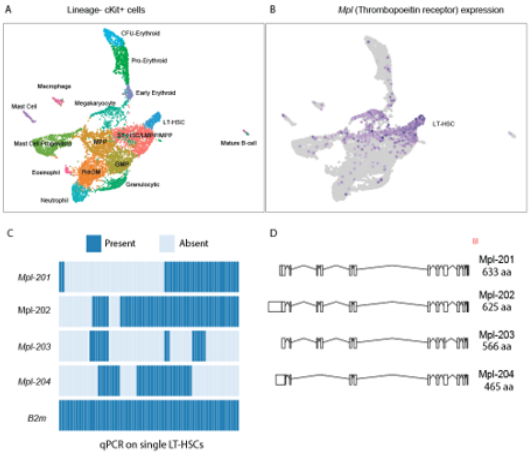


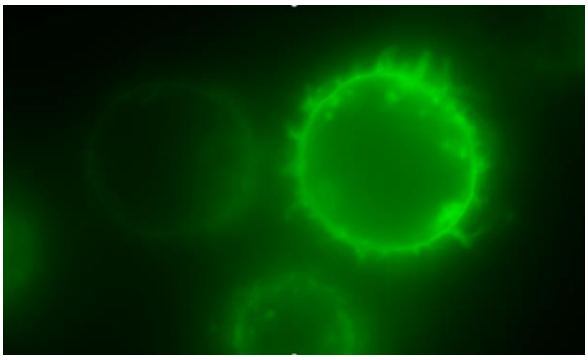
Figure 1: Analysis of alternative splicing in single blood stem cells (A) Short-read single-cell RNA-seq reveals the diversity of cell ty present in the blood stem and progenitor cell populations from mouse bone marrow and **(B)** enables detection of cell type-specific g expression – here the expression of the gene *Mpl*, which is restricted to long-term reconstituting stem cells (LT-HSC) and megakaryocy is shown. **(C)** Using qPCR assays targeting specific isoforms in single cells, we confirmed that individual blood stem cells can express m than one of the isoforms of *Mpl* **(D)**, each of which can encode a distinct protein differing in size and potential function.

We are keen to apply these tools in a wider range of clinical applications and would be happy to consider projects from any clinical area that would benefit from single-cell genomic analysis.

Contact: iain.macaulay@earlham.ac.uk or see my online research profile.

Leukaemia and the bone marrow microenvironment

We study the tumour microenvironment in both acute myeloid leukaemia (AML) and multiple myeloma (MM). With increasing understanding of tumour pathogenesis, we have recognised the vital role the BM microenvironment plays in supporting tumour growth. We have investigated how interactions between tumour cells and the bone marrow microenvironment drive metabolic changes within the tumour cell. By improving our understanding of how tumour cells manipulate their microenvironment to promote tumour growth and survival, we hope to identify new targets that could be used in the treatment of AML and MM to improve the outcome for patients.

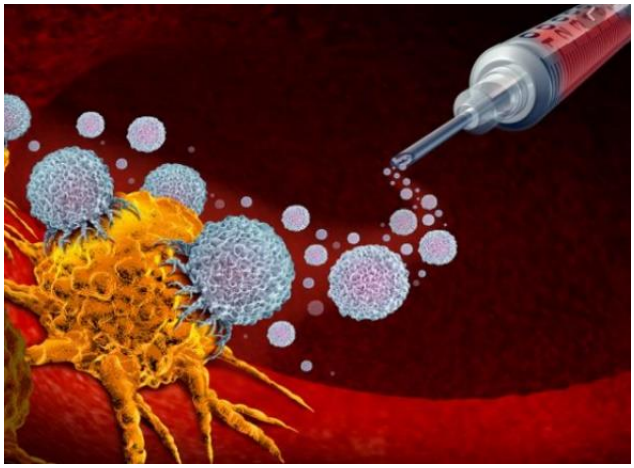


Using our knowledge of the bone marrow microenvironment in malignancy we now study the physiology of haematopoietic stem cells (HSC) in infection. We have investigated the metabolic changes in HSC in response to infection and the role of the bone marrow microenvironment in supporting these changes. We also study the role ageing and senescence in changing bone marrow function both in response to infection and in the malignant setting. An improved understanding of the bone marrow response to infection and the impact of ageing and senescence on its function will help to improve treatments for cancer and age-related diseases.

Further details are on the group's website.

Contact details: s.rushworth@uea.ac.uk **or** kristian.bowles@nnuh.nhs.uk

Oncology and Radiation Oncology Research



There is ongoing research on the different areas of oncology practice such as antineoplastic therapies, early symptom identification and management. The discovery of various targeted systemic agents and immunotherapy as well as technological advances in radiotherapy have led to improved outcomes across different tumour sites.

I shall aim to retrospectively and prospectively study the outcomes and side effects of stereotactic body radiation therapy (SBRT) for lung cancer and oligometastatic disease.

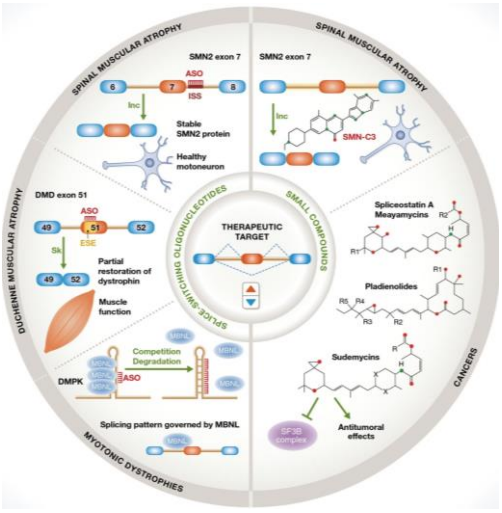
There is a need for better understanding of how these advanced oncological treatments impact patient care including late side-effects, quality of life and patient outcomes.

Contact: pinelopi.gkogkou@nnuh.nhs.uk

Targeting RNA splicing in human diseases

The RNA (epi)Genetics group's research focuses on how RNA modifications, RNA processing and non-coding RNAs regulate gene expression during development and disease. Our group combines biochemical approaches with genetics to reveal essential RNA-mediated cell processes. We use Oxford Nanopore Sequencing to study isoform-level gene expression and RNA modifications, mass-spectrometry to quantify modified RNAs, genetics for mutational analysis and microbiology to change animals' diets.

An exciting research area in our group is the sequence-specific regulation of RNA splicing by snRNA modifications. snRNAs are essential components of the spliceosome and recognise correct RNA splice sites. Human cancers and many other human diseases, such as neurological disorders, are associated with changes in the alternative splicing of genes. Targeting the RNA spliceosome or the splice site sequences are a developing area of RNA therapeutics.



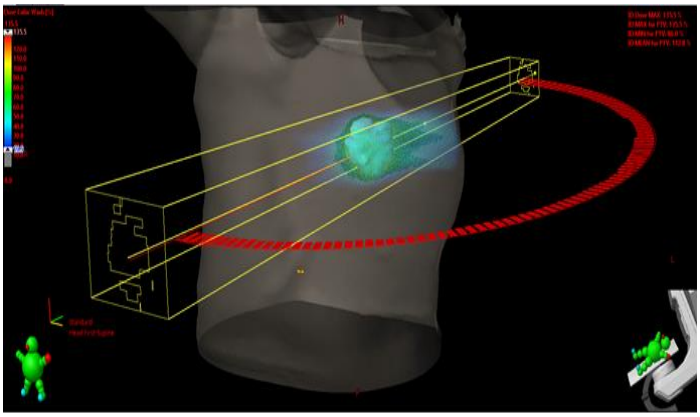
Daguenet et al. EMBO Reports, 2015

This research area offers projects to study the effects of targeting RNA splice sites and snRNAs to alter splicing patterns in human genes. These projects will allow opportunities to use genetic and biochemical methods, including RNA interference, RNA sequencing, qRT-PCR, etc.

Contact: a.akay@uea.ac.uk or view the group's online profile

Urology

Urology is a surgical speciality dealing with problems of the Genito-urinary tract. The major share of the work involves dealing with five major cancers sites namely Prostate, Bladder, Renal, Testes and Penile cancer. Norfolk and Norwich University Hospital is the main tertiary referral centre for treating penile cancer. We are also the major cancer centre in Norfolk treating bladder and prostate cancer patients. The Urology department at NNUH is involved in various multicentre and local clinical trials. Salient multicentre trials recruiting at present include BladderPath (MRI and Bladder cancer) and InPACT (Role of Neoadjuvant chemotherapy in treatment of node positive penile cancer).



Current research opportunities:

Penile cancer

- Lymph node staging in penile cancer
- Use of novel tracers in sentinel node imaging in penile cancer
- The role of Human Papilloma Virus in penile cancer

Prostate cancer

- Dietary factors and prostate cancer
- Novel diagnostic techniques in prostate cancer
- Minimally invasive surgery and Robotics in prostate cancer

Bladder Cancer

- Radiological risk stratification of patients with high risk non-muscle invasive bladder cancer
- Optimisation of patients before major surgery in muscle invasive bladder cancer.

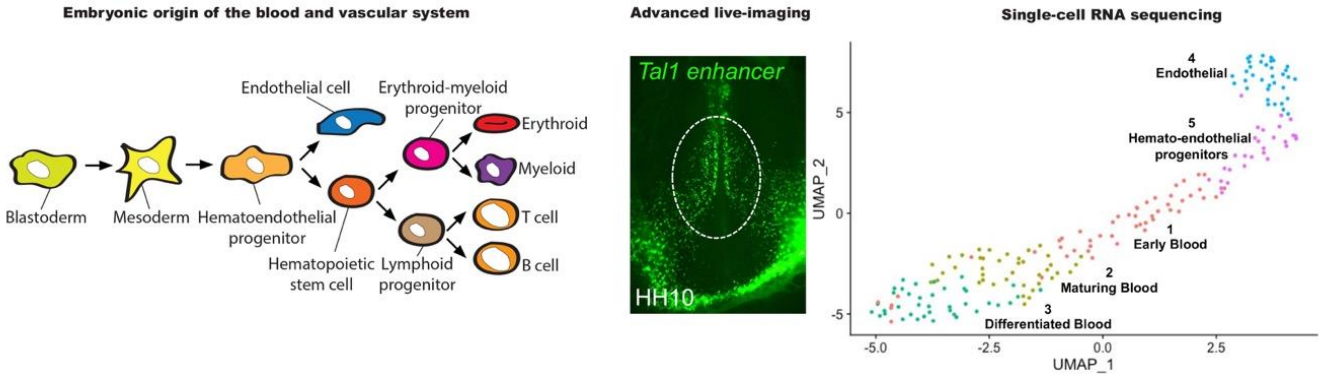
Contact details: Vivekanandan.kumar@nnuh.nhs.uk

Hematopoietic and vascular system development

Hematopoietic stem cells (HSCs) are at the initiation of the hematopoietic hierarchy and give rise to all blood lineages in the adult organism. Understanding the molecular, cellular, and developmental biology of HSCs is of fundamental importance, but also clinically relevant for the progress of cell replacement therapies and transplantation protocols in blood-related genetic diseases. The primary research interest of the lab focusses on how the early hematopoietic and vascular system (made up of blood and blood vessels) arise during embryonic development – specifically a group of cells called **hemato-endothelial cells** – using the avian (chick) embryo as a model organism which shares great similarities to human embryo development. We use a combination of experimental and computational approaches to study 1) how transcription factor networks (also known as **gene regulatory networks**) control the function of the hematopoietic and vascular system; 2) the role of the **ECM** (extra cellular matrix) in cell migration; and 3) **signalling mechanisms** in cell fate determination. We use an integrated approach of genomics (single cell RNA sequencing, ATAC sequencing) and molecular and cellular biology (live imaging) to discover new

combinatorial interactions between key hemato-endothelial cell regulators. This work is currently funded by the **British Heart Foundation** (BHF).

Contact: Dr Gi Fay (Geoffrey) Mok g.mok@uea.ac.uk



Skin Cancer Epidemiology

Our group is focused on tackling key questions in skin cancer epidemiology by leveraging national or regional databases, including data from the National Disease Registration Service which are openly available therefore often no ethical approval is required. Our research spans both common and rare skin cancers, with the goal of understanding trends in incidence, survival, and patient demographics to inform prevention and treatment strategies.

Why Choose Skin Cancer Epidemiology Research?

- **Nationally Representative Data**: Projects involve working with large, high-quality national datasets, enabling robust analyses of population-level trends in skin cancer.
- **Impactful Research**: Skin cancer, particularly cutaneous squamous cell carcinoma (cSCC), is one of the fastest-growing cancers in terms of incidence. Improving our understanding of the disease can lead to enhanced prevention and better outcomes.
- **Focus on Both Common and Rare Cancers**: Our work includes studying well-known cancers like cSCC and melanoma, as well as rarer subtypes, providing a broad research scope.

Current Research Opportunities:

- **Trends in Skin Cancer Incidence and Survival**
  - Analyse national data to identify patterns in skin cancer diagnoses and outcomes over time.
  - Investigate demographic disparities, including age, gender, ethnicity, and regional variations.
- **Understanding Rare Skin Cancers**
  - Use national databases to improve understanding of rare but aggressive skin cancers, uncovering novel insights into their risk factors and prognosis.

This research is ideal for motivated students interested in dermatology, oncology, public health, or epidemiology. It provides the opportunity to contribute to a growing field while developing skills in data analysis, critical thinking, and communication.

Contact: zoe.venables@nnuh.nhs.uk

Chronic inflammation – novel ways to target the macrophage

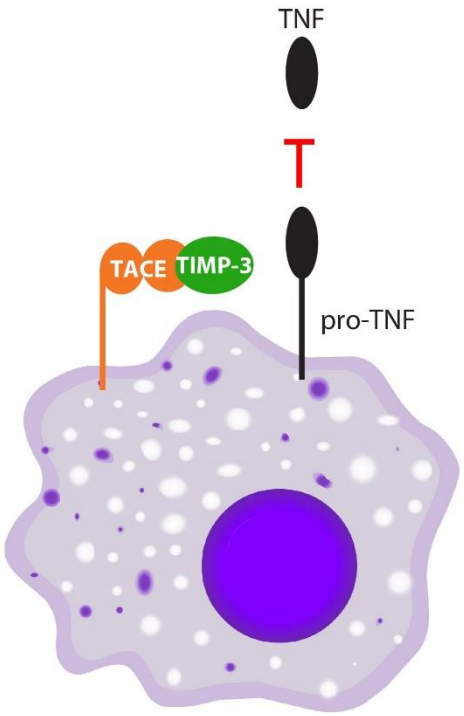
Regulated inflammation is a vital component of the body's defence mechanisms, playing a central role in eliminating pathogens and initiating tissue repair during wound healing. Macrophages are key to this process, driving both the inflammatory response and its resolution. If this resolution is impaired, inflammation can persist, contributing to chronic diseases such as diabetes, cardiovascular disease, and neurodegeneration.

We study the molecular mechanisms that regulate resolution of inflammation in macrophages, with the aim of developing new therapies to treat chronic inflammation.

Specifically, we are studying how release of the key pro-inflammatory cytokines TNF is controlled, focusing on how a key inhibitor of TNF release accumulates in activated macrophages (see PMID: 30659107). This is a laboratory-based project, giving the opportunity to learn molecular analysis techniques like primary cell culture, molecular biology (qPCR, siRNA) and protein analysis (immunoblotting, ELISA). A follow-up paper is close to completion, giving the opportunity to contribute to a scientific publication.

Contact: l.troeberg@uea.ac.uk

Activated macrophages release the pro-inflammatory cytokine TNF using the enzyme TACE (aka TNF alpha cleaving enzyme). This process can be inhibited by a protein called TIMP-3. We are studying how TIMP-3 accumulates in activated macrophages.



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Cardiovascular Research

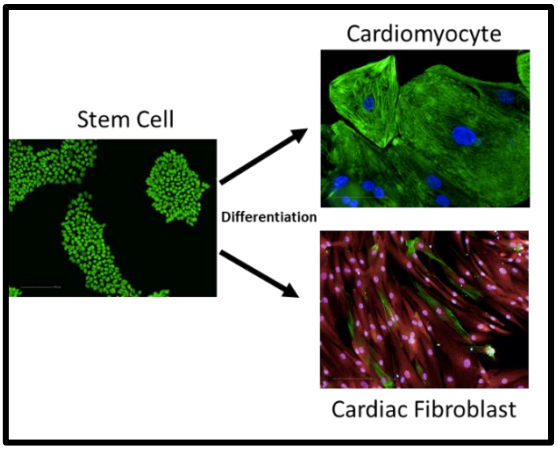
Cardiovascular Research

Cardiovascular research is a growing activity at University of East Anglia and Norfolk and Norwich University Hospital and across the Norwich Research Park. All researchers mentioned in this summary would be delighted to discuss research in this field with students and are very happy to be contacted about opportunities. Such opportunities could be for both SSS and importantly for MRes related research, SFP and ACF. The Cardiology department publishes over 50 papers annually.

Current Research Opportunities

- Stem cell models of heart disease - *Dr James Smith*
- Heart function/heart failure – *Prof Vass Vassiliou*
- Acute coronary syndromes – *Dr Alisdair Ryding*
- Interventional cardiology – *Dr Simon Eccleshall and Prof Vass Vassiliou*
- Valvular heart disease - *Prof Vass Vassiliou*
- Advanced MRI Imaging – *Dr Pankaj Garg*
- Atrial fibrillation – *Dr Gareth Matthews and Dr Pankaj Garg*
- The impact of n-3 fatty acids and APOE genotype on cardiovascular and cognitive health – *Prof Anne Marie Minihane*
- *Echocardiography – Dr Ciaran Grafton-Clarke & Dr Pankaj Garg*
- Cardiovascular Regenerative and Translational Medicine - *Dr Amer Rana*

Stem cell models of heart disease



Fibrosis is a prevalent and hard-to-treat condition. Of all deaths in the developed world, 45% are associated with chronic fibro-proliferative disease. Cardiac fibrosis disrupts the mechanical and electrical activity of the heart, which can lead to sudden cardiac death. Many heart diseases, such as hypertrophic cardiomyopathy (HCM), are associated with a fibrotic phenotype.

This group, led by Dr James Smith, uses human induced pluripotent stem cells (hiPSCs) and CRISPR-Cas9 gene editing technology, to create new human *in vitro* models of cardiac disease. Gene edited hiPSCs can be differentiated to produce force-generating cardiomyocytes, and secretory active cardiac fibroblasts. We investigate the interplay between these cell types, creating models that recapitulate the impact of cardiac fibroblasts on cardiomyocyte function. The role of disease-causing mutations (including HCM mutations) can be investigated in such models to gain better insights into these diseases and identify new potential therapeutic targets.

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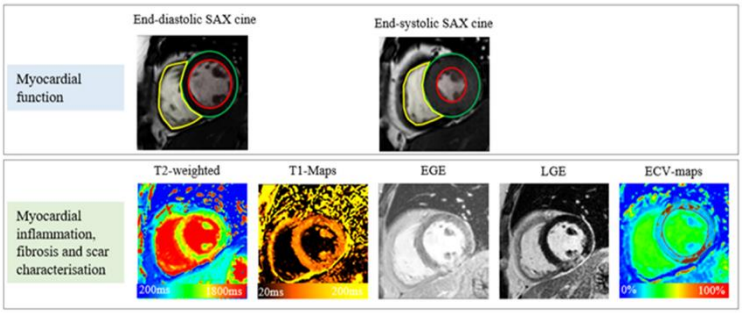
Heart function/heart failure



There is ongoing research on understanding the basic mechanisms of cardiac contractility. Energy requirements and response to exercise are key aspects of this work leading to an understanding of novel therapies to support the failing heart.

The group has developed the concept of diastolic ventricular interaction (DVI), where right ventricular overload can impact on left ventricular function, and is testing ways to improve this including pacing. Enhancing nitric oxide at a cellular level may lead to improved cardiac energetics and a randomised trial of nitrate supplements in dilated cardiomyopathy is underway to understand the mechanistic response to this therapy and safety.

The group also uses advanced imaging such as cardiac MRI parametric mapping and 4D flow to characterise the heart.

Contact: v.vassiliou@uea.ac.uk **or** p.garg@uea.ac.uk

Interventional cardiology

Norfolk and Norwich University Hospital (NNUH) is one of the busiest coronary interventional centres in the UK. Norwich has pioneered the introduction of Drug Coated Balloon (DCB) technology in which coronary stenosis are dilated with DCB without the placement of a stent. NNUH has one of the largest case series of DCB treatment and these cases are being analysed for a report that can inform future research (Dr Simon Eccleshall, Prof Vass Vassiliou). Projects in acute coronary syndromes interventional programme are being carried out by Dr Alisdair Ryding.

Recent examples of published work include:

- Drug coated balloons for coronary artery bifurcation lesions
- The role of inflammation in percutaneous coronary intervention, from balloon angioplasty to drug eluting stents
- Long-term safety of paclitaxel drug-coated balloon-only angioplasty for de novo coronary artery disease

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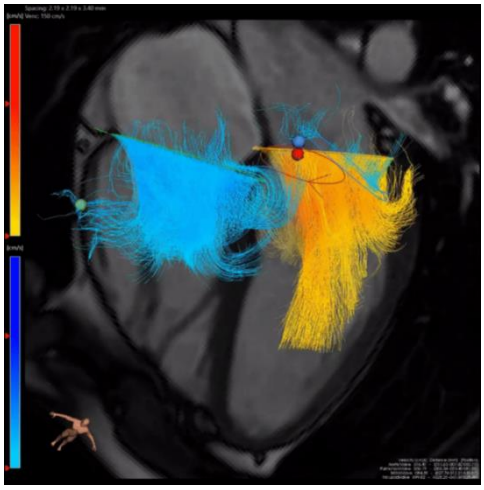
Valvular heart disease

With an ageing population, valve disease is becoming a significant burden to the NHS services. Prof Vassiliou leads this work in identifying adverse predictors in patients with valve disease and mortality. This work is undertaken in collaboration with the Royal Brompton Hospital and specifically looks at the role of cardiac MRI and the presence of scarring in associating with mortality.

Recent examples of published work include:

- Management of asymptomatic severe aortic stenosis
- Effect of sex and surgical incision on survival after isolated primary mitral valve operations
- Validation of aortic valve pressure gradient quantification using semi-automated 4D flow CMR pipeline

- A novel cardiovascular magnetic resonance risk score for predicting mortality following surgical aortic valve replacement
- Biomarkers Associated with Mortality in Aortic Stenosis



In addition, we have translated 4D flow MRI for patients with VHD. Dr Garg's group is prospectively collecting data of 1000s of patients through REC approved and funded programme. There are research opportunities for MRes students to work on several projects investigating the clinical value of 4D flow MRI in quantifying and grading several valvular heart diseases - mitral regurgitation, aortic regurgitation and aortic stenosis.

Illustration of three-dimensional flow over time (the fourth dimension) not on 4D flow MRI through all the four valves. This is the reference imaging method for intracardiac flow quantification.

Recent papers:

- Validation of time-resolved, automated peak trans-mitral velocity tracking
- Mitral regurgitation quantified by CMR 4D-flow is associated with microvascular obstruction post reperfused ST-segment elevation myocardial infarction

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Advanced MRI Imaging

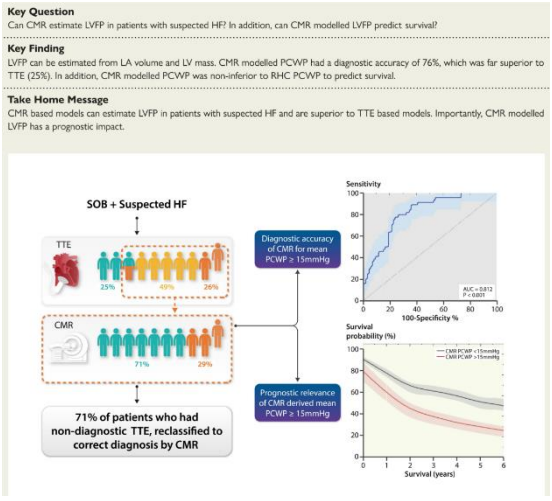
Advanced non-imaging Heart MRI for intra-cardiac pressures

Students and SFP, ACF also have the opportunity to work within the Garg lab, on projects funded by the Wellcome Trust into developing advanced intra-cardiac physiology models using cutting-edge non-invasive methods of imaging the heart by MRI and pioneering in 4D flow MRI technology.

Students and SFP/ ACF will have unique opportunities to analyse heart MRI data and learn cardiac physiology.

Recent related publication:

- Cardiac magnetic resonance identifies raised left ventricular filling pressure: prognostic implications



Contact: p.garg@uea.ac.uk

Atrial fibrillation

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. In the UK, it affects 3.29% of the population in 2016 having increased from 2.14% in 2000. The increasing prevalence reflects the aging population and the increase in cardiac risk factors such as obesity, diabetes, hypertension, and sleep apnoea. The risk factors for AF and heart failure with preserved ejection fraction (HFpEF) are shared. 50% of patients with HFpEF also have AF.

Our group is a unique collaboration between cardiac imaging and cardiac rhythm specialists. We have developed state-of-the-art cardiac magnetic resonance imaging to assess structure, tissue characterisation and haemodynamics. We also have cutting-edge invasive mapping tools for the assessment of cardiac electrical activity in patients undergoing ablation procedures to treat AF. By integrating both assessments we will develop methods for complete pathophysiological characterisation of AF and its relation to HFpEF.

Projects would be tailored to the phase of the overall work as well as the interests of the individual student. This might include clinical data collection, imaging analysis, electrical signal processing and big data handling.

Contact: gareth.matthews@uea.ac.uk or p.garg@uea.ac.uk

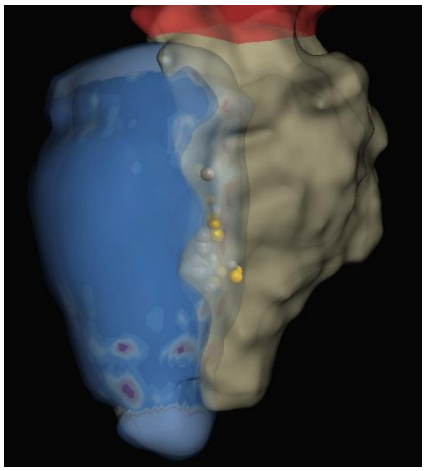


Figure 1: Combined cardiac MRI left ventricular fibrosis map (blue with fibrotic patches in red) merged with contact anatomical map of the right ventricle (grey) during a live ablation case.

Echocardiography

Echocardiography is an incredibly useful diagnostic tool within cardiovascular medicine and is used to assess heart structure and function. We have successfully compiled the largest worldwide echocardiography database, which includes technical data and mortality data from over 180,000 patients. You will have the opportunity to explore cutting-edge hypotheses which may provide crucial insight into disease processes that have value for patients with cardiovascular disease. Key research areas will comprise determining the significance of repeat examinations across pivotal diagnostic states, such as aortic stenosis and heart failure; exploring the correlation between cardiac rhythm and image quality; and pinpointing essential imaging markers for prognosis across various disease states.

You will be supported throughout and mentored directly by an Academic Clinical Fellow in Cardiology and an Associate Professor in Cardiology, both of whom boast a formidable track record in academic supervision and cardiovascular imaging publication. Beyond this, there is the potential to contribute to other imaging projects within our cardiovascular magnetic resonance imaging portfolio. This will provide interested students with exposure to advanced imaging techniques at the cutting edge of cardiovascular medical research.

Beyond this, there is the potential to contribute to other imaging projects within our cardiovascular magnetic resonance imaging portfolio. This will expose interested students to advanced imaging techniques at the cutting edge of cardiovascular medical research.

We anticipate this MSc has the potential to offer 5-10 publications and presentations at conferences, which will be an integral part of your academic growth. There will be abundant opportunities to hone your academic writing skills within a supportive, dynamic, and research-intensive group.

Contact: C.Grafton-Clarke@uea.ac.uk or P.Garg@uea.ac.uk

Cardiovascular Regenerative and Translational Medicine

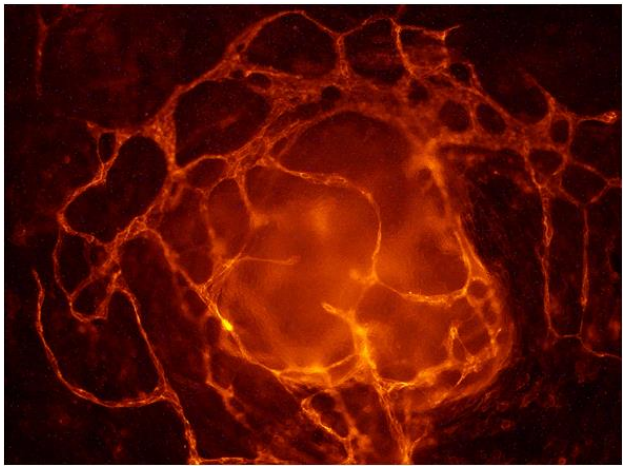


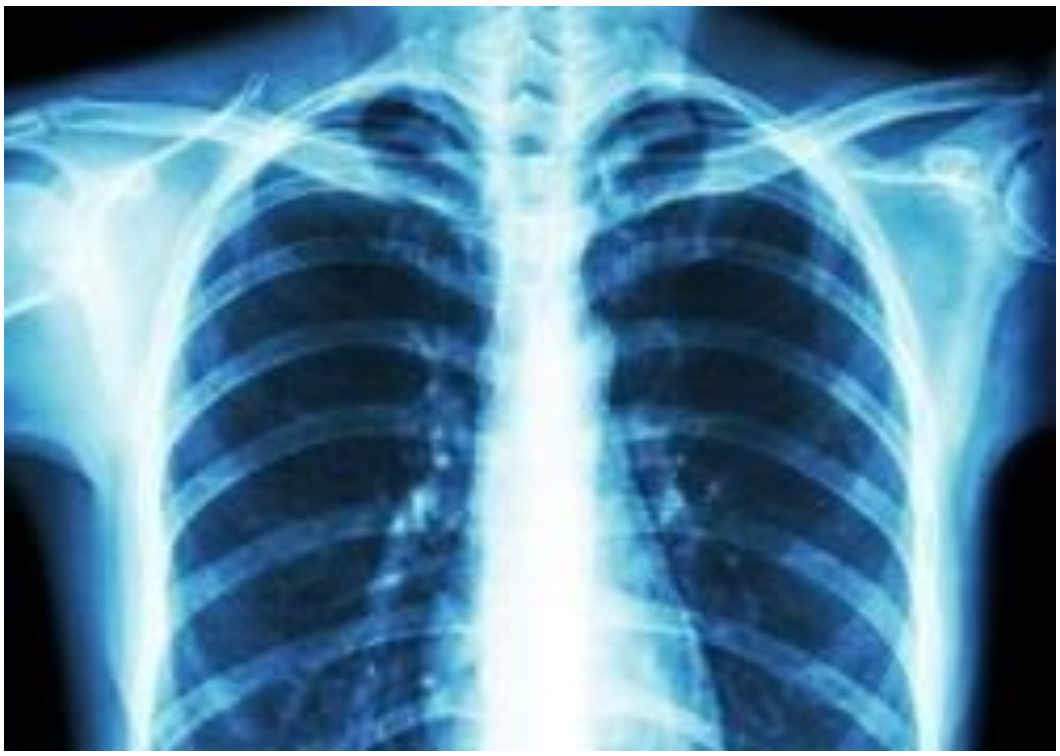
Figure 2: Blood vessel grown in the lab by a student-maybe this could be you?

Cardiovascular and cardiopulmonary diseases are the largest health burden. Development of therapeutics has been hampered by a lack relevant models to help understand disease pathology and for drug and toxicology screening. Our lab's goal over the past 12 years has been to translate developmental and stem cell biology into medical therapies. Our seminal and unique contributions include pioneering the development of patented and licensed methods to improve the generation of induced pluripotent stem cells (iPSC) for disease modelling and clinical applications. We also have world leading expertise in genetic engineering/gene editing, including the use of CRISPR-Cas9 technologies, and development of iPSC differentiation protocols to generate cells of the cardiovascular and cardiopulmonary linages for studying disease and development. and to be used for drug and toxicology screening. They are developing this further and using these cells to develop way to regenerate the cardiovascular and cardiopulmonary systems after trauma or disease, including post-myocardial infarction and curing pulmonary hypertension and coronary disease. They have a very broad gamut of possible projects available, so Dr Rana recommends any student who is interested in his lab's work to contact him and develop something unique!

Contact: Amer.Rana@uea.ac.uk

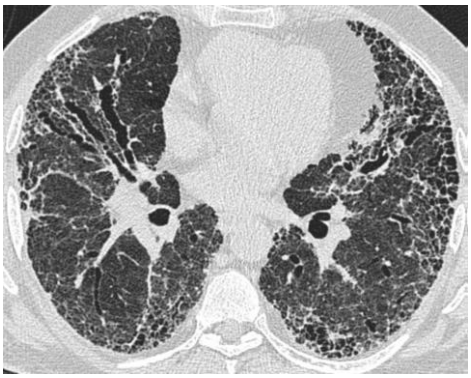
University of East Anglia | NORWICH MEDICAL SCHOOL

Respiratory Medicine



Respiratory Medicine

The Respiratory Research Group includes academic researchers covering all the main domains of Respiratory Medicine including Airways Disease, Pleural Disease, Pulmonary Vascular Disease, and Interstitial Lung Disease. They have an international reputation for designing and delivering high quality multicentred national clinical trials with current research focusing on at risk registers in asthma, anti- reflux therapy in pulmonary fibrosis and fish oil supplements in asthma.



Ongoing research projects include assessment of biomarkers and predictors of re-accumulation of pleural fluid, prognosis in pulmonary hypertension, and outcomes in sarcoidosis and pulmonary fibrosis; development of exercise interventions in asthma; and evaluation of vascular dysfunction in asthma.

Previous students have shown social deprivation to result in poorer outcomes for people with pulmonary fibrosis, explored the role of breath and blood biomarkers in interstitial lung disease, examined the symptomatology of pleural effusions, reviewed the role of interventions to improve activity in asthma and investigated the use of online health forums by patients with chronic cough.

Potential novel projects, supported by ongoing work, for students to ask about, include

- What are the patient and researcher's opinions about their involvement in clinical trials and how can these be made more efficient?
- Do people with IPF cough more on exercise than those with other cause of cough?
- What factors help people living with asthma and obesity lose weight more quickly?
- What is the influence of patient demographics on their perception respiratory related of quality of life?
- What factors influence the re-accumulation rate of pleural fluid?
- Which physiological and blood biomarker combination predicts outcomes in secondary pulmonary hypertension?
- How can we support the carers of people with chronic lung disease?
- How do different scores of breathlessness compare?

For more information contact

Prof Andrew Wilson a.m.wilson@uea.ac.uk
Dr Eleanor Mishra eleanor.mishra@nnuh.nhs.uk
Dr Charaka Hadinnapola charaka.hadinnapola@nnuh.nhs.uk

We can accommodate primary (qualitative and quantitative) research, systematic reviews, and secondary analysis of trial data in most areas of respiratory medicine so please get in touch to discuss more.

Current Research Opportunities

- Self-efficacy in respiratory disease – *Prof Andrew Wilson*
- Breathlessness and quality of life in interstitial lung disease – *Prof Andrew Wilson*
- Identifying Progressive Pulmonary Fibrosis in Inflammatory Arthritis – *Prof Andrew Wilson and Prof Alex Macgregor*
- The relationship between cough and physical activity in IPF – *Prof Andrew Wilson and Dr Allan Clark*
- Virtual Clinical Trials: mixed methods research – *Prof Andrew Wilson, Megan Jones and Leanne Tyson*
- Vascular function in asthma and obesity following weight loss – *Prof Andrew Wilson and Dr Peter Curtis*

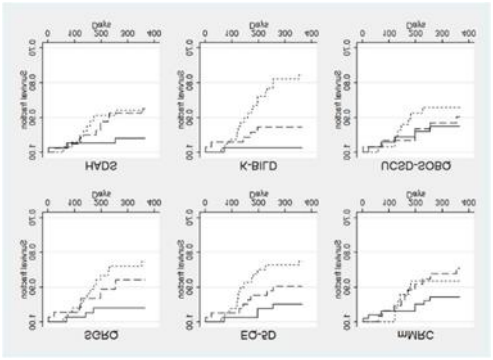
- Models for Patient Centred Care and Self-efficacy in Life Limiting Respiratory Disease – *Prof Andrew Wilson and Caroline Barry*
- Combined asthma and cardiovascular disease – Prof *Andrew Wilson, Malcolm Marquette and Leanne Tyson*
- Development of a biofilm resistant silicon indwelling pleural catheter - *Prof Eleanor Mishra and Prof Mark Webber*
- Asthma – *Dr Sadiyah Hand, Prof Jane Cross and Dr Allan Clark*

Self-efficacy in respiratory disease

Living with chronic disease results in considerable financial and emotional burden for patients. Innovative methods are required to increase the quality of patient care, improve patient choice and provide care closer to home, in an expedient and productive manner. Modern healthcare approach encourages a change in the doctor:patient relationship from paternalistic to shared decision making. Self-efficacy is the confidence patients have in their ability to successfully deal with their condition and make decisions that affect their care.We have a programme of work investigating self-efficacy in patients with chronic disease and exploring options of improving self-efficacy though patient education and patient self management plans (PSMP). We have designed a PSMP for bronchiectasis called BET (see figure) and are currently evaluating its utility. Other workstreams investigate the influence of self-efficacy on health related quality of life. Opportunities are available to evaluate self-efficacy further in different contexts in patients with different respiratory diseases.

Contact: a.m.wilson@uea.ac.uk

Breathlessness and quality of life in interstitial lung disease: secondary analysis of multiple databases.



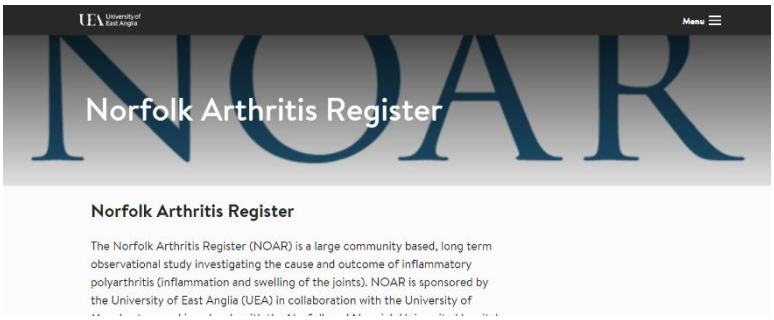
Breathlessness is the cardinal symptom of respiratory disease. Being a symptom, there is no objective measure, and it is difficult to quantify. There are numerous questionnaires which record and rate breathlessness symptoms but no measure that can capture the extent of breathlessness (Bausewein Respir Med 2007). The most commonly utilised of which is the modified Medical Research Council dyspnoea score, which scores between 1 and 5, however patients report that this is confusing to complete. The St Georges Respiratory Questionnaire (SGRQ) also captures breathlessness as one of the questions – which has 7 different responses and may be more suitable for patients.

The TIPAC study evaluated co-trimoxazole in pulmonary fibrosis using the MRC, SGRQ, Euro-Qol (which captured health related quality of life) and lung function in 198 participants (Thorax. 2013 Feb;68(2):155-62), and the Psychometric Properties of outcomes in Pulmonary Fibrosis Study (PPoPF study) in 238 participants (Chron Respir Dis. 2021 Jan-Dec;18:1479973121103392) also captured these variables. In addition, we have been recording these for clinical purposes in Norfolk and Norwich University Hospital and have ethical approval for evaluating them. Both the PPoPF and the EME-TIPAC study captured, MRC, EQ-5D, kings brief interstitial lung disease (KBILD) and the global rating of concept scale, which permits determination of the minimum important clinical difference (used to understand clinically relevant changes) using the anchor-based method.

The purpose of the study will be to create a database from clinical records and combine the three datasets and examine the relationship between MRC and SGRQ versus HRQOL. The influence of age, gender and disease severity can also be explored. The minimum important difference for MRC, K-BILD, EQ-5D can be calculated.

Contact: a.m.wilson@uea.ac.uk or allan.clark@uea.ac.uk

Identifying Progressive Pulmonary Fibrosis in Inflammatory Arthritis



Pulmonary fibrosis is a non-articular complication of people with inflammatory arthritis and is an important cause of death in these individuals. Until recently there was no specific treatment but in 2022 National Institute of Clinical Excellence (NICE) approved the use of anti-fibrotic therapy in individuals with progressive pulmonary fibrosis. Identifying and monitoring those most at risk is therefore important clinically.

The Norfolk Arthritic Register (NOAR) is a large observational study of people with inflammatory polyarthritis who were diagnosed while living in Norfolk. It started in 1989 and has recruited over 4500 individual patients. The lung function laboratory at Norfolk and Norwich University Hospital (NNUH) has recently been upgraded and it is now possible to interrogate the data. This provides an excellent opportunity to review the lung function results of people within NOAR.

The student will work within the Norfolk Epidemiology Centre to undertake record linkage, data management and analysis of people with NOAR, the NNUH lung function laboratory and radiology databases, to identify those people with arthritis related progressive pulmonary fibrosis. Baseline characteristics assessed at diagnosis including age, gender, routine blood serological clinical markers, respiratory and rheumatological symptoms will be obtained from NOAR and clinical records to generate a predictive algorithm.

Contact: a.m.wilson@uea.ac.uk or a.macgregor@uea.ac.uk

The relationship between cough and physical activity in IPF

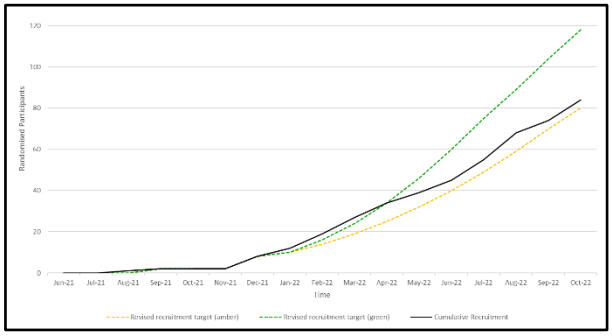
Cough is a disabling symptom for people with interstitial lung disease and occurs in three quarters of patients. It is related to disease severity and is an independent predictor of survival. It is an important problem in end-of-life care but is also present at an early stage of the disease with a third of people with IPF having at least one consultation for cough in the year before diagnosis.

Exercise is a common trigger for cough in people with airways disease such as asthma but the association with exercise and cough is not clear in people with interstitial lung disease. We have been captured cough counts using a validated cough monitor and activity using a wrist worn accelerometer in people with idiopathic pulmonary fibrosis as part of the TIPAL study.

The project will involve examining the cough and activity data to explore the relationship between the onset of activity and onset of cough. The proportion of cough episodes during activity and during rest will be reported. The relationship between cough and amount of activity (light, moderate or vigorous activity) can be reported. The project will also involve the calculation of time spent in moderate or vigorous physical activity (MVPA) and sedentary time. The relationship between MVPA and sedentary time versus lung function and quality of life can be determined.

Contact: a.m.wilson@uea.ac.uk or allan.clark@uea.ac.uk

Virtual Clinical Trials: mixed methods research



Clinical trials are the cornerstone of evidence-based medicine however are expensive, time-consuming and frequently fail to recruit to time or target. There is a considerable desire to make clinical trials more efficient to overcome these hurdles. Inefficient trial design includes platform trials, step-wedge design and remote or virtual clinical trials (VCT). Understanding the strengths, weaknesses, and patient and researcher experiences of trials methodology is important for researchers and funders, alike.

We have developed a VCT to evaluate proton pump inhibitors in 300 people with idiopathic pulmonary fibrosis (IPF), in light of the COVID pandemic. Participants have all of the trial related procedures undertaken at home. Consent is being provided electronically by email, home spirometers provide with training on-line and computer tablets are used to upload spirometry and questionnaire data to the trial server. Initial qualitative findings from research nursing staff supporting the trial highlighted the time-saving potential and lack of experience.

There is an opportunity to undertake a mixed methods study to explore the patient experiences of VTCs and expand on the findings of existing research. Participants and researchers will be mailed a questionnaire to capture their experiences and views about participating in the trial. On line semi-structed interviews and focus groups will be conducted for in depth exploration of their responses, with purposive sampling to enrol those with good and bad experiences. Triangulation of these experiences will be reported and discussed.

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Vascular function in asthma and obesity following weight loss

Asthma, cardiovascular disease, and obesity are interlinked medical conditions with considerable morbidity and cost. Both asthma and obesity are risk factors for cardiovascular diseases, which have multiple vascular pathophysiology's including arterial stiffening. This can be assessed non-invasively, via a surrogate marker known as pulse wave velocity (PWV) – which calculates the speed (i.e. transit time in *m/s*) that pulse pressure waves travel across the vasculature e.g. carotid to femoral vessels (cfPWV). Quicker speeds indicate greater arterial stiffening.
Glucagon like protein 1 receptor agonists (GLP-1 Ra), like Semaglutide, promote significant weight loss, and meta-analysis has confirmed they reduce arterial stiffening in people with type 2 diabetes. In our funded randomised placebo controlled trial, which is principally investigating the effectiveness of semaglutide in people with asthma plus obesity, we would like to concurrently evaluate whether arterial stiffness (cfPWV) decreases over 12 months. The project offers a student the opportunity to support the enrolment of 72 patients with asthma and obesity, and assess cfPWV before and after treatment with once weekly subcutaneous semaglutide (2.4mg for 36 weeks following a 16-week up-titration phase). We can explore the inter-relatedness of changes in cfPWV with 12-month changes in anthropometry and body composition, asthma control and serum adipokines, cytokines and markers of oxidative stress. We expect that this will elucidate mechanism of action of semaglutide on vascular function in asthma and obesity and help reduce cardiovascular disease in these people.

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Models for Patient Centred Care and Self-efficacy in Life Limiting Respiratory Disease

Idiopathic Pulmonary Fibrosis is a progressive, incurable condition with a prognosis similar to lung cancer; a median survival of only 4 years. Lower levels of confidence in IPF are associated with higher levels of depression and fatigue, and worse health related quality of life. Living with a terminal illness results in considerable financial and emotional burden for patients, and innovative methods are required to increase the quality of patient care, improve patient choice and provide care closer to home towards the end of life.

Models for patient centred care used for palliative care patients may be useful in IPF to help address patient expectations when there is a poor prognosis, encompassing the three pillars of care model: disease centred management, symptom centred management and education/self-management.

We have a programme of work investigating self-efficacy in patients with chronic disease and exploring options of improving self-efficacy though patient education and patient self-management plans (PSMP). Previous MRES students have published on the impact of confidence on patients' mental health and ability make decisions that affect their care.

MRES students will be supported in undertaking primary research to investigate the models of improving self-efficacy and self management in particular to managing cough, breathlessness and fatigue under joint supervision from respiratory and palliative medicine, making use of the new purpose built £12 million 'Priscilla Bacon' hospice on the Colney Lane campus. The student will be able to undertake questionnaires and semi-structured interviews with people with life-limiting pulmonary fibrosis and their relatives.

Contact: a.m.wilson@uea.ac.uk

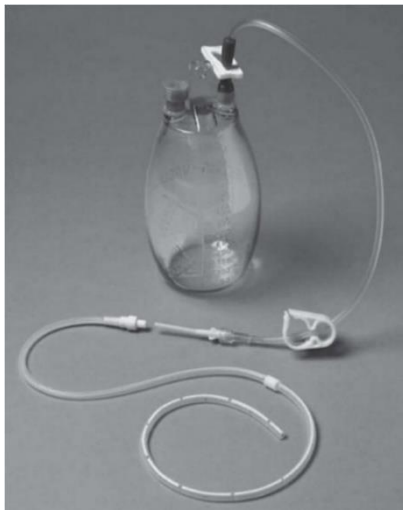
Combined asthma and cardiovascular disease; what is the experience of affected patients?

Multimorbidity is a major healthcare issue. There is growing evidence in the literature about the link between asthma and increased cardiovascular disease (CVD) risk. We recently completed a meta-analysis which provides evidence that this increased CVD risk in people with asthma is likely related to physiological and morphological changes leading to atherosclerotic disease formation. This high CVD risk has also been observed in young people and children. Asthma management can be complex and varied, especially considering the different disease processes contributing to asthma (asthma phenotypes). Therefore, understanding the impact of this co-morbid condition on the overall health and well-being of people with asthma is essential to ensure a good and holistic quality of care. The perspective of the patient with asthma is lacking in the literature.

We want to explore the personal perspectives of living with comorbid asthma and cardiovascular disease. The student will be able to undertake semi-structured surveys to examine the personal issues that patients may experience. We will ask how this impacts lifestyle choices (e.g., exercise) and, more importantly, different symptom recognition and the implication on medication adherence and concerns for asthma and CVD. The student will be involved in survey design and data analysis, and report writing.

Contact: a.m.wilson@uea.ac.uk, m.marquette@uea.ac.uk or Leanne.Tyson@uea.ac.uk

Development of a biofilm resistant silicon indwelling pleural catheter



Malignant pleural effusion (MPE) is a build-up of fluid in the space between the lungs and the chest wall due to advanced cancer, causing disabling breathlessness. Indwelling pleural catheters (IPCs) are tunnelled semi-permanent chest drains which relieve breathlessness by enabling regular drainage. IPC infections occur in about 5% of patients. One solution to reducing the infection rate is to optimise the catheter design to reduce bacterial colonisation. This proposed project aims to use novel physical approaches to add surface texture to the silicon catheter surfaces. We will manufacture silicon disks with variable surface properties including differences in charge, wettability, roughness, topography and stiffness using 3D printing and laser technology available in the Material Sciences department. We will use these disks in our established laboratory model of IPC infection which utilises pleural fluid collected from patients with MPE and bacteria which have clinically caused IPC infection and quantify biofilm formation on these silicon disks. The aim is to develop a biofilm resistant silicon surface to reduce infections.

Contact: eleanor.mishra@nnuh.nhs.uk or mark.webber@quadram.ac.uk

Asthma Research

Asthma is a common condition affecting 12% of people in the UK, and it costs the healthcare system over £1 billion every year. The Office of National statistics (ONS) data shows asthma deaths are increasing and that in the East of England, asthma deaths are higher than the national average.

Although there is new treatment called ‘biological therapy’ for severe asthma, this treatment works better for a specific type of asthma called "TH2 high asthma," where high levels of inflammation are the main cause of asthma. However, half of asthma patients have "TH2 low" asthma, which is harder to treat and doesn’t always respond to common medications like steroids.

Since 2017 we have been regularly using biological therapy on patients with severe asthma. We wanted to see if regular use of biological therapy has reduced the number of patients attending A+E regularly.

The asthma research group at NNUH has hospital numbers of patients who attended A+E between April 2018 and September 2024 and were discharged from A+E with a diagnosis of asthma. This was the period of the COVID pandemic. We have obtained approval from the confidentiality advisory group (CAG) to collate hospital data on these subjects. Using this data we hope to understand how the COVID pandemic and lock down affected asthma presentation to A+E but with particular reference to two factors that are associated with deprivation: obesity and adverse childhood experiences.

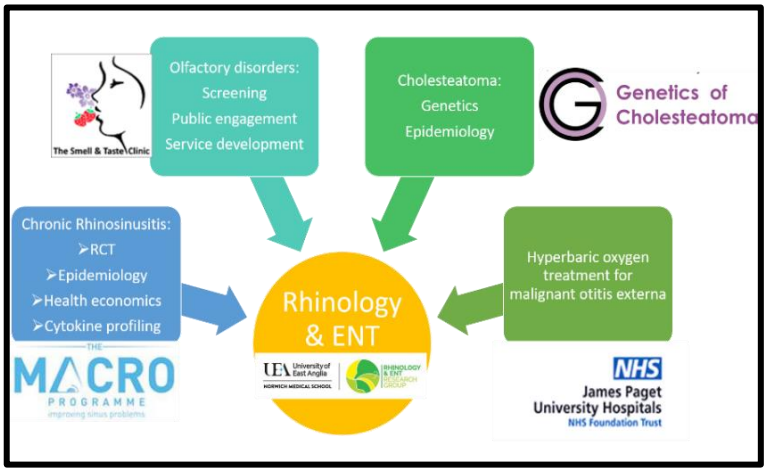
The MRES students involved in this project will investigate those subjects who have recurrent presentations to A+E with particular attention to either obesity or information related to adverse life events before the age of 18 years.

The expectation will be that the student will undertake a literature search on asthma and obesity or asthma and adverse childhood experiences and will prepare methodology for data analysis aiming for writing an abstract for an international conference and aiming to write a paper that could be accepted for publication.

Contact: SADIYAH.HAND@nnuh.nhs.uk or J.Cross@uea.ac.uk or Allan.Clark@uea.ac.uk

Rhinology and the Eye

Rhinology



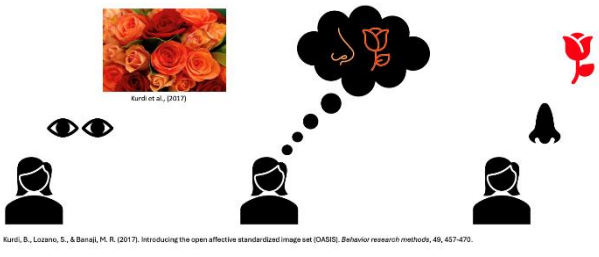
The Rhinology Research Group led by Professor Carl Philpott has a portfolio of research ranging from lab based to clinical and engagement projects. Our team includes 2 PhD students, an academic clinical fellow, 7 specialist foundation doctors, a clinical research fellow, 2 research associates and an MRes student. Currently active research includes chronic rhinosinusitis, olfactory disorders and cholesteatoma as subject areas with opportunities to develop research skills in collection and processing of tissue samples, cytokine analysis, data interpretation, genetics, health economics, qualitative analysis, recruitment to clinical trials, observational studies and public engagement and education. MRes students will be supported in undertaking primary research activities as well as presenting their findings to national and international meetings and contributing to the publication of research papers. The group receives funding from various sources including NIHR which funds the £3.8 million MACRO programme grant for chronic rhinosinusitis and a proof-of-concept study for post-viral olfactory dysfunction based in the new UEA Brain Imaging Centre. The latest project is the Digital Smell Care project.

Contact: c.philpott@uea.ac.uk

Current Research Opportunities

- Olfaction and Memory – *Tabitha James*
- The APOLLO trial – *Zhu Yeap*
- The DSC Study – *Sanjoli Mathur*
- EDI Strategy – *Sanjoli Mathur*
- Age-related macular degeneration – *Dr Linda Troeberg*

Olfaction and Memory

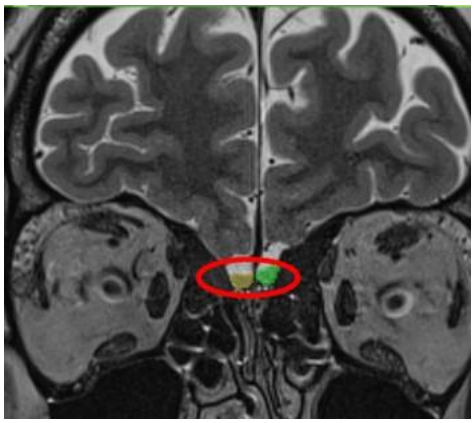


Kurdi, B., Lozano, S., & Banaji, M. R. (2017). Introducing the open affective standardized image set (OASIS). *Behavior research methods*, 49, 457-470.

Currently we are working on an fMRI study which aims to investigate the potential overlap in neural representations in olfactory regions when individuals are presented with olfactory information using three different modes of presentation (pictures, mental imagery, and olfactory perception). Given that the imagination of an odour can lead to memories associated with the odour being retrieved, mental imagery could be an avenue to target the established connections between smell and memory. This may allow for the design of novel olfactory training techniques. The current study will help us to understand how similar imagining an odour may be to perceiving an odour, and therefore how the imagination of odours could be used in a novel olfactory training approach. The study will finish testing at the end of October 2024, currently 26 participants have completed part one of the fMRI study and 17 have completed part 2. Once data collection has commenced the data will be analysed using multivariate pattern analysis (MVPA) and will be prepared for publication.

Contact: Tabitha.L.James@uea.ac.uk

The APOLLO Trial



Loss of smell affects an estimated 5% of people leading to depression, anxiety and isolation as well as changes in weight due to reduced appetite. Viral infections in the nose, including common colds and Covid-19, are the second most common cause of this smell loss. A recent limited study in Germany using vitamin A nasal drops showed that those in the treated group improved twice as much as those in the untreated group, lasting at least 10 months. It is thought that this treatment works to help repair tissues in the nose damaged by the viruses. This study will see if the size and activity of smell pathways in patients' brains increases when they are treated with vitamin A nasal drops. This would show recovery of the damage caused by common viral infections in the nose. We will invite people with smell loss due to a previous viral infection to join the study the Norfolk Smell & Taste Clinic or Fifth Sense (smell and taste disorders charity). The trial has recruited participants who have been randomly allocated to one of two groups: 38 patients received a 12-week course of nasal vitamin A drops and 19 received a placebo (inactive drops). Both sets of patients received brain scans before and after the treatment. We will look for changes in the size of the olfactory bulb (an area above the nose where the smell nerves join together and connect to the brain), that can be measured. We will also look at activity in areas of the brain linked to recognising smells. The patients were smelling odours (roses and rotten eggs) while special brain scans are taken that use a magnetic coil to create images. A smell test and a questionnaire also measured smell loss and its impact at the two visits. The study has now entered an analysis phase.

Contact: Z.Yeap@uea.ac.uk

The DSC Study

The Digital Smell Care study investigated the feasibility of a digital olfactory training device in 18 households across London and Norwich. The deployment was 6 months long where participants were encouraged to do olfactory training twice daily. The data collection for the study has now been completed and researchers are currently conducting analysis. In Sept, the team organised an event 'Smell Above All: Where the Nose Meets Technology Event' where all participants, funders, project partners, academics, and industry professionals were invited. You can read more about the event on the Smell Care website.

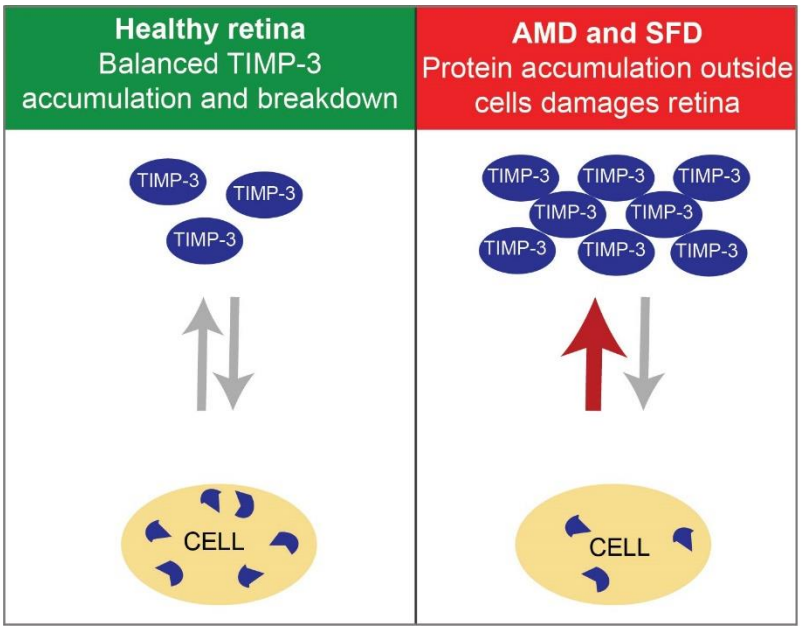
Contact: Sanjoli.Mathur@uea.ac.uk

EDI Strategy

The aim of the study was to determine the factors that need to be addressed to improve the Equality, Diversity, and Inclusion (EDI) of people with smell and taste disorders to enable them to seek and receive support without hurdles. The aim is also to use these findings to ensure that future research includes a representative population within studies. We conducted 7 focus group discussions and 2 interviews with a total of 15 participants, as well as a survey that received 89 responses. The data is now being analysed and prepared for publication.

Contact: Sanjoli.Mathur@uea.ac.uk

Age-related macular degeneration



Age-related macular degeneration (AMD) is a leading cause of sight loss worldwide. Anti-VEGF therapies are effective for many people living with the “wet” neovascular form of the disease, but there are not currently any therapies for the “dry” geographic atrophy form of the disease. To address this need, we are studying Sorsby’s fundus dystrophy (SFD), a rare genetic form of sight loss with many similarities to AMD (see PMID: 38601018). This simpler model gives us insights into the molecular events of AMD and potentially new avenues to treat geographic atrophy in both conditions.

SFD is caused by mutations in a gene called Tissue inhibitor of metalloproteinases 3 (TIMP3). We recently showed that SFD variants of TIMP-3 accumulate in the retina because they escape cellular pathways that normally clear TIMP-3 from the extracellular environment. So far, we have studied clearance by retinal pigment epithelial cells, and the next step is to study clearance by other cells of the retina. We are also interested in understanding how factors like diet and smoking affect TIMP-3 clearance. These are laboratory-based projects, giving the opportunity to learn molecular analysis techniques like cell culture, molecular biology (qPCR, siRNA) and protein analysis (immunoblotting, ELISA).

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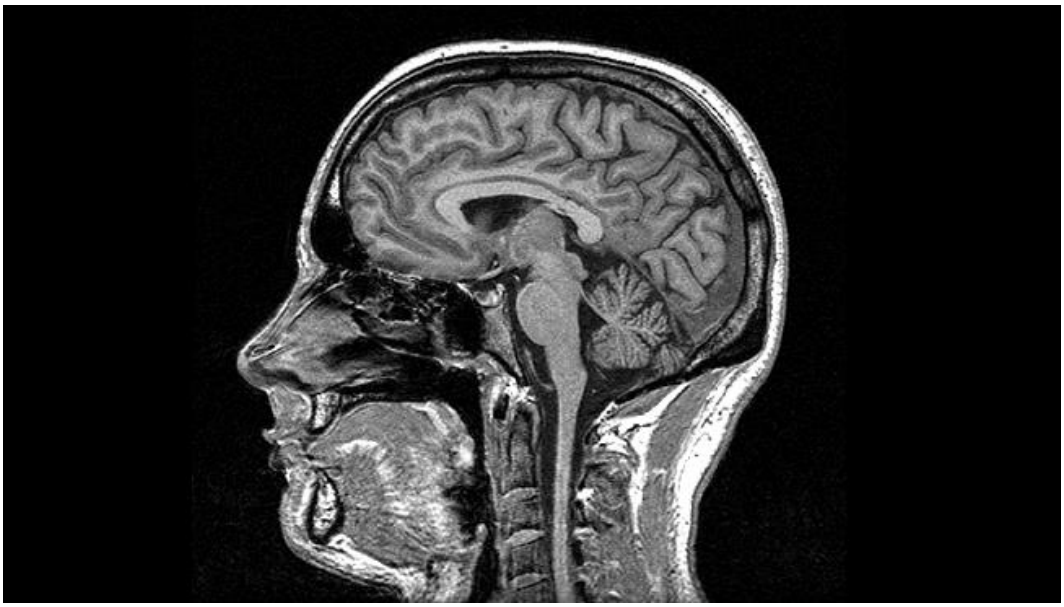
Mental Health and Dementia



Current Research Opportunities

- Anxiety Intensity Scale Circles (AISCs) and the Yale-anxiety: exploring the validity of two anxiety screens and Natural Language Processing in stroke – *Dr Joshua Blake*

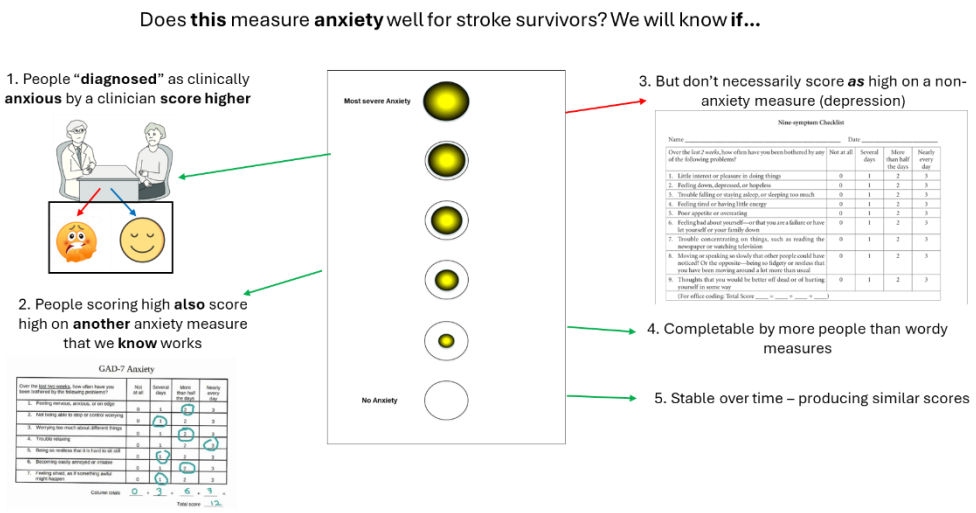
Anxiety Intensity Scale Circles (AISCs) and the Yale-anxiety: exploring the validity of two anxiety screens and Natural Language Processing in stroke

Background and aims: Screening tools are often used in stroke services to assess anxiety, but many of these tools are unsuitable for people with cognitive or communication difficulties. We therefore aim to evaluate the validity of two brief anxiety measures, designed to be accessible for such difficulties: the Anxiety Intensity Scale Circles (AISCs) and the Yale-anxiety (Yale-a). The AISCs is a one-item visual analogue scale, and the Yale-a is a simple closed-ended question. We will also investigate whether Natural Language Processing (NLP) models can identify mood disorders and predictive linguistic features.

Methods: One hundred forty-two stroke inpatients will be recruited from five sites in East Anglia. Participants more than two weeks post-stroke capable of giving informed consent will be included. Participants will complete the AISCs, Yale-a, the Depression Intensity Scale Circles (DISCs), Yale-depression (Yale-d), Patient Health Questionnaire-9 (PHQ-9), Generalised Anxiety Disorder-7 (GAD-7), an anxiety number line named the Numeric Graphical Rating Scale for anxiety (NGRS-a), the State-Trait Anxiety Inventory State subscale (STAI-S), and Western Aphasia Battery-Revised bedside version (WAB-R). Participants will then complete a structured clinical interview, acting as a reference standard. They will also complete a brief questionnaire of post-stroke emotionalism (TEARS-Q) and a novel worries identification task. The AISCs, DISCs, Yale-a, and Yale-d will be re-administered during a third contact to assess test-retest reliability. Contacts will be voice recorded to enable NLP analyses.

Analysis: Convergent validity of the AISCs will be assessed via correlations with the STAI-S and GAD-7. Divergent validity will be assessed using the PHQ-9. Classification accuracy of the AISCs and Yale-a against the reference standard will be calculated via a Receiver Operating Characteristic analysis. Test-retest reliability will be calculated using Intraclass Correlation Coefficients. Voice recordings will be transcribed. An existing NLP model will be trained using half of the recorded sample and the predictive value of NLP will be evaluated using the second half. Feature analysis will be used to identify relevant linguistic features.

Timeline for delivery: The project will take place over two years. Data collection will commence within ten months of award and last approximately eight months.



Population Health, Primary Care and Health Care Delivery

Population Health, Primary Care and Health Care Delivery

The focus of population health research is to improve health and quality of life through prevention and treatment of disease and other physical and mental health conditions. Our work combines state-of-the art research in several clinical, public health and health service fields: health economics, clinical trials, epidemiology, health geography and medical statistics, and our research addresses a wide range of clinical, health service and public health problems. We have particular strengths in research on: the organisation and delivery of primary health care; diabetes; cardiovascular risk factors; obesity; smoking; musculoskeletal disease; HIV; tuberculosis; respiratory disease; mental health; diagnostic screening; and environmental influences on health.

MRes students can get good hands-on research experience and can produce original publishable papers themselves, with expert guidance. For example, statistical analysis of pre-existing *survey data* already held by academic staff, but yet not fully exploited, can answer interesting research questions in new ways. Students can collect their own data using questionnaire surveys or by going through medical records. *In depth-interviews* with individual patients, health professionals or groups of people can provide deeper insights into issues and problems that are not captured by numerical evidence. It is quite feasible for students to collect and analyse these qualitative data themselves. *Systematic reviews and meta-analyses* (statistical summaries) of previously published research are also feasible for students to do by themselves, often producing high impact publications. With any of these methods, the process of identifying problems, asking questions, defining hypotheses and analysing data provides transferable skills which can be used in many different areas of medical research.

Current Research Opportunities

- Effectiveness, cost effectiveness and epidemiology of health care – *Prof Max Bachmann*
- Measuring population health – *Prof Nick Steel*
- Musculoskeletal epidemiology – *Prof Alex MacGregor (academic rheumatologist), Dr Max Yates (academic rheumatologist), Dr Jack Dainty (statistician) and Prof Elena Kulinskaya (actuary/statistician in Computer Science)*
- Economic evaluation/cost effectiveness – *Prof Garry Barton* Public health and clinical intervention – *Prof Fujian Song*
- Addiction Research – *Prof Caitlin Notley*
- Antimuscarinic use for overactive bladder – *Dr Kathryn Richardson*

Palliative Care Research

- Pharmacogenomics in Palliative and Supportive Care – *Dr Caroline Barry or Dr Martyn Patel*
- Understanding the Complexity of Living with, and Managing Secretions in Motor Neurone Disease – *Dr Caroline Barry*
- Inequalities in palliative care in coastal communities – *Dr Abigail Hensley*

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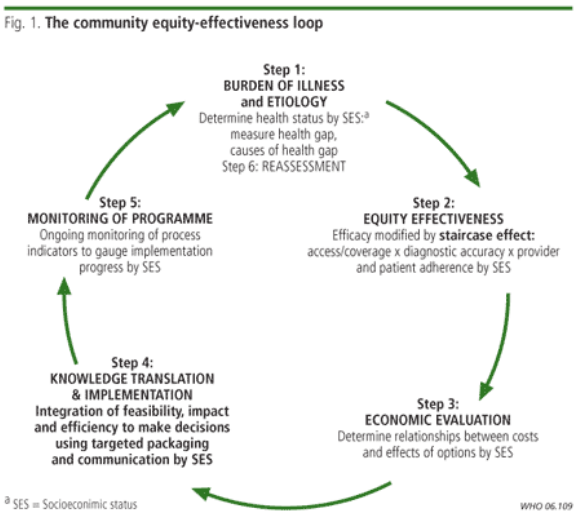
Effectiveness, cost effectiveness and epidemiology of health care

Max Bachmann is Professor of health services research. He is a public health physician interested in quantitative evaluation of the effectiveness and cost-effectiveness of health care, especially of primary care interventions intended to improve the health of populations. Disease areas of interest include HIV, tuberculosis, diabetes, and chronic illness in general. He works with South African colleagues on a research programme to improve primary care through training and clinical guidelines, based on a series of randomised trials and related research. For medical student research he is able to supervise systematic reviews and synthesis of evidence about the effectiveness of health care, and the epidemiology of these conditions. We may be able to extend this to statistical analysis of epidemiological data.



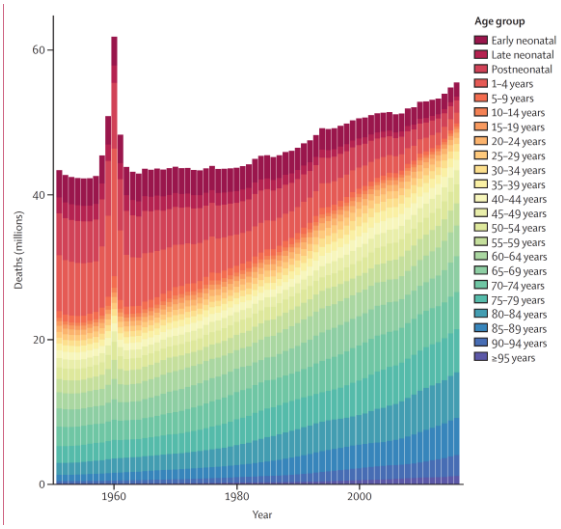
Contact: m.bachmann@uea.ac.uk

Measuring population health

Professor Nick Steel leads the Health Services and Primary Care Research Group within the Public Health and Health Services Research Theme at Norwich Medical School. His research interests focus on measuring health at population level with a view to improving the health and quality of life of people in need. He is currently working on two major projects that offer excellent opportunities for quantitative analysis of existing data for MSc and PhD students: the English Longitudinal Study of Ageing (and the Global Burden of Disease Study in England.

Nick has also been involved with a local evaluation of primary health care for vulnerable people, including the homeless and migrants, and there may be opportunities for further research in this area.

Contact: n.steel@uea.ac.uk



Global total number of deaths,1950-2017 (www.healthdata.org/gbd)

Musculoskeletal epidemiology

In 2013, the Centre for Epidemiology (CfE) Versus Arthritis was jointly awarded to Manchester University and UEA, recognising the strengths and potential for musculoskeletal epidemiology research across the two institutions. This has placed UEA and Manchester at the centre of a UK collaborative network in musculoskeletal epidemiology that includes the universities of Oxford, Southampton, Keele, Nottingham, Aberdeen and Bristol. The UK Research in Musculoskeletal Epidemiology (UK-RiME) partnership facilitates collaboration and partnership between these institutions.

Here at UEA, within the centre for epidemiology, we are a dynamic group with links to other national and international centres. We include academic rheumatologists, statisticians, MRI physicists and computer scientists. In addition, we collaborate with “wet-bench” scientists here at UEA. Our work includes descriptive and aetiological work on the two large and long-running cohort studies based in Norfolk: The Norfolk Arthritis Register (NOAR) and The European Prospective Study into Cancer and Nutrition (EPIC-Norfolk). NOAR was set-up in 1989 and represents one of the longest and best-characterised inception cohorts of patients with inflammatory arthritis in the world. EPIC-Norfolk recruited participants between 1993 to 1997 and has an unrivalled rich phenotype allowing interrogation of purported aetiological factors for disease onset and progression.

In addition, we have experience of working with other large datasets such as the CPRD, EPIC, ECLIPSE, UK Biobank, UK Twins Registry and National Joint Registry. Another big advantage is that the Centre has recently obtained an institutional site licence for access to CPRD. We are always delighted to have those interested in risk factor assessment, be that medical students to junior doctors, work with us on small well contained projects which enhance studies of morbidity and disease progression within these data sources. Other opportunities include pilot studies from translation work up to, and including, clinical interventional trials.

The range of projects carried out addresses research questions across the life course of musculoskeletal disease, and, as such, would be suitable for all students interested in pursuing an academic career. Specialities particularly aligned include: rheumatology, orthopaedics, public health, general practice and radiology. We are very happy to meet and informally discuss research ideas with potential interested parties.

Contacts:

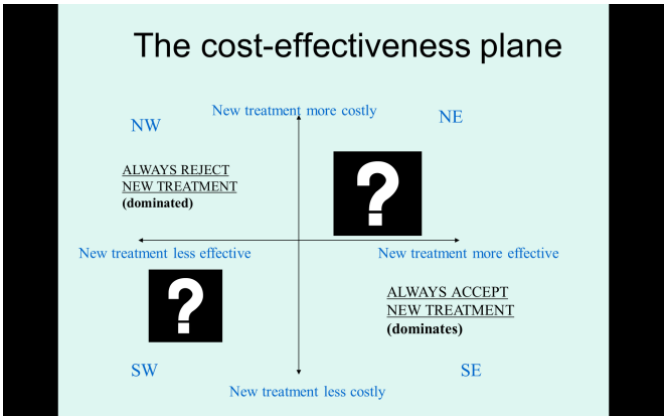
Prof Alex MacGregor (academic rheumatologist): A.Macgregor@uea.ac.uk

Dr Max Yates (academic rheumatologist): m.yates@uea.ac.uk

Dr Jack Dainty (statistician): jack.dainty@uea.ac.uk

Prof Elena Kulinskaya (actuary/statistician in Computer Science)**:** e.kulinskaya@uea.ac.uk

Economic evaluation/cost effectiveness



Professor Garry Barton's main area of expertise is in the application and development of the methods of economic evaluation. As a health economist, Garry is a co-applicant on a number of pragmatic randomised controlled trials in a variety of clinical areas. His role is generally to assess the costs and benefits associated with different interventions, in order to make judgments about cost-effectiveness. Methodological work which Professor Barton has undertaken includes the comparison of two measures of utility (the EQ-5D and SF-6D) which can be used to measure the benefits of interventions, where the practicality, construct validity and responsiveness of these two measures were assessed.

Contact: g.barton@uea.ac.uk

Public health and clinical intervention

Fujian Song has experience in systematic reviews and simulation modelling for evaluating healthcare interventions, conducted methodological research concerning evidence synthesis, including heterogeneity in meta-analysis, publication and related biases, assessment of non-randomised studies, indirect and mixed treatment comparison for evaluating competing healthcare interventions, and methods for synthesizing evidence for the evaluation of complex healthcare interventions.

Current research projects potentially suitable to MBBS students:

- Systematic review/meta-analysis of selected public health or clinical interventions and epidemiological studies;
- Literature-based methodological research related to clinical trials and research synthesis (e.g., systematic review methods, complex healthcare interventions, indirect comparison, and publication bias);
- Evidence based global health.

Contact: fujian.song@uea.ac.uk

Addiction research

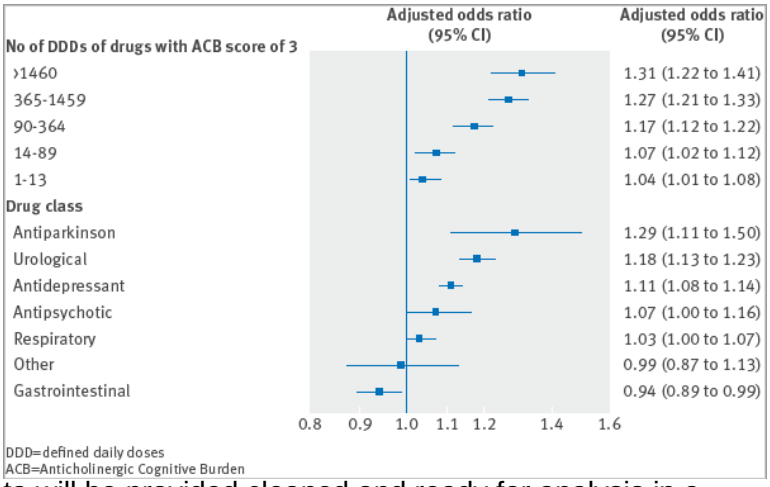
Prof Caitlin Notley leads the Addiction Research Group: The group produces high quality multidisciplinary research evidence to impact upon people who are affected by addiction, including service users, carers, health professionals and policy makers. The research approach emphasises responsiveness to social, cultural and pressing health needs, and supporting high risk or disadvantaged groups. Caitlin is a social scientist, and an expert in qualitative research methodologies applied across health and social sciences. She has extensive experience of running qualitative studies as stand-alone projects or alongside clinical trials, intervention development and systematic reviewing. Caitlin is a Cochrane author situated within the Cochrane tobacco addiction review group. Her particular areas of research expertise, that she would welcome students to work with on, are tobacco smoking cessation, relapse prevention and electronic cigarette use. She could also supervise projects more broadly in the fields of substance dependency, misuse and addiction, alcohol misuse, mental health and young people, health needs assessment and qualitative systematic reviewing.

Currently Caitlin has projects funded by the National Institute for Health Research, focused on smoking relapse prevention postpartum (the Babybreathe trial) and smoking cessation provision within neonatal intensive care units ('Love my Lungs'). She co-leads the CoSTED trial, 'cessation of smoking trial in the emergency department'. She has also led Cancer Research UK funded projects, most recently focused on dual use of e cigarettes and tobacco smoking.

Contact: c.notley@uea.ac.uk

Antimuscarinic use for overactive bladder

Dr Kathryn Richardson is an epidemiologist and statistician experienced in analysing primary care and secondary care data. Her research interests include the long-term effects of taking medications with anticholinergic properties. Through a project funded by the Alzheimer's Society, she has opportunities to examine long-term antimuscarinic use for overactive bladder and outcomes such as stroke, delirium, fractures or motor vehicle accidents. She has access to primary care records on 700,000 patients in England prescribed bladder antimuscarinics with linkage to hospital admissions data. The data will be provided cleaned and ready for analysis in a simpler format, and there is the opportunity to be involved in the publication of study findings. The student will have flexibility to explore and describe the data, and will be supported by Dr Richardson as well as the Norwich Epidemiology Centre.



Contact: kathryn.richardson@uea.ac.uk

Palliative Care Research

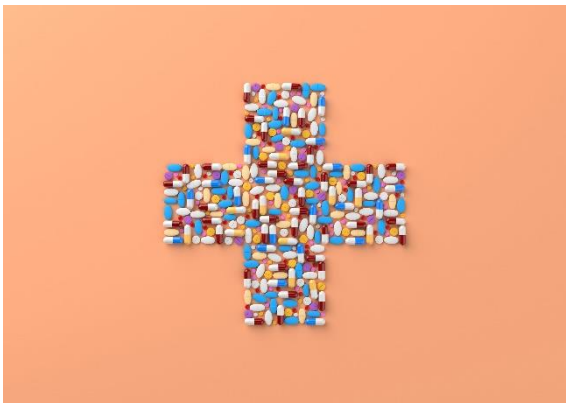
Palliative care research at the Norfolk and Norwich University Hospital is an expanding area of practice, with many opportunities to be involved in research, across the hospital campus, and working in collaboration with community trusts.

Key Research Interests include:

- Pharmacogenomics in Palliative and Supportive Care – Dr Caroline Barry and Dr Martyn Patel
- Understanding the Complexity of living with, and managing secretions in Motor Neurone Disease – Dr Caroline Barry
- Understanding inequalities in palliative care in coastal communities – Dr Abi Hensley

Pharmacogenomics in Palliative and Supportive Care

We are leading a UK first exploring the potential for pharmacogenomics to improve symptom management in people living with incurable illness. We will be offering genetic testing to patients receiving treatment at the Norfolk and Norwich University Hospital to understand whether genetic changes may influence how effective medications used are to manage pain and other symptoms, and a wider programme of work to understand whether this can improve patient care. This project is an opportunity to be involved in a local observational study, including data analysis, writing for publication, and development of a large scale clinical trial.



Contact: caroline.barry@nnuh.nhs or martyn.patel@nnuh.nhs.uk

Understanding the Complexity of Living with, and Managing Secretions in Motor Neurone Disease

Motor neurone disease is a progressive, incurable neurological condition, affecting most muscles of the body. Many people with this condition struggle to manage mucous and saliva as the muscles controlling speech and swallow get weaker. This leads to adverse effects such as pneumonia, and poor quality of life. We are undertaking a programme of work to further explore the complexity of living with, and managing this condition, with the aim of developing a decision support aid and/or service model to improve the management of this condition. Research activities include assisting in a complex intervention systematic review, focus groups / interviews, stakeholder meetings and/or decision aid development.

Norfolk MND Care and Research Network

Contact: caroline.barry@nnuh.nhs.uk

Inequalities in palliative care in coastal communities

Dr Abi Hensley is a palliative medicine consultant with St Elizabeth Hospice in Great Yarmouth and Waveney, and a UEA and MRes alumni. Her project is evaluating the differences in access and provision of palliative and end of life care to those that live in coastal and rural communities compared to those that live further in land.

Her project is a mixed methods research study, with quantitative data analysis and qualitative focus groups of healthcare professionals.

This project already has ethical approvals in place and would make an ideal MRes project to lead to achievable academic submissions within the 12 month time frame.

Contact: abigail.hensley@stelizabethhospice.org.uk