NHS Endowment call 2021 – successful applications

Bittersweet- the impact of anti-diabetic therapy on susceptibility to fungal infection

Decision fatigue in General Practitioners and Advanced Nurse Practitioners: detecting changes in decision making over the work period

The return to work experiences of people with communication disorders post-stroke: a qualitative study

The Effect of Coronary Artery Disease Prevention on Periodontal Health

Music as Adjunctive Epileptic Seizure TReatment Option (MAESTRO): a pilot study

Towards Avoiding Conflict in Difficult Care Management Decisions: understanding the causes of local disputes in paediatrics in order to develop pathways to dispute resolution in NHS Grampian.

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Seeing through the chemofog: Neural correlates of chemotherapy induced cognitive impairment

Are antiepileptic drugs associated with immune system dysfunction?

Identifying the meaningful clinically important difference (CID) for two validated patient reported outcome measures (PROMs) for women with stress urinary incontinence.

Omics as deteRmInants Of fitNess – the ORION Study

PI	Project Title and Summary
Professor Heather Wilson	**Bittersweet- the impact of anti-diabetic therapy on susceptibility to fungal infection**
	Summary People with type 1 and type 2 diabetes are more susceptible to fungal infection, especially Candida albicans (thrush) infections. The increased susceptibility is because the immune cells that are key to clearing infection, can be less efficient in people with diabetes. In addition to diabetes itself making people more susceptible to fungal infection, it is now recognised that type 2 anti-diabetic therapies can also increase susceptibility. For example, one newer type of medication, SGLT2 inhibitors (e.g., dapagliflozin), increases the incidence of genital thrush infections amongst people with diabetes. Another common treatment for diabetes, metformin, lowers glucose levels. Experimental model systems indicate that immune cells are defective as a result of glucose depletion and cannot fight the fungal infection properly. However, little is known about the exact mechanisms driving this infection susceptibility and whether revised practices could be put in place to prevent this. The aim of this project is to compare effects of common type 2 anti-diabetic medication on the function of the immune cells that are key to fighting fungal infections. Experiments will be performed under conditions of both high and normal glucose levels. Results from these experiments could provide information on the potential infection risks as a result of both diabetes itself, and also its treatments, and consequently may help to develop future preventative measures.
Dr Julia Allan	**Decision fatigue in General Practitioners and Advanced Nurse Practitioners: detecting changes in decision making over the work period**
	Summary Demands on healthcare workers are high: services are stretched, shifts are long and doctors regularly work lengthy periods without a break. In addition to reducing wellbeing, spending time continuously 'on task' changes decision making in predictable ways. Specifically, people make decisions that are progressively easier or more conservative as the period of time worked without a break increases; a phenomenon known as 'decision fatigue'. In the healthcare context, this could lead health professionals to make different, and sometimes less appropriate treatment and management decisions later in their shifts if adequate breaks are not provided. The present project aims to explore decision fatigue in General Practitioners (GPs) and Advanced Nurse Practitioners (ANPs), two essential professional groups, currently under high, and increasing levels of demand. The project will use data routinely captured by the Adastra clinical patient management system during out-of-hours consultations and qualitative interviews to determine if, when and how the decision-making of health professionals in Grampian changes over time. By studying when GP/ANPs' decision making starts to change during a work shift, we will be able to estimate how often they should take breaks during periods of continuous work to maintain their clinical judgement at the best possible level.
Dr Emma Coutts	**The return to work experiences of people with communication disorders post-stroke: a qualitative study**
	Summary Approximately a quarter of stroke survivors are of working age, and it is well-known that disabilities caused by stroke can lead to difficulties returning to work. Communication problems (potentially affecting reading and writing, as well as producing and understanding speech) are not as visible as other stroke-related problems such as a weak arm or difficulties walking. However, they can cause major problems for returning to work. We need to know more about the effects of communication problems on returning to work after a stroke. Specifically, we want to find out what helps and what hinders people with communication disorders following a stroke when they attempt to return to work; what information and support is most helpful to them; how this information and support should be given. We aim to do this by interviewing people across NHS Grampian who have the experience of attempting to return to work with post-stroke communication problems. We will then look at all the interviews together and find the common feelings or experiences that the participants mentioned. The findings will be

	written up and shared widely. The knowledge gained will help us to plan a programme to help people with these problems to return to work.
Dr Karolin Hijazi	**The Effect of Coronary Artery Disease Prevention on Periodontal Health**
	Summary The risk of heart attacks is increased by genetics, other diseases and lifestyle choices. Apart from these known risk factors, we recently demonstrated that bacteria associated with gum disease also contribute to a further increase in the risk of heart attacks. After a heart attack, medications and life-style modifications are prescribed. In this study we will explore if these secondary prevention measures for heart attacks contribute any improvement in gum disease. If gum disease is not reduced by these secondary prevention measures, we will in the future propose an oral intervention strategy aimed at the bacteria associated with gum disease, to further reduce the risk of recurrent heart attacks.
Dr Domenico Serino	**Music as Adjunctive Epileptic Seizure TReatment Option (MAESTRO): a pilot study**
	Summary Epilepsy is a neurological condition characterised by disruption to normal electrical brain activity, which can severely affect a child's cognitive functioning, learning and development. Mozart's Sonata for two pianos in D major (K448) has been found to reduce electrical abnormalities in patients with epilepsy. This study will examine the long-term effects of listening to the K448 sonata on seizure frequency and cognitive functioning in children with drug-resistant epilepsy. Patients' parents will complete a seizure diary for the whole study period, during which antiepileptic drug therapy of the child will remain unchanged. Baseline seizures diarisation and cognitive testing will be performed. The study group will listen to K448 for 8 continuous minutes every day for 2 months, while those in the control group will listen to of Mozart's Fantasia for Piano in C Minor, for the same amount of time. Cognitive testing will be repeated at two months and change from baseline examined. Seizure frequency during periods of exposure to music will be compared to baseline in both groups. Feedback questionnaires and parent focus groups will be used to gather information around the practicalities of taking part in the study and suggestions for how future studies might be improved.
Dr Sarah Sivers	**Towards Avoiding Conflict in Difficult Care Management Decisions: understanding the causes of local disputes in paediatrics in order to develop pathways to dispute resolution in NHS Grampian.**
	Summary Conflicts over the care of children with life-limiting conditions can reach the point where the only resolution is to ask courts to decide what is best, incurring costs in time and money. Having parents and NHS staff give evidence in court results in distress, unwanted publicity and social media attention. This was seen in the English case of Charlie Gard where the judge pleaded for parties to try to resolve disputes without court intervention in future. The law in Scotland is different to that in England. No case has yet come to a Scottish court. A toolkit designed to reduce the risk of a Scottish court being asked to make such a decision is needed. The proposed study is the first step in creating a toolkit. We will interview Grampian families and clinicians to gather their experiences and views of disagreements about care. Our results will be used by our medical and legal team members to develop resources to assist in understanding and recognising conflict, and pathways to resolution to allow NHS Grampian and parents to avoid court costs. Our ultimate step (in a future proposal) will be to develop a toolkit for conflict resolution across all Scottish Health Boards.
Dr Magdalena Rzewuska	**Understanding digital appointment inequalities in NHS Grampian: exploring digital exclusion and identifying solutions to address it with our rural and urban communities**
	Summary NHS Grampian (NHSG), like the rest of NHS Scotland, is rolling out a new type of online outpatient consultation service, where the patient and doctor do not have to be available at the same time. The hospital asks the patient to fill in details of their symptoms and situation on a website and maybe attach photos. The doctor then reviews these and decides on the next

	steps, e.g., tests, treatment, discharge or further face-to-face contact. We know that a significant proportion of people do not take up the offer of this new approach to care provision. There might be many reasons for this. When unexamined those reasons may lead to this service being calibrated in a way that disadvantages people ('digital exclusion') or is inappropriate for others ('digital choice to opt-out'). We propose to start exploring what digital exclusion means to people locally and the sources of digital exclusion and digital choice to opt out. We also want to start identifying what could be done practically to improve the inclusivity of our online outpatient consultations. This would be done by reviewing literature and holding discussions with people in our urban and rural communities affected by this issue.
Professor Anne Kiltie	**Kidney, colon and lung tumour metabolites and their dependence on the tumour microbiota**
	Summary Recently, the healthy bacteria living in the intestines of patients with cancer (the 'gut microbiota') have been found to determine how well their tumours respond to some cancer treatments. However, tumours themselves also have a microbiota. These bacteria come from the gut, skin, mouth (oral cavity) or other mucosal surfaces, after being 'eaten' by immune cells, and take up residence inside cancer cells and associated immune cells. Such bacteria produce chemicals (known as 'metabolites'), including short chain fatty acids (SCFA), tryptophan and bile acids. These act as signals to either shrink or grow the tumours. Bacteria differ between some tumour types and in the metabolites they produce but more work is needed. We therefore wish to study three very different tumour types, kidney, colon and lung cancers, with different exposures to oral and gut microbiota, and normal tissue from the same specimens. Tumours contain low numbers of bacteria (if any) which can make contaminating bacteria a problem in experiments. We shall test the feasibility of measuring bacteria and their metabolites in fresh-frozen tumour samples, looking for associations and generating pilot data to explore new cancer treatment approaches based on drugs, dietary supplementation or manipulation of the oral/gut microbiota.
Dr Callum Kaye	**Improving recruitment to emergency research trials – Making the consent process acceptable for all**
	Summary Clinical trials provide the strongest evidence to determine whether treatments are effective. In the emergency setting, these trials can be very difficult to perform and often struggle to recruit patients. This can be due to a number of different reasons, including around how we ask patients or their relatives for their consent to take part in the trial. This is even more important in the setting of life-threatening emergencies, where the patient is not able to give consent and relatives have only just been told that their next of kin is critically unwell. In this project, we will speak to members of the public, specifically people from a diverse range of backgrounds, to explore their thoughts of how consent should be sought in this setting and propose a future trial led from Aberdeen recruiting patients with severe brain injuries. We will also speak to research nurses with experience of recruiting to such trials, to understand the realities of seeking consent in such settings and give best practice advice to support a future NHS Grampian led trial.
Dr Fiona Clegg	**Primary human hepatic 3D organoid culture as a new method to study liver disease.**
	Summary Liver disease is a major cause of illness and death in Northeast Scotland and is becoming more common. The understanding of liver disease and development of medications to treat it have been hampered by a lack of realistic laboratory models. We have developed a new method for growing human liver cells from fresh liver tissue removed during operations within NHS Grampian. These cultures (hepatic organoids) can be kept alive for many months, frozen and regrown on thawing. Hepatic organoid culture offers the opportunity to test experiments from preliminary work in animals or cell line culture on more representative models of the human liver. The method we have created is affordable and efficient compared to those published to date. It is essential we can demonstrate the hepatic organoids we have generated produce cells with similar features of those seen in the human liver. We plan to do this by comparing the expression of genes and proteins in our organoids with that in human adult liver.

Dr Elaine Wainwright	**What helps people with musculoskeletal pain stay in the labour market, if they are self-employed, precarious or portfolio workers? Patients' and First Contact Practitioners' views**
	Summary Persistent musculoskeletal pain is a major health problem, leading to poorer physical and psychological outcomes. Safe, appropriate work can be protective: healthcare professionals including First Contact Practitioners (FCPs) are increasingly asked to see work as a health outcome. However, most return-to-work research concerns organisational full and part-time contracts. We know little about supporting people living with MSK pain to stay in work if they are: self-employed; in precarious work; have portfolio working patterns like freelance or contract work. These working practices are getting more prevalent. We also know little about how FCPs can support people in pain with these working lives; this is important as they may see patients first. We will interview workers living with MSK pain to explore their experiences of using these working practices, and of FCP consultations. We will also interview FCPs to investigate their experiences of supporting such workers. Data analyses will consider what patients and FCPs think works to keep people in pain in modern labour market patterns, and what supports the FCP role when discussing work and health. The findings will also enable a larger bid whereby stakeholders co-create summaries of key points, and solutions to the issues raised, using Accelerated Experience-based Co-design.
Dr Dana Kidder	**Expanding Grampian vasculitis biorepository to support current and future vasculitis research**
	Summary A biorepository is a storage facility that collects, stores and processes biospecimens for clinical and laboratory research studies. Biorepositories are critical in enabling molecular research using powerful technologies that allow identification of new disease mechanisms and treatment targets. In Grampian, we established a vasculitis biorepository in 2017. Vasculitis mean inflammation of blood vessels and are divided into small, medium and large vessel vasculitis based on the size of affected vessels. We received strong patient engagement for our biorepository that was key to our research in small vessel vasculitis. We aim to expand the biorepository to include large vessel vasculitis, namely temporal arteritis. It is the commonest type of vasculitis and manifests as headaches and feeling unwell. The condition affects individuals above age of 50. Left untreated, it can cause blindness. Half of patients experience relapses. There are unmet needs in the care of temporal arteritis including knowledge gaps on why and how the disease happens, improving the diagnosis, identification of targeted and less toxic therapies and predicting disease course. We started two PhD studentships tackling a number of these unmet needs. The proposed expansion is critical for our success in addressing these unmet needs and improving health and care of our patients.
Professor Lynda Erskine	**SLC38A8: the missing link in the visual system deficits associated with albinism?**
	Summary Individuals with albinism, lacking ocular pigmentation, or with mutations in SLC38A8, which causes no detectable changes in ocular pigmentation, display strikingly similar visual system deficits (foveal hypoplasia and optic nerve misrouting). These visual deficits result in decreased visual acuity and impaired ability to see in depth. There is no cure and only limited measures can be taken to improve visual function. Quality of life for individuals with severe visual impairment is poorer than for those with other serious conditions such as breast cancer and arthritis. This project will test the hypothesis that SLC38A8 acts downstream of ocular pigmentation to regulate events during eye development important for fovea development and optic nerve routing. We will use chicken embryos to establish the impact of knocking down SLC38A8 on retina development and the inter-relationship between SLC38A8 and genes important for albinism in humans. The results obtained will advance our understanding of the cellular and molecular mechanisms underlying the visual deficits associated with albinism and SLC38A8 mutations. In collaboration with relevant experts across Europe we will use this data to underpin a larger funding application. The long-term aim is to develop new therapeutic strategies of benefit to patients with albinism/SLC38A8 mutations.

Dr Arimantas Lionikas	**Screening assay for sarcopenia drug development**
	Summary Decline in muscle mass and strength, known as sarcopenia, erodes quality of life of the elderly and increases the risk of falls, fractures, institutionalization, and mortality. No effective medication currently exists to treat sarcopenia. This project targets this unmet need by developing a screening assay for the compounds designed to improve muscle strength. A series of recent studies highlighted two key proteins that are the focus of this project. First, the insulin-like growth factor 1 (IGF1) is an important stimulator of growth and survival of healthy muscle cells. Second, the IGF binding protein 5 (IGFBP5) is a key regulator limiting availability of the IGF1. The IGFBP5 binds the IGF1 and prevents its stimulatory effect. Small synthetic compounds can be designed to interfere with the IGFBP5 and IGF1 binding and that would increase the growth promoting signal in muscle cells. A screening assay is an integral part of a full-scale drug development programme. It is required for determining which variant of the synthetic compounds can block the IGFBP5 ability to bind the IGF1 most effectively.
Dr Heidi Gardner	**A qualitative interview study with adults living in remote and rural areas of Grampian to explore barriers and facilitators to participation in clinical trials**
	Summary Improving healthcare for rural communities is a priority for Scotland, to do this we need to ensure that rural communities can engage with health research. Clinical trials are an essential part of health research but delivering trials with people living in rural areas is difficult. In this project, we will use semi-structured interviews to gather views of people living in rural areas of our region to: • Understand how adults living across rural and remote parts of Grampian feel about participation in clinical trials. • Explore how rurality contributes to and intersects with these views, and how trial teams can alleviate barriers and enhance facilitators to improve engagement with this group. Alongside this qualitative project, we have secured separate funding to conduct a systematic review that will enable us to bring together evidence from the published literature around ways in which researchers have tailored their trial recruitment strategies to rural communities, this will help us to understand what has been done before in other rural areas. Funding from NHS Grampian's Endowment Grants will support us to gain insights directly from Grampian's rural communities. These two projects will together provide new knowledge so that researchers can design trials with rural communities in mind.
Dr Joanna Shim	**Development of a prehabilitation program informed by cognitive behavioural therapy (pR-CBT) to improve outcomes in total knee arthroplasty (TKA).**
	Summary Knee replacement is a common approach to treat severe osteoarthritis and knee injury, with more than 100,000 knee replacements performed in the UK annually. Although knee replacement surgery usually improves pain and function (e.g. walking and climbing stairs), around 1 in 5 patients are still not satisfied with the outcome of their surgery. Prehabilitation, a form of pre-surgery rehabilitation to improve overall physical health, is really important because it may help with some of the physical and mental barriers one might experience prior to surgery; therefore, reducing the overall interventions required afterwards. Prehabilitation before knee replacement has also been reported to shorten the length of hospital stay and help speed the return to normal daily life activity after surgery. However, most of the existing prehabilitation only focuses on exercises and education to improve knee function and does not currently take into account important modifiable psychological or individual factors such as patient expectations and coping ability which play a significant role in recovery. Therefore, there is a need to develop a prehabilitation intervention for patients undergoing knee replacement surgery that provides the necessary psychological support and this study will do that.

Dr Nicola Mutch	**Improving patient selection for thrombolysis in acute ischaemic stroke**
	Summary Patients suffering strokes can die or end up with devastating disabilities. Strokes due to blood clots can be treated with a clot buster drug if the patient comes to hospital quickly and the brain scan does not show blood or other changes. Only around half of those treated with the drug respond, however, we can't predict who will improve or who might have bleeding after the treatment. Knowing more about the patients' blood clotting before treatment might help us identify the best patients for treatment and those who are likely to be harmed. We have access to a new analyser which can very quickly tell us about how a patients' blood clots and how 'tough' these clots are. Fifteen patients admitted with stroke will be asked to provide blood samples at various time points which will be run on the analyser: we will compare their clotting profile with how well they recover after their stroke. We will also compare with patients who have had a stroke but could not get the clot buster drug. An ability to identify good or bad responders to the drug based on how their blood clots, may help to improve stroke patient safety and care.
Dr Kathryn Martin	**Involve Grampian: Enhancing wellbeing <u>for all</u> through involving patients and the public from our diverse community in health-related research**
	Summary Academic and medical institutions across the NHS Grampian area have traditionally struggled to involve and recruit to research people from underprivileged or deprived groups, including those from cultural, religious, and disabled communities. Often such research activities would be of greatest benefit to these seldom heard groups. This project aims to better understand the reasons why certain groups are underrepresented and develop strategies to remedy this. We will work collaboratively with researchers, patient and community partners, NHS Grampian Consultation and Engagement Advisors, and community organisations to identify barriers to involvement in research and best practices locally and nationally to engaging with seldom heard groups. We will design inclusivity, accessibility, and diversity training materials for University researchers, as well as research empowerment training for Grampian community members. These will be sense-checked by community organisations to ensure they are fit for purpose. We will create newsletters and podcasts advising the Grampian public on the meaning of involvement and research opportunities. The project outcomes will enable those wishing to conduct research in future to do so in a way that is more inclusive, accessible, and engaging, and will enable diverse groups within the Grampian community to feel empowered to participate to a greater extent.
Dr Carrie Stewart	**Exploring health professional views towards a patient empowerment approach to reducing use of anticholinergic medications**
	Summary Anticholinergics, a group of medications, are prescribed for several common conditions including irritable bladder, allergies and sickness. Around half of all older adults use one or more of these medications. However, the more anticholinergic medications taken by a person, the greater their risk of heart attack, dementia, falls and death. Several attempts to reduce prescribing of anticholinergic medications have been reported. They typically involve educating prescribers, providing alerts to prescribers, or adding an expert prescribing service. These approaches target the prescriber. One different approach proposed to reducing medication harms involves targeting the patient. Our team has co-developed a flyer and animated video with our lay volunteers. The materials provide information as to why we are interested in reducing use of anticholinergic medications and what they (the patient) can do. The purpose is to empower patients to ask more questions about their medications. To progress our work in identifying ways to reduce anticholinergic medication related harms, we want to explore the patient empowerment approach further. Specifically, we want to find out how health professionals view these materials and their opinions towards this approach. We will do this through three online focus groups with health professionals from across Scotland.

Dr Tiberiu A. Pana & Professor Dana Dawson	**Importance of Gender Differences in Secondary Prevention and Long-term Outcomes of Cardiovascular Diseases in Scotland**
	Heart attacks and strokes are the leading causes of illness and death in Scotland. Women are less likely than men to suffer these conditions. However, we do not know whether men and women fare differently in terms of dying in the long-term or having further heart attacks or strokes. Several studies from other parts of the world suggest that women have higher risk of death and repeated heart attack/stroke than men. Such differences may at least partly be driven by differences in prescription of medications proven to reduce the risk of further disease, such as lipid-lowering drugs or blood thinners. In this study, we aim to describe for the first time the differences between men and women in appropriate prescription of these medications after heart attack/stroke in Scotland. We also aim to understand factors which may explain these differences using an anonymised national dataset. Importantly, we will also determine if such differences in prescribed medications also translate into differences in death and subsequent heart attack/stroke. Knowledge of such differences is an essential step in Scotland's ambition of reducing health inequalities for women, highlighted by the recent launch of the Women's Health Plan by the Scottish Government.
Dr Gordon Waiter	**Seeing through the chemofog: Neural correlates of chemotherapy induced cognitive impairment**
	Chemotherapy is toxic and most chemotherapy side-effects are known and well documented. However, the phenomenon of "chemo fog" or "chemobrain" is less well understood. Changes in thinking ability, like lack of concentration or loss of memory has a significant impact on the lives of cancer patients. Without understanding what "chemobrain" is, and what causes it, there is little that doctors can do to help. The team proposing this study believe that chemotherapy causes chemicals associated with inflammation to attack parts of the brain that are important for concentration and making new memories. Unfortunately, it is not possible to measure these chemicals directly in the brain, but we believe that a brain scan sensitive to brain inflammation, can help. This project will measure thinking ability, take a blood sample, and do a brain scan before, during and after a patient has chemotherapy. We will then look for changes in brain inflammation in areas that are important for concentration and memory and compare those to changes in thinking ability and to levels of inflammation chemicals in the blood. This information will be essential to help plan our next step which is to test ways to reduce the effects of "chemobrain".
Dr Angus Macleod	**Are antiepileptic drugs associated with immune system dysfunction?**
	Antibodies and white blood cells are an important part of the immune system and help fight infections. We previously looked after a patient with epilepsy, treated with an antiepileptic drug, who developed a life threatening infection in association with low antibody and white blood cell levels. She unexpectedly recovered after her antiepileptic drug was stopped, and her antibody and white blood cell levels returned to normal. There are a few published cases of low antibodies and white blood cells in people treated with antiepileptics but no studies have investigated how commonly this occurs. As a potentially serious side effect, it is important to understand more about it. We will use the Grampian Data Safe Haven to anonymously link prescribing data, laboratory data, and data about health conditions, for people in Grampian since 2009. We will identify everybody who has had antibody or white blood cell levels measured and investigate whether they were prescribed antiepileptic drugs. We will assess whether low antibodies or low white blood cells are more likely with higher exposures of antiepileptic drugs, and also investigate if those treated with antiepileptic drugs are at an increased risk of infections, as this can occur as a consequence of an impaired immune system.
Dr David Cooper	**Identifying the meaningful clinically important difference (CID) for two validated patient reported outcome measures (PROMs) for women with stress urinary incontinence.**
	Urinary incontinence is a common condition in women that reduces quality of life. Because of this, when testing new treatments patient reported outcome measures, or PROMs, are the most relevant things to measure. For urinary incontinence there are many ways to measure

	different PROMs, but for some we don't know what constitutes important differences. This is problematic, without an understanding of a worthwhile difference women and their doctors struggle to adequately trade-off the benefits and harms of available treatments. In this study we intend to use data already collected from two of our clinical trials (SIMS and OPAL) to derive important differences for a range of PROMs. We're going to do this by comparing what women told us about their quality of life using a PROM called the Patient Global Impression of Improvement (PGI-I) to what they reported on the other PROMs we measured. The PGI-I is well understood, allowing us to map changes in PROMs measuring incontinence-related quality of life and sexual function onto PGI-I scores to derive meaningful differences.
Dr Alice-Mihaela Mezincescu	**Omics as deteRmInants Of fitNess – the ORION Study**
	Physical exercise is good for health and reduces the development of heart disease, obesity, and type 2 diabetes; whilst being inactive is one of the main risk factors for developing these conditions. Despite knowing that exercise is good for us, we do not fully understand how exercising leads to all these health benefits. By studying comparatively a group of recreational athletes i.e. the fittest, who have a low risk of developing cardiovascular diseases and diabetes and comparing them with a group of type 2 diabetes patients who are at risk of cardio-vascular disease and who are unfit, we are aiming to uncover the missing link between exercise and cardiometabolic risk. The plasma (i.e. the liquid part of the blood) contains a multitude of very small molecules and fats (lipids) that play many roles in the body. In this project, we are aiming to characterise these small molecules and fats in the plasma in relation to one exercise session and an exercise program in these two populations situated at opposite ends of fitness. Using special techniques that improve the separation of small molecules and fats in a sample, we are aiming to determine a 'molecular blood signature' of fitness versus one of disease. This may lead to the development of new drugs that could mimic the beneficial effects of exercise or new drugs for treating type 2 diabetes.