Igniting our potential

Health Research Classification System Coding Examples

Identifying the main aim

Identification and mapping of osteoporosis genes in the general population by DNA pooling

Osteoporosis is a common disease with a strong genetic component characterised by reduced bone mineral density (BMD) and an increased risk of fragility fractures. The molecular-basis of osteoporosis is incompletely understood, but current evidence suggests that susceptibility is influenced by the combined effects of several genes. Linkage disequilibrium mapping (LD mapping) using DNA pooling is a novel and potentially powerful tool for fine mapping of loci for polygenic diseases such as osteoporosis. In preliminary studies we successfully used DNA pooling to fine map a candidate locus for regulation of BMD on chromosome 1p36. We now wish to explore the possibility that LD mapping may be used to characterise other candidate loci for regulation of BMD and identify the genes responsible. We will prepare DNA pools from individuals with high and low BMD and use these to fine map candidate loci which have been implicated in the genetic regulation of BMD by previous linkage studies. Positional candidate genes within these regions will then be screened to identify the casual mutations and polymorphisms. These studies will advance knowledge about the genetic basis of osteoporosis and offer the prospect of identifying novel genes which are involved in the regulation of BMD. This information will be of clinical value in fracture risk assessment and in identifying new molecular targets for anti-osteoporotic therapies.

Title can be a good summary of main aim

Background information

The past

Lifetime of award

The future

Aim

Identification and mapping of osteoporosis genes in the general population by DNA pooling

Osteoporosis is a common disease with a strong genetic component characterised by reduced bone mineral density (BMD) and an increased risk of fragility fractures. The molecular-basis of osteoporosis is incompletely understood, but current evidence suggests that susceptibility is influenced by the combined effects of several genes. Linkage disequilibrium mapping (LD mapping) using DNA pooling is a novel and potentially powerful tool for fine mapping of loci for polygenic diseases such as osteoporosis. In preliminary studies we successfully used DNA pooling to fine map a candidate locus for regulation of BMD on chromosome 1p36. We now wish to explore the possibility that LD mapping may be used to **characterise other candidate loci for regulation of BMD and identify the genes responsible.** We will prepare DNA pools from individuals with high and low BMD and use these to fine map candidate loci which have been implicated in the genetic regulation of BMD by previous linkage studies. Positional candidate genes within these regions will then be screened to identify the casual mutations and polymorphisms. These studies will advance knowledge about **the genetic basis of osteoporosis** and offer the prospect of identifying novel genes which are involved in the regulation of BMD. This information will be of clinical value in fracture risk assessment and in identifying new molecular targets for anti-osteoporotic therapies.

Aim
To characterise genes involved in the development of osteoporosis

HRCS Coding

Health Categories
Musculoskeletal - 100%

Research Activity Codes
2.1 Aetiology - 100%

M1

Over two years for an investigation of the sarcoplasmic reticulum in human myometrium.

This project will increase our knowledge of the sarcoplasmic reticulum (SR) in human myometrium. Ultimately this may help in the treatment or prevention of pre-term or difficult term labours. Studies on animal uterus have shown that Ca2+-induced Ca2+ release from the SR may not be functionally significant. Rather, the SR may release Ca2+ spontaneously when Ca2+-loaded, which activates membrane ion channels thus altering excitability. Both Ca2+-activated K+ (K+Ca) and Cl- (Cl-Ca) are expressed in the uterus. I will determine in single cells the effects of altering SR function on these currents. In intact myometrial preparations, I will also determine the functional effects of these manoeuvres. The role of the SR in sequestering Ca2+, via the SR Ca-ATPase, and contributing to relaxation is largely unexplained in human myometrium. We have developed methodology for making simultaneous measurements of changes in cytosolic and SR [Ca2+] in uterine myocytes. Using this new approach, I will investigate the changes in SR and cytosolic Ca2+ during agonist - induced and spontaneous Ca2+ transients. This will provide much new data and advance our understanding of the role of the SR in excitation and relaxation of the uterus

Aim
To study the normal biology of the uterus

Website Links

Pregnancy Underpinning

HRCS Coding

Health Categories
Reproduction - 100%

Research Activity Codes
1.1 Underpinning - 100%

M2

Regulation of macrophage function by Th2 cytokines in atherosclerosis.

Cardiovascular disease is the leading cause of death in the UK. The underlying cause of angina, myocardial infarction and cerebral stroke is the development of atherosclerotic lesions in the major arteries. Monocytes bind to activated endothelium and differentiate into macrophages which endocytose modified low density lipoprotein (LDL) to form lipid-laden foam cells. Continued recruitment of mononuclear cells including CD4+ T cells into the atheromatous lesion leads to the development of complex atherosclerotic plaques.

The aim of this project will be to determine the role of the Th2-type cytokines Interleukin-4 (IL-4) and Interleukin-13 (IL-13) in regulating macrophage function in atherosclerosis 1. We want to test the hypothesis that the Th1/Th2 cytokine balance within atherosclerotic lesions critically affects cardiovascular disease progression. For these studies we will use animals that are defective in the IL-4 receptor alpha chain which can not respond to either IL-4 or IL-13.

This programme of research will offer new insights into the pathophysiology of atherosclerosis. Specifically, we hope to identify key components of the host immune response that modify the development of atherosclerotic lesions. These experiments may identify new targets for drug design or suggest new therapeutic approaches to cardiovascular disease.

Aim
To study biological factors involved in the cause and development of a circulatory disorder

Website Links
Inflammatory & Immune Atherosclerosis

HRCS Coding

Health Categories
Cardiovascular - 100%

Research Activity Codes
2.1 Aetiology - 100%

M5

Life-course Persistent Antisocial Behaviour

Objective: The proposed research programme aims to build knowledge about life-course persistent antisocial behaviour. Offenders having this disorder account for the bulk of violence. Hypotheses address: (a) developmental etiology, (b) how persistent antisocial behaviour is expressed in family life and the workplace, (c) how persistent antisocial behaviour is related to personality disorders, drug and alcohol dependence, and major mental disorders, (d) whether persistent antisocial behaviour leads to poor physical health, (e) how parental antisocial behaviour affects children. Methods: A birth cohort will be used. Analyses will ascertain relations between the study members antisocial status and variables drawn from extensive data gathered over many years about study members, their parents, their partners, and now their children. Significance: The proposed research will generate (a) disconfirming or supportive tests of our published theory of antisocial behaviour, (b) recommendations for tailoring the timing and content of interventions to fit offenders developmental histories, (c) documentation of the full scope of the health burden of antisocial behaviour, (d) information about the co-incidence of adult life problems for coordinating disparate service-delivery systems, (e) knowledge about origins of family violence, which can be used for prevention of partner and child abuse

Aim
To study the psychological/social determinants of a behavioural disorder

Website Links
Mental Health Cohorts (2.4)

HRCS Coding

Health Categories
Mental Health - 100%

Research Activity Codes
2.3 Aetiology - 100%

M6

Randomised controlled trial of the effectiveness of a schools-based, peer-led smoking intervention

The intervention to be evaluated is a 'diffusion of innovation' approach to reducing teenage smoking prevalence, an approach previously used successfully to promote HIV-risk reduction. An earlier feasibility study of two intervention and two control schools indicated an impact on smoking uptake in Year 8 pupils. The intervention is being further modified following the experience of the feasibility study. This proposal aims to assess the intervention's effectiveness in a cluster randomised controlled trial, with 33 schools in each arm of the trial. Control schools will be offered a conventional, classroom-based anti-smoking package. Smoking behaviour will be monitored for two years post-intervention by self-report data and by cotinine testing of saliva samples. If no intervention effect is observable at one year post-intervention, then the trial will be terminated early. A process evaluation and a health economics evaluation will also be undertaken.

Aim
To test an intervention to modify behaviour and prevent uptake of smoking

Website Guidance
Smoking
Trials
Economic evaluation

HRCS Coding
Health Categories
Cancer - 25%
Cardiovascular – 25%
Respiratory – 25%
Stroke – 25%
Research Activity Codes
3.1 Prevention - 100%

M7

Molecular profiling of epithelial ovarian and breast cancer with simultaneous cDNA and CGH microarrays

Advances in cDNA microarray technology now make it possible to rapidly determine the expression ratios of thousands of genes within a single cancer. Analysis of these large data sets can discover clusters of gene expression patterns that may determine new cancer classifications or prognostic information. However, none of these studies have validated the candidate genes on large independent sample sets. This proposal sets out to improve the current approach to expression profiling by 1) tightly integrating expression analysis with array CGH; 2) developing robust RNA amplification methods for expression analysis from microscopic biopsies; and 3) using tissue microarrays for high-throughput validation of candidate markers. These techniques will be used in two stages: 1) To carry out pilot projects that will investigate a series of platinum-resistant ovarian cancers and high risk breast cancers to identify candidate clusters for prognosis. 2) To validate the predictive value of smaller subset of markers from these clusters, using tissue microarrays of tumours from patients in phase III clinical trials. The validated markers should have high utility of routine pathological assessment of patient material.

Aim
To discover **and** evaluate biological markers with predictive value for ovarian and breast cancer

Website Guidance
Biomarkers
Methodology

Coding

Health Categories
Cancer - 100%

Research Activity Codes
4.1/4.2 Detection & Diagnosis - 50%/50%

M8

Scanning for cystic fibrosis

Hyperpolarized 3-Helium MR is a novel technology that combines static imaging of the airways with real time dynamic information on gas inflow together with regional information on airspace size and oxygen uptake. It has the ability to relate structural change to function and may prove to be a more sensitive methodology to evaluate lung function and extent of disease than existing imaging techniques. 3-Helium MR has been performed safely in young patients with asthma and in a few patients with cystic fibrosis. We will perform 3-Helium MR scans on a cross-section of 20 patients with cystic fibrosis (CF). This pilot study will establish the feasibility, reproducibility and safety of the technique in CF and correlate results with conventional methods of assessment. Subjects will be chosen from both paediatric and adult CF units to ensure a wide age range and reflect disease of varying severity. Data from this pilot study will form the basis of future clinical applications of the technique to assess the impact of neonatal screening on lung disease and the efficacy of new therapies in cystic fibrosis

Aim
Pilot study in patients to evaluate a new diagnostic monitoring technology for cystic fibrosis

Website Guidance
Congenital Screening

HRCS Coding

Health Categories
Congenital - 100%

Research Activity Codes
4.2 Detection & Diagnosis – 100%

M9

Molecular mechanisms of steroid efficacy in inflammatory bowel disease.

Crohn's disease and ulcerative colitis are common causes of gastrointestinal morbidity in the developed world. Gluco-corticosteroids remain the mainstay of treatment for active disease, in spite of real problems associated with drug toxicity, and efficacy.

The molecular mechanisms involved in steroid efficacy in the gastrointestinal tract remain poorly characterised, although recent data implicate multi-drug resistance (P-glycoprotein 170) gene expression (MDR), gluco-corticoid receptor expression, together with allelic variation in a number of key immunoregulatory genes.

We aim to document the molecular mechanisms underlying steroid efficacy in the gastrointestinal tract.

Using a rat model, the effect of circulating gluco-corticoids in modulating gene expression in the gastrointestinal tract will be investigated. Expression of MDR genes, gluco-corticoid receptor genes, alpha and beta, and transcription factor expression/activity will be investigated in steroid treated animals, animals which have undergone adrenalectomy, and sham-operated animals. .

Gene expression in the human gastrointestinal tract will be investigated using samples taken from healthy controls, and samples from patients with active ulcerative colitis, both steroid responsive and non-responsive.

Aim
To study, in model systems and patient samples, the mechanisms of action of steroid drug therapy for Crohn's disease

Website Links
Pharmacogenetics

HRCS Coding

Health Categories
Oral and Gastro - 100%

Research Activity Codes
5.1 Treatment Development – 100%

M10

The potential of retinal stem cell transplantation in attenuating retinal dystrophic disease.

The primary objective of this project is to generate immortalised human foetal retinal progenitor (stem) cells and to evaluate their potential to integrate and differentiate into photoreceptors in the adult rat retina. Stable immortalised clonal cell lines expressing various fluorescent reporter proteins will be generated and thoroughly characterised in vitro prior to transplantation into the normal and lesioned rat retina. Using state-of-the-art non-invasive high resolution in vivo imaging techniques graft survival, integration and differentiation will be evaluated in real time in both control retina and following co-transplantation of encapsulated cells secreting known soluble differentiation factors.

Aim
To develop a stem cell line for potential therapeutic application in the retina and test it in a model system

Website Guidance
Stem cells

HRCS Coding

Health Categories
Eye - 100%
Research Activity Codes
5.2 Treatment Development – 100%

R2A

Randomised controlled trial of the use of three dressing regimens in the management of chronic ulcers of the foot in diabetes

The study is determining the comparative effectiveness of older and newer dressing preparations in an observer-blind, parallel group, randomised controlled trial. Three dressings are being assessed: 1.a simple, non-adherent traditional preparation (NA), 2. a widely used antiseptic preparation (Inadine), 3.a modern hydrofibre (Aquacel). The primary endpoint will be complete healing at 24 weeks. Secondary outcomes include costs, taking into account the cost of dressings, dressing frequency and professional costs. As professional time is partly determined by the frequency with which dressings are undertaken by the patient and/or their carer, this will be formally assessed - as will aspects of patient, pain, satisfaction and health-related quality of life. The completion of this study will provide clinical data for three dressings used in routine clinical use, using clinical and patient relevant endpoints.

Aim
Clinical test of a new dressing treatment for foot ulcers resulting from diabetes

Website Guidance
Sequelae
Quality of life

HRCS Coding

Health Categories
Metabolic - 50%
Skin – 50%
Research Activity Codes
6.3 Treatment Evaluation - 100%

M11

Antidepressant drug therapy vs a community-based psychosocial intervention for the treatment of moderate postnatal depression: a pragmatic randomised controlled trial (RESPOND)

The study will compare the effectiveness and cost-effectiveness of antidepressant drug therapy versus a community-based psychosocial intervention (Health Visitor delivered non-directive counselling) in the treatment of moderate postnatal depression. A two arm multi-centre pragmatic randomised controlled trial, with randomisation at the level of the individual woman, is proposed. Women who do not respond to the allocated therapy in their group will be offered the opportunity to either switch or combine therapies after the primary outcome has been measured (4 weeks for antidepressants, 18 weeks for counselling). Thus the research design allows women to receive both antidepressants and psychological therapy if required. In addition, the protocol allows for the dose of antidepressant to be increased or for a different drug to be prescribed. The primary outcome measure is the EPDS at 4 weeks, 18 weeks and 44 weeks. In addition, we will use the SF-36 as a generic measure of functional quality of life and the EQ5D for economic analysis.

Aim
Clinical comparison of drug therapy and psychological therapy for treatment of depression following birth

HRCS Coding

Health Categories
Mental Health - 50%
Reproduction - 50%

Research Activity Codes
6.1/6.6 Treatment Evaluation - 50%/50%

M12

The psychosocial impact of dysarthria on the individual and their carers

Dysarthria, a communication impairment, is experienced by approximately 20 – 30% of individuals in the early stages of stroke. There is little indication of what the impact of dysarthria is on the individual and their carer post stroke. The literature to date has focused primarily on the pathology and impairment elements of the disorder, which has supported the development of a range of impairment focused speech and language therapy interventions, whose success, in turn, is evaluated using impairment focused measures. We propose to develop an understanding of the impact of post stroke dysarthria by working with the patients and carers, specifically focusing on their experiences of participation (including barriers and support) within family, social and community circles. This research will facilitate the development of patient focused functionally relevant outcome measures that will in turn encourage the expansion (and evaluation) of therapeutic interventions that address participation focused patient/carer identified priorities.

Aim
To study needs and social impact in patients with communication impairments as part of a stroke

HRCS Coding

Health Categories
Stroke - 100%

Research Activity Codes
7.1 Disease Management - 100%

M13

Doctor-patient communication and physical examination in Upper Respiratory Tract Infections in primary care consultations

Aims: Consultations for upper respiratory tract infections (URTIs) in primary care take place in potentially difficult contexts. URTI illness is vaguely defined, and there is contested legitimacy for consulting with 'minor' illness. Doctors face dilemmas in consultation such as regulating demand for services and prescription of antibiotics. These factors provide contexts for interaction which may mean that communication between doctors and patients consulting with URTIs is problematic. I am using techniques of discourse analysis to ask:

How well does communication go in consultations for URTIs ?

Are there problems in communication, and if yes, what are their nature ?

What are the sources of communication problems ?

Methods: Qualitative approach

Consultations have been video recorded and doctors and patients interviewed afterwards.

Dialogue in consultation will be analysed by drawing on some of the principles of conversation analysis. Interview data will be analysed thematically and using socio-linguistic discourse analysis.

Aim
Study of doctor patient consultations for upper respiratory tract infection

Website Guidance
Case studies

HRCS Coding

Health Categories
Infection - 100%

Research Activity Codes
7.3 Disease Management - 100%

M15

Pharmaceutical care for elderly patients shared between community pharmacists & GP's a randomised evaluation

This project aims to investigate the effectiveness and cost implications of "pharmaceutical care" provided by community pharmacists to elderly patients in the community. The study design is a randomised multiple interrupted time series. We will recruit five general practices each associated with one to three community pharmacies from each of the four PCGs in the East Riding - 20 practices and about 40 pharmacies in all. 7- patients will be recruited. We shall randomise the resulting four groups of practices, pharmacies and patients to begin pharmaceutical care in four successive phases. All four will be controls until they receive the intervention in a random sequence. The community pharmacists will receive training in pharmaceutical care for the elderly. Once trained, they will meet recruited patients either in the pharmacies (in a consultation room or dispensary to preserve the patient's confidentially) or at home, in order to identify the drug-related problems, and design the "pharmaceutical care plan" in conjunction with both the GP and the patient. Pharmacists will implement, monitor, and update the plan. Until they receive process. The primary outcome measure is the Medication Appropriateness Index; secondary measures are quality of life, compliance, adverse events and patient knowledge. We shall also investigate the cost of treatment to the NHS, to patients and to society as a whole.

Aim
To evaluate delivery of services by community pharmacies

HRCS Coding

Health Categories
Generic - 100%

Research Activity Codes
8.1 Health Services - 100%

M16

Application of Modeling Techniques and Analysis of Uncertainty in the economic evaluation of health technologies

To investigate the areas of application of different modelling techniques in economic evaluations of health technologies, methods of models allocation and analysis of uncertainty in the economic evaluations

Methodology: Various techniques and (Decision trees, Markov models, Discreet Event Simulations; Neural Networks) to be applied in order to extrapolate, synthesise and/all analyse he available evidence in the most appropriate way and to inform the healthcare decision making. This have three main focuses:

1 Aspects of models validation in economic analysis - no explicit criteria for moral validation exists. Aspects of validation by using part of the primary data comparing the results with those from other studies and comparing the results from different models have been used.

2 The social welfare function, health costs cared decision makers (loss) function and their optimisation. - the social policy objective is to maximise the social welfare. Similar to all other policy areas the healthcare decision makers have the problem to identify the actual social way of welfare function even if only healthcare benefits are concerned. The main area interests are the solicitation of public views on the aspects of efficiency and equity and their application in the decision-making.

3 Analysis of uncertainty and the application of probabilistic sensitivity analysis to address uncertainty in the economic evaluations in the context of health care decision-making. - The use of prompt probabilistic sensitivity analysis to analyse the joint uncertainty in parameters is highly valued but its application in economic evaluations is still underdeveloped. Some of the areas of further research are the end of analysis of parameter uncertainty, then interaction and the inference based on Monte Carlo Simulations.

Aim
To evaluate different economic models for assessing cost effectiveness of health technologies

Website Guidance
Methodology
Economic Evaluation

HRCS Coding

Health Categories
Generic - 100%

Research Activity Codes
8.2 Health Services - 100%

M4

THE PEOPLE'S DNA BANK: a national DNA banking and genotyping facility

The objective of this project is to facilitate current and future work of investigators in the discovery and evaluation of associations between human disease phenotypes and genotypes. The aim of this project is to store safely and make widely available 13 case-control collections; to provide capacity to house and to make available other collections; and to improve access to high throughput genotyping at many loci. These aims and objectives will be achieved by collaborations. The principal umbrella organisation for this will be the People's DNA Bank (PDB). Scientifically, this bank will be directed collaboratively by investigators who deposit their samples in the bank. Operationally, we will develop, run and maintain integrated and flexible facilities for the receipt, processing and storage of subject samples; for DNA extraction, DNA amplification and genotyping; and for database management. Investigations will be undertaken into improvements in biological and biochemical amplification of genomes.

Aim
To establish a resource for wide use by the research community

Website Guidance
Resources and infrastructure

HRCS Coding
Health Categories
Generic - 100%
Research Activity Codes
1.5 Underpinning - 25%
2.6 Aetiology – 25%
4.5 Detection – 25%
5.9 Treatment – 25%


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