

## Research Themes



Across the University of Birmingham there are many principal investigators examining all aspects of obesity, crossing different schools and disciplines. This has created a platform of excellence within obesity research upon which the Centre for Obesity Research plans to build, cementing the University of Birmingham as the leading international centre for research and intervention in obesity.

The current central research themes upon which the Centre for Obesity Research focuses are listed below, along with the principal academic lead for that area.

### Mechanisms of Disease : Dr Jeremy Tomlinson ...

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The health consequences of obesity are severe; on average, being obese decreases life expectancy by nearly 10 years. In addition, it is associated with dramatic increases in the risks of developing type 2 diabetes, hypertension, coronary artery disease and hyperlipidaemia. It is tightly linked to the development of fatty liver disease which can progress to cirrhosis and also to the development of some cancers. Indeed, it has been suggested that in the not too distant future, obesity could not only become the leading cause of liver failure, but also the leading cause of cancer worldwide.

Despite the severe health impact, we still understand relatively little about the cellular process that contribute to the accumulation of fat and its distribution within the body; Importantly, fat carried around the abdomen (often called central obesity) rather than around the hips (gynoid obesity) is far more detrimental to health.

Within the University of Birmingham there are a number of investigators trying to understand the cellular process that contribute to the regulation of fat mass and the complications of obesity, including the genetic predisposition to diabetes, role of steroid hormones and immune function, sleep disturbance as a risk for the development of obesity, the causes of fatty liver disease and insulin action and the heart. Our aim is to understand these process such that we can identify, design and trial novel treatments in an attempt to halt the epidemic of obesity and its devastating consequences.

#### Specific project examples

**Glucocorticoids and insulin signalling in human adipose tissue**

This project seeks to explore the mechanisms by which glucocorticoids (e.g. cortisol) impact upon insulin action within human adipose tissue. Understanding how endogenous and exogenous glucocorticoids interact with insulin signalling will help us determine the mechanism underpinning insulin resistance which is often regarded as being pivotal in the consequences and complications of obesity

Contact: Dr Jeremy Tomlinson

**Impact of glucocorticoids upon insulin signalling in skeletal muscle**

Glucocorticoids are widely used in medical practice, but are associated with significant complications including insulin resistance and obesity. We are trying to understand how glucocorticoids (both synthetic drugs and those produced naturally by the body) cause insulin resistance in muscle and therefore help to identify ways in which to maximize the benefits of these drugs and minimize side effects

Contact: Dr Jeremy Tomlinson

**Glucocorticoid metabolism and fatty liver disease**

Glucocorticoids in excess can cause fatty liver. We are exploring the hypothesis using cell models and clinical studies to see if limiting the generation of natural endogenous glucocorticoid by the liver can improve fatty liver disease and insulin resistance.

Contact: Professor Paul Stewart, Dr Phil Newsome and Dr Jeremy Tomlinson

### Exercise and Nutrition: Professor Janice Thompson ...

Physical activity and poor diet will soon become the number one cause of death, ahead of smoking and alcohol consumption. The World Health Organisation identified that a reduction of physical activity in combination with an increased consumption of more energy-dense, nutrient-poor foods with high levels of sugar and saturated fats, have led to obesity rates that have risen three-fold or more since 1980 in some areas of North America, the United Kingdom, Eastern Europe, the Middle East, the Pacific Islands, Australasia and China. Although it is clear that a combination of reduced physical activity and an increased consumption of energy dense foods is responsible, the underlying mechanisms are still incompletely understood. Exercise plays an important role in terms of energy expenditure but also in the regulation of appetite. Dietary composition has also been found to have an important effect on weight loss or weight gain. In addition various nutritional supplements have been claimed to increase fat metabolism and reduce fat mass, although evidence for this is scarce. Therefore more research is needed to study the interactions between nutrition and exercise. More specifically in this theme the aims are:

- Understanding the effects of exercise training interventions in obesity
- Understanding the effects of exercise on appetite regulation
- Understanding the effects of nutrition interventions in obesity
- Understanding the nutrient-exercise-gene interactions in obesity
- Understanding the acute and long term effects of exercise
- Developing practical ways to implement exercise training programmes or promote physical activity

#### Specific project examples

**Exercise training and fat metabolism**

Although it is known that physical activity results in several improvements in fat metabolism and metabolic control, and can result in weight loss, it is yet unclear which types and intensities of exercise are most effective. Several studies are addressing this issue. These studies will help to give more targeted and detailed advice to the patient who has been told to "exercise". It will also help the businessman who has very little time in his day to use the available time as effectively as possible and it will

answer questions like how little exercise is needed to get health benefits.  
Contact: Dr Michelle Venables

### **Exercise and appetite**

It is long known that exercise affects appetite. The underlying mechanisms are most likely related to various hormones and substances that are secreted during exercise. It is not known which types of exercise and which intensities reduce or increase appetite. Also, the longer term effects of exercise training programmes on energy intake (appetite control) and body weight and the relationship between post-exercise fat metabolism and subsequent energy intake and body weight is currently unknown.  
Contact: Dr Andrew Blannin

### **Green tea and fat oxidation**

Green tea (and the active compound EGCG in particular) has been linked to increases in fat metabolism and greater weight loss. However most of the research was carried out in animal models and little information is available in humans. In an initial study we saw increased fat oxidation during exercise and improved insulin sensitivity. Future studies will investigate the underlying mechanisms as well as the dose response relationship  
Contact: Dr Michelle Venables

### **Childhood Obesity: Prof Tim Barrett ...**

In 1987 less than 10% of UK children were overweight or obese. This has increased to a third of all children in 2007, and the Government predicts that two thirds of our children will be overweight or obese by 2050. Our aim is to prevent this prediction becoming a reality. West Midlands children are already some of the fattest in England – 34% of boys are either overweight or obese and 30.6% of girls; and in some Birmingham districts, up to 50% of 11 year olds are overweight or obese. Some of these children already have diabetes, hypertension, fatty livers, depression, and early markers for future heart disease. When these children reach their late teens and early twenties they are likely to suffer from diseases normally associated with much older adults, exemplified by the growing number of cases of Type 2 diabetes (previously called "adult-onset diabetes") in obese children. The global health consequences of this will be severe, and prompted The Lancet to report in 2006 that "We may be the first generation in history where our children will die before their parents".

### **Current projects**

#### **Evaluation of different types of exercise intervention and maintenance in childhood obesity**

Taking place at Birmingham Children's Hospital in the new Wellcome Trust Clinical Research Satellite Facility, a project generously supported by University of Birmingham alumni and the School of Sports and Exercise Sciences is aiming to explore what forms of exercise work best at helping obese children to shed their excess weight. This includes computer game-related dance mats, which are used for half an hour three days a week, coupled with exercise bikes and indirect calorimeters to estimate how beneficial this exercise really is for children, taking into account physical fitness, body composition, blood sugar and body mass index. Encouragingly, meaningful weight loss has already been observed in these children, and the work will be extended through to other exercise interventions in the near future.  
Contact: Professor Timothy Barrett

#### **Promoting adolescent health through an intervention aimed at improving the quality of their participation in physical activity**

With respect to the need for encouraging active lifestyles, The White Paper on a Strategy for Europe on Nutrition, Overweight and Obesity and the Commission White Paper on Sport point to the significance of community sports organisations in public health and primary prevention, with a special reference to young people. Funded by the EU Commission and endorsed by the English FA and Professional Football Association, this project centres on the formation, implementation, and testing of a sustainable and cost-effective coach education program aimed at improving the quality of children and adolescents' participation in leisure-time physical activity, enhancing their psychosocial development, and empowering young people to adopt and sustain healthy lifestyles.  
Contact: Professor Joan Duda

#### **Promotion and assessment of effective physical activity engagement in children**

At present we don't have accurate measures of how effective different sporting activities are for keeping children healthy. With this project, we want to develop valid and reliable field-based assessments of objective physical activity, energy expenditure, caloric intake, fitness and body composition for UK children taking part in leisure-time sport. We plan to use these objective assessments to test the biomedical effectiveness (complementing paper-and pencil measures of self-reported physical activity, motivation, self perceptions) of a large-scale intervention in the community. This will be centred on the creation of more positive youth sport experiences for boys and girls. Within the larger intervention project, we will also follow a sub-sample of children over the course of one year and examine the objective levels of physical activity, energy intake and energy expenditure necessary to the maintenance normal weight.  
Contact: Professor Joan Duda, Professor Timothy Barrett

### **Motivating Health Lifestyle : Professor Joan Duda ...**

**Vision:** "To develop effective person-centred interventions centred on fostering motivation for and participation in physical activity and healthy eating and associated well being in children and adults."

There is currently a considerable amount of evidence regarding the impact of regular engagement in physical activity and healthy eating on physical and mental health. We also now know more about the mechanisms by which exercise and dietary patterns contribute to health as well as the means by which inactivity and high calorie diets lead to disease states. However, despite these marked advances in our knowledge base, there is a large and increasing percentage of the population who do not participate in physical activity at the intensity and frequency necessary to accrue the health benefits associated with regular exercise. Insufficient levels of physical activity have been implicated in the aetiology of obesity. In the case of individuals who are overweight or obese, dietary modification is also necessary. Thus, there is a striking need for viable interventions that can successfully influence the adoption and maintenance of physical activity and healthy eating in the general and clinical populations.

Results of interventions centred on individual behavioural change have been inconsistent. Much of this work is not grounded in theories of motivation or does not adequately test our current theoretical understanding of what contributes to healthy lifestyles. Whether directed toward primary or secondary prevention, we need theory-based interventions which can effectively promote individuals' efficacy and personal autonomy regarding behavioural change. Key staff members represented in this theme have expertise regarding the environmental (social, physical) factors and motivational processes underpinning sustained health behaviour patterns and optimal functioning in children and adults. The applied and basic research we do considers physical activity engagement in the largest sense: i.e., physical activity accrued within exercise classes, physical activity referral programmes, sport, dance, physical education, hospital-based exercise programmes, the workplace and daily life physical activities (e.g., taking the stairs, gardening). The importance of motivational processes is also considered to whether physical activity is more or less likely to result in positive mental health outcomes.

### **Current Projects**

#### **An evaluation of the Birmingham Exercise on Prescription service: Standard provision and a self-determination focussed arm**

Personal autonomy for health behaviour change is a central concept of Self-Determination Theory (SDT). People are autonomously motivated when they engage in an activity or cease an activity for reasons that come from within the self and are freely chosen. Funded by local PCTs and Birmingham City Council, this trial is comparing the effect (at 3 and 6 months) of an exercise consultation delivered by SDT-trained health and fitness advisors with an exercise consultation provided by currently trained HFAs in Birmingham on participants' self-reported physical activity, associated health behaviours, physical health, and well-being/quality of life.  
Contacts: Professor Joan Duda, Dr Kate Jolly

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their psychosocial development, and empowering young people to adopt and sustain healthy lifestyles.  
Contact: Professor Joan Duda

### **“Step by step”: A feasibility study on the promotion of lunchtime walking to increase physical activity and improve mental well-being in sedentary employees**

Funded by the BUPA Medical Grant Programme, this project examines the feasibility of a theory-based 16-week lunchtime walking intervention designed to a) promote regular walking and b) improve psycho-social well-being and work performance, in sedentary employees. The workplace has been targeted as an important location for health promotion, particularly with regard to mental health and also obesity prevention. More direct benefits of physical activity to employers may accrue in terms of enhanced employee work satisfaction, performance and productivity.  
Contact: Dr Cecilie Thøgersen

### **Environmental prompts for physical activity: Targeting calorific expenditure with stair climbing.**

Current approaches to physical activity promotion target the accumulation of physical activity as part of daily life. The studies are part of a series using point-of-choice prompts positioned between the stairs and the escalator/lift encouraging stair climbing for health. Our previous work has shown a greater response to a worksite campaign in overweight individuals, suggesting stair climbing is a physical activity the overweight perceive as achievable. A current study targeting calorific expenditure has reversed the lower rates of stair climbing by overweight people relative to those with normal weight. Thus a ratio of 1.9:1 of normal to overweight people on the stairs at baseline was changed to a ratio of 1.3:1 in favour of overweight pedestrians. These simple, cheap interventions function by interrupting habitual behaviour at the time of its occurrence. The techniques we use should generalise to calorific intake at point-of-purchase. These studies at public access sites and workplaces have been funded by the NHS in England, Scotland, Hong Kong and Spain.  
Contact: Dr Frank Eves

### **Is exercise, in addition to usual care, an effective treatment for postnatal depression?**

It has been estimated that depression will be the second most common cause of disability worldwide by 2020. Postnatal depression (PND) is a serious problem across cultures and affects about 10-15% of women some time in the first year after giving birth. After giving birth, many women have excess weight and decreased fitness levels. New mothers have reported weight gain to be a significant concern for them. Studies of pregnant and postpartum women have indicated high risk for inactivity and reductions in previously established levels of activity. These health concerns would apply equally to women with PND. A recent systematic review and meta-analysis of five randomised and quasi randomised controlled trials concluded that it was uncertain whether exercise reduces symptoms of PND and called for a large trial that compared exercise with standard treatment(s). Funded by the National Institute for Health (NIHR) and the NIHR School for Primary Care Research this RCT aims to investigate the effectiveness of exercise as a treatment for PND. Other outcomes such as weight, BMI and physical activity levels (objectively) will also be assessed. This trial will run for three years (2009-2012).  
Contacts: Dr Amanda Daley, Dr Kate Jolly, Professor Christine MacArthur

### **The acceptability and feasibility of aerobic exercise as a treatment for vasomotor and other menopausal symptoms in symptomatic women**

The risk-benefits profile of HRT has been questioned recently and many menopausal women are keen to use non-pharmacological alternatives. There has been a lack of robust research on the effects of exercise upon vasomotor symptoms (hot flushes and night sweats) as evidenced by the recent Cochrane review. Low rates of exercise participation have also been recorded for menopausal aged women, which may also increase their risk of diseases in later life (e.g. depression, osteoporosis, stroke, cardiovascular diseases); thus exercise might provide additional health benefits in this population of women. On the basis of very limited evidence the Royal College of Obstetricians and Gynaecologists recently advised that regular aerobic exercise may help relieve menopausal symptoms. Further research is clearly required before menopausal symptomatic women could be advised that we know that exercise is an effective treatment option for these symptoms. Funded by the National Institute for Health Research (NIHR) we aim to determine the feasibility and acceptability of exercise as a treatment for vasomotor symptoms. We will also consider whether feasibility varies according to BMI status. This programme of research involves a series of observational studies and a RCT that will take place over five years (2008-2013).  
Contact: Dr Amanda Daley

## **Obesity in the Community : Dr Neil Thomas ...**

The Obesity in the Community theme of the Centre for Obesity Research aims to provide the platform that integrates the investigations of the other themes providing access to patient groups and appropriate samples to further our understanding of the mechanisms underlying the association between obesity and the diseases it causes. Additionally we wish to explore the reasons and cultural and other barriers to adherence to recommended treatments, access to and utilisation of health services, which is contributing to existing health disparities.

This will be achieved by further developing and characterising our existing obesity-related disease cohorts (as described below) to compare and contrast determinants between ethnic groups in order to enhance our opportunity to detect those of importance. Asians, generally, relative to others, are very susceptible to the development of diabetes. South Asians have a preponderance of heart and renal disease, yet less peripheral disease than expected; whereas Chinese tend to have more stroke and renal disease with less heart disease and minimal peripheral disease. It is important to remember that our ability to detect the contribution of disease determinants is dependent on the range of variation in the parameter. Distinctions across racial groups can provide sufficient differences to enable adequate investigation, which can be readily examined given the ethnic diversity of Birmingham providing an ideal setting for such investigations. These cohorts will also provide an ideal opportunity to investigate differences in the development of diabetes and vascular disease in the different ethnic groups.

Additionally, access to children, the community and patients with obesity gives us the opportunity to readily initiate investigations to target obesity and where those interventions appear beneficial to translate the work into preventative and medical practices.

We thus, through the Centre for Obesity Research, aim to make a major contribution to not only our understanding of the causes of obesity and how it leads to disease, but also to provide effective, cost-effective strategies to prevent and treat the condition.

Existing active cohorts include: 1: The Guangzhou Biobank Cohort Study, China, 30,000 older ( $\geq 50$ y) Chinese subjects with comprehensive fasting biochemical includes plasma and live white cells stored in liquid N<sub>2</sub>), anthropometric and questionnaire-based parameters to investigate genetic and environmental determinants of chronic disease. First 5 year follow-up is now underway.; 2: Hong Kong Cardiovascular Risk Factor Study, 2,900 subjects (24-75y). 13 year follow-up just concluding. A similarly intensively phenotyped study investigating determinants of vascular disease; 3: Isfahan Cohort, Iran, 6,500 subjects ( $\geq 18$ y) with 6 year follow-up similarly to investigate determinants of vascular disease with a particular emphasis on lifestyle parameters; 4: Heart failure (ECHOES) study examining prevalence, determinants and impact of ethnicity on heart failure; 5: Type 2 diabetic cohort 7,500 to investigate the impact of ethnicity on the development of diabetes and its associated complications.

Pharmacological and lifestyle interventions include 1: investigation of a polypill for the primary prevention of vascular disease; 2: investigation of buddy vs pedometer to increase physical activity in the elderly; 3: exercise, including use of prescriptions, in the rehabilitation of patients with heart failure; 4: development of interventions to prevent the development of obesity in minority children

### **Key theme investigators**

Dr G. Neil Thomas (Theme lead) has worked extensively investigating environmental and genetic determinants of obesity-related disease, particularly in Chinese populations, as well as instigating novel lifestyle and pharmacological approaches in the treatment of obesity and other vascular disease risk factors. He is closely involved in conducting a number of cohort studies of chronic disease, in particular obesity, and has established a treatment centre for obesity-related disorders in China to translate existing knowledge into improved patient care.

Dr Shahrad Taheri (Levels 3-4 obesity intervention) is the Director of the Obesity service at Heartlands Hospital, the largest and most comprehensive service in the UK. This presents an ideal opportunity to instigate novel therapeutic options into obese patient groups for treatment and the prevention of the onset of complications and to assess their prognosis.

Dr Paramjit Gill (Community based obesity interventions) has already been assessing the health impacts of obesity on a number of conditions including heart failure in ethnic groups. Dr Gill has access to the Midlands Research Practices Consortium (MidRec), which is a major primary care research network of over 500 practices within

the West Midlands who are actively involved in high quality, externally peer-reviewed and funded research. This presents an ideal platform to take high quality intervention studies directly into the community.

Dr Peymane Adab (Childhood obesity interventions) has extensive experience in conducting large-scale, complex, school-based interventions targeting lifestyle patterns relating to obesity in children both locally (focusing on south Asians) and internationally. The children taking part in these studies are generally healthy, and part of the community. This provides an opportunity to extend follow up after the intervention and establish a community cohort to further understand the determinants and aetiology of obesity and related morbidities.

Professors KK Cheng and AH Barnett, the principle investigators of the existing cohort data in Chinese and both Caucasian and South Asian populations, respectively, will play an integral advisory role, as well as providing access and support for the existing cohorts.

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