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

Coding based on main research 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

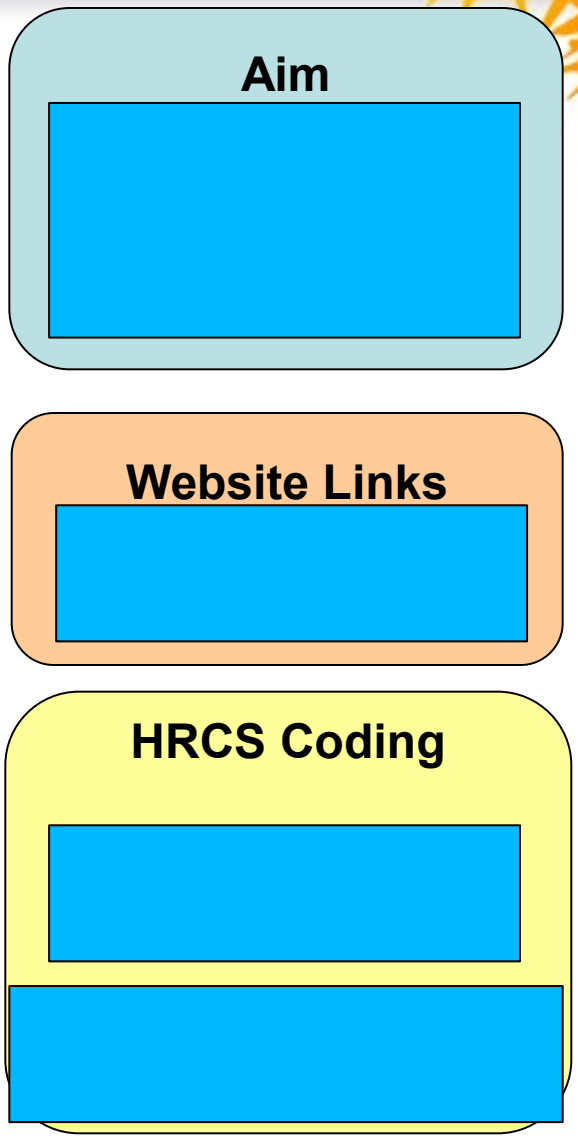
Website Links

HRCS Coding

M5

Life-course Persistent Antisocial Behaviour

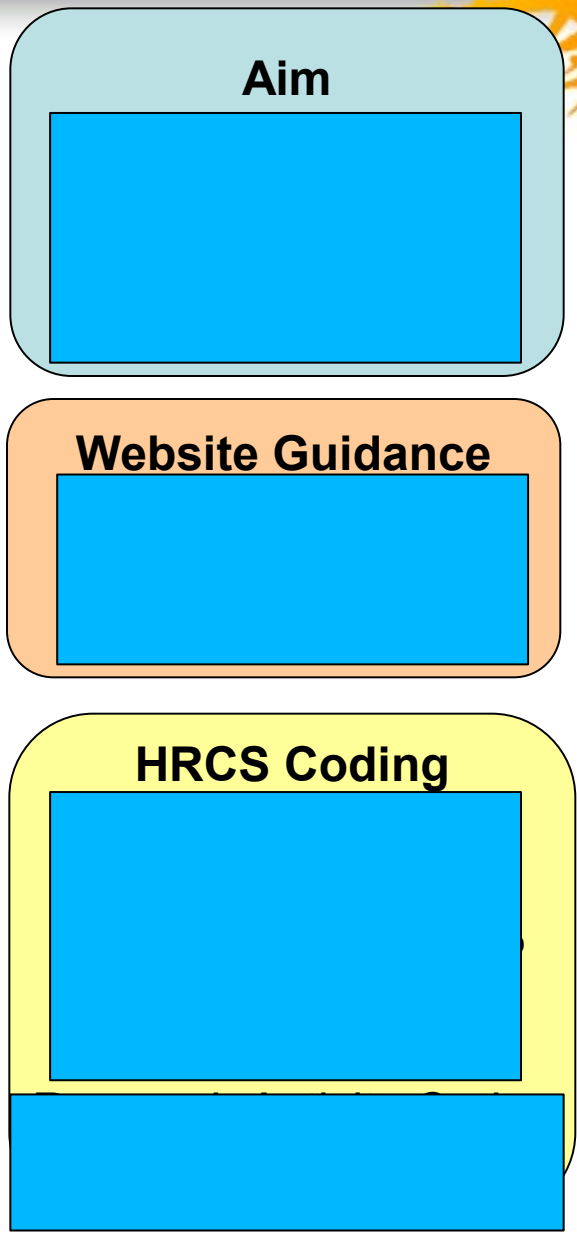
Objective: The proposed research programme aims to build knowledge about life-course persistent antisocial behaviour. Offenders having this disorder account for the bulk of violence. Hypotheses address: (a) developmental etiology, (b) how persistent antisocial behaviour is expressed in family life and 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



M6

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

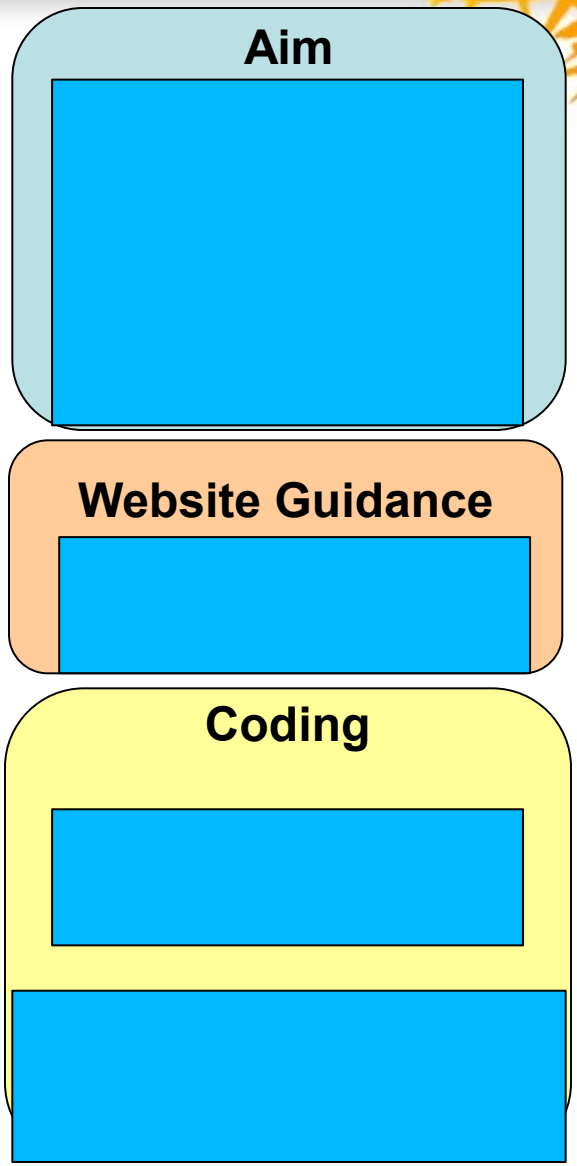
The intervention to be evaluated is a 'diffusion of innovation' approach to reducing teenage smoking prevalence, an approach previously used successfully to promote HIV-risk reduction. An earlier feasibility study of two intervention and two control schools indicated an impact on smoking uptake in Year 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.



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.



M9

Molecular mechanisms of steroid efficacy in inflammatory bowel disease.

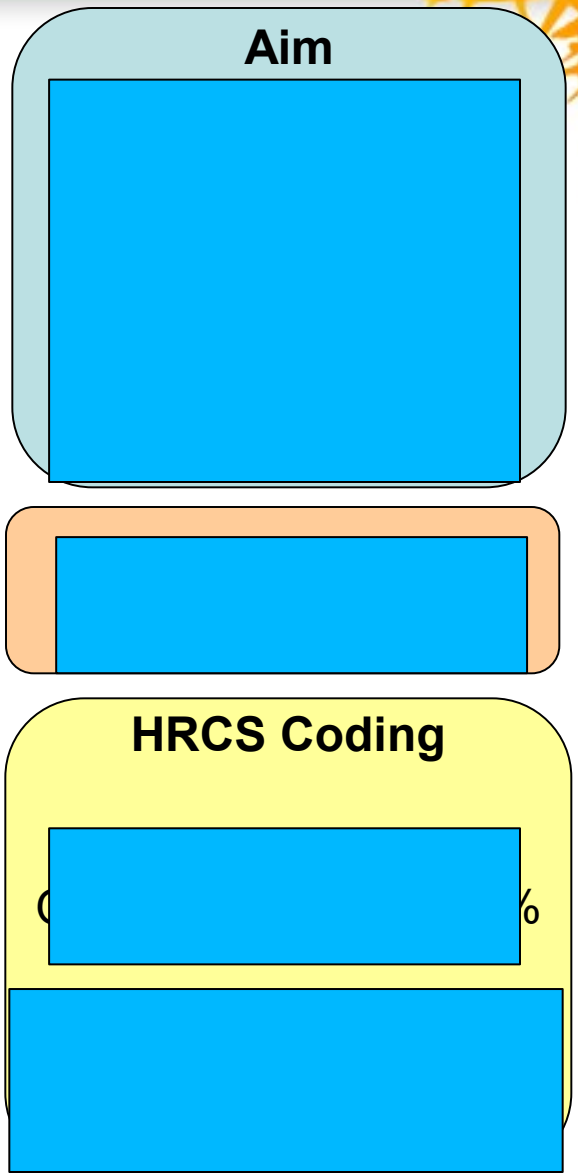
Crohn's disease and ulcerative colitis are common causes of gastrointestinal morbidity in the developed world. Gluco-corticosteroids remain the mainstay of treatment for active disease, in spite of real problems associated with drug toxicity, and efficacy.

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. .

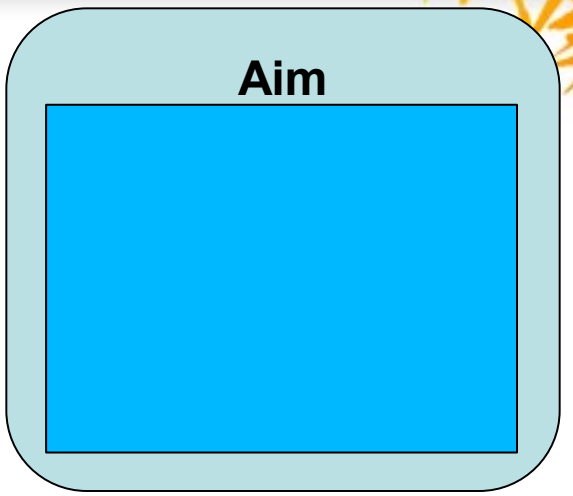
Gene expression in the human gastrointestinal tract will be investigated using samples taken from healthy controls, and samples from patients with active ulcerative colitis, both steroid responsive and non-responsive.

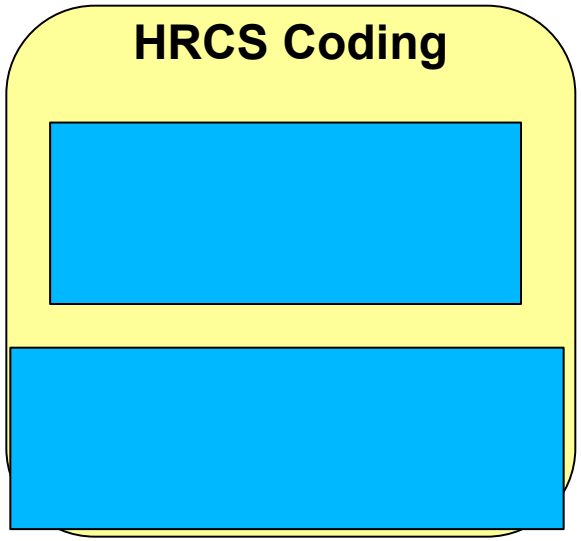


M11

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.





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 ?

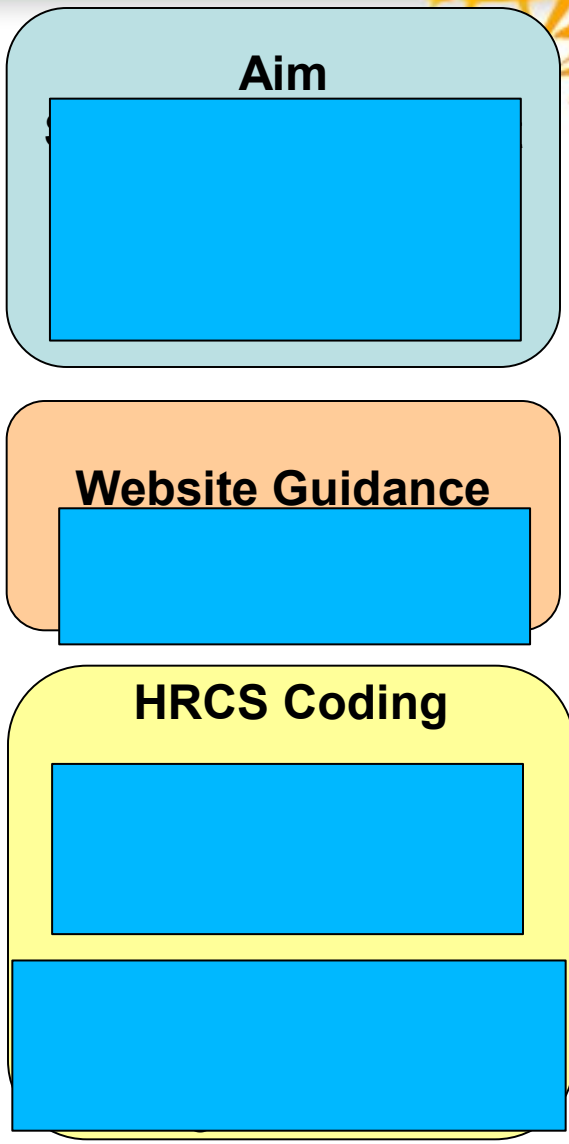
Are there problems in communication, and if yes, what are their nature ?

What are the sources of communication problems ?

Methods: Qualitative approach

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

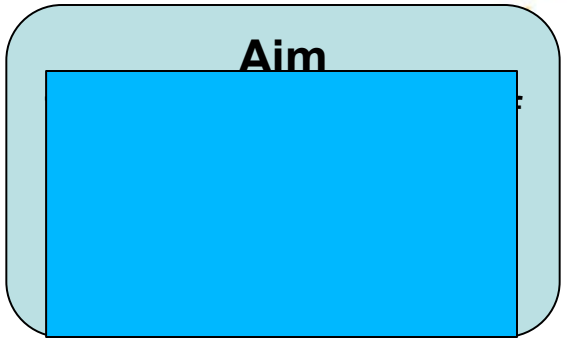
Dialogue in consultation will be analysed by drawing on some of the principles of conversation analysis. Interview data will be analysed thematically and using socio-linguistic discourse analysis.

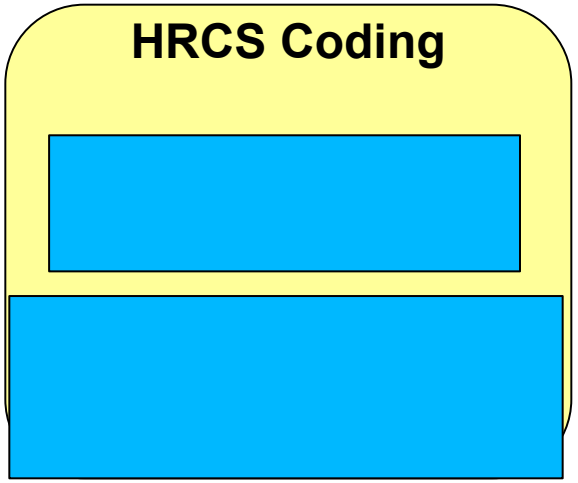


M15

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.





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