PATIENTS FREQUENTLY REFERRED FROM PRIMARY CARE TO HOSPITAL OUTPATIENT CLINICS FOR MEDICALLY 'UNEXPLAINED' SYMPTOMS

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DECLARATION

I declare that I wrote this thesis and conducted the research outlined under supervision. This work has been submitted only for the degree of Ph.D.

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LIST OF ABBREVIATIONS

A&E	Accident and Emergency Department
AHP	Allied Health Practitioners
ASD	Abridged Somatisation Disorder
ANS	Autonomic Nervous System Questionnaire
CBT	Cognitive Behavioural Therapy
CI	Confidence Interval
DNA	Did Not Attend (a consultation)
DSM	Diagnostic and Statistical Manual of Mental Disorders (III - 3rd Edition, IV - 4th Edition, V - 5th Edition).
ECA	Epidemiological Catchment Area surveys
ED	Emergency Department
ENT	Ear, Nose and Throat (Outpatient clinic)
FA	Frequent Attenders
FR	Frequently Referred (Three or more referrals)
FRMES	Frequently Referred for Medically Explained Symptoms
FRMUS	Frequently Referred for Medically Unexplained Symptoms
FSS	Functional Somatic Syndromes (or symptoms)
GAD	Generalised Anxiety Disorder
GP	General Practitioner
GPSI	General Practitioner with a Specialist Interest
GPASS	General Practice Administrative System for Scotland
IBS	Irritable Bowel Syndrome
ICD-10	Tenth Revision of the International Classification of Diseases
IPQ	Illness Perception Questionnaire
IR	Infrequently Referred (once only)
IRS	Infrequently Referred for Symptoms
ISD	Information and Statistics Division of the NHS
LA	Low Attenders (to medical consultations)
LREC	Local Research Ethics Committee
MCS	Mental Composite Score (SF-12, v2)
MDD	Major Depressive Disorder

LIST OF ABBREVIATIONS (Continued)

MOPD	General Medicine (Outpatient clinic)
MUS	Medically 'Unexplained' Symptoms
N	Number
NHS	National Health Service
OPD	Outpatient Department
OOPD	Orthopaedics Outpatient Department
OR	Odd Ratio
PAC	Privacy Advisory Committee of ISD
PCS	Physical Component Score (SF-12, v2)
PHQ	Patient Health Questionnaire
SCAN	Schedules for Clinical Assessment in Neuropsychiatry
SCID	Structured Clinical Interview for DSM-IV
SD	Used both for Standard Deviation and Somatisation Disorder
SF-12 (v2)	Short Form Health Survey - 12 Item (version two)
SOPD	General Surgery (Outpatient clinic)
WI	Whitely Index

DEFINITIONS

For the purposes of this thesis:

Primary care: Community-based general medical care which is often the first point of contact for a patient with the health care system. Although this care may be provided by a community nurse, midwife or health visitor, this thesis is concerned with care provided by a General Practitioner (GP). For a more detailed definition of general practice and the role of the GP, see Olesen and colleagues(1). The terms 'primary care' and 'general practice' will be used interchangeably in this thesis.

Secondary care: Hospital-based specialist medical services. Patients generally access these health care services from primary care. Although this term also includes inpatient admissions, this thesis is particularly concerned with care provided in outpatient clinics. The doctors who work in this setting are referred to as 'specialists'.

Symptom: An individual's experience, or heightened awareness, of a change in bodily function or sensation.

Disease: the presence of an objective structural change in the body.

Medically 'unexplained' symptoms (MUS): If no bodily change can be observed or objectively measured by a medical specialist, then a symptom is classified as medically 'unexplained' by disease.

ABSTRACT

BACKGROUND

One third of frequent attenders to UK outpatient clinics have symptoms that are inadequately explained by disease according to specialist opinion (medically 'unexplained'). Some of these patients are frequently referred for similar symptoms to multiple specialties. The characteristics and treatment needs of these frequently referred patients are poorly understood.

AIM

The aim was to identify and describe patients frequently referred from primary care to hospital clinics for medically 'unexplained' symptoms (FRMUS) and compare them with patients frequently referred with medically explained symptoms (FRMES) and patients infrequently referred for symptoms (IRS).

HYPOTHESES

Compared to FRMES and IRS patients, a greater proportion of FRMUS patients would have anxiety or depression and this would be inadequately treated. Subsidiary hypotheses relating to: consulting multiple doctors, health care costs, perceived general health, satisfaction with care, and health beliefs, as well as the general practitioners' (GPs) expressed difficulty managing the patient, were also tested.

METHODS

The methodology employed for this study involved three phases as follows: (1) Identification of cases and controls from five Edinburgh general practices using a combination of National Health Service (NHS) referral data and primary care case notes. (2) A case-control study to describe and compare FRMUS patients with the two control patient groups. This comprised a questionnaire survey of GPs and

patients, and a lifetime case note review for a 15% random selection of FRMUS and FRMES participants. (3) An economic analysis of the health care contacts.

RESULTS

FRMUS patients made up 1.1% (293/26252; CI 0.01-0.013) of the primary care population aged 18-65 years, and nearly two thirds (218/293, 74.4%) were female. The FRMUS patients had statistically more anxiety (67/193, 34.7%) when compared to 37 of the 162 FRMES (22.8%, OR 1.8, CI 1.12-2.88) and 23 of the 152 IRS (15.1%, OR 2.98, CI 1.75-5.09) comparison patient groups. Although there was no statistical difference for diagnoses of depression between the FR groups, the FRMUS patients had a significantly greater mean score for depressive symptoms than the FRMES control patients (mean difference 2.03, CI 0.66-3.41). Of the 67 FRMUS patients with an anxiety disorder 41(61.2%) were receiving adequate treatment, and this was considerably more than the six of 37 FRMES (16.2%, OR 8.147, CI 2.99-22.21) and the six of 23 IRS (26.1%, OR 4.47, CI 1.56-12.8) comparison patients who had an anxiety disorder. Treatment for those patients with depression was also significantly greater for FRMUS patients (43/64, 67.2%) compared with the FRMES (10/41, 24.4%, OR 6.35, CI 2.62-15.36) and IRS (5/21, 23.8%, OR 6.56, CI 2.11-20.32) groups. FRMUS patients were also more likely to: be female, reside in a deprived area of Lothian, referred by multiple doctors, have problems considered to be more difficult to help by a GP, have high health care costs, and report poor general physical and mental health.

DISCUSSION

A third of FRMUS patients had anxiety and depression, the majority of whom were receiving 'adequate treatment'. Factors other than undetected anxiety and depression may better explain why these patients are repeatedly referred to outpatient clinics for 'unexplained' symptoms.

INTRODUCTION

"Grief that has no vent in tears makes other organs weep"

H. Maudsley (1868) 'The Physiology and Pathology of the Mind'(2)

CHAPTER 1. BACKGROUND

SYMPTOMS

Physical symptoms are a subjective sensation of a change in normal body awareness or function. Symptoms are a *normal* phenomenon. Most people in the general community experience symptoms most days. Examples include tiredness, neck pain, bloating, headache, and so on.

The Oxford Dictionary(3) defines a symptom as *"a change in the body or mind which is the sign of disease"*. This definition highlights the contribution of both physical and mental processes that can bring about the experience of a symptom.

It is important to understand the extent that somatic[1] symptoms are present among healthy non-patient populations to provide a comparison for those in medical settings. A noteworthy study which provided prevalence data on symptoms in the community, as well as psychiatric and related disorders, was the Epidemiological Catchment Area surveys (ECA) in the United States(4). Using a multi-stage, random and clustered sampling technique provided a large epidemiologically sound sample of 13538 subjects who were interviewed. Subsequent analyses of the data by Kroenke's research group found that 10% of people surveyed had been bothered by 24 of 26 selected symptoms at some point in their life(5). The most common non-menstrual symptoms included joint pains (36.7%), back pain (31.5%), headaches (24.9%), chest pain (24.6%), arm or leg pain (24.3%), abdominal pain (23.6%), fatigue (23.6%), and dizziness (23.2%).

A cross-sectional survey conducted in the UK found an overall three-month headache prevalence of 70.3%, which rose to nearly 77% for women(6). The 1998 UK Omnibus Survey(7), found that 40% of adults had suffered back pain lasting more than one day in the previous 12 months(8). A similar study in Italy found a mean of 46.4% individuals reporting one or more gastrointestinal (GI) symptom(9). Sloane and colleagues(10) found that the prevalence of dizziness in the community ranged from 1.8% in young adults to more than 30% in the elderly.

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[1] Where somatic means physical; affecting or characteristic to the body

Although symptoms are prevalent in the community, they vary in frequency and intensity. Perception of, and reaction to, them depends on the individual. Some may shrug them off as a temporary bother. Others may self medicate e.g. take paracetamol for a headache. If a symptom is of concern or bother, individuals may seek a medical opinion. Unless an individual becomes a 'patient' by consulting a doctor, their symptoms remain unlabelled.

CONSULTATION AND PREVALENCE OF MEDICALLY UNEXPLAINED SYMPTOMS IN PRIMARY CARE

If individuals seek help for their symptoms, most will enter the health care system via their registered general practice(11). Physical symptoms are by far the most common reason for patients to consult a GP. In primary care, symptoms account for up to 73% of patient visits(12-14).

The usual procedure during a consultation is that the GP takes a medical history, i.e. asks patients questions about the symptom and their general health, and then examines the relevant area of the body. Investigations may also be ordered with the aim to determine if there is any disease.

The response of GPs to manage these symptoms may simply be to reassure the patient, or 'watch and wait'. They might decide to treat symptoms empirically or investigate further. However, if the GP has cause for concern about the symptoms, or the patient is particularly anxious about them, the patient may be referred to a hospital outpatient clinic for a specialist opinion.

The prevalence of MUS depends on how this phenomenon is defined and which patient group is under study. Consequently, there is no definitive figure to be quoted. A range of prevalence figures from epidemiological studies have been published.

Kurt Kroenke's research team in Indianapolis have completed considerable research in the area of symptoms in primary care. One study found 140 of 1000 (14%) primary care patients had 'unexplained' symptoms(15). A later study by the same group found MUS in 600 of 6000 (10%) patients surveyed(16). A random sample of patient records for all visits made to a single primary care clinic during four one-month

periods were reviewed by physician raters. These raters classified nearly half (48%) of the symptoms as MUS. As many as 84% of symptoms studied in an American primary care population had no identifiable pathology(17).

A Danish primary care study found that 60.6% of patients had at least one 'unexplained' symptom(18). More locally, the lowest prevalence estimate of 1.1% (17/1492) of patients with unexplained physical symptoms (UPS) was provided by a pilot study conducted in a single general practice in Edinburgh(19). A cross-sectional survey of consecutive general practice attenders identified 25% to have MUS(20). Finally, a British study asked ten GPs to identify 'unexplained' physical symptoms as the main reason for patients to attend. GPs identified 19%, and the administration of screening instruments identified 35% of patients to have multiple MUS(21).

Prevalence rates of MUS or somatisation in primary care are wide ranging from as low as 1% and up to 84% of the population studied. A common figure quoted in the literature is that approximately one third of primary care patients present with MUS(22). MUS is a problem in primary care which makes up a substantial amount of the workload for GPs(23-26).

REFERRAL TO AND PREVALENCE OF MEDICALLY UNEXPLAINED SYMPTOMS IN SECONDARY CARE

Many of the symptoms seen by GPs are self-limiting. An important role of GPs is to identify and conservatively maintain patients with benign physical complaints in primary care. The term 'gate keeper' has been applied to GPs and their role of controlling patient access to expensive secondary care services(27;28).

A low percentage of somatic complaints presented to GPs end up being referred to hospital(29;30). A study of referrals for 'unexplained' bowel symptoms (irritable bowel syndrome, IBS) found GPs were more likely to recognise and maintain these patients in their practice rather than refer them to hospital(31). However, Carson and colleagues found that GP reasons for patient referral to neurology clinics were not associated with "organicity"(32). The inter-rater reliability between GP and neurology specialist diagnoses was also low.

Although rates of referral from primary to secondary care services are relatively low, studies have found high variation in GP referral rates(33-36). Patient deprivation has explained some of this variation(37). Although patient characteristics account for around 40% of the difference, variations in referral rates remain largely unexplained(38;39).

Hospital services are designed to diagnose and treat disease. Symptoms presented to hospital clinics are assessed to exclude physical disease. This may include invasive and expensive investigations such as colonoscopies or magnetic resonance imaging (MRI).

If no evidence of disease can be found after these assessments, the symptom remains medically 'unexplained' by disease. The patient may be sent to another specialist for a further opinion, but the majority are sent back to the GP to manage in their practice.

Reassurance (for patient and GP) is a less common reason for referral to hospital services, and these are usually for self-limiting or non-threatening problems(40;41). Even if this need for reassurance is explicit in the referral letter, studies have shown that this can be translated into something different as a result of the referral process. As an example, Warner and colleagues found that broad menstrual complaints were often reframed as excessive bleeding at referral(42). Their concern was that a number of women had received hysterectomies inappropriately as a consequence.

Somatisation and MUS have been linked with above average use of secondary health care services(43-45). Despite high health care attention, patient outcomes generally remain poor(46). This is partly because hospital services are designed to diagnose and treat disease, and if none is present, it is not surprising that disease management is ineffective. Ironically, as a result of often invasive procedures patients with MUS can be left with a medically induced problem (iatrogenesis), which may require further intervention(47-51). Prevalence estimates of MUS in secondary care have shown less variation compared to figures cited in primary care studies.

Prevalence of medically unexplained symptoms in outpatient clinics

Most studies of MUS in outpatient clinics have sampled from new or consecutively attending patients. Of 191 patients newly referred to a general medical outpatient

clinic, no medical diagnosis could be made in 58 (30%) patients, and 42 (22%) of the diagnoses remained uncertain(52). One third of new referrals to a Scottish neurology outpatient clinic had either completely 'unexplained' or 'somewhat explained' symptoms according to the assessing neurologist(32). New referrals to cardiology, gastroenterology and neurology clinics identified 35% of these to have functional diagnoses, whilst 5% remained undiagnosed(45). A study including seven outpatient specialities found that 51% were considered to have 'unexplained' symptoms following medical investigations. One of the largest studies reviewed three years of 1000 patient records from an internal medicine clinic. At least one symptom was reported for 38% of these outpatients, but organic aetiology was found in only 16% of them(17). Other than the latter figure from Kroenke's study, it seems reasonable to summarise from these prevalence estimates that approximately one third of symptoms in outpatients remain 'unexplained'.

Prevalence of medically unexplained symptoms in inpatient admissions

There have been few studies which have estimated the prevalence of MUS among hospital inpatients. Some of the earliest work, by De Gruy's group in Alabama (USA), reported a 9% prevalence in patients admitted to surgical and general medical wards of a teaching hospital(53).

A study by Creed and colleagues had two neurologists provide an 'organicity rating' of symptoms experienced by 133 females admitted to a neurology ward(54). Of the sample, 24% had symptoms that could not be explained by organic disease, and a further 35% had symptoms of doubtful organic significance. A later study used a similar methodology to assess 100 consecutive male and female admissions to a neurology ward, and found 40% to have MUS(55).

Per Fink used the national Danish computer register to identify members of the general population with 10 or more admissions over an eight year period(56;57). Half (50%) of the 282 hospitalised patients identified had 'unexplained' complaints.

Once determined as 'unexplained' by a specialist, MUS often persist, and an organic diagnosis is rarely determined. At the conclusion of a six year follow-up of 64 patients previously admitted with neurological MUS, only three (less than 5%) had new

organic neurological disorders diagnosed to fully or partly explain their initial symptoms(58).

FREQUENT ATTENDERS TO OUTPATIENT CLINICS FOR MEDICALLY UNEXPLAINED SYMPTOMS

Only two known published studies have identified a group of patients with MUS who re-attended outpatient clinics. The first study was of frequent attenders to gastroenterology clinics(59). A diagnosis was uncertain in 3% (23/762) of these patients, but 21% (159/762) had symptoms that were not at all associated with disease.

A second study looked at re-attendance to a range of medical outpatient clinics in London for MUS(60). 'Unexplained' symptoms were shown to be prevalent among high users, and the clinics associated with the most MUS presentations included gastroenterology (54%), neurology (50%), cardiology (34%), rheumatology (33%), and orthopaedics (30%)(60). This study indicated that the prevalence of MUS varies depending on the specialty.

By frequently attending hospital outpatient clinics, patients are more likely to have a number of tests performed in the search of a somatic diagnosis, which in the case of MUS is rarely found(61). Health care costs rise exponentially when patient care is transferred from primary to secondary care. Few studies have actually quantified the costs resulting from consultations, tests and procedures of patients with 'unexplained' symptoms(62;63). However, high using patients with 'unexplained' symptoms can cost up to nine times more than the average patient(64).

Patients who use hospital outpatient services have a greater 'risk' of being admitted for further investigation. A study of high users of inpatient hospital care showed this group represented 15% of all the patients hospitalised in one year. In terms of the total hospital bed days used, this patient group made up 54.4% overall(65). Although the majority of inpatients have the most severe and complex medical disease(66;67), a small proportion have no significant disease to warrant such intensive care.

Per Fink's study of 'persistent somatisers' found that 56 (50%) were persistently admitted (six or more admissions in eight years) for MUS(68). From a population

aged 17-49, the prevalence of 'persistent somatisation' equated to 0.6 per 1000 men and 3.2 per 1000 women. 'Persistent somatisers' were all aged less than 35 years and had been admitted to hospital for 'unexplained' complaints for up to 20 years prior to the study.

FREQUENT REFERRAL FROM PRIMARY TO SECONDARY CARE OUTPATIENT CLINICS FOR MEDICALLY UNEXPLAINED SYMPTOMS

Rather than frequent *attendance*, this thesis is concerned with patients who are frequently *referred* from primary care to hospital outpatient clinics for symptoms deemed by a hospital specialist to be medically 'unexplained'. Frequent attendance can involve the same care episode (e.g. a patient is asked to return for review by the specialist). Frequent referral in this research relates to the phenomenon of multiple symptoms, multiple GPs and multiple specialties.

There are many ways to study the phenomenon of medically 'unexplained' symptoms (MUS), and the patients who experience them. Some of the alternative approaches will be outlined in Chapter 4. However, I have chosen to study 'FRMUS' patients for the following reasons. Firstly, there is little research published on patients who are frequent attenders in secondary care, and no known study about patients frequently referred. Secondly, secondary care attendance is usually assessed in secondary care settings, but this does not advise on why this occurs from the primary care perspective.

In the UK, GPs make most of the patient referrals to hospital services. However, it is the decision of hospital doctors or specialists to send the patient back to the GP or to keep them in the secondary care system for review or admission. The patient consults both primary and secondary care services, but the interactions between the three (GP, patient and hospital doctor) are poorly understood.

Identification of patients from their health service use is a practical approach. Frequent referral (FR) from primary to secondary care provides an indicator of difficulty managing the symptoms in primary care and high health care costs. Specialist opinions that symptoms are 'unexplained' indicate a mismatch with disease-based management.

CHAPTER 2. MEDICALLY 'UNEXPLAINED' SYMPTOMS (MUS)

The concept of what MUS actually are is complex, and currently there is no consensus as to what the appropriate term is to describe them, let alone how they should be defined and operationalised for study. In this chapter, I shall attempt to summarise what is already known about MUS. This begins with a brief overview of some historical perspectives of dualism (the mind-body problem). Terminology, definitions and approaches to identifying and studying MUS in current circulation will be discussed. It is important to understand each of the various definitions adopted by researchers, as these determine which patient groups have been studied and in turn how prevalent MUS are in that particular study population. I have also outlined my own working definition for MUS at the conclusion of this chapter.

HISTORICAL PERSPECTIVES OF DUALISM

Around 360BC, Plato was perhaps the first to contend that the soul was distinct from the body and capable of maintaining a separate existence from it. He asserted that if any one of the three parts of the soul (appetite, spirit, and reason) became inactive, this would bring about an imbalance and result in ill health; for example the war within the soul between reason and desire(69). In contrast, Aristotle argued that body and soul were two aspects of the same underlying substance (form and matter)[2]. From the perspective of Christian writers, such as St. Paul to the Corinthians, they too were puzzled by the Platonic conception of the soul (or psyche) as separate and independent from the body as this went against the Jewish teachings of the person as a unity(70). It was along these lines that Thomas Sydenham took the view of hysteria which realised a range of illness and included a mental component. His view was that all activity lay in the nervous system, and that physiological forces brought about the mental symptoms of disease. This approach related to the person as a whole, with the body and mind interacting with one another to bring about illness(71).

[2] It should be noted that it is by no means unanimous that Aristotle was not a dualist.

Rene Descartes is most famous for implementing a dichotomous view of mind and the body dualism in the 1600s(72). He disagreed with Plato, and felt that the soul was one entity with no different parts. Descartes' main contribution was to exclude the soul from the scope of physical enquiry. He purported that the body and mind (or soul) were separate; a patient's symptoms were due to either physical illness or mental illness, not a combination of both. The dualistic approach asserts that a symptom is deemed to be 'unexplained' if no physical disease, structural change or substance can be objectively identified. This view advocates that there are mind illnesses and body illnesses. Even into the 21st century, this black and white dichotomy has continued in the practice of medicine(73). Most in medicine would agree that separating the mind and body does not aid the understanding of psychosomatic issues and should not be a part of any diagnostic classification. However, the separation persists, and some would give the classifications in the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association, Fourth Edition (DSM-IV) as an example of this persisting dualism in medicine(74).

TERMINOLOGY AND DEFINITIONS RELATED TO THE CONCEPT OF MEDICALLY UNEXPLAINED SYMPTOMS

Differing terminologies have hampered research in the field of MUS. Alternative terms used in the literature include: functional somatic symptoms or syndromes (FSS), idiopathic physical symptoms, conversion disorder, somatisation, somatoform disorder, hypochondriasis, psychosomatic illness, abnormal illness behaviour, neurasthenia, alexithymia, hysteria, and Briquet's syndrome. There are some subtle differences in these terms, and the definitions of each are outlined below.

Abnormal illness behaviour was a term developed by Issy Pilowsky(75). She put forward that this described the reactions of patients to symptoms that seemed out of proportion to the presence of any disease.

Alexithymia is a disruption of both affective and cognitive processes, where individuals have difficulty identifying and describing feelings. It is also the inability to distinguish between feelings and the bodily sensations of emotional arousal(76). Although initially described in the context of psychosomatic illness, alexithymic characteristics

may be observed in patients with a wide range of medical (e.g. stroke) and psychiatric disorders. As such, it is not appropriate to use this term interchangeably with MUS.

Briquet's syndrome is now more commonly known as somatisation disorder. This syndrome referred to patients who presented with numerous symptoms in a number of organ systems and who visited several different doctors. Patients studied with Briquet's syndrome tended to have high rates of surgery and inpatient admissions(77).

Conversion disorder is classified as one of the somatoform disorders in the DSM-IV. It is defined as the alteration or loss of physical function presumed to be the expression of an underlying psychological problem.

Functional somatic symptoms, syndromes (FSS) or disorders were originally thought to have been caused by some sort of lesion of the nervous system according to the French neurologist, Charcot(78). Since then, term 'functional' has been approached using two different schools of thought; the first to relate to a disturbance in bodily functioning, and the second to describe general psychiatric illness. Trimble(79) advocated the emphasis on the physiological use of the term i.e. an alteration of function rather than of structure. In terms of functional somatic syndromes, a substantial overlap (i.e. in symptoms and case definition) exists between the individual syndromes, and similarities between them outweigh the differences(80).

The core features of *hypochondriasis* are preoccupation with symptoms and the fear or belief of having a serious disease. This is also categorised as a somatoform disorder in the DSM-IV due to excessive focus on bodily symptoms for a period of at least six months. Both the DSM-IV and the Tenth Revision of the International Classification of Diseases (ICD-10) classification systems define hypochondriasis as a chronic condition that is distinct from anxiety and depressive disorders. However, a contemporary view is that hypochondriasis represents an intense form of health anxiety, and recent evidence has shown that anxiety and/or depressive disorders are significantly associated with both onset and persistence of hypochondriasis in primary care patients(81).

The term *hysteria* derived from the Greek word for womb, reflecting the belief that the condition resulted from disturbances of the uterus. Literally, it means 'the wandering womb'(82). The chauvinistic, male dominated, origins of this term make it unpopular and as a diagnosis, it is generally avoided. When made, the diagnosis is based on three assumptions: 1) symptoms can arise without an adequate pathological source; 2) the

patient experiences the symptoms and they are not purposefully contrived; and 3) psychological distress can be 'converted' into physical symptoms. Although the first of these assumptions has validity, the unreliability of the other two renders it unacceptable as a classification(83).

Idiopathic physical symptoms is a term mainly used by American researchers(84). Idiopathic means of unknown cause. However, any disease that is of uncertain or unknown origin may be termed idiopathic.

Neurasthenia was dropped from the DSM-IV in 1980. However, the ICD-10 outlines criteria for the diagnosis which includes the following core symptoms: mental and/or physical fatigue, accompanied by two or more of seven symptoms (dizziness, dyspepsia, muscular aches or pains, tension headaches, inability to relax, irritability, and sleep disturbance. The illness must be persistent, with no evidence of any mood, panic, or generalized anxiety disorders(85).

Psychosomatic illness relates to an illness or symptoms that can not be traced to any organic cause, but are more likely the result of some interaction between the mind and the body(86). The symptoms are really experienced by the patient, but they are thought to be caused or worsened by psychological factors, i.e. depression, anxiety, or stress, and not some underlying physical disease.

Somatoform disorder, once termed psychosomatic disorder, was devised by the DSM-III. The physical symptoms, and their severity and duration, cannot be adequately explained by any underlying physical disease. Under this umbrella of somatoform disorders comes: conversion disorder, hypochondriasis, body dysmorphic disorder, pain disorder, undifferentiated somatoform disorder and somatoform disorder not otherwise specified (NOS). There is no clear operational definition for the whole category and some of these disorders can be so chronic that they are arguably more in line with personality disorders(87).

In the nineteenth and early twentieth centuries, *somatisation disorder* was known as hysteria(88), and subsequently Briquet's syndrome(89). Steckel, a psychoanalyst, was the first to introduce the term 'somatisation' in 1943(90). He asserted that 'unexplained' physical complaints were manifestations of mental pathology, and somatisation was a "disease of the conscious" (pg. 580).

Along with most of his peers, Lipowski's views of somatisation changed and evolved over time. In 1968 he defined it as the tendency to experience, conceptualise or communicate psychological states as bodily sensations, functional changes or somatic metaphors(91). Years later in 1986 he defined it as the tendency to experience and communicate psychological distress in the form of somatic symptoms that the patient misinterprets as signifying serious physical illness(92). His 1988 definition of somatisation involved symptoms, distressing enough for the patient to seek medical help, that were unaccounted for by pathological findings, but the patient attributed to physical illness(93). His assumption that psychosocial stress played a part in these presentations remained.

Somatisation disorder (SD) as described in the DSM-IV, is defined as "..a polysymptomatic disorder that begins before age 30 years, extends over a period of years, and is characterised by a combination of pain, gastrointestinal, sexual, and pseudoneurological complaints." pg. 445(94). These distressing symptoms are not fully explained by a medical condition, the direct effect of a substance, or by another mental disorder. It is a chronic condition in which there are numerous physical complaints which can result in substantial impairment. The physical symptoms are thought to be caused by psychological problems, where no underlying physical problem can be identified. The diagnostic criteria for somatisation disorder are thought to be too restrictive for application in clinical settings(87).

As evident above, there is some overlap between all of the above terms and definitions. However, there is no consensus on the most appropriate term to use, and the validity and reliability of all of them have been called into question to some extent. This complicates research and management in clinical practice(78;95;96). Somatisation, medically 'unexplained' and functional somatic symptoms are perhaps the most commonly used in the literature and, rightly or wrongly, are often used interchangeably to refer to the same phenomenon(97-99).

I have used the term medically 'unexplained' symptoms (MUS) in this thesis. Unlike the term 'somatisation' which assumes underlying psychiatric morbidity, the term MUS makes no such assumptions. However, in line with the literature, I have also referred to studies which used the term 'somatisation' or 'functional somatic symptoms/syndromes'.

A working definition of medically unexplained symptoms

Symptoms are not necessarily indicators of pathology. They can represent a combination of physical, psychological, social and environmental changes(99-101). The contribution of each factor varies. We lack the vocabulary with which to deal with or describe mind-body-society-environment interactions.

The term MUS refers to the ill-defined nature of symptoms and the absence of objective physical and laboratory findings(102). A simple definition of MUS is therefore symptoms lacking an organic basis(103). This would effectively incorporate no detectable structural abnormalities, infection or metabolic causes. However, this does not take into account recent evidence that neuro-endocrinological, neuro-chemical and psycho-physiological factors can play a part in stress-related bodily disorders(104-106).

Kellner defined somatisation to be the presence of one or more physical complaints where either appropriate evaluation discovers no organic pathology (or patho-physiological mechanism), or when there is related organic pathology, the physical complaints or resulting social or occupational impairment is far in excess of the physical findings(107). Sharpe defined MUS more succinctly as symptoms disproportionate to identifiable physical disease(108).

In agreement with the above views put forward by Kellner and Sharpe, my working definition of medically 'unexplained' symptoms (MUS) for this study was: symptoms presented to a general practitioner (GP) for which there was no (or inadequate) objective evidence of disease or structural bodily change according to the opinion of a medical specialist.

Summary

The different terms and definitions show the complex nature of identifying and studying MUS. This makes reviews of the evidence confusing and comparisons difficult. It is unlikely that we will ever find a simple label or definition that will adequately encompass all of these perspectives.

MUS are present in all medical settings; more so in primary than in secondary care. A small proportion of patients with no objective disease use a substantial amount of

health care resources designed to treat disease. This represents a mismatch of health care provision and unmet patient needs. However, what these needs actually are is unclear.

CHAPTER 3. ASSOCIATIONS WITH MEDICALLY UNEXPLAINED SYMPTOMS

Patients who consult for MUS commonly have a complex mix of other possibly related characteristics and problems. This chapter will outline the main associations found by research conducted prior to the commencement of this thesis (November 2002); for example anxiety and depression.

ANXIETY AND DEPRESSION

MUS are associated with high rates of anxiety and depression. Kroenke found that one third of symptoms are considered to be either psychiatric or unexplained. There were common symptoms associated with at least a two-fold increased lifetime risk of a common "psychiatric disorder"; predominantly anxiety and depression(109). He later showed that the more symptoms experienced at one time, the more likely they would be 'unexplained' by disease, and associated with anxiety or depression(110). Symptoms more commonly associated with anxiety and depression disorder include: pains in the joints, back, head, chest, arms or legs, and abdomen, as well as fatigue and dizziness(111-113). These physical symptoms have caused patients considerable discomfort and have persisted.

Symptoms such as chest pain, shortness of breath and excessive sweating can be indicators of serious disease (e.g. myocardial infarction/heart attack). However, many of these symptoms also make up the criteria for anxiety and depression. The symptoms associated with anxiety, panic and depression will be briefly outlined in this next section.

Depression

The overall prevalence of depression in primary care has been reported in the range of 3.5% to 27%(114;115). As with MUS, the prevalence of depression found depends on how it is measured.

Depressive disorders have characteristic symptoms affecting thoughts, emotions, and functioning. Common symptoms and diagnostic features of a depressive episode include disturbed sleep, loss or increased appetite, and fatigue(116).

Another common physical complaint of patients with depression is pain. In part, this may be due to altered mood affecting individuals' perception and reporting of pain. A common neuro-chemical pathway has been implicated where serotonin and noradrenaline both affect the perception of pain and the pathogenesis of depression(117).

Somatic symptoms are common with depression and increase the burden of depression(118). Whether depression causes symptoms, or patients become depressed because of their symptoms, is debatable(119). Symptoms can be both predictive and consequential of depressive episodes(120;121).

Anxiety

Anxiety can affect numerous body systems as well as produce psychological symptoms of fear, irritability, sensitivity, restlessness, and poor concentration. The symptoms of generalised anxiety disorder (GAD) do not necessarily come about through exposure to any particular environment or situation, but are more persistent. Patients with anxiety disorders may have physiological hyper-arousal at rest and heightened physiologic responses to any external stressors. Figure 1. below outlines the physical symptoms often experienced by patients with GAD(122).

The physical symptoms of anxiety are commonly associated with 'unexplained' symptoms and anxiety has been correlated strongly as a predictor for MUS(123-125). Anxiety is the most prevalent psychiatric diagnosis for chronic somatisers(126), and can make a diagnosis of somatisation difficult(127).

Figure 1. Physical symptoms of generalised anxiety disorder

Gastrointestinal

- Dry mouth
- Difficulty swallowing
- Epigastric pain
- Excess wind
- Frequent or loose bowel motions

Respiratory

- Difficulty inhaling
- Over-breathing (hyperventilation)

Cardiovascular

- Chest pain or constriction
- Palpitations or awareness of missed beats

Genitourinary

- Frequent or urgent micturition
- Erectile dysfunction
- Menstrual discomfort or no periods (amenorrhoea)

Neuromuscular

- Tremor
- Prickling sensations
- Tinnitus
- Dizziness
- Headache
- Muscle aches and pains
- Insomnia

N.B. Adapted from the Oxford Textbook of Psychiatry(122)

Panic

Panic disorder is an anxiety disorder. The central feature of a panic attack is when physical symptoms overwhelm the individual. This is often accompanied by fear of serious consequences, for example having a heart attack. Although distinguishable from one another, the symptoms of a heart attack and a panic attack may be similarly distressing to a patient(128). Due to the similar presentations of panic with other cardiac, gastrointestinal and neurological conditions, misdiagnosis of a panic disorder for a somatic condition can continue for months or even years(129).

The DSM-IV(116) describes a panic attack as a discrete period of intense fear or discomfort in which any four or more of the following physical symptoms develop suddenly and peak within 10 minutes:

- Palpitations, pounding heart, or accelerated heart rate
- Sweating
- Trembling or shaking
- Sensations of shortness of breath or smothering
- Feeling of choking
- Chest pain or discomfort
- Nausea or abdominal distress
- Feeling dizzy, unsteady, light-headed, or faint
- Paresthesias (numbness or tingling sensations)
- Chills or hot flushes.

Katon and colleagues found that half of all visits to primary care providers are precipitated by the somatic symptoms associated with this disorder(130). Analysis of the data from the ECA study found panic disorder in up to 8% of primary-care patients and that it was strongly associated with multiple MUS(131). Frequent attenders to

primary care in the ECA study had high prevalence of current (12%) and lifetime panic disorder (30%).

Undetected anxiety and depression

There is a large body of evidence to suggest that doctors do not detect or adequately treat a substantial proportion of patients who have emotional problems accompanying their physical symptoms(45;132;133). There has been much research and published literature on this based in the primary care setting(20;29;134-146). If undetected or sub-optimally untreated, depression can result in significant morbidity, and has been associated with high rates of morbidity, disability and mortality(147;148).

Bridges and Goldberg reported that GPs did not diagnose more than 50% of psychiatric conditions in patients who presented with physical symptoms(149). Non-diagnosis or non-detection of anxiety and depression by GPs has been associated with new patients to a general practice and those forming new doctor-patient relationships(150;151).

Other reasons, such as perceived stigma of mental illness(152;153) or patient fears of serious physical disease(154;155) may contribute to the fact that patients or their treating doctors may not recognise or acknowledge symptoms of anxiety and depression(119). Studies have shown that a normalising attributional style of patients significantly contributes to the low detection of psychiatric disorders by doctors(136;137;143;156-159). In an international study where 1146 patients were identified to have major depression, 45% to 95% of these patients (depending on the centre of recruitment) presented only somatic symptoms to the doctor(160). Symptoms of anxiety, particularly comorbid with depression, are more likely to be recognised by GPs than symptoms in patients with pure depression(161-163).

Interventions directed at GPs have shown improved detection of anxiety and depression(164). However, a review performed by Kroenke and colleagues found conflicting results. In at least 70% of studies, improved diagnosis and treatment of psychiatric disorders could be achieved through intervention. However, improved patient outcomes were only evident in 36% to 50% of studies reviewed(165). Detection was only found to be useful if GPs had the skills and resources to deliver adequate mental health therapies and interventions(162).

Effective alternatives are available

There is evidence that there are effective alternative treatments for patients with MUS which can reduce both health care costs and risk of patient iatrogenic harm. Systematic reviews of pharmacological(166-169) and behavioural therapies(170), or a combination of both(171) have shown to reduce the impact of symptoms and improve patient wellbeing. Even if patients do not have diagnoses of anxiety or depression, there is evidence that some psychological and psychiatric therapies can improve patients' symptoms. A meta-analysis showed that antidepressants (notably selective serotonin reuptake inhibitors, SSRI) were about seven times more effective than placebo in the treatment of physical and behavioural symptoms of severe pre-menstrual syndrome (PMS)(172).

OTHER ASSOCIATIONS WITH MEDICALLY UNEXPLAINED SYMPTOMS

Patient demographics

It has been established that women use more health care services than men(173;174). This is often necessary due to screening, gynaecological problems and childbirth. However, females are also more likely to present to a doctor with symptoms than males(175-177). Also, patients with low levels of education and living in deprived areas are at greater risk of developing MUS(178-181).

Abuse and neglect

There is evidence linking childhood neglect and physical or sexual abuse with consulting for 'unexplained' symptoms(182-194). Common symptoms linked to abuse include pain in the pelvis, abdomen and during sexual intercourse (dyspareunia).

Illness beliefs of the patient

Linked in part to low levels of patient education and unmet expectations, 'unexplained' symptoms have also been associated with certain beliefs or worries about the cause of illness such as viruses, pollution or cancer(97;143;177;195-197). Patients with MUS are more likely to consider themselves as more vulnerable to, and suffering from, poor health. Salmon's group found that patients believed stress and lifestyle caused the disturbances in their bodily function, and were less convinced of any pathological disease(198).

Organic disease

Symptoms can be an indicator of disease (e.g. cancer) or normal bodily changes (e.g. pregnancy). However, patients with these conditions can also develop symptoms that cannot be explained by, or are out of proportion to, the disease or structural change present(199-205). It is not uncommon for patients who have suffered a stroke or cardiac event to develop MUS associated with their anxiety about experiencing similar events in the future (206;207).

Poor outcomes

A large proportion of patients who have attended secondary care clinics with MUS continue to be troubled by their symptoms after their secondary care contact(208). At six months and even three years of follow-up, three quarters of patients with non-cardiac chest pain, studied by Mayou and colleagues, reported continued limitation of function, concern about the cause of their symptoms, and dissatisfaction with medical care(209).

Similar findings have been evidenced among neurology outpatients. At eight months follow-up, Carson and colleagues found over half of the patients under study had no improvement from their original neurological symptoms(210). Even after ten years, Mace and Trimble found that 30 of 73 (41.1%) patients had no relief from their original symptom.

Iatrogenesis

Kouyanou and colleagues found that over-investigation, over treatment, inappropriate prescribing, and misdiagnosis brought about negative health care interactions and an increased risk of iatrogenic harm(49;50). The 'harm of healing' becomes an issue for patients with no organic disease(47). Those patients who frequently consult doctors for MUS, and are exposed to more intensive and invasive medical investigations and procedures, are at increasing risk for iatrogenic harm with each contact(51).

Functional impairment and disability

Despite the absence of pathology, patients with MUS often have equal or greater functional disability than patients with objective organic disease(64;110;211-217). Impairment was often compounded when comorbid with an affective disorder(218). This has been evidenced not only by patient self reports of limited function, but also societal costs in the form of time off work, lost productivity, lost wages, receipt of sickness or disability benefits, medical retirement and the impact on other usual activities and relationships(16;58;177;219).

Dissatisfaction with health care

Jackson and colleagues have studied the effects of unmet or misinformed expectations held by patients presenting to a doctor with physical symptoms(220-222). If doctors did not meet patient expectations, i.e. of a diagnosis or somatic treatment, then patients were more likely to leave dissatisfied. Similarly, doctors who used language that rejected patient interpretations or did not provide helpful explanations were likely to leave patients dissatisfied(223).

Difficult doctor-patient relationships

Although GPs mostly feel that unexplained symptoms or minor ailments are best managed in primary care, they find the consultations frustrating and difficult(24;25;212;224-229). The difficulty in the doctor-patient relationship may be due to a number of factors including doctor discomfort with the uncertainty(228;230), dissatisfaction with poor patient progress, or the unrealistic patient expectations and demands on the doctor. Such difficult interactions have been shown to bring about inappropriate patient labelling and suboptimal care(231). A mismatch between patient and GP explanatory models of symptoms may result in leaving both the doctor and patient dissatisfied with the outcome(223).

Attitudes of doctors

Linked to difficult doctor-patient encounters outlined above, doctors' attitudes to, and beliefs about, MUS have been found to have an effect on patient management, outcomes and satisfaction(232;233). A study of doctor's attitudes to functional gastrointestinal disorders found that only half the surveyed GPs believed the symptoms represented diagnosable disease(26). Contrastingly, the majority of specialist participants believed functional gastrointestinal symptoms represented "real disease" and were more likely to treat as such.

Some GPs have reported feeling unsupported or 'out of their depth' in caring for these patients. Wayne Katon and colleagues determined that there were a set of commonly held beliefs by doctors which inhibited them from dealing with the wider psychosocial, rather than just physical, health of their patients(234). These included the belief that their role was to rule out organic disease first and foremost, the belief that patients only want organic problems dealt with, and their fear that the patients' problems would be beyond them to be able to help.

A somewhat disillusioned account by two Canadian doctors summarised their belief that patients, consciously or subconsciously, developed functional somatic syndromes (FSS) in order to achieve secondary gain such as benefits, sympathy, and absolution from responsibilities(235). FSS such as chronic fatigue and fibromyalgia defy easy

categorisations of illness and remain difficult to treat, and patients with these syndromes can be disbelieved by their doctors(236). A survey of family doctors found that they acknowledged their part in some difficult consultations with patients due to their own impatience and judgemental beliefs(237).

Multiple doctors

Studies have observed that patients with MUS are more likely to see multiple doctors. Neal and colleagues found that their frequent attenders to general practice consulted with most or all of the doctors within practices(238).

A group of frequent user patients were identified as they had obtained ambulatory care from more than 20 physicians within the year of study(239). This group received 10 times more medical services than the average patient, and the mean cost per patient for ambulatory care was also 10 times higher. Nearly all (98.9%) of these patients received specialist care. Diagnoses of anxiety (36.0%) and depression (16.4%) were common in this frequently attending group.

Patients referred to secondary care for MUS were more likely to have changed general practices, and were still forming new doctor-patient relationships. Rounds of specialist referrals have been shown to be a consequence of a change in GP or general practice(240;241).

Another association with 'unexplained' symptoms, which is particularly pertinent to this thesis, is high use of health care services. This shall be addressed in more detail in Chapter 5.

SUMMARY

Previous research has repeatedly shown the following features to be associated with medically 'unexplained' symptoms:

- Psychiatric morbidity (anxiety, depression and panic) which is often undetected by health care professionals
- Patient demographics (i.e. female gender, deprivation and low levels of education)
- Abuse and neglect
- Dissatisfaction with health care
- Functional impairment
- Organic disease
- Iatrogenic risk and poor outcomes from biomedical care
- Inappropriate health beliefs
- Strained doctor-patient relationships which can result in patients seeking different and multiple doctors

Clearly, patients with MUS are a needy group of patients. However, their needs are not adequately being met as evidenced by continually poor outcomes, dissatisfaction with health care received and undetected (therefore inadequately treated) anxiety and depression. There is evidence that there are effective alternatives to biomedical treatments. However, if left undetected, patients with MUS will not receive them, and risk developing an unhelpful (and at worst harmful) pattern of seeking help from medical care.

CHAPTER 4. APPROACHES TO STUDYING MEDICALLY UNEXPLAINED SYMPTOMS

Chapter three outlined that patients with MUS have a level of unmet need from disease-based medical management. In an attempt to identify and single out a group of patients to help, researchers have developed approaches to identify and study MUS. The two main approaches have been provided by psychiatry and medical specialties. There is also a relatively new argument that MUS are the product of doctor-patient interactions. This chapter will outline these approaches.

PSYCHIATRIC APPROACH

Over the past century, psychiatric explanations and diagnostic criteria have dominated the field of 'unexplained' symptoms(242-244). In 1985, Goldberg and Bridges attempted to operationalise the concept of somatisation. Patients under assessment were required to have positive evidence of an emotional disorder that could potentially explain their symptoms. This set of operational criteria is outlined below in Figure 2(149).

These criteria highlight a number of features which are possibly related to the development of MUS. These included that a patient consulted a doctor, and that their belief was that their symptoms were due to a physical problem. However, the main hypothesis was that somatisation represented 'hidden psychiatric morbidity'. This was based on the assumption that a causal relationship existed between physical symptoms and psychiatric disorders.

Figure 2. Goldberg and Bridges criteria for somatisation

Consulting behaviour – the patient sought medical help for somatic manifestations of psychiatric illness but did not present psychological symptoms.
Attribution – the patient considered the somatic manifestations to be caused by a physical problem when they visited a doctor.
Psychiatric illness – they reported symptoms to the researcher (in this case a psychiatrist) which indicated a psychiatric diagnosis based on standard criteria (such as the DSM).
Response to intervention – in the opinion of a psychiatrist, treatment of the psychiatric disorder would cause the somatic manifestations either to disappear or to return to a tolerable level.

Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) and Somatoform Disorders (SD)

The Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) is perhaps the most widely used psychiatric classification which provides rigid criteria to diagnose and classify mental disorders(116). Somatisation disorder (SD) is outlined by the DSM as a psychiatric diagnosis based on multiple lifetime 'unexplained' symptoms(94). It includes the fact that patients present for medical help without attributing psychological distress to their physical manifestations. For a diagnosis of SD to be made, eight or more symptoms across four different systems must be present.

A diagnosis of SD is made based on lifetime counts of 'unexplained' symptoms. These symptom counts involve relatively arbitrary cut off points. Patients with fewer symptoms can pose equally difficult management problems. As such, this diagnosis may miss or not apply to many somatising patients in primary care(245). A diagnosis of SD is also rarely made. A pilot study in Edinburgh by Brown found that only 1.1% (17/1492) of patients under study met the criteria for somatisation(19).

At the other end of the spectrum, undifferentiated somatoform disorder (USD) or somatoform disorder not otherwise specified (SD-NOS) require only one 'unexplained' symptom for the diagnosis. These diagnoses have proved unhelpful, as they are too inclusive and of questionable validity(246). Using DSM-IV criteria, one study found that 59.9% of patients had at least one somatoform disorder(18). However, this reduced

to 13.1% when the not otherwise specified (SD NOS) or undifferentiated diagnostic (USD) groups were excluded.

The diagnostic categories themselves were derived from specialist hospital-based clinics and the majority of people outside these settings would likely end up in the catch-all category, undifferentiated somatoform disorder, which is of doubtful research and clinical usefulness. Another problem with the somatoform diagnoses is the bias arising from patients' recall of a lifetime of symptoms. In a large international study of somatisation and somatic symptoms, only 39% of 'unexplained' symptoms recorded at baseline were still recalled by the patient 12 months later(247).

Tenth Revision of the International Classification of Diseases (ICD-10)

Other than the DSM-IV, the other major psychiatric classification system is the ICD-10(85). It too developed a primary care edition specifically for GPs(248). After this was instituted, there was a substantial increase in the number of patients diagnosed with depression or 'unexplained' symptoms(144). GPs also made increased use of psychological interventions.

The ICD-10 has the potential to allow reliable comparisons of epidemiological data between countries, levels of health care systems, or different periods of time. However, for general practice, it has been found to be too specific to describe problems relevant to the work of GPs(249). These guidelines have shown little impact on the overall detection and diagnostic accuracy of mental disorders, and the ability of the guidelines to bring about change in primary care remains uncertain(144).

Abridged Somatisation Disorder (ASD)

Javier Escobar, a research psychiatrist, established the construct of 'abridged' somatisation disorder (ASD)(250). This was developed as a result of his recognition that the majority of patients with MUS did not have somatisation disorder. Like most other psychiatric approaches, this basically involved symptom counting using the Somatic Symptom Index (SSI). ASD was diagnosed when six concurrent symptoms

were present for women and four for men. This diagnosis has shown association with use of medical services(251).

ASD is prevalent in primary care, with approximately one fifth of patients meeting this criteria(252). Studies which have used either DSM-IV or ICD-10 classifications reported lower prevalence rates than the ASD criteria. For example, of 685 Canadian primary care patients, 26.3% met criteria for one or more forms of somatisation, such as ASD(253). However, by applying the DSM criteria, somatisation disorder was prevalent in only one percent.

ASD was originally developed with the Hispanic community in mind, so one could argue that generalisability to, in this case, a Scottish population, where less than one percent of the population comprises people of Hispanic origin, may be limited. In contrast to this argument, a large World Health Organisation (WHO) study conducted across 14 different countries involving 5438 primary care patients, found modest differences between cultures. This construct has relatively successfully discriminated between cases and controls, or mild somatisation from severe, in other health care settings such as Germany(243;254), but has mainly been applied to American populations(243;245;252;255;256).

The WHO study found only a 2.8% prevalence of somatisation using the ICD-10 definition which rose to nearly 20% when using the less restrictive ASD(257). However, many patients do not fit the criteria for ASD(258). This approach does not specifically address what constitutes an 'unexplained' symptom, but rather more the numbers of symptoms that are experienced. The abridged construct has not been validated as a diagnosis. It is simply a dimensional construct with demonstrated usefulness for defining cases that can be used for further epidemiologic and clinical inquiry(244). Given the reservations above, its use in UK primary care may not be ideal(259).

Multisomatoform Disorder (MSD)

GPs need diagnostic measures suited to the realities of their practice. Consequently, the primary care edition of the DSM-IV (DSM-IV-PC) was developed by a team of

psychiatrists and primary care physicians(260;261). In this manual, it describes multisomatoform disorder (MSD), a relatively new diagnosis based on current 'unexplained' symptoms(259). MSD is defined as three or more medically 'unexplained' and currently bothersome physical symptoms, as well as a history of somatisation lasting two or more years(15). Kroenke and his team operationalised this using a list of 15 common symptoms in the primary care evaluation of mental disorders project (PRIME-MD)(245). This is arguably the most useful diagnosis because it identifies patients with perceived impairment of comparable severity to full SD, whilst avoiding recall bias by using a more efficient diagnostic approach based on current symptoms.

Limitations with the psychiatric approach

The core of the psychiatric approach involves counting symptoms. Classifications of somatisation involve rigid operationalised criteria according to the DSM-IV(116) and ICD-10(262). As such, somatisation disorder is extremely rare with a prevalence ranging from 0.2% to 2% of the population(94). By contrast, the somatoform classifications have become highly contested diagnoses, as they are too inclusive. These have proved to be unhelpful constructs needing revision or plain abolition(74). The diagnoses of undifferentiated somatoform disorder (USD), or somatoform not otherwise specified (SD NOS) are of disputed validity as patients usually obtain a medical or another psychiatric diagnosis after being given this label(94). Specific somatoform diagnoses are made less often outside a psychiatric setting(263).

Studies of psychological morbidity and medically 'unexplained' symptoms, have shown that a considerable proportion of patients, particularly those in primary care, have no psychiatric diagnosis which excludes them from the psychiatric classification systems and re-emphasises the dualistic perspective. For example, Kroenke and colleagues determined that a depressive or anxiety disorder was present in 29% of their study subjects(264). What of the other 71%? Although a substantial number of patients with MUS have anxiety and depression, it is not appropriate to assume that this is the cause for their symptoms.

In summary, there is conflicting evidence about the validity of many of the psychiatric classifications used to identify MUS. Many diagnoses such as USD and SD NOS are unreliable and not discriminating. Although the diagnosis of MSD shows the most promise, it still relies on basic symptom counting. The number of symptoms a patient has does not necessarily tell us anything further about the symptom or the patient experiencing them. As has already been shown in chapter one, symptoms are extremely common in the community, but most people do not seek help for them. So the number of symptoms an individual has is generally unhelpful.

MEDICAL APPROACH: FUNCTIONAL SOMATIC SYNDROMES

Ian Deary coined the terms 'lumping' or 'splitting' when referring to somatic symptoms(265). Medical specialties take the 'splitter' approach when making a functional somatic syndrome (FSS) diagnosis. Patients experiencing symptoms in one area or organ of the body may be referred to the corresponding medical specialty for an opinion. Predominantly based on the presence of specific symptoms, there are operationalised criteria available to help specialists diagnose functional system-based disorders (syndromes) such as chronic fatigue, fibromyalgia or irritable bowel (IBS). For example, the most stringent criteria for accurately diagnosing IBS are considered to be the Rome criteria(266).

FSS diagnoses derive from the clustering of 'unexplained' symptoms of relevance to the particular medical specialty and reflect, at least in part, a medical speciality bias(267). A list of functional syndromes associated with the relevant medical specialties is provided below in Figure 3.

Limitations with the medical specialty approach

Although organ-specific, FSS often have overlapping symptoms with other syndromes from other medical specialties. Deary's term 'lumping' refers to the assertion that MUS share so many other characteristics that they could all be 'lumped' in the one grouping. An extensive literature review by Wessely and colleagues in 1999 provided evidence in support of this, concluding that substantial overlap exists between individual functional

somatic syndromes to the extent that the similarities outweighed the differences(80). The review argued that FSS create artificial distinctions even though they are not entirely distinct entities(80). Findings from this review have been supported by more recent studies in the community(268), primary care(269) and secondary care settings(155;270). A review by Aaron and Buchwald found that patients with one 'unexplained' clinical condition frequently met the criteria for a second 'unexplained' condition(271).

Figure 3. Medical specialties and associated functional somatic syndrome diagnoses (FSS)

Cardiology	Atypical or non-cardiac chest pain
Chest medicine	Hyperventilation syndrome
Dentistry	Temporomandibular joint dysfunction, atypical facial pain
Ear, nose, throat (ENT)	Dysphonia, globus syndrome
Endocrinology	Reactive hypoglycaemia
Gastroenterology	Irritable bowel syndrome, spastic colon, non-ulcer dyspepsia
Gynaecology	Pelvic pain, premenstrual (tension) syndrome
Infectious diseases	Chronic (post-viral) fatigue syndrome
Neurology	Tension headache, chronic daily headache
Occupational medicine	Gulf War syndrome, multiple chemical sensitivity, repetitive strain injury, sick building syndrome
Orthopaedics	Low back pain, chronic whiplash
Pain clinic	Chronic pain syndromes
Renal medicine	Loin pain haematuria syndrome
Rheumatology	Fibromyalgia
Urology	Irritable bladder syndrome, detrusor instability

These functional syndromes are defined by arbitrary symptom cut-offs and offer no intrinsic validity. Effectively, FSS are simply a form of re-labelling a group of 'unexplained' symptoms. The diagnoses are generally only made after referral of the patient to the medical specialty relevant to the organ system of their presenting symptoms.

MEDICALLY UNEXPLAINED SYMPTOMS AS A PRODUCT OF THE DOCTOR-PATIENT INTERACTION

Slater hyothesised that 'unexplained' symptoms (using the diagnostic term of hysteria) applied to a disturbance of the doctor-patient relationship(272). In his view, MUS were evidence of poor communication and of mutual misunderstanding. Bridges and Goldberg described somatisation in 1988, not as a disease, but as a common and important human mechanism involving both doctor and patient(29). Malterud suggested that MUS commonly arose after female patients consulted male doctors for their symptoms(273). Thus it was more a product of male doctor-female patient interaction. These researchers proposed that 'unexplained' symptoms were not just a patient attribute, but the result of inappropriate somatic fixation of doctors, family members, or others, on patients' complex problems(274;275).

More recent qualitative evidence has advocated that MUS are a product of the interaction between doctors and patients(276). Salmon's research group have meticulously studied the consultations of different patients and doctors in different medical settings. In an earlier study, (female) patients and doctors were likened as 'opponents' with contrasting areas of expertise; that is that the patient was the expert in the intimate knowledge of their subjective symptoms, whilst the doctor was the expert with the technical knowledge of the human body(277).

The interaction between patient and doctor during a consultation can determine whether symptoms continue as a medical problem. There is contention as to whether it is the patient who medicalises their symptoms, or the doctor, or both to a certain extent(278). A consultation for symptoms can be influenced by many different doctor and patient factors, some of which may include:

1) *The doctor-patient relationship*: how well they know each other and previous experiences affect how patients and GPs feel about each other. This in turn affects how they communicate with one another(279).

2) *Communication*: a consultation relies on the doctor asking for all the relevant information and the patient's ability to identify and impart all the relevant information. Communication between doctor and patient relies not only on what is said, but also what is heard and understood(223). There is evidence

linking the quality of communication between doctors and patients to clinical outcomes(280).

3) *Time*: the time allotted per consultation can affect how much information can be shared between doctor and patient. Consultations in the UK average a mean of 8.4 minutes which is much shorter than international comparisons, e.g. 15 minute consultations in Canada, and 21 minutes in Sweden. Although GPs may be aware of patient distress, they may not have the time to address the related issues(281).

4) *Documentation*: a concise summary in patient notes of past physical, emotional, social and environmental health issues, as well as past health care encounters, may assist the doctor by providing information relevant to the current presentation. This is particularly important when the doctor does not know the patient very well(282).

5) *Individual factors*: both the doctor and patient's ability to cope with uncertainty is affected by their past experience, level of education, belief systems and attitudes. Some of these associations have been outlined in more detail in chapter three.

Limitations with the doctor-patient interaction approach

Arguably, the interaction between doctors and patients cannot solely explain the phenomenon of MUS as there is often an objective validity to the physical nature of some symptoms prior to the consultation and any interaction with a doctor. For example, one can objectively measure diarrhoea for a patient presenting with an irritable bowel. There are also symptoms that are subjectively experienced by the patient, such as chest pain and headache, which can not objectively be measured by the doctor. The doctor-patient interaction argument does not dispute patients' experiences of symptoms. The majority of symptoms (both objectively and subjectively measurable) are the result of normal bodily processes. An aspect of this argument is that there are a number of factors within the doctor-patient encounter which iatrogenically maintain normal bodily function so that they become MUS, and it has

been asserted that this could be overcome by the use of appropriate interview techniques(283). In a similar light, Biggs and colleagues(284) stated that high health care use has been associated with depression and anxiety in patients in whom there are demonstrable pathological findings (e.g. myocardial infarction, angina, inflammatory bowel disease, and general medical symptoms). They suggest that studies assessing psychosocial variables as predictors of high health care use should also be applied to patients who consult for objective pathological symptoms as those with functional disorders.

The merits of the approach that MUS are a product of the interaction between the doctor and the patient are acknowledged. These interactions represent the reality at the coal face of general practice. However, in research terms, the concept is an extremely difficult one to operationalise and measure.

SUMMARY

Reviews of the available evidence about classification and MUS have been conducted in an attempt to clarify the situation and bring about some consensus(244;265;271;285-292). However, even the findings and suggestions from the reviews conflict with one another, and some reviews have been unable to reach a conclusion. For example, an attempt to simplify somatisation down to two distinct forms, as originally proposed by Kirmayer and Robbins(253) (i.e. "presenting somatisation" secondary to psychological distress, and "functional somatisation" characterised by 'unexplained' symptoms), provided a useful review of the merits of the concepts(293). Although these categories of MUS have been shown to have face validity in a UK primary care setting(208), the review failed to provide a definitive answer as to what concept was most useful from both clinical and research perspectives. Overlap of these forms of somatisation, including hypochondriasis, has been shown(294).

The problem with the psychiatric approach is that it basically involves counting symptoms and tells us little about the symptoms or the patient experiencing them. FSS diagnoses are specific to particular organ systems. However, there is now strong evidence that criteria for these syndromes overlap with one another and merely provide

artificial distinctions. The association between doctor-patient interactions and MUS is unclear, and difficult to operationalise.

Unexplained symptoms may not represent a medical nor a psychiatric problem for some patients(295). Although the psychiatric and medical approaches to MUS are readily applicable in psychiatric and specialist medical settings, they are relatively unhelpful outside of these settings. The majority of patients with 'unexplained' symptoms present initially to GPs rather than to psychiatrists or medical specialists.

There are no rights or wrongs in this field, and the three approaches to MUS as outlined in this chapter have developed in the quest to answer the many grey areas associated with studying and identifying MUS. A broader, pragmatic approach to the identification and study of MUS is yet to be established. One that could be readily applied in primary care has been advocated(21;288).

CHAPTER 5. STUDYING MEDICALLY UNEXPLAINED SYMPTOMS BY CONTACTS WITH HEALTH CARE

There are various different ways of operationalising MUS and defining a patient group with MUS to study. Chapter 4 outlined the limitations of the psychiatric and medical approaches. Recommendations from authorities, such as the World Health Organisation (WHO)(296), advocated that MUS should be managed in primary care to contain unnecessary iatrogenic harm to the patient and health care costs for the Health Service. However, current means of identifying patients with MUS in primary care are inadequate.

As outlined in Chapter 3, patients who have MUS are more likely to consult multiple doctors than the average patient. There appears to be a link between anxiety and depression, high health care use and high numbers of 'unexplained' symptoms(297;298). Given that a characteristic of patients with persistent somatisation is to seek medical attention, rates of medical use have been suggested as a criterion for identifying patients with MUS(299).

In health services research, patients of interest are those who have high health care use and high health care costs, i.e. 'persistent', 'repeat' or 'frequent' attenders and 'high users'. Health service use provides a simple, quantitative approach that can act as an indicator of symptom severity and high health care costs. The measurements and ratings are a proxy for what is actually going on in practice.

A simple and practical method of identifying a group of patients who are obviously seeking help, is to identify the number of times they have seen a doctor for their symptoms. This approach is not only applicable in primary care, but could be applied in any health care setting of interest. This chapter outlines an argument for the identification of MUS by quantifying patients' health care use.

FREQUENT ATTENDERS TO PRIMARY CARE

Frequent, persistent or repeat attenders to health care services, also called high users, make up a small proportion of the population. However, they consume a disproportionately large amount of health care resources. Frequent attenders have been shown to account for nearly a quarter of the workload in general practice(300).

Reasons behind seeking medical attention are complex and varied. However, the majority of patients who use a high level of health care services are extremely sick. Heywood and colleagues found that 94% of 'very frequent attenders' (defined as 15 or more face to face consultations with a GP) had a diagnosed chronic health condition(301). However, one of the earliest studies by Robinson and Granfield compared frequent consulters with infrequent consulters in primary care, and found that frequent consulters had more functional somatic symptoms (FSS) and were more inclined to negative mood(302).

Barsky and colleagues found that medical use correlated with the number of somatic symptoms reported, depressive symptoms, and the number of medical diagnoses in the medical record(303). As a result of multiple regressions, symptoms were the second most powerful predictors of medical use, followed by hypochondriacal attitudes and the presence of a major psychiatric diagnosis in the medical record. A later study found that medical care utilisation was associated with female gender, age, number and duration of symptoms, fatigue and psychiatric disorder, especially somatoform disorders(304).

A random selection of community respondents from the ECA study were interviewed to determine if they had somatisation, according to the criteria for ASD(305). Compared to individuals with no evidence of ASD, somatising respondents had more contacts with medical health care services, as well as more time off work and disability. An association between MUS and frequent health care attendance has been found(294).

A helpful systematic review of factors associated with frequent attendance to general practice found high use was related to physical disease, psychiatric disorders, or a combination of both(174). The main findings from this review are summarised in Figure 4.

Figure 4. Summary of Gill and Sharpe's findings of frequent consulters in general practice

- A cut-off of 9 to 14 consultations per year was used to define subjects
- Patients saw multiple doctors, often for similar problems
- A highly heterogeneous patient group
- A small proportion of patients used disproportionate amounts of health care resources
- Female gender, low socioeconomic status, poor education level, and older
- High rates of physical disease
- A high proportion had one or more psychiatric diagnosis
- Comorbid physical and emotional problems often presented
- Impaired function and perceived poor physical health
- Multiple current somatic symptoms
- More likely to believe normal or common bodily sensations were abnormal
- Stressful life events were modestly predictive of GP visits
- Approximately a third of symptoms in primary care were deemed medically 'unexplained' by disease

Since the Gill and Sharpe review, the figure of approximately one third of frequent primary care attenders having 'unexplained' symptoms has been estimated(306). Anxiety and depression have further been shown to be predictors of, or the main associations with, frequent attender status(307-310). Depressive symptoms were the major predictor of frequent attendance in a primary care study conducted by Dowrick and colleagues(311).

However, disease and mental illness are not the only reasons behind a patient consulting a doctor. Medical services are used by some patients as a means of coping with life stresses(312;313). Bellon and colleagues found family dysfunction and the need for emotional support to be associated with high primary health care use(314). Combinations of physical symptoms, difficult cultural and social factors, and negative mood can be difficult for an individual to express. One way of expressing them can be by frequently attending a doctor(279).

The following thesis section outlines a selection of relevant research that identified patient groups with MUS to study based on their number of health care contacts. The

methods, strengths and weaknesses used by these research projects will be outlined and discussed. This section was included to demonstrate various approaches to defining and identifying high users of health care with MUS.

STUDYING FREQUENT ATTENDERS TO PRIMARY CARE

The Edinburgh pilot study

An unpublished pilot study was conducted in a single general practice located in Edinburgh(315). Brown identified cases by reviewing the five year medical history documented in the case notes of all patients with surnames beginning with the letter 'A' through to 'F', as well as patients considered by GPs to be frequent consulters.

The case note screening method for identifying MUS included the following consultation outcomes:

1) no organic explanation for the symptom could be found
2) there was no organic explanation on the first visit, and the patient made no return visit
3) symptoms of physical disease were 'exaggerated' or had an element of functional overlay[3]. If the symptom could feasibly have been caused by known illness, a conservative approach to classification was taken, and the symptom was scored as organic. Similarly, if the symptom could feasibly have been caused by known illness, a conservative approach to classification was taken, and the symptom was scored as organic.

The prevalence of patients with 'unexplained' symptoms according to GP case note review was 1.1% (17/1492), with a mean of 11 symptoms recorded (range 1-20). The most commonly 'unexplained' symptoms included: low libido/problems with intercourse, abdominal bloating, back pain, menorrhagia, limb pain, food intolerance, joint pain, abdominal pain, palpitations, nausea, fainting or loss of consciousness, and

[3] Functional overlay refers to a psychological condition which has caused or aggravated the physical symptoms.

dyspnoea. Fifty percent of patients identified had a past psychiatric history, and the prevalence of somatisation was 0.5% (ten patients).

Limitations with the Edinburgh pilot study

The prevalence rates of MUS were dramatically lower than those quoted in other primary care studies (see Chapter 1). The reasons for this are unclear. However, there were some limitations in the methodology employed, and the findings should be interpreted with the following in mind:

1. GP identification of frequently attending patients may have introduced selection bias; it is possible that patients with surnames G-Z had more MUS.
2. Only one researcher conducted the ratings to determine MUS, and there was no inter-rater reliability performed
3. Numbers of patients studied were small, and this affects generalisability

The first contact patients with symptoms have with the health care system is with a GP. Therefore identification of MUS in the primary care setting would prevent many referrals to expensive and intensive secondary care services. However, identification of patients in general practice can prove problematic. As Brown's study illustrated, there are several options available to identify patients. These include:

- asking GPs or practice staff is unsystematic and prone to selection bias. The bias would come in the form of over-representation of frequent or 'heartsink' *primary care* attenders, but perhaps omit frequent secondary care users from the process. Primary care staff are generally stretched for time and resources, and less able to engage in such an activity[4].
- trawling through patient case notes is a labour intensive, time consuming and generally inefficient process to identify patients.

[4] Anecdotally, Brown stated in his thesis that at the conclusion of three years of painstakingly reviewing case notes and identifying patients, he found that asking the receptionists provided the same list of names, with some extra patients that had been missed by his methods(298).

- accessing information from the practice computer system can provide a biased sample. Although UK general practice is highly computerised, comprehensive use of these computers is often limited to registration data and the issue of repeat prescriptions. The recording of diagnostic data is unsystematic and varies between practices. A recently published study of 78 English general practices found marked variability in inter-practice data quality(316). It also found that some clinically important codes were lacking, and there were multiple ways that the same clinical concept could be represented. The study recommended that manual searching was still required to find data from primary care practices.

Patients will likely be omitted by these unsystematic means. With these issues in mind, the use of combined methods to identify subjects, i.e. using both automated patient record data and case note data (a "hybrid" method), have been advocated(317).

STUDIES OF FREQUENT ATTENDERS TO BOTH PRIMARY AND SECONDARY CARE

The healthcare system in the United States is conducted differently to the system in the UK. In the US, patients are registered with a health maintenance organisation (HMO) which includes both primary and secondary care clinics. Unlike the UK, primary care doctors act less as a 'gatekeeper', and attendance driven more by the patient and their insurance cover. Accordingly, American studies define frequent attenders as those with high numbers of face to face ambulatory contacts with a health care provider (e.g. physician, physician assistant, nurse practitioner, specialist or emergency room). This makes comparisons between US and UK studies of frequent attendance problematic. Arguably frequent attenders to HMOs are equivalent to UK frequent primary care attenders in the way patients can access these services. Four American studies of frequent attenders with MUS had some applicable methods and findings to this research and shall be outlined in this section.

The Michigan high user study

A research group led by Robert Smith in Michigan used management information system data and patient case notes to identify patients with somatisation. Initially, patients were flagged by high numbers of primary care visits(318). High users were defined as those with six or more visits in the year (arbitrarily the 65th percentile). Somatisation was defined as the presence of physical symptoms of at least six months duration with no organic disease explanation, or where the frequency or intensity of the symptoms were not fully explained by the presence of any organic disease.

The procedure identified 35% of the HMO to be "high users". A random selection of 1000 high using patients aged 18-55 years was chosen for a case note review. The study showed that patients were more likely to screen positive for somatisation the more contacts they had per year. Using a somewhat complex operationalised criteria to identify patients with somatisation, 14% had somatisation and 51% had what they termed 'minor acute illness' (MAI) as their main problems(99).

Limitations with the Michigan study

This study was limited by having only one rater to apply the operational criteria to the case notes, and there was minimal attention to inter-rater reliability. The criteria developed by this pilot work were complex and protracted. In the publication of the study, it was admitted that the method likely excluded significant numbers of somatisers and also brought about high numbers of false positives (i.e. classifying patients as somatisers when they do not have the condition).

It can be problematic defining what constitutes high health care use or a 'frequent attender'. The first difficulty arises in the definition of a consultation, and the second in quantifying frequency(319). The Smith study showed that definitions of 'frequent' can be based on arbitrary numerical definitions.

The Arkansas multiple 'unexplained' symptoms study

One of the earliest studies, conducted in 1986 by Smith and colleagues, identified a group of 41 high using patients with somatisation(320). Patients were referred to the

study by an internist or a family doctor because they had recurrent and multiple somatic complaints of several years duration for which medical attention had been sought but no physical disorder could be found. Two and a half years of health care use was measured along with somatisation and psychiatric morbidity according to DSM-III criteria and a diagnostic interview.

The majority of this group were female, of low socioeconomic status and poor educational background. There were a large number with marital problems. Patients reported at least 12 'unexplained' symptoms. A history of depression was present in 85%, 68% had a history of anxiety and 58.5% had experienced an emotionally traumatic event in their life. They rated their health as poor as patients with chronic respiratory and diabetic medical illnesses.

The study subjects' high health use was determined by comparison with the general population and was recorded as over six times the amount of hospital care and associated expenditure and almost 14 times more physician costs. These patients were more likely to have uncoordinated care from a variety of doctors.

Limitations with the Arkansas study

The numbers involved in this study were small and generalisability must be called into question. As patients were selected by their treating doctor for entry into the study, sampling bias was likely introduced.

The Seattle "distressed high utilizer" study

For the purpose of conducting a randomised trial of psychiatric liaison in primary care, Katon and colleagues identified patients who made the top 10% of all ambulatory health care visits in a year within one HMO (which incorporated 23 primary care clinics and two hospitals)(321). Male 'high utilizers' were defined as those aged 18-44 years who had seven or more visits in the year prior to study, or 10 or more visits for those aged 45-65 years. For the females aged 18-65 years, patients had 11 or more visits within the previous year. These high users averaged 15 medical visits and 15

telephone calls to a medical facility for the year. Most of the 767 high users identified were under the age of 65 years, and 60% were female.

Of the high using patients 51% (392) screened positively for anxiety, depression and somatisation, and defined as "distressed high utilizers". Of this group, a random sample of 119 subjects was assessed using the Diagnostic Interview Schedule (DIS). Twenty percent met the DSM criteria for SD and 73% met criteria for ASD[5].

"Distressed high utilizers" were more likely to report poor physical health than the non-distressed patients. However, one third of the distressed patients had no chronic disease diagnoses to account for such high use or disability. The study determined that 91 (76.5%) patients had unmet diagnostic and treatment needs for their anxiety and depression, and 51 (43%) patients were associated with some sort of doctor-patient relationship problem.

This study found that a substantial number of patients with depression used considerable non-psychiatric medical care services. However, over three quarters had inadequate treatment for their anxiety and depression.

Limitations with the Seattle study

Determination of chronic medical disease was based on patient self report, rather than case note review, and this may have introduced bias for this outcome. This was a rigorous study using a 'gold standard' psychiatric interview to determine anxiety, depression and somatoform disorders. Limitations were difficult to identify. However, the training, resources and time required to undertake a psychiatric interview could be seen as a limitation in the primary care setting.

The Boston "high utilizers" study

Pearson and colleagues addressed the issue of defining what constitutes high use, by asking the participating HMOs to set their own threshold number of ambulatory

[5] In contrast, analysis of the ECA study data reported a lifetime population prevalence rate of SD of 0.1%(322) and 4.4% met the criteria for ASD(250).

contacts per year(323). The study used the HMO's computer database to identify patients in the top 15% of ambulatory visits for each HMO during each of the previous two years. The number of face to face ambulatory contacts was selected as their identification criterion. This was because consultations correlated highly with health care costs and were thought to be easier to use in everyday practice as the basis for a depression screening program than would a measure of overall costs.

This large study used the Structured Clinical Interview for DSM-IV (SCID(324)) to screen 7,203 high users for depression, of whom 1,465 (20.3%) screened positive for current major depression or depression in partial remission. Among the depressed patients, 621 (42.4%) either had seen a mental health practitioner, had a diagnosis of depression, or both within the previous two years. The prevalence of well-defined medical conditions was the same in patients with and patients without depression (41.5%). Patients screening positive for current major depression averaged more outpatient visits and inpatient days over the two years of study compared with patients with past or no depression. High users who had not made a visit for a non-specific complaint were at significantly lower risk of depression.

The findings suggested that depression screening could be made more efficient by focusing on high users who have frequent medical contacts for non-specific symptoms and complaints. The association between depression and high use of medical services was supported as depressed high using patients had more outpatient visits, hospital admissions, and total number of days in hospital.

Limitations of the Boston study

The generalisability of this study was limited by the fact that the patient population comprised privately insured individuals. The HMOs involved in this study integrated mental health care with the general medical health care services. The findings of adequate treatment for depression from this study may not be extrapolated to other health care services where mental health care is provided by separate organisations.

HIGH USERS OF SECONDARY CARE

There has been little systematic investigation of frequent attenders to secondary care for MUS. This is surprising considering it is more important from a healthcare service perspective to identify the more expensive high users of secondary care. Frequent attendance to secondary care provides an indication of the severity of symptoms and a much higher cost of investigations and management when compared to frequent attenders to primary care. The resulting specialist opinion acts as a 'gold standard' diagnosis of symptoms as 'explained' or 'unexplained' by disease. A discussion of the use of specialist opinions as 'gold standard' will follow later in this thesis (see pages 95 and 236).

Inpatient studies

Admission patterns of *'persistent somatizers'*

Per Fink conducted a series of studies to identify and describe persistent inpatient somatisers in Denmark. In his earlier work, he used a hospital database to identify patients with a high number of inpatient stays(48;68). In a later study, the Danish National Patient Register was used to identify members of the general public (aged 17 to 49 years) who had been admitted 'persistently' to hospital during an 8 year study period(325). Approximately 1% (n = 282) were identified as having been admitted to hospital 10 or more times. The case notes of 113 patients were reviewed and categorised according to whether their physical symptoms could be explained adequately by disease. Of the 2930 admissions, 1126 (38%) were considered MUS. Patients with greater than six MUS admissions (the median number of admissions) were classified as 'persistent somatizers'. Persistent somatisers were compared to other patients from the sample. Documentation from the case notes was used to derive ICD-10 psychiatric diagnoses using the SCAN. Panic disorder, depression and phobias were the most common diagnoses in the persistent somatizers(326). The only main limitation with these findings was that no patient contact had been made, and although the SCAN checklist allowed diagnoses to be made from the notes, the range of diagnoses was restricted and did not include somatoform disorders. Even though 82%

of these inpatients had seen a psychiatrist, the nature or outcome of these consultations was unknown.

Neurology inpatients with conversion disorder

Chapter 2 indicated that patient attributes are not the sole contributor to high use of health care. The following example, a study of the referrals of a group of previously admitted neurology patients with a diagnosis of 'conversion disorder'[6], indicates that frequent attendance may involve a complex series of interactions between patients, GPs and specialists. In fact, this study indicated that referrals for MUS may even be a product of how the current health care system is managed.

Crimlisk and colleagues (241) followed 64 patients (31 women) for six years after admission to neurology for MUS(58). Prior to admission, GPs made most of the referrals (64%) and over 60% of GPs clearly stated that the symptoms were likely to be non-organic, and that they were after a 'final' second opinion. However, patients were admitted for a mean of eight days and underwent a series of expensive and invasive investigations including electrophysiological tests (61%), imaging (53%) and lumbar puncture (31%).

After discharge from hospital with a diagnosis of conversion disorder, 51% were referred back to neurology and 42% were re-admitted. Twenty two (34%) of patients were referred 48 times to other clinics including rheumatology, general medicine, infectious diseases, orthopaedics or immunology. GPs made most of these referrals. Of interest was that 61% of patients had changed GPs during the six year follow-up (one patient changed five times) and the new GPs tended to refer soon after the patient registered. Although patients may have acknowledged psychological distress, 75% of patients did not believe this played any part on their symptoms; more it was the symptoms that made them distressed. Nearly 80% had contact with psychiatry by this time, but this did not seem to alter the pattern of referral. Of concern to the researchers

[6] Conversion disorder is defined as a mental disorder in which an unconscious emotional conflict is expressed as an alteration or loss of physical functioning, usually controlled by the voluntary nervous system(327).

was the fact that patient care did not seem to be coordinated by any one practitioner, and I quote:

> "Perhaps the most striking finding of the study is that few of these patients had a consistent pattern of care during the follow-up period despite the chronicity and severity of their symptoms." ((241), pg. 219)

It must be noted that, although this group of high using inpatients are likely expensive to the health care system, they are at the 'extreme end' of somatisation and unexplained symptoms. Arguably it is of less value to study these intensive users of inpatient services. Ideally, we should be identifying these patients much earlier in their patterns of health care use to direct them to more appropriate services which may better meet their needs and reduce iatrogenic risk and cost.

The most appropriate setting for identification is primary care. However, MUS and associated psychiatric illness often goes undetected in general practice, and some patients are referred to hospital outpatient services. If undetected in outpatient departments, patients risk becoming 'persistent somatizers' as the two examples above have described.

Outpatient studies

Of most relevance to this thesis are two studies which looked at patients who were frequent outpatient clinics attenders. Although, I wish to emphasise that frequent attendance and frequent referral to outpatient clinics represent a different phenomenon, and identify a different group of patients to study. With that said, these studies used the number of secondary care contacts as a means of identifying and studying patients seeking help for symptoms which are classified by specialist assessment to be MUS. A more in-depth critique of these studies is outlined in the discussion section (see pages 252-261).

The Oxford frequent gastroenterology attenders study

Bass and colleagues studied frequent attendances to a gastroenterology clinic at an Oxford general hospital(59). The hospital computer system was used to identify frequent attenders who were defined in this study as those aged 18-65 years, who had attended any general hospital outpatient clinic on four or more occasions in the previous year. Of the 2530 consecutive outpatients who attended a gastroenterology appointment during the 11 month study period, 762 (30%) were identified as frequent attenders.

There were 159 frequent attenders who were assessed to have no organic disease, and 23 with uncertain diagnoses of organic disease. Thus 24% of the outpatient population were identified as frequent attenders with MUS. The first 50, of the 159 frequent attenders with MUS (35 women, 15 men), to attend outpatients again were studied more closely(328).

These patients reported a mean number of 5.7 specialist appointments in the previous year. Of these frequent attenders with 'unexplained' gastrointestinal (GI) complaints, 35% were also deemed frequent attenders in primary care (≥12 visits in the previous year), and were often patients of other hospital specialist clinics. A gastroenterologist interviewed, examined (and investigated where appropriate) the participants to diagnose whether symptoms were explained or 'unexplained' by organic disease. Approximately 20-25% of the patients assessed had MUS.

Patients had a mean number of 5.9 lifetime somatic symptoms. Psychiatric diagnoses were made using the SCID (DSM-III-R), and 45 of the 50 patients (90%) had at least one current psychiatric diagnosis and 24 (48%) had at least two. Somatoform disorders were the most common, but only three had somatisation disorder.

Limitations with the Oxford study

This study proved that hospital computer records could be reliably used to identify frequent attenders to outpatient clinics, and that high medical use was associated with MUS and a high proportion of psychiatric illness. The limitation with this study was that only 50 patients were closely examined. Although the subjects were also attending

other outpatient departments, the findings only really apply to gastroenterology outpatients.

The London frequent attenders study

The majority of previous secondary care studies of MUS focussed on new patients(45) or psychiatric referrals(62). The most relevant study to the research described in this thesis was conducted in the South Thames (West) NHS Trust of London by a research psychiatrist, Steven Reid and colleagues(60). Their aim was to identify 'unexplained' symptoms in frequent attenders to a range of secondary care outpatient clinics, and describe their characteristics. Frequent attenders were defined as the top 5% of outpatient users for those in the age groups of 18-45 and 46-65 years.

Reid addressed all the concerns I have already raised about the previous studies. To summarise, these included:

1) An identification procedure which combined computerised outpatient activity data with hospital case notes (i.e. hybrid method)

2) Assuring inter-rater reliability of the operationalised criteria employed when reviewing the case notes(329)

3) Identification of high users to a range of medical and surgical outpatient clinics situated in more than one hospital

4) Psychiatric illness was identified using both a psychiatric interview (Schedules for Clinical Assessment in Neuropsychiatry - SCAN(330)), patient case notes, and patient self report by means of the Hospital Anxiety and Depression Scale – HADS(331), and

5) An estimate of the health costs of these frequently attending outpatients(61). This will be addressed in more detail in chapter 15 of this thesis.

A random selection of 400 patients, drawn from two age groupings, was made and 361 case notes were reviewed. There were 97 frequent attenders (26.9%) who had one or more consultation episode for MUS, and 61 (16.9%) who had two or more episodes of MUS (defined as somatisers). Of the 971 consultation episodes reviewed, 21% were classified MUS. Abdominal pain, chest pain, headache, and back pain were the most common MUS. These frequent attenders reported high levels of disability and spent between 1.3 and 4.9 days in bed each month. In comparison, patients with serious medical conditions averaged a day or less.

A three year follow-up study of 48 of the 61 (78.7% response rate) frequent attending somatisers was conducted by the same research group(208). The sample continued to be high users of a range of health services and continued to report functional impairment. Psychological morbidity as identified by the HADS found 69% reached the cut-off score for anxiety and 52% for depression. At least one current psychiatric diagnosis was determined in 33 (69%) patients and 23 (48%) had at least two. Approximately 50% met the DSM-IV criteria for any anxiety disorder or mood disorder according to the SCAN. Inadequate psychiatric treatment was indicated by the fact that of 208 medically 'unexplained' episodes assessed, only 14 (6%) resulted in antidepressants being prescribed and only four (2%) unexplained episodes resulted in a psychiatric referral.

This was an important series of studies for the following reasons:

1. it found that MUS account for a substantial proportion of secondary care use by frequent attenders, and in most hospital outpatient specialties.

2. Frequent attenders had high levels of functional impairment and psychiatric illness.

3. Although frequent attenders with MUS had levels of service use and expenditure comparable to frequent attenders with organic disease, their use and cost of investigations was significantly greater.

Limitations with the London study

There were limitations with this study, and these are addressed in more detail in the discussion section (see summary on page 260). In brief, the final number of patients interviewed was small (48, 13.3% of the case notes originally reviewed). Over 61,200 frequent outpatient attenders were originally identified and a random sample of 400 was selected from those. It is therefore questionable how generalisable results from only 48 frequently attending outpatients actually can be. As 'somatisers' were defined as having two or more attendances with MUS, and the comparison group had one or no MUS, the control group was poorly defined and of questionable difference to the study cases.

A NOVEL APPROACH TO STUDYING MEDICALLY UNEXPLAINED SYMPTOMS: FREQUENT REFERRALS

In summary, the high user studies, particularly the two frequent outpatient attender studies, provided important information about patients who are high users of health care services. However, the frequent outpatient studies identified their subjects solely in secondary care. Such specific focus is of limited value for informing interventions in primary care aimed at reducing unnecessary hospital referrals. Other questions left unanswered included:

1. How do patients with MUS become frequent attenders to outpatient clinics? Most patients are referred to outpatient clinics by GPs. A survey of GP attitudes to MUS was conducted by Reid(25), yet it did not adequately address GP and patient factors for frequent referral to outpatient clinics.

2. Are disorders of anxiety and depression one of the main associations with frequent referral for MUS?

3. How specific is anxiety and depression to being frequently referred with MUS compared to other patient groups? e.g. do other patients have anxiety and depression?

4. If undetected anxiety and depression are associated with frequent referral, what psychiatric or psychological treatment are these patients receiving?
5. Reid assessed health care costs for the frequent attenders with MUS, but did not assess the most expensive, which were inpatient costs(61).

Although GP consultations are less costly than outpatient consultations, they are the gateway to accessing expensive and intensive secondary care services. Referrals to outpatient departments are not as expensive as admissions to hospital, but they are often the precursor.

This thesis is concerned with patients frequently referred from general practice to hospital outpatient clinics for symptoms diagnosed as 'unexplained' by a specialist (MUS). This is an appropriate group to study because:

- the patient has sought some sort of help by consulting a GP
- the GP has sought help from medical specialists by frequently referring the patient to hospital outpatient clinics
- their management is expensive to the health care system but ineffective (as they keep getting referred for MUS),
- they are at risk of iatrogenesis, and
- the classification of MUS is valid in so far as it has been made after specialist assessment in the outpatient clinic.

The advantages of this approach are that both patient and GP assessments can be undertaken to determine GP management difficulties and reasons for referral. GP case notes can provide extensive information allowing in-depth analysis of a patients' lifetime use of healthcare services, which is a neglected area of research into MUS. Case notes include documentation of a lifetime's worth of symptoms(57;247). The first step towards using this novel approach was an unpublished pilot study undertaken by a research psychiatrist, Ben Smith(332).

Single practice pilot study

This pilot study[7] was conducted in a single Edinburgh-based general practice with nine GPs and had approximately 10000 registered patients. With ethical and privacy advisory council approval, centralised computer records of all referrals made from the practice were obtained from the Information and Statistics Division (ISD) of the National Health Service (NHS). The activity data were reviewed for all patients aged 18 to 65 years who had been referred five or more times in the last five years of available data. Using this arbitrarily chosen threshold, 76 patients were identified. For the purposes of research, they were classified as frequently referred (FR).

The hospital correspondence, between the referring GPs and assessing specialists, was reviewed in the GP case notes of the identified FR patients. Each referral and the outcome as outlined by the letter from the specialist to the GP were noted in detail. Based on the example of Reid's study of frequent outpatient attenders(60), a set of operationalised criteria (See Appendix 1) were developed to define MUS using specialist opinion as the 'gold standard'. This was assessed for inter-rater reliability which was found to be good (kappa 0.73). Each completed referral episode was then coded according to the operationalised criteria.

Two thirds of the FR patients had at least one referral that had resulted in a diagnosis of MUS. Twenty three (30%) patients had at least three referrals for MUS; these patients were defined as FRMUS cases. Twenty five (33%) of the FR patients had outcomes explained by organic disease processes and were defined as FRMES controls. An attempt was made to recruit a second control group of patients who had not been referred at all. However, this brought about such a low response rate from those invited (5%) that further analysis of these patients was abandoned.

This pilot showed that patients could be reliably identified using a combination of centralised activity data and GP case notes. The FRMUS cases had a lifetime history of repeated referrals to secondary care for MUS. These patients had higher rates of physical impairment and anxiety and depression. Almost all FRMUS patients

[7] I shall be making further reference to this research in this thesis in order to compare some of the methodology and findings with the current larger study. This pilot shall be referred to as 'the single practice pilot study'.

identified by ISD and case note review had a somatoform disorder according to the SCID.

GPs perceived more FRMUS patients as difficult to manage when compared to FRMES patients. However, not all FRMUS patients were considered difficult. Reasons for this were unclear, but possibly once a patient had been referred, they did not re-attend the practice again until they had been seen by a specialist months later. Alternatively, patients may remain in the hospital system as a result of the referral, and the GP loses control as coordinator of care.

Limitations of the single practice pilot study

A limitation with this pilot study was the small study sample of 16 FRMUS cases and 13 frequently referred patients in the comparison group. Such a small sample size brought statistically insignificant findings and comparisons were of limited meaning. The fact that the study was only conducted in one practice limited generalisability. A larger multi-practice study involving more general practices, GPs and patients was necessary to determine if the identification procedure and findings might be generalised to a wider primary care setting. Such a multi-centre study, the 'Referral Study', is described in this thesis. The aims and hypotheses of the study will now be outlined in the following chapter.

CHAPTER 6. NEW DEVELOPMENTS DURING THE CONDUCT OF THIS STUDY

The literature included so far in this thesis has outlined studies published before the current research got underway (i.e. November 2002). This chapter specifically deals with the most relevant studies which came to light after this project commenced and up until submission of the thesis in January 2006. There have been no studies which have specifically looked at patients with high numbers of referrals from general practice to secondary care services for medically unexplained symptoms. However, for the purposes of this chapter, those published studies which looked at frequent medical consultation, or high health care utilisation, for patients with medically unexplained symptoms have been outlined.

The first section addresses recent studies conducted in primary care, and the second outlines studies of MUS in secondary care. The third section looks at high users of medical care identified by overall health care use or cost. This also incorporated the most recent American studies of 'high utilisers' with MUS which tend to cover all ambulatory health care contacts (including primary care and secondary care outpatient, and A&E contacts). I have also included a section each on recent intervention studies and some of the latest thinking about the classification of MUS. Further discussion of later studies of interest, as well as developments in classification of MUS, can be found later in this thesis in regards to study findings (pages 228-9), limitations (from page 231), and discussions of other new studies of relevance to the topic (from 258 onwards). I bring this chapter to a close with a section outlining my conclusions of what MUS actually are as a result of my review of the literature.

RECENT DEVELOPMENTS IN THE STUDY OF PATIENTS WHO FREQUENTLY ATTEND PRIMARY HEALTH CARE WITH MEDICALLY UNEXPLAINED SYMPTOMS

The Utrecht Study

A large survey conducted in Utrecht, the Netherlands(333), identified patients over 18 years of age who had consulted their GP at least four times in one year for persisting symptoms but received no defined organic medical diagnosis by the end of the year (medically unexplained physical symptoms - MUPS - group). This study identified two comparison groups where the first was based on average patients from the general population minus the MUPS group (average patients group), and the second were patients who had consulted their GP at least four times with "real"[8] medical diagnoses (diagnosis group).

The MUPS group consisted of 5507 primary care patients out of a total population of 225013 (2.45%). Further supporting the evidence that functional somatic syndromes overlap with one another, patients in this group had a great deal of overlap between clusters of functional symptoms as collated by Robbins and colleagues in 1997(334).

There was an over-representation of over 75 year olds in the MUPS group which mostly explained the reason why the MUPS group were significantly older than the other two patient groups. This group also had significantly more females and patients with low levels of education; two very common findings in studies of patients with MUS. Compared to the two other patient groups, the MUPS group were more likely unemployed but both frequent attender groups were equally likely to be retired. Generally the MUPS group showed greater indicators of deprivation or low socioeconomic status than the other patients. The MUPS group had significantly more GP consultations for illness, and episodes which resulted in a psychological diagnosis, than either of the other two patient groups. The study group of interest also reported far worse health than the two comparison groups.

The main limitation with this study was its *a priori* assessment of symptoms. The authors acknowledged that assessment should ideally be dependent on context. The

[8] The authors' term.

study concluded that further research was needed to 'disentangle' the relationship between frequent attendance and MUPS.

RECENT DEVELOPMENTS IN THE STUDY OF PATIENTS WHO FREQUENTLY ATTEND SECONDARY HEALTH CARE WITH MEDICALLY UNEXPLAINED SYMPTOMS

The Los Angeles Study

In an attempt to assess the association between levels of somatisation and health care use, a large cross-sectional survey of 1410 patients with irritable bowel syndrome (IBS) was carried out in California, USA(335). Consecutive attenders to a specialty gastrointestinal out patient clinic were identified as they were aged between 18 to 49 years and had tested positive for the Rome Criteria for IBS. As this was an American health service unit, it is worthy to note that one third of patients self refer themselves to this clinic and two thirds are referred by their GP or other gastroenterologists.

Health care use and cost data were derived from patient self-report. This is a major limitation of the study due to likely bias introduced by patient recall. With this in mind, the large majority of the cohort was female (68%) and over 52% had gone on to further education after high school. Out of a maximum somatisation score of 100 (using the symptom checklist SCL-90-R), the mean somatisation score of this cohort was 59.7. Forty seven percent of the cohort had not used gastroenterology resources in the previous year. In a regression analysis, high levels of somatization did not predict physician visits, but symptom severity and postgraduate education did act as predictors. Interestingly, once evaluated for care in the gastroenterology clinic, patients with high somatisation scores were more likely to expend significantly more health care dollars than patients with low somatisation scores. This study suggested that outpatient doctors/gastroenterologists, more so than patients, played a part in mediating the relationship between somatisation and health care use and costs.

The Manchester Study

A study conducted in Manchester, UK, identified consecutively attending patients presenting to a secondary or tertiary outpatient clinic with upper abdominal or chest pain(284). Participants completed a battery of self-report measures to assess general health, anxiety and depression, illness perception, childhood abuse, and life event outcomes. The main outcome variable was the total number of consultations with GPs, hospital specialists (outpatient visits), and allied health visits (e.g. physiotherapist, occupational therapist, and district nurse) obtained from patients' notes for 12 months before the index visit and 6 months after (18 months overall). A multiple regression analysis was used to identify the factors most closely associated with health care use.

Biggs and colleagues' study found that patients had a median number of 14 visits over an 18 month study period (9 were at the GP). Women were more likely to consult more. One quarter of the patients made 20 or more visits, and the numbers of visits were consistent during the 12 months before and the 6 months after the index clinic visit. There was no significant difference in the number of health care visits between those for demonstrable pathological abnormalities and those of functional origin. Health care use was significantly associated with the health anxiety outcome variable, but not with anxiety or depression scores derived from the HADS. Illness perceptions were significantly associated with number of health care visits. Ongoing social stress was not a significant predictor for health care use. Of interest from this study was the fact that higher health care use was associated with a poor relationship with the father and with sexual abuse. People who reported two or more childhood adversities showed the clearest increase in number of health care visits and this occurred only in patients with functional gastrointestinal disorders. The predictor variables for number of hospital medical specialists and non-medical health professionals were: physical function scores, mental health, health perception, gender, and pain severity.

The Manchester Study was followed up by the same research group to determine if there were any psychological mediators for the relationship between childhood adversity and frequent medical consultations(336). This study is outlined in detail on pages 266-267. However, their later findings indicated that a history of severe childhood adversity was associated with frequent primary and secondary care medical

consultations in patients attending neurology, cardiology, and gastroenterology clinics. This relationship was confined to patients with medically unexplained symptoms.

The London Study

For completeness, I should add that the final follow-up phase of the London Study by Reid and colleagues was published in 2003(208). This has been outlined previously on pages 67 to 69, addressed in relation to the health economic phase of the study on pages 209 to 210, and finally discussed in great detail in the Discussion Section from pages 252 to 261. However, of importance from the final phase of this study was the fact that during three years of follow-up, the sample continued to use high levels of secondary health care services. The majority of frequently attending outpatients with MUS had one or more diagnoses of an anxiety and/or mood disorder. There were indications that this group of patients were receiving inadequate or no treatment for their anxiety or mood disorders.

RECENT DEVELOPMENTS IN THE IDENTIFICATION AND STUDY OF FREQUENTLY ATTENDING PATIENTS WITH MEDICALLY UNEXPLAINED SYMPTOMS BY OVERALL HEALTH SERVICE USE OR COST

The Harvard Study

Barsky's research group has been interested in the interactions between psychiatric disorder (specifically somatisation) and health care resource use since the 1980s. One recent study by this group identified consenting participants, over the age of 18 years, by consecutive attendance to two primary care practices(337). Of those identified, 1546 patients completed the Patient Health Questionnaire (PHQ) and Somatic Symptom Inventory (SSI) as well as outcomes of functional status and medical morbidity. Although patients were identified by primary care attendance, the health care use data and associated costs calculated encompassed all primary care, mental health care,

specialist care, and emergency visits, as well as hospital admissions. One year of health care contacts and costs were obtained from the affiliated hospital's computer database.

Over one year, patients averaged 3.7 primary care visits, 5.6 visits with a specialist and 0.3 contacts with mental health care services. A provisional diagnosis of somatisation from the PHQ was assigned to 20.5% of participants (299 patients). Compared to non-somatising patients, somatisers were more likely to be female, less educated and belong to an ethnic minority group. Somatisers with comorbid anxiety and depression used more health care resources than those with anxiety or depressive disorders alone. Total annual health care costs came to US$6354 as opposed to US$2762 for non-somatising patients. A limitation of this study was that patients likely sought medical attention at other hospitals, and this was not accounted for. However, if anything, these findings were an underestimate of the total use and costs of the study sample. Somatisation was found to be a highly significant predictor of health care use and costs even when fully adjusted for potentially confounding variables such as medical comorbidity and sociodemographics.

The data from the above study was further used to differentiate somatising patients from non-somatising patients from their characteristics and patterns of medical care use(338). Using predictive modelling techniques, the following were considered to be predictor variables for distinguishing somatising from non-somatising patients:

- female gender
- black or Hispanic
- low levels of education
- younger than 60 years of age
- more specialty visits than primary care visits
- greater secondary care costs
- any number of mental health visits and ambulatory care procedures

However, there were still high proportions of false positives (i.e. classified as somatising when they did not have the condition) and false negatives (i.e. classified as

not somatising when they did have the condition) when these criteria were applied. Thus the study's algorithm was unable to distinguish the two groups well enough to be practically useful.

The Connecticut Study

Patients over 17 years of age (including up to 103 years!) were identified by an index ambulatory care visit in 1998, and were defined as high utilisers (HU) if they had a number of visits two standard deviations beyond the mean (i.e. more than 8 for women and 7 for men)(339;340). A random sample of 125 men and 125 women were selected. A comparison group of 125 men and 125 women were randomly selected from those patients with two consultations in 1998. Computerised medical practice data were used to determine diagnoses, medical visits, and demographics. Although not specifically looking at symptoms, a regression analyses were used to determine if psychiatric conditions, such as anxiety and depression, contributed to high health care use independent of other variables.

Compared to the control group, the HU group was more likely to be younger, from an ethnic minority, and not working. Current medical conditions attributed for a great amount of the medical visits. However, the HU group was more likely to not attend appointments. A diagnosis of anxiety was independently associated with HU status, and this group of patients had higher rates of anxiety, depressive and addictive disorders. In terms of patterns of health care use, low utilisers mostly remained low utilisers, where as the HU group had two sub groups that had transient or stable high use. Persistent high use was associated with medical morbidity and anxiety. Psychiatric disorders were not associated with persistent HU for specialty or emergency services, but did play a role in persistent high health care use that was distinct from medical illness.

The Mainz Study

In the quest to identify patients for an intervention study, a research team in Mainz (Germany) defined high health care use as healthcare expenditures of ≥€2500[9] during the previous two years(341). Somatoform disorder (SFD) was determined by an initial screening questionnaire and confirmed by the Structured Clinical Interview for DSM-IV (SCID) upon inpatient admission to a special clinic for patients with psychophysiological and mental disorders. Patients were selected only if they had a positive SFD diagnosis, and for whom cost calculations were obtainable from their health insurance companies (n=95). Three groups were devised on high utilising SFD patients, average use SFD patients and average use patients with other mental disorders, namely mood disorders and phobias.

In contrast to the two other comparison patient groups, the high utilising SFD patients had higher scores for illness behaviour, occupational disability, self-perceived bodily weakness, more hypochondriasis-related somatic symptoms (from the Whitely Index), and a higher level of disability in different areas of psychosocial functioning. The cases reported more subjective distress from symptoms. A subgroup of 27 extremely high utilising SFD patients (≥€5000) showed a higher proportion of women and the tendency to catastrophise or be intolerant of bodily discomfort.

Summary of Frequent Attender Studies

Consistent findings from these studies show similar patient characteristics, such as a high preponderance of females and patients with low levels of education. Psychological and mood problems tended to be more prevalent in the frequent attender groups with MUS. However, there is new evidence that other influences, such as childhood adversity and patient attributional styles, may explain the background behind some of the high number of attendances. Although these patients only account for a small proportion of the total patient population, the frequent attenders have high health care costs which are disproportionate to their numbers. There is continued evidence that the high health care costs are not matched by improved patient outcomes.

[9] Where the average 2-year per capita expenditures published by the German public health insurance companies were about €700 for outpatient medical care and about €1400 for inpatient care(341).

RECENT DEVELOPMENTS IN THE TREATMENT OF FREQUENTLY ATTENDING PATIENTS WITH MEDICALLY UNEXPLAINED SYMPTOMS

Psychological Interventions

The Mainz Intervention Study

Following on from the identification phase of the German study by Rief's research group(341) outlined above, patients were entered into an intervention study to evaluate the effects of cognitive-behavioural therapy (CBT) on physical symptoms, mental health status, and healthcare use of newly admitted patients with somatoform disorders(342). A psychiatric interview identified 172 patients with a somatoform disorder (SFD i.e. 54 patients with somatisation disorder, 51 with abridged somatisation disorder, and 67 with an other defined SFD), and a clinical non-SFD comparison group of 123 patients. Patients were treated within a broad interdisciplinary approach based on the principles of CBT and behavioural medicine. Health care costs before and after CBT were compared. Those health care costs calculated included: inpatient, outpatient, outpatient dental, prescriptions, and other related services charges (such as transport, glasses, hearing aids and crutches).

Patients were aged between 19 and 72 years. The only significant difference between the two groups in terms of demographic characteristics and comorbidity was the number of somatisation symptoms according to the DSM-IV checklist. However, the SFD patients had higher scores for hypochondriasis and dysfunctional body-related cognitions. The mean period of treatment time received was significantly more for the SFD patient group at 58.6 days (range 21–114), compared to 52.2 days (range 15–84) for the non-SFD comparison group ($p \leq 01$). As a result of the intervention, the outpatient charges of the entire SFD group decreased by 24.5%, and inpatient charges reduced by 36.7%. The inpatient charges of the non-SFD patient group also decreased substantially by 27.9%. Days off work in the SFD group were reduced by 35.3% and 30.6% in the comparison patient group. Significant correlations were found between total cost changes and corresponding changes of the somatisation, hypochondriasis and depression scores, but not with changes of catastrophising symptoms.

A subsequent publication of a randomised controlled trial by Reif's research group in Mainz provided further evidence of the potential benefits from CBT for patients with

multiple somatoform symptoms in tertiary care(343). At one year follow-up, all outcome criteria were significantly reduced. Patients who received the intervention of additional group management training of somatisation had a significant reduction of visits to the doctor. Greatest longitudinal effect sizes were found for the reduction of somatoform symptoms in treated patients.

The Amsterdam Study

This randomised controlled trial from the Netherlands set out to test the effect of psychological intervention on multiple MUS, psychological symptoms, and health care resources use(344). Ninety eight patients were assigned to either one of the following two groups: psychological intervention by a qualified therapist plus usual care by a GP, or usual care only. Self-reported and GP reported MUS decreased from pre-test to the two other follow-up time points of six and 12 months. Psychological symptoms and consultations also decreased. However, intervention and control groups did not differ in overall symptom reduction.

General Practitioner Education and Training

Three Danish studies attempted to assess the effect of providing GPs with specialised communication skills, and reattribution training, to better detect and manage patients with MUS. Although GPs stated a more positive attitude towards, and confidence in, managing patients with MUS(345), they did not improve in terms of diagnostic accuracy(346). However, patients did state greater satisfaction with their care as a result of GPs receiving this training(347).

Summary of Intervention Studies

The above studies have provided mixed evidence in terms of benefits from psychological treatments for patients. The Mainz studies targeted inpatients who would be higher along the spectrum of MUS in terms of severity. Arguably, any

improvements in such a high using group of patients must be viewed as a positive finding. Increasingly, studies of reattribution training in general practice are finding minimal benefit in terms of patient outcomes, symptom relief, or reduction of health care resources consumed. These findings question whether a psychological approach alone is the answer to minimising this phenomenon. There are further recent studies outlined in the Discussion Section (see pages 247, 283 and 284) which provide evidence of the benefits of antidepressants in the treatment of MUS.

RECENT DEVELOPMENTS IN THE CLASSIFICATION OF MEDICALLY UNEXPLAINED SYMPTOMS

In preparing the latest version of the DSM (the DSM-V), experts have gathered to discuss alternatives to the somatoform category(348). As outlined previously in Chapter 2, there is much controversy about what to call MUS and how to diagnose them in a meaningful way which is helpful for both doctor and patient. From a research perspective, it is also essential to have a classification which is easy to operationalise. In an attempt to eliminate unhelpful dualist thinking, the group have proposed to abolish the category of somatoform disorders altogether, and reassign specific somatoform diagnoses to other parts of the DSM. Diagnoses could also be elaborated on by using an additional multidimensional description.

A new term for somatic symptoms and syndromes has been called for. This could simply be called "somatic symptoms" with an associated disease diagnosis specified later if found (e.g. "abdominal pain" and perhaps later, "pain associated with bowel cancer"). The term "functional" was suggested as an adjective to emphasise the lack of association with a general medical condition. Ultimately, this new classification should be acceptable to patients (with or without medical conditions), and to clinicians at the coal face where it should relate effectively to the functional disorder classification currently used by many doctors. The classification should be etiologically neutral but provide help in planning future patient management. Ideally, the classification would also provide an effective basis for further research. However, whether this

classification suggested by Mayou and colleagues will be implemented, or indeed be feasible in practice has yet to be evaluated.

CONCLUSIONS OF WHAT MEDICALLY UNEXPLAINED SYMPTOMS ACTUALLY ARE

To provide a definitive conclusion on what MUS are is no easy task. The literature demonstrates that clinicians and academics across the board have found these symptoms difficult to name, conceptualise, and classify. Perspectives are different within and between medical specialties, and this includes differences between primary and secondary care. The Mayou paper outlined above, along with the evidence outlined in Chapter 2, demonstrates that experts in the field are still unsatisfied and grappling with current classifications.

Simply put, medically unexplained symptoms are symptoms of an unknown or unidentifiable physical or structural cause. Psychiatric experts in the field tend to align these with an underlying psychological problem (thus its inclusion in the DSM). Some doctors who manage patients with functional somatic syndromes believe that these are bona fide organic-based diagnoses to some extent(233;349). However, there are others in medicine (evidence suggests in the majority) who believe these diagnoses to be predominantly unexplained by disease(155;350-352). There is no 100% agreement.

There is a growing awareness or belief that a purely psychiatric approach towards MUS is unacceptable to many patients and their attending doctors. More recent literature has again questioned the common notion of somatisation as physical manifestations of psychological problems, such as anxiety, depression and panic. Somatisation disorder, hypochondriasis or MUS cannot be conclusively regarded as psychiatric disorders(353). Although associated with MUS, reviews of the literature have shown that emotional disorders do not fully explain the phenomenon(102;354). The evidence remains that there are patients who present with medically unexplained somatic symptoms, but are without an underlying anxiety or depressive disorder(355;356). Patients with a medical diagnosis, such as heart disease or stroke, can still have symptoms that are not plausibly explained by their disease. There is a complex relationship between psychological and

somatic distress(293). Others would argue there are other mediators in between such as doctors' attitudes(223;357;358), life context(359), childhood adversity(284;336), and environmental factors(100;292) which contribute to the phenomenon.

To quote Laurence Kirmayer and colleagues in their recent 2004 article(360):

> "The term 'medically unexplained symptoms' names a social and clinical predicament, not a specific disorder... rather, a way of drawing attention to a situation in which the meaning of distress is contested." (pg. 663).

With this predicament comes uncertainty of how to operationalise the problem for clinical management and research purposes. In this study, I have sought to assess documented evidence in order to classify symptoms on a spectrum of explanation by physical disease or structural changes according to specialist opinion (see pages 106-7). Whether there is some psychological basis, or perhaps other contributing factors, to this phenomenon of MUS is one of the main research questions posed by this study.

METHODS

"For each ailment that doctors cure with medications (as I am told they do occasionally succeed in doing), they produce ten others in healthy individuals by inoculating them with that pathogenic agent a thousand times more virulent than all the microbes — the idea that they are ill."

Marcel Proust (1920) 'Le Cote de Guermantes' (The Guermantes Way)

CHAPTER 7. AIMS AND HYPOTHESES

AIMS

The aims of this research were to:

1. identify patients frequently referred (FR) from general practice to hospital outpatient clinics for symptoms that a specialist has diagnosed as medically 'unexplained' (MUS).
2. quantify the prevalence of FRMUS patients in primary care.
3. describe the characteristics of FRMUS patients. The characteristics studied include the following:
    - Demographics: i.e. age, gender, deprivation, marital status, living arrangements, education, employment, and benefits received
    - Number and specialty of outpatient contacts attended (and those appointments that the patient did not attend – DNA)
    - Other health care contacts including: investigations, A&E visits, out of hours GP contacts, days admitted
    - The number of referring GPs involved in each patient's care
    - GP 'difficulty' in managing these patients' problems
    - Number of years registered with the practice
    - Medical diagnoses and surgical procedures
    - Past documented, and current self-reported, symptoms of anxiety, depression and panic
    - Past and current documented psychiatric treatment (antidepressants and mental health contacts)

- Past documented and current self-reported somatic symptoms
- Physical and mental health function
- Illness perceptions and beliefs
- Attitudes to medical and psychiatric treatment
- Attitudes to disclosing problems to doctors
- Satisfaction with health care received
- Time off work and usual activities

4. compare each of the above characteristics of FRMUS patients with those of two other patient groups using a case-control study design. One group was frequently referred for medically 'explained' symptoms (FRMES); the other group was infrequently referred for physical symptoms (IRS).
5. calculate the five year health care costs of FRMUS patients

HYPOTHESES

1. A greater proportion of FRMUS patients will have symptoms and diagnoses of anxiety or depression compared to FRMES patients and IRS patients.
2. A greater proportion of FRMUS patients will have received inadequate treatment for their anxiety or depression compared to FRMES patients and IRS patients.

Secondary Hypotheses

Compared to FRMES patients and IRS patients, FRMUS patients will:

1. be referred by a greater number of different GPs
2. have problems regarded by their GP as more 'difficult' to help
3. have higher health care costs
4. be more dissatisfied with the health care they receive
5. perceive their health to be worse
6. report more current symptoms
7. be more worried about their health
8. state more discomfort in disclosing emotional problems to doctors, and
9. have more time off work and other activities due to ill health

OVERVIEW OF THE STUDY DESIGN

The current study was designed to address the research aims and hypotheses as outlined above. This involved three related phases which were as follows:

Phase 1

The first phase involved identification of patients frequently referred with medically 'unexplained' symptoms (FRMUS) and two other patient groups. Eligible patients were identified using a combination of national secondary care data from the Information and Statistics Division (ISD) of the National Health Service (NHS) and patient case notes in their registered general practice. Operationalised criteria were

applied to all referral episodes documented in the case notes for a five year time frame. The prevalence of FRMUS patients was calculated. The characteristics of this patient group were determined (i.e. basic demographic information, symptoms, health care utilisation, specialist diagnoses and medical treatments).

Phase 2

Information for this phase was derived from four main sources: ISD data, primary care case notes (collected in phase one), as well as GP and patient questionnaires. Patients identified in the first phase were invited to participate in a questionnaire study that formed the second phase of the study. The questionnaire assessed variables as outlined in the hypotheses (e.g. anxiety and depression, satisfaction with health care, etc.). Characteristics of FRMUS cases were compared with two control patient groups. The first group were patients frequently referred with medically explained symptoms (FRMES); the second group were patients infrequently referred for symptoms (IRS).

Phase 3

The health care contact data, as collected in Phase One, was given a monetary value. These were added together to provide an estimate of health care costs for each FRMUS patient. A 15% random selection of those FR patients who participated in Phase Two of the study had a further lifetime review of their case notes. A lifetime health care cost was estimated for each of these randomly selected FR patients.

CHAPTER 8. IDENTIFICTION OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS AND TWO OTHER COMPARISON PATIENT GROUPS (PHASE-1)

CROSS-SECTIONAL STUDY DESIGN

A cross-sectional study is well suited to the task of identifying and describing a group of patients with a characteristic of interest. This design facilitates calculations of prevalence, and patterns of distribution, in the population sampled from(361). It is called a cross-sectional study as it takes a cross-section of subjects from the population of interest (e.g. general practice patients) and studies them for variables of interest for a given period of time.

I used a cross-sectional study design to identify eligible patients for this research. Central to the cross-sectional phase of the study was identifying patients with a pattern of frequent referral (FR) for medically 'unexplained' symptoms (MUS) and the prevalence of this group of patients in general practice.

SOURCES USED TO IDENTIFY PATIENTS (INFORMATION AND STATISTICS DIVISION DATA AND CASE NOTE DATA)

Information and Statistics Division (ISD) Data

The Information and Statistics Division (ISD) is the Common Services Agency for the National Health Service (NHS in Scotland). Its broad remit is to collect, validate, and disseminate health service activity, manpower and finance data. ISD receives this data at regular intervals from health boards, NHS trusts and general practices. The data are processed securely and in accordance with the requirements of data protection legislation.

ISD provides important information services to health care organisations in Scotland. For Scottish primary care practices, it can provide information on:

- GP prescribing and dispensing
- general practice activity
- items of service
- immunisation and screening levels
- patient demographics and deprivation profiles
- GP diagnoses, and
- GP workload.

The systematically collected ISD data offered an opportunity, unique in the UK, to efficiently identify patients frequently referred to hospital. There were five Scottish Morbidity Recording (SMR) secondary care datasets obtained from ISD for this research (see Figure 5).

Figure 5. SMR ISD data of secondary care contacts

SMR00	outpatient department contacts
SMR01	inpatient admissions
SMR04	Psychiatry contacts
SMR06	Oncology contacts
99B	deaths

The SMR00 data contained information relating to outpatient contacts of patients registered with five general practices (described further in this chapter on pages 97-9). Information included: a unique patient identifier number (PIN), patient first name, surname, maiden name (if applicable), unique Community Health Index (CHI) number, source of referral (GP, prison/penal establishment, accident and emergency

(A&E), specialist from same or another specialty), medical specialty, date of clinic attendance, procedures, and diagnoses. Basic demographic information was also available from this dataset and included patient date of birth, gender and deprivation category (DepCat) of residence.

Justification of Information and Statistics Division data use

The majority of general practices in Scotland use computers to record patient health care contacts, and the software most commonly used is GPASS (General Practice Administrative System for Scotland)(362;363). The accuracy and detail of information entered into these computing systems varies between practices(364). Although there is a function on GPASS to manually enter referrals made from the practice, some practices do not use this. For example, one participating practice recorded their referrals by writing them on separate pieces of paper and filing them in a drawer. Paper copies of referral letters are filed in patients' notes, but it is impractical to identify eligible subjects by trawling through thousands of case notes at multiple practices.

Other software such as 'Second Opinion' provides templates for referral letters and the capacity to send directly to the appropriate hospital department. At the time of conducting this study, there was no way to link referrals made through 'Second Opinion' to the main patient record on GPASS. According to personal communication with Dr. John Donald(362), approximately 20% of GPs reported using this software as of 2002.

The ISD of the Scottish NHS provides arguably one of the best national databases of all hospital attendances and admissions in Europe. An annual in-house audit by ISD indicates the accuracy of their data. Compared to referrals documented in GP case notes, the single practice pilot study indicated that ISD data enabled valid identification of referred patients (Pearson's correlation coefficient 0.84, $p=0.01$). The number of referrals from a participating general practice could readily be quantified. The outpatient specialty referred to could also be identified from this data. This was useful given some specialties are more likely to receive referrals for MUS than others.

The single practice pilot study showed that data from ISD were unable to reliably identify patients referred with MUS. Although ISD aims to provide diagnoses or outcomes of secondary care consultations, these are often absent. If provided, the diagnostic coding system is extremely complex and time consuming to decipher.

Primary care case notes

A more detailed description of the case note audit procedure is described further into this chapter from pages 105-9. However, in brief, the case notes of patients referred to hospital outpatients as identified from the ISD data were retrieved for audit at the respective general practices. The hospital correspondence section of each set of GP case notes was reviewed for several reasons. The first was to ascertain GPs' reasons for referral i.e. symptoms, from their referral letter to the specialist. The second was to confirm the patient had actually attended the outpatient consultation. Finally any assessments, investigations, findings and diagnoses according to 'gold standard' specialist opinion were obtained from specialists' letters back to the GP, i.e. symptoms were 'explained' or 'unexplained' by disease.

Justification of using case note data

The hospital correspondence section of GP case notes contains written documentation of all secondary care contacts (although patchy and less complete prior to the 1990s). Letters from the referring GP detail the reasons and symptoms for referral, whilst returning letters from the hospital specialist confirmed attendance, outlined assessments conducted and the detail of findings and diagnoses.

The combination of ISD and GP case notes enabled identification of patients (frequently) referred from participating primary care practices, detailed symptoms being referred, and provided specialist opinion to the extent symptoms were 'explained' by disease.

Justification of specialist diagnoses as the 'gold standard'

An ideal gold standard has a sensitivity of 100% (it identifies all individuals with a disease process) and a specificity of 100% (it does not falsely identify someone with a condition that does not have the condition). There are no known measures that can provide 100% certainty. Optimal case definition is important in epidemiological research, but can be difficult when there is no satisfactory gold standard available. This is certainly the case for establishing a diagnosis of MUS. The value of a case definition lies in its practical utility in distinguishing groups of people to study(365).

For the purposes of this study, I took a pragmatic approach to classify subjects with or without MUS. I rated referral episodes based on specialist opinion and results of investigations. Arguably, a 'gold standard' for diagnosing MUS would involve multiple different independent specialist assessments accompanied by a series of investigations, with a measure of inter-rater reliability, to ensure diagnostic accuracy. The fact that these patients were frequently referred and assessed is evidence that they did have multiple examinations and investigations. However, this is ultimately what this study is seeking to avoid for this group of patients. In the absence of a gold standard, Knottnerus and colleagues suggest an appropriate clinical follow up, using a cross sectional study design and final assessment by independent experts, as the best approach(366). Although specialist diagnoses are an imperfect gold standard, they are a practical option, and are commonly cited in the literature as the expert opinion upon which diagnoses of MUS have been based(32;59;60;356;367).

Deprivation

Before describing the characteristics of the practices involved in the study, I must first explain what I mean by deprivation. Peter Townsend(368) outlined deprivation as people lacking .. "the types of diet, clothing, housing, household facilities and fuel and environmental, educational, working and social conditions, activities and facilities which are customary, or at least widely encouraged and approved, in the societies to which they belong." (p.126)

Deprivation can be measured at the individual and area level, in relation to material deprivation (e.g. having adequate food, clothing and shelter) and social deprivation (e.g. access to services and isolation). Measurement at the individual patient level is obviously more desirable, as it is more specific. Measures at the area level are less robust, but provide a proxy measure of those living within a small locality.

This research used a measure of deprivation at the area level i.e. the Carstairs index. This composite deprivation measure was created by calculating scores from 2001 UK area-based Census data on percent of: over crowding, male unemployment, no car ownership, and low social class(369). These scores act as a measure which reflects access to those material resources which provide access to "those goods and services, resources and amenities and of a physical environment which are customary in society"(370). The scores are not directed at the individual level of material wellbeing or disadvantage. They are a summary measure applied to populations contained within small geographic localities; i.e. populations of postcode sectors in Scotland where a postcode sector is the set of unit postcodes that are the same apart from the last two characters.

It is acknowledged that there are two other measures of deprivation commonly used in the literature, e.g. the Townsend index and the Jarman score. Both the Carstairs and Townsend indices involve the same three variables, but instead of lower social class in the Carstairs Index, the fourth for the Townsend index is home ownership. The Under-privileged Areas (UPA) score, was developed by Jarman and colleagues(371)[10]. The UPA score comprises eight variables, including the four already mentioned plus: the proportion of single-parent families, children under age five, retired persons living alone and recent immigrant status. The weight given to each of these variables in constructing the index differs according to the perception that physicians have of that variable's impact on their workload. A comparative analysis of the three indices showed the first two correlate more closely with a set of health indicators than the third(370).

[10] Incidentally, it has also been used in determining remuneration for physicians in Britain.

At the time of writing this thesis, the Carstairs index of deprivation was the measure of choice used by the ISD[11]. Due to the ready availability of these scores (a score provided by ISD for each patient) and that the data was specifically derived from Scottish Census data, this was the deprivation measure chosen for use in this study. The dataset that I received from ISD provided two index scores for each patient, i.e. deprivation categories from one to five (DepCat 5), and deprivation categories from one to seven (DepCat 7).

To corroborate these scores, other measures of deprivation were assessed as part of the study. Included in these were: years of education, living arrangements, employment status and receipt of government benefits. These were determined by patient self-report (as outlined further on in this thesis on pages 113 and 118).

THE GENERAL PRACTICE POPULATION

The study sample was derived from a mixed primary care population who were registered with five general practices in Edinburgh. A total of 30 GPs worked at these practices during the five year study period.

Seven practices were originally invited to be involved in the study. However, two practices who served more deprived areas of Edinburgh declined participation. One of these had a high number of requests for research and felt they had reached their limit at the time. Although GPs from the other practice agreed to be involved, and ISD referral data had been obtained, the practice withdrew due to major computing and staff changes. The data from this practice were not used.

It should be noted that the ISD provided deprivation category for the practice was derived from aggregated data at the general practice level (i.e. one quintile per general practice). As such, the deprivation score has been based on the geographical location

[11] It is acknowledged that it is less appropriate in the 21st century to only include male unemployment and not take into account those single female parent families, for example. Although ISD provided deprivation scores based on the Carstairs index for patients and practices involved in this study, because of the somewhat outdated measures used in this index, ISD have since recommend the use of the new Scottish Index of Multiple Deprivation (SIMD) published in June 2004 (see http://www.isdscotland.org/isd/401.html).

of the practice and may not necessarily be entirely representative of the actual population registered at that practice. However, further information from ISD indicated our five practices were representative of the other general practices in Lothian (see page 132 for a detailed description, and the table in Appendix 2).

The five participating general practices

This section describes the characteristics of the five participating general practices in this study. The Carstairs DepCat 7 measure of deprivation has been provided to describe the residential area each practice was situated in. As previously highlighted above, this is not a robust measure and these deprivation scores can only provide a proxy measure of the deprivation of the surrounding patient population they care for. A summary of practice information is provided in Table 1.

Practice 1.

According to ISD, there were 10731 patients were registered at this practice, and the patients were from heterogeneous backgrounds. It was closely situated to an army barracks, a private boys' school, an elderly residential care settlement and a council housing estate. This practice was located in a DepCat '1' area indicating the highest category on this socio-demographic scale. Approximately 10% of referrals from the practice were made to private medical specialists. There were three full time (F/T) males, one F/T female and two part time (P/T) female GPs working at this practice.

Practice 2.

This practice had 9336 registered patients. A minority of patients lived in council housing and more deprived areas of Edinburgh. This practice sent approximately 10% of referrals to private specialist care, reflecting low levels of deprivation. In theory it comprised four separate practices; three male solo practitioners and a fourth practice consisting of one F/T male and two P/T female GPs. However, all six GPs (three solo

practitioners with their own patient lists included) shared the same practice support staff and facilities.

Practice 3.

Much of this practice population derived from inner city council housing estates. There were also students and university staff (although the practice was not the official health service for the University). There were 5206 patients registered with this practice at the commencement of this research. There was a small number of private referrals from this practice; no more than 5%. There were two F/T GPs employed in the practice; one male and one female. The other GPs worked P/T in the practice due to academic and teaching commitments associated with the University, and comprised three males and three females.

Practice 4.

Practice four was situated in the most deprived residential area of the five with a DepCat of '6'. Teenage pregnancy, domestic violence, mental illness, alcohol abuse and other drug misuse were common presentations at this practice. Private referrals were rarely made. There were 5838 patients were registered with this practice. One male GP worked at this practice F/T, two males and two females worked P/T.

Practice 5.

Practice-5 became involved in the study in 2004/2005 to increase the primary care population available to sample from and maximise generalisability; this was a year later than the other four practices. Located in a DepCat '1' residential area, this practice had similar characteristics to Practice-1 and was more likely to provide the required response rate. There were 8451 registered patients at this practice at the commencement of this study. There were three F/T male GPs and two P/T females.

Justification of the primary care population

These particular participating practices were chosen for two main reasons. The first was on the grounds of representativeness of general practices around Edinburgh, and the second on their likelihood of participating. My sample of practices provided a good mix of practice types, GPs, and a sociodemographic mix of patients.

ACCESS TO PATIENT DATA: CONFIDENTIALITY ISSUES

The Data Protection Act (1998) states that only those involved in direct patient care may access confidential and identifying patient information. The signed consent of patients and their treating doctors is required before any patient information can be made available for purposes other than direct patient care. This is impractical from a research perspective as it would be time consuming, labour intensive and costly. It would also cause patients undue worry to seek their consent for research that most would be ineligible for(372).

Patient autonomy is important, and seeking their consent to participate in research is generally the best approach. However, there are times when it is not possible or inappropriate. Willison and colleagues(373) outlined some of these situations (see Figure 6).

Figure 6. Problems associated with obtaining consent for research

1. Size of population being researched
2. Difficulty of contacting participants, either directly or indirectly
3. Resultant risk of introducing bias into the research
4. Risk of breaching privacy or inflicting psychological, social, or other harm by contacting the individual
5. Undue hardship imposed on organisation when additional financial, material, human, or other resources are required
6. Determination of impracticability made by a duly constituted research ethics board

All determinants applied to this research. Contacting large numbers of patients would substantially reduce response rates making the findings meaningless and unrepresentative.

Medical practitioners can request free access to their patients' health activity data from ISD. However, they typically do not have the time or resources. Thus an additional, dedicated practice member would be required to request and review the ISD data. My role in the practice was to assist GPs with an audit of their referrals from the practice; particularly to identify those patients who had been 'frequently' referred. To be able do this, I was required to hold an honorary Lothian Primary Care Trust (LPCT) contract to work in the Lothian primary care setting. I also had to be made an honorary member of each participating practice to access patients' notes. Before practices became involved in the study, GPs had to agree to participate in the research given the proposed methodology.

A representative GP from each of the five participating practices and the Medical Directors of the three NHS Trusts servicing Edinburgh signed confidentiality statements to allow release of the relevant patient identifying data. The Trusts included: the Lothian Primary Care Trust (LPCT, now known as the Primary and Community Division) to grant access to patient information from general practices; the Lothian Hospital and University Trust (LHUT) to permit access to outpatient information; and, West Lothian Trust (WLT) to authorize access to data of those patients referred to St. John's Hospital.

This process required not only the approval of participating practices and the relevant NHS Trusts, but also the Local Research Ethics Committee (LREC), and the NHS ISD Privacy Advisory Council (PAC). Approval from all of these regulatory bodies was obtained.

ISD and case note data were entered directly into a purpose designed Microsoft Access database(374) held on a password protected lap top computer. Data were entered according to the PIN allocated by ISD. In order to identify the appropriate case notes to review, lists of patient names and corresponding PINs were stored in each practice. No identifying patient information left the practice (until patients provided informed consent for the case-control phase of the study which will be outlined later in this chapter).

INCLUSION AND EXCLUSION CRITERIA

In order to be eligible for the initial identification phase of the study, patients had to meet the inclusion criteria as outlined below in Figure 7. If patients did not meet all the criteria they were excluded. However, patients were also excluded if the following criteria were met, as outlined below in Figure 8.

Figure 7. Inclusion criteria of eligible cases and controls

- currently registered with one of the five participating practices,
- referred to selected outpatient specialties as identified by ISD, i.e. Cardiology, Dermatology, Ear, Nose and Throat (ENT), Endocrinology/Metabolics, Gastroenterology, General Medicine (MOPD), General Surgery (SOPD), Gynaecology, Neurology/neurosurgery, Ophthalmology, Orthopaedics (OOPD), Respiratory Medicine, Rheumatology, and Urology.
- referred within a defined five year study time frame: between the dates of 1st March 1997 to 31st March 2002[12].
- referred three or more times, or referred once only[13] (to be eligible for the IRS control patient group of phase two.)
- at least one referral was made during the last year of the five year time frame[14],
- a GP was the source of at least three referrals (for the FR patients) or one referral only (for the IRS controls)
- main purpose for referral was physical symptoms
- aged 18-65 years at the time of the latest referral.

Justification of criteria

Currently registered with the practice

Patients were required to be currently registered with the participating practices so that both their ISD data and case notes would be available for review. Although identified

[12] Practice-5 joined the study over 12 months after the other four practices, thus the time frame for this practice was 1st March 1998 to 31st March 2003.
[13] Although patients had only one referral in the five year study period, they were deemed ineligible as an IRS if they had subsequent referrals after the study period.
[14] Given minor inaccuracies of ISD data and to obtain adequate numbers to achieve power, I audited all FR patient notes and applied this criterion at the time of audit. However, this was applied from the outset to the IRS due to large numbers.

as having been referred by ISD, if patient case notes were unavailable, there was no reliable means of confirming their referral, symptoms and outcomes.

Figure 8. Exclusion criteria

- identified as deceased by ISD data (99B records) or GP records
- left the practice since the ISD data was released
- no record of the patient ever being registered with the practice
- case notes missing or unavailable during the entire case note audit
- no documentation in the case notes of ever having been referred
- referred only for reasons other than symptoms e.g. diagnosed disease management reviews, medication advice, or abnormal blood tests, etc.
- referred only to the following outpatient departments: Clinical Genetics, Palliative Medicine, Transplantation Surgery, Obstetrics, Oncology, and Psychiatry.

Referral to selected hospital outpatient departments

There were 15 outpatient departments chosen for review. These were chosen based on previous studies(60;332;375) which identified these specialties as receiving higher proportions of referrals for MUS. It could be argued that had all referrals to all secondary care departments been included, not only would more patients be identified, but the total magnitude of health care contacts and associated costs could have been more accurately estimated. However, this would have brought about a case note audit load too large for one researcher which would only bring about diminishing returns. As this was a study to identify MUS, for pragmatic reasons I focussed on the specialties which were more likely to receive referrals for MUS.

Referral within a five year time frame

Participants are more likely to be engaged in a study of relevance or interest to them. To maximise response rates for the case-control phase of the study, it was important to recruit patients who had been recently referred. This was to facilitate recall about their

past health concerns and the nature of referrals. As the latest complete ISD dataset was available up to March 2002, referrals for five years prior to this were selected .

A time frame longer than five years would involve a greater number of patient referrals and data to assess, as well as identifying a greater number of patients who had left the practice or died since the release of the ISD data. Due to the large number of patients expected to be identified, lifetime review of too many case notes would have been impractical and time consuming. However, given one of the main reasons for conducting the study in primary care was to access lifetime patient information, a 10% random sample of lifetime case note reviews were performed. This is outlined in more detail in Chapter 14, from page 198.

GP made the referral

This is a study of the primary-secondary care interface. However, the focus is on GP referrals as most patients in the UK access hospital outpatients by referral from a GP. Focussing on referrals made by GPs eliminated one source of confounding i.e. source of referral.

Patients aged between 18-65 years

This has been an accepted age group used by other studies in this field. The reasons for this are as follows:

1. Patients under the age of 18 years are likely to be subject to parental influence in terms of access to and use of health services. Children would not be able to provide informed consent, nor complete a written questionnaire without the help of a parent or carer.

2. Adults aged 65 and over are more at risk of developing organic and degenerative medical conditions which would necessitate more health care contacts than the general population.

IDENTIFICATION PROCEDURE

The ISD SMR00 data were initially sorted in an Excel(376) spreadsheet by outpatient specialty. Referrals made to any of the excluded departments were deleted. The data were then sorted by date of consultation and referrals made outside the five year study period were removed. Data of patients aged younger than 18 years or older than 65 years at the last eligible referral were also removed. Finally the data were sorted by the unique PIN and a count of outpatient contacts for each patient was totalled.

For the purposes of this study 'FR' was defined as three or more referrals to selected outpatient specialties of patients within the five year period. Those patients referred three times or more were flagged for case note review. Patients with only one outpatient contact were also flagged for case note review as potential 'infrequently referred' (IR) control patients.

Case note audit

The GP case notes of those patients identified as FR, and a random selection of IR patients, were reviewed. Reasons for referral, symptoms documented and outcomes of referrals were recorded. A list of symptom categories was derived. Symptoms mentioned less than five times were put into a 'miscellaneous' category.

A 10% random sample of the FR case notes was selected for a lifetime review (this is reported separately in Chapter 15). The time it took for each patient's case notes to be reviewed was recorded.

The review period was for the same five year time frame as for the data from ISD data, i.e. from 1997 to March 2002 (or 1998 to March 2003 for Practice-5). Any documented referrals made after this period were noted but not included in the final identification of potentially eligible cases and controls.

Operationalised criteria

To ensure systematic and reliable identification of MUS, a set of rules or guidelines were devised. These were based on those developed during the single practice pilot study. The core of the criteria was that the GP had referred a patient with one or more physical symptoms and the specialist opinion determined how explained the symptom was by disease. These criteria were applied to each referral episode.

A referral episode was defined as all subsequent hospital clinic appointments resulting from a single referral to one speciality until:

- a final diagnosis was made
- the patient was discharged or referred to a different specialty
- diagnosis was no longer the objective, or
- the patient had died.

Referrals for reasons other than symptoms were noted but did not contribute towards the classification of study subjects. The operationalised criteria were applied to each referral episode where the main reason for referral was for symptoms (see Figure 9). Where the specialist had stated some or no medical explanation for the patient's symptoms, the referral episode was rated as 'somewhat explained' or 'not at all explained' respectively (i.e. MUS). Patients who were found to have two or more of these referral episodes were classified as FRMUS. However, in the event that clear objective evidence of disease was discovered from subsequent consultations for those symptoms previously deemed MUS, this was taken into account when identifying eligible cases and controls.

Figure 9: Operationalised criteria applied to each referral episode for symptoms documented in the GP case notes

0 = Completely explained: when positive findings of disease resulted from a medical history, physical examination or investigations and the specialist deemed these to clearly explain the presenting symptom.

1 = Largely explained: the specialist stated the symptom was largely and most likely explained by disease, but there were some inconclusive findings on assessment. If no specialist diagnosis was stated, this category still applied if positive clinical examination or investigation findings of disease likely to be pertinent to the aetiology of the presenting symptom were documented.

2 = Somewhat explained: when the specialist stated that the symptom was unlikely to be explained by disease. This may have been due to equivocal assessment results or the specialist considering the symptom to be out of proportion to any underlying or incidental finding of an "organic" condition, e.g. lower back pain and associated disability when only early mild degenerative osteoarthritis found on x-ray.

3 = Not at all explained / medically unexplained (MUS): results of a thorough examination or investigation of the symptom were negative. If the specialist concluded that there was "no organic basis" or a psychosocial basis for the symptom e.g. anxiety, depression, stress or problems at home, this was rated as MUS. Functional somatic syndrome (FSS) diagnoses were automatically rated as MUS (e.g. irritable bowel syndrome, etc.)*

* for a full list of FSS diagnoses which were rated as MUS, see Chapter 3. Figure 3, page 48.

Consensus ratings

Supervision meetings were held monthly between me, the Professor of Psychological Medicine and Symptoms Research, Michael Sharpe, and the Professor of General Practice, David Weller. Throughout the case note review, referral episodes which were too difficult to rate on my own were summarised. Summaries included symptom presentation, information documented by the referring GP, information documented by the hospital specialist, investigations performed and their results, and any diagnoses documented by the specialist. Each case was presented to the two professors, discussed as a group and a consensus rating made. In the uncommon event that consensus could not be reached, the episode was rated as 'largely explained' by

disease. For the purpose of this research, consensus ratings erred on the side of caution towards explained by disease to give the clinician the benefit of the doubt.

Quality assessment of ratings – intra-rater reliability

An intra-rater reliability assessment of the first ratings made was conducted early in the identification phase. This was deemed necessary for two reasons. The first was to ensure my comprehension and consistency of applying the criteria. Anecdotally, my perceptions and understanding of the project and the criteria changed with the experience of reviewing more case notes over time. Secondly, a five year break from clinical nursing at this time, meant my medical terminology also improved with reading and rating more case notes.

Twenty patient records were randomly selected, their notes extracted, and each referral episode re-rated independently of the initial ratings. Upon completion of this exercise, the new ratings were compared with the original ratings and intra-rater reliability assessed.

Revision of the operationalised criteria

Consensus meetings also identified some shortcomings in the current operationalised criteria. Some statements were clarified and altered in December 2003 (the original operationalised criteria adopted from the single practice pilot study is included as Appendix 1). This became an opportunity for a second quality assurance check, and records reviewed and rated prior to December 2003 were re-examined to ensure adherence to the revised criteria.

Justification of operationalised criteria

It is important to extract data for research purposes systematically. Due to the great volume of information contained in patient case notes, methodical data collection is

challenging. Case note reviews rely on observer interpretation of investigations and written opinion which may or may not reflect the true opinion of the assessing doctor.

Robust and comprehensive operational criteria applied to case note reviews for MUS were available from Reid and colleagues(329). Inter-rater reliability between three raters showed considerable agreement (combined kappa was 0.76) suggesting that case note review can be a reliable method of determining whether a symptom is medically 'unexplained' by disease. These criteria were further developed during the single practice pilot study, with a similarly high inter-rater reliability(332).

Subject group classification

Referral episode ratings were sorted in the database by unique PIN. Those patients with two or more ratings of '2 – somewhat explained' or '3 – not at all explained' by organic disease were classified as FRMUS. Those patients with ratings only scored as '0 – totally explained' or '1 – largely explained' by organic disease were classified as FRMES. Patients were defined as IRS if they had been referred only once to the selected specialties for symptoms; specific symptom outcome did not impact on inclusion and could be rated anywhere on the spectrum of explanation by disease. Specific definitions of subject groups are outlined below in Figure 10.

Justification of definitions

The single practice pilot study defined frequent referral as five or more times within a five year time frame. This was a practical decision taken to bring about manageable numbers of subjects to study. However, as a general definition, it was a somewhat arbitrary number of referrals, consistent with previous research on definitions of 'high' or 'frequent' users of health care services(174). The decision to use this cut off was made to detect patients at the more extreme end of the health care utilisation spectrum and to ensure manageable numbers for the researcher to interview. To detect a larger number of patients to achieve power for the present study, the referral threshold was lowered to three referrals.

Figure 10. Definitions of cases and controls

Cases

Frequently referred with medically unexplained symptoms (FRMUS)

A patient referred from primary care to selected outpatient departments three or more times in five years for symptoms, where two or more of the referral episodes were deemed MUS by specialist assessment and opinion.

Controls

1. Frequently referred with medically explained symptoms (FRMES)

A patient referred from primary care to selected outpatient departments three or more times in five years for symptoms, where all referral episodes were deemed explained by disease according to specialist opinion.

2. Infrequently referred with symptoms (IRS)

A patient referred from primary care to selected outpatient departments once only in five years for symptoms which may or may not have been determined as MUS by a specialist.

Justification of control groups

To test if the characteristics of FRMUS cases were not merely an artefact of being ill, a control group of patients frequently referred for medically explained symptoms (FRMES) was required. To ensure adequate difference between the cases and controls for the main factor under study (i.e. MUS), FRMES controls were required to have no referrals for MUS. In this way all of their referrals were considered explained by disease according to specialist opinion.

However, to make sure the findings were not just a result of being referred frequently, a second control group was necessary. The single practice pilot study had invited a group of general practice patients, who had never been referred, to participate in the study. However, only a 5% response rate was achieved. Clearly patients who had not been referred to hospital were not engaged in a study about referrals. I chose to identify a group of patients who had been referred once only in five years (infrequently referred, IR) as they had been engaged with the secondary care service.

CHAPTER 9. DESCRIPTION AND COMPARISON OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS (PHASE-2)

CASE-CONTROL STUDY DESIGN

A case-control study involves identifying a group of subjects with a condition of interest (cases), and another without it (controls). The two groups are then studied for differences in characteristics which might explain why the cases have the condition and the controls do not (361).

Justification of study design

There were other designs I could have used to conduct this research. I could have done a big survey, or a prospective cohort study. However, I used a case-control study design. Case control studies have several advantages over cohort studies. The study design is relatively quick and inexpensive to conduct as it does not involve waiting on uncommon or slowly developing conditions to arise (as is the case for FRMUS). This design is also good for testing hypotheses and associations of other variables with the condition under study. The main limitation with a case-control study design is that it is well known to introduce various sources of bias which may bring about spurious findings. Case-control studies assume homogeneity of all characteristics among the designated study groups, and if not taken into account, this can produce confounded results. As this is mainly a descriptive study to advise a possible future intervention, the use of a case-control design was deemed a reasonable approach.

ASSESSMENTS OF SUBJECT CHARACTERISTICS

As FRMUS patients were a novel group to study, it was important to collect as much descriptive data about them as possible. Information already collected in the first phase from both ISD and case note data partly contributed to the description of subject characteristics. Up to this point, the ISD data had identified referred patients and provided basic demographic information about them. The case note data confirmed the number and nature of all health care contacts.

Following recommended steps proposed for the design of a questionnaire(361), I made a list of variables to assess(see Figure 11). This list enabled me to easily identify information already obtained via ISD and case note data, and the information that was still required to meet the aims and test the hypotheses (as stated in Chapter Six). Remaining information was to be collected via patient self-report questionnaire.

Justification of questionnaire

Postal questionnaires are widely used for the collection of data in epidemiological studies and health research. Questionnaires are a relatively inexpensive and efficient way to reach, and gather data from, a potentially large number of respondents.

To enhance validity and facilitate comparison with other studies, I used existing validated instruments to measure study variables not available from ISD or case note data. There were several validated instruments used in the "Referral Study"[15] questionnaire, as well as some specifically devised items to address the study's main hypotheses (see Figure 11). The questionnaire is included as Appendix 9.

[15] From this point onwards, this research project will be referred to as "The Referral Study".

Background to the self-report instruments

The following measures were chosen as previously validated, applied to a primary care patient population, and brief to minimise response burden and maximise response rate.

Figure 11. List of variables to describe characteristics of subjects and data sources used

Variables	Source of data
Age, gender, deprivation (DepCat 5 & DepCat7)	ISD data
Number & specialty of outpatient contacts attended & not attended (DNA)	ISD data & GP case notes
Other health care contacts including: investigations, A&E visits, out of hours GP contacts, days admitted	GP case notes
Main referring or registered GP	GP case notes
GP 'difficulty' rating	GP questionnaire
Number of years registered with the practice	GP case notes
Medical diagnoses	GP case notes
Past psychiatric diagnoses (anxiety, depression & panic)	GP case notes & patient self-report
'Adequate' psychiatric treatment: antidepressants & mental health care contacts	GP case notes & patient self-report
Current symptoms & diagnoses of anxiety & depression	Patient self-report (PHQ)
Past five year symptoms of anxiety, depression & panic	Patient self-report
Current symptoms & diagnosis of panic	Patient self-report (ANS-2)
Past documented somatic symptoms	GP case notes
Current somatic symptoms	Patient self-report (PHQ-15)
Physical & mental health function	Patient self-report (SF-12 v2)
Illness perceptions & beliefs	Patient self-report (IPQ & WI)
Attitudes to medical & psychiatric treatment	Patient self-report
Attitudes to disclosing problems to doctors	Patient self-report
Satisfaction with health care received	Patient self-report (GPAS items)
Demographic information including: marital status, living arrangements, education, employment, & benefits	Patient self-report
Time off work & usual activities	Patient self-report

Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PHQ)

Although I could have obtained some diagnoses of anxiety and depression from ISD data or case note data, these were unreliable sources for the following reasons. Firstly, ISD derived diagnoses were complex codes to decipher and often incomplete. Also, anxiety and depressive disorders were less likely to be coded with ISD if a patient had been referred to gastroenterology, for example. Secondly, diagnoses of anxiety and depression from case notes were not reliable because some GPs do not make the diagnoses and some GPs may not document the diagnoses. Even if mentioned in case note summaries, information about *when, who and how* the diagnoses were made had rarely been provided.

There are a range of validated measures designed to detect anxiety and depression. The PHQ was developed specifically for primary care populations with reported 75% sensitivity and 90% specificity. It has comparable diagnostic validity to the clinician-administered PRIME-MD interview(139) which was developed from the SCID as a shortened version for epidemiological surveys. However, it is more time and cost efficient as it can be self-administered(377). A growing number of international studies have chosen to administer the PHQ to patients in primary care(378-380), as well as hospital outpatient settings(201;381) to screen for anxiety and depression.

I used the PHQ-9 depression module as it scores each of the nine DSM-IV criteria as "0" (not at all) to "3" (nearly every day). Scoring of the instrument provides a final score between 0-27, where a score of 10 or more provides an indicator of clinical major depressive disorder (MDD). Scores over 15 equate to moderate MDD and over 20 represents severe MDD. In addition to making criteria-based diagnoses of depressive disorders, the PHQ-9 is a reliable and valid measure of depression severity. Provision of diagnosis, severity of depression and brevity make the PHQ-9 a useful clinical and research tool(382). I also used items from the PHQ to assess current anxiety and panic disorders and self-reported somatic symptoms. Alcohol and eating disorder questions from the PHQ were omitted.

Patient Health Questionnaire Symptom Checklist (PHQ-15)

The PHQ-15 is a brief instrument which includes 15 somatic symptoms from the PHQ. Although developed as a tool to identify and monitor somatic symptom severity in research and clinical practice, it has also shown to be a useful screening instrument for somatisation(16). Using the scoring system of 0 for "not bothered", 1 for "bothered a little" and 2 for "bothered a lot", participants could score a maximum of 30 for the PHQ-15. Current symptom numbers of 5, 10 and 15, respectively represent cut-off points for low, medium, and high somatic symptom severity.

The two-question version of the Autonomic Nervous System Questionnaire (ANS-2)

This is a brief two item screening tool to detect panic disorder in the primary care setting. It has shown excellent sensitivity and negative predictive value (NPV). Some issues with low specificity and positive predictive value (PPV) are acknowledged(383). The limitation with studying panic disorder in primary care is the lack of an adequate measure and the lack of effective treatment.

Past anxiety, depression and panic

The time frame used to identify cases and controls (March 1997- March 2002) was more than two years before the questionnaires were completed by subjects. A gauge of depression for the previous five years was sought. Five years was chosen in line with the rest of the study's timelines and to be consistent throughout the questionnaire. Also, asking for lifetime depressive episodes was more likely to be subject to recall bias. Similar questions to those in the PHQ were adapted using the five year time line. Five years is still a long period of time for some patients to remember, so recall bias is acknowledged. However, this self-reported data has been corroborated by information documented in the case notes.

Version two of the Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12 v2)

The SF-36 (used in the single practice pilot) is one of the most extensively administered general health measures in the international literature. The SF-12 is a shortened form of the SF-36(384). Twelve items from the SF-36 were grouped into two six-item subscales, one measuring physical functioning (PCS) and the other measuring emotional functioning (MCS). This has shown considerable accuracy and far less respondent burden(385). The SF-12 (version two) was chosen as a short generic measure to provide summary information on physical and mental health status of participants(386). Mean population norm scores have been calculated to be 50 for both PCS and MCS. A higher score indicates better health.

There are several internationally recognised and validated measures of general physical and mental health status. Other measures of general health status, such as the EuroQol (EQ-5D), were also considered for inclusion into the present study. However, comparison of the EQ-5D and SF-12 showed the latter to be more sensitive (387).

Items from the General Practice Assessment Survey (GPAS)

The GPAS was a survey designed for a UK primary care population. It addresses nine key areas of primary care (access, technical care, communication, inter-personal care, trust, knowledge of patient, nursing care, receptionists and continuity of care) (388). However, three of the four single items, relating to patients' perceptions of the GP's role in referral and co-ordination of care, and their overall satisfaction with care, were included in the Referral Study questionnaire. Given that patients were seen by both primary and secondary care doctors, a question was included to ask patients about their overall satisfaction with the care received from each setting. The satisfaction items provided a score from 7 "completely dissatisfied" to 35 "completely satisfied" with health care.

Items from the Illness Perception Questionnaire (IPQ)

This is a lengthy instrument designed to assess patients' thoughts and interpretations of illness(389). This questionnaire has been widely administered by studies looking at patients experiencing MUS and disability. There are a number of core items in the IPQ, but I only chose the four which related specifically to the Referral Study's hypotheses. These four assessed perceptions of the consequences of illness, ability to change health problems, stress or worry affecting health, and patient worry about health. Numerous items were not considered for inclusion due to their overlap with items already included from the PHQ.

One item from the Whiteley Index (WI)

The WI was originally developed by Pilowsky in 1967(390) as a 14 item instrument. Fink and colleagues reduced this to a seven item questionnaire developed to assess health anxiety(391). This has shown to be good at discriminating hypochondriasis in patients. However, I only chose to include the final one item in my questionnaire. This asked patients to rate how much they agreed or disagreed with the statement: "I find that I am bothered by many different symptoms". I felt the other items e.g. being told by a doctor "there is nothing to worry about" were inappropriate to be administered to the FRMES patients.

Disclosure

The literature has indicated that one of the reasons GPs find it hard to detect underlying anxiety and depression in physical presentations is that patients may not be willing or not given the opportunity to disclose emotional and psychosocial issues with their doctors(392-394). As there were no known validated measures of patient perceived ability to disclose personal problems to doctors, two items were specifically designed in the present study questionnaire. Patients were asked how comfortable they were discussing physical and emotional issues with their treating primary care and hospital doctors.

Contacts with medical and mental health care professionals

Due to time lags between ISD, case note and questionnaire data, patients were asked if they had seen a medical or a psychiatric specialist within the last twelve months. This was to obtain a measure of more recent use of health care services since the case note audit. Patients were also asked to indicate to what extent they felt they may benefit from seeing a medical or psychiatric specialist. This was included expressly to address recent psychiatric or psychological care and perceived need for it.

Time off work and usual activities

General health measures tend not to include items asking whether illness or disability has caused patients to take time off work. I not only included time off from work in this questionnaire, but also added a question about taking time off from usual activities, so as not to place any greater importance on working for those participants who were not in paid employment. Again, these two items were designed and included in the questionnaire to address this study's subsidiary hypotheses.

Demographic information

Demographic information is crucial in describing and comparing research participants. These include data such as education, employment, marital status and living arrangements. However, there are no 'gold standard' measures systematically used by researchers.

A national UK survey of NHS patients conducted in 2002 used items which were brief and easy to answer, even for members of the public with low level literacy skills(395). I adopted those for employment status and living arrangements for the Referral Study. A list of possible relevant benefits was obtained from the social security website (http://www.hmrc.gov.uk/manuals/eimanual/EIM7600.htm).

As 16 years is the legal working age in the UK, I determined participant educational attainment by asking how many years of education they had completed after the age of 16. A similar format was used by the UK Omnibus Survey in 1998(7)

Initially, I had included a list of ethnicities for participants to select from. However, I removed this as Scotland has a small minority ethnic population (only 2% according to the 2001 Scottish Census). This omission was a pragmatic decision to reduce the size of the questionnaire given the item was likely to provide minimal returns.

Free text comments

To enable participants to write comments about their experiences of being referred (or other health information participants wished to share), a large open text box was placed at the end of the questionnaire.

Determining 'adequate' treatment for depression

To address the second part of the main hypothesis, a means of determining 'adequate' psychiatric or psychological treatment for subjects was required. The concept of 'adequate' is debatable and shall be addressed in more detail in the discussion of this thesis. However, for the purposes of the study, the assumption was made that conventional evidence-based treatments for depression would be applicable to this group of patients(396).

Information about prescribed antidepressants was collected from the GPASS records of the five participating general practices. Contacts with mental health care professionals were extracted from both the case notes and patient self-report.

Definition of 'adequate treatment' of depression included the following:

- *Antidepressants:* Prescribed minimum therapeutic dose of an antidepressant drug, as per guidelines specified in the British National Formulary (BNF, www.bnf.org) (397). However, recent evidence from Furukawa suggested that tricyclic antidepressants may be effective at a minimum dose of 75 mg(398).

- *Psychological or psychiatric treatment*: was defined as a course of treatment with a recognised mental health professional of at least two treatment sessions. Referral to mental health services was defined to include referral to any discipline in the

local NHS services. If referred for cognitive behavioural therapy (CBT) this was only considered adequate if the course had been completed(399).

Determining 'adequate' treatment for anxiety

Adequate treatment for anxiety is perhaps more problematic than deciding if treatment is 'adequate' for depression. There are fewer known effective medications for anxiety disorder than depression. However, for the purposes of this study, adequate treatment for anxiety was defined the same for depression, including the minimum effective dose of an anxiolytic as per guidelines specified in the British National Formulary (BNF, www.bnf.org)(397).

PILOTING STUDY MATERIALS

A draft questionnaire was composed of the above measures and items. Although similar measures were administered in the single practice pilot, I interviewed individual patients and asked them to complete the questionnaires in my presence to obtain their feedback. An unknown was the feasibility of mailing out a questionnaire to these patient groups and the likelihood of them responding. Therefore I had to conduct a pilot of my own to determine the likely response rate from mailing out the questionnaires.

Study materials, including the patient information sheet, consent form, and self-report questionnaire, were piloted twice. The first was to assess the acceptability of language used and layout of the materials. The second was to determine how feasible it was to send out hundreds of study packs and what the likely response rate would be. This was particularly the case for the IR control group. The single practice pilot was only able to obtain a five percent response rate from control patients that had not been referred at all. As such, I was uncertain how patients referred only once (IR controls) would be engaged in a study about referrals.

First pilot – questionnaire content and format

Thirteen volunteers were asked to read and complete all study materials and provide their comments, particularly about the questionnaire. Three volunteers with recent referrals to hospital were recruited through members of staff at in the division of General Practice at the University. Ten outpatient volunteers were approached in the waiting rooms of gynaecology, neurology and rheumatology outpatient departments.[16] Responses to, and concerns or difficulties encountered during completion of, the questionnaire were discussed with the participant.

This pilot informed my decisions to:

- provide more detailed introduction and explanation at the beginning of each section
- clarify difficult terms
- reorganise the order of questions asked, and
- to make the layout of the document more logical, easier to complete and aesthetically appealing.

Second pilot – response rates

Further piloting of all study materials, including the recruitment process[17] was conducted to ensure patient comprehension of the study materials and to assess for any potential problems with response rates. Twenty patients identified as FR (frequently referred) with one MUS episode (not eligible for the main study) and twenty patients selected that had been referred only once were randomly selected from the practice in the most deprived area, Practice-4. Also, a random selection of 10 FR and 10 IR

[16] A senior consultant at each of three outpatient departments was contacted about the present study and asked if I would be able to attend one of their outpatient clinics to talk to a small number of their patients. The three consultants agreed. The consultant first talked to the patient and if the patient verbally consented, the consultant directed them to me to pilot the study materials.

[17] The GP agreed to the patient being suitable to participate, signed the invitation letters to patients, and provided a 'difficulty rating' of how difficult they found the patient and the problems they presented with.

patients from Practice-2 were chosen. In total 60 pilot questionnaires were mailed to patients from their practice.

As will be outlined in the results chapter of this thesis, the response from my pilot mail out was disappointing. I had followed all recommendations of a recent systematic review of how to maximise response rates to postal questionnaires(400). This included a total of three mail outs; the initial mail out with two reminders of all study materials to non-responders sent at fortnightly intervals. All measures, as determined from Edwards and colleagues' systematic review, are outlined below in Figure 12.

Figure 12. Measures used to increase response rates to the Referral Study questionnaire

- research topic of relevance or potential interest to the subject
- a brief (five paged) questionnaire
- the use of coloured ink
- good quality paper and envelopes
- a booklet format
- the use of the funding body (i.e. CSO), university, and registered general practices' logos
- a personal invitation letter signed by their GP
- the inclusion of a reply-paid envelope to return the questionnaire
- mail by first class post
- follow up contact of non-respondents with two further mail outs of all study materials and courtesy telephone calls from practice staff.

Edwards' review found that the odds of response more than doubled when a monetary incentive was used. Returns almost doubled when incentives were not conditional on response. Providing financial incentives is becoming common practice in research projects conducted in North America and has been shown to improve response rates(401;402). This has not been usual practice in UK health services research. However, given the low pilot response rates and evidence that unconditional monetary incentives more than double response rates, the CSO and LREC agreed that a five pound (£5) voucher could be included in the first mail out of study materials to

compensate subjects for their time and efforts during participation. This was included with the first mail out of study materials, but not piloted.

GENERAL PRACTITIONER AGREEMENT FOR PATIENTS TO BE INVOLVED IN RESEARCH

The main referring GP was consulted for their opinion about the suitability of each patient's participation in the research. If it was unclear who referred the patient most, because the patient had been referred by multiple doctors or a doctor no longer working at the practice (e.g. a GP registrar or locum), the patient's registered GP was asked.

GPs were consulted about the appropriateness of patients' inclusion into the study for a number of reasons. The first was to make patient selection more appropriate, i.e. avoid asking patients who had recently died, had become very ill, or in one case, had commenced a legal suit against the practice! It was also a form of 'public relations' to engage the GP in the project. The final reason was to obtain the GP's perspective of the complaints the patients presented with.

General Practitioner difficulty rating

At the time of signing the invitation letters, GPs also completed a one item 'difficulty rating' for each of their patients (See Appendix 5). GPs were asked to provide a response on a five point Likert-type scale to the question: *"To what extent do you feel this patient's problems are difficult to help?"*

The single practice pilot had administered the Difficult Doctor Patient Relationship Questionnaire (DDPRQ-10)(226) to participating GPs. I chose not to use this as it was too long and most of the items were not appropriate to the concept being measured. GPs have limited or no allocated time to participate in external research. As such I felt it appropriate to ask GPs this one question to minimise the burden of their participation

and to directly target our hypothesis that FRMUS patients' problems would be perceived as more difficult to manage.

I piloted this question with five GPs. Anecdotally, they particularly liked the use of the word 'feel', and that the focus was on the patient's problems, not the patient per se. They stated the question was open enough to enable comment about particular issues with the patient as appropriate. There was an opportunity to make hand written comments at the bottom of the form if GPs wished to do so.

At this stage, patients were excluded from the study if they had:

- left the practice after the case note audit was completed, or
- been excluded by their treating GP

If the GP agreed for the patient to be involved, they signed an accompanying letter inviting the patient to complete the questionnaire. Those letters not suitable to be sent were collected and reasons for exclusion recorded. The signed letters were included with the information sheet, consent form (see Appendices 6-8), questionnaire (see Appendix 9), reply-paid envelope and £5 voucher for mailing to the eligible subjects.

CONFIDENTIALITY OF PATIENT DATA

Once eligible subjects had been identified, and their GP was agreeable for each to be involved, study materials were mailed out using the process piloted earlier. Returned completed consent forms and responses from questionnaires were recorded directly into the SPSS database (403) according to their anonymous ISD provided PIN (personal identification number). The paper copies were filed into individual patient folders (labelled by their PIN). No identifying patient information left the practice until patients provided informed consent and returned their completed questionnaire. Hard copies of study materials were stored in a locked filing cabinet in an office in the University division of General Practice.

STATISTICS

Power calculation

Numbers required for the study were based on the sample size required to determine a clinically significant difference in the primary variable of interest i.e. the proportion of patients with anxiety and depression in each of the study groups. The study team (the two Professors and I) determined that a 20% difference between the study groups for anxiety and depression scores was clinically meaningful. Based on estimates from the single practice pilot study, approximately 1000 patients would be identified as FR. Assuming a 70% response rate, 200 patients would need to be identified for each group to achieve a minimum of 140 participants and detect a 20% difference ($p<0.05$ and 90% power).

Statistical analysis

All quantitative statistical analyses were performed using SPSS for Windows(403). Basic descriptive statistics, such as the mean and standard deviation (S.D.), were calculated for scaled variables e.g. age. The proportions of referrals to particular specialties, for particular symptoms, and how many were for MUS according to the operationalised criteria were calculated. Referrals for non-symptom problems, e.g. review of chronic diseases, were noted but excluded from further analysis.

The number of FRMUS, FRMES and IRS patients identified overall was counted. The prevalence of FRMUS patients was calculated by dividing the number of eligible cases by the number of registered patients aged 18-65 at the time of the study. The number of referrals and eligible participants was also contrasted between practices and GPs to assess if a patient was more likely to be referred according to the practice or the GP they consulted.

To determine how specific FRMUS characteristics differed from the FRMES and IRS control groups, the chi-squared test was employed; FRMUS characteristics compared with each control group in turn. This test was used specifically to compare categorical variables. As the number of current symptoms formed a normal distribution on a histogram, the mean number of symptoms checked and overall score on the PHQ-15

were calculated and compared between the groups using the T-test for normal distributions. Mean scores of the SF-12 (v2), PHQ-9, and satisfaction instruments were calculated using a non-parametric statistic for skewed distributions; the Mann Whitney U.

Confounding occurs when another factor (e.g. age) for a condition is also associated with the factor under study (in this case, anxiety and depression, and treatment for these conditions), but acts separately. One way to test for variables which may confound the study's results is to perform a simple linear or logistic regression depending on whether binary or quantitative variables(404). This was performed to assess for any association of four key variables with anxiety and depression. Potential confounding variables included in the model were:

- study group
- age
- gender, and
- deprivation (i.e. area of residence by postcode).

The free text comments provided by patients and GPs were recorded verbatim and coded for themes.

MAXIMISING RESPONSE RATES

Three weeks from the first mail out, non-responders were re-mailed all study materials (with the exception of the voucher). A third and final mail out of all study materials, for all but Practice-3, was undertaken at the sixth week.

Practice-3 opted for their Practice Secretary to telephone non-responding patients as a courtesy phone call. She was given a script to ask non-responders if they recalled receiving the study materials, and *if so*, to encourage them to participate for the opportunity to feed back about their care. If patients had not received the materials, she was to confirm their contact details and ask the patient if they would be agreeable

to receiving the study materials by mail. Alternatively, patients were given the option if they would prefer to complete the survey over the phone with me, have it faxed or placed on their case notes for their next GP visit.

The secretary made three attempts to contact the patient at various times of the day. Patient responses were recorded. If unable to make contact, she was to leave a message on their answering machine or if there wasn't one, to record 'unable to contact'.

Regardless of all efforts employed, at this point in time, the response rate remained below the desired 70%. The five Practice Managers were consulted for their opinion about how to follow-up non-responding patients. Practice-3 agreed to another mail out of those patients not contactable by telephone. Practices one, two and five agreed to a telephone follow-up, with the same script as outlined above. This was conducted by the Practice Secretary in Practice-1 and the Practice Manager in the other two practices. The practice in the most deprived area declined a third reminder of any kind contending that it was "bordering on patient harassment" and may compromise the already delicate relationship the GPs had with their patients. The practice did, however, agree to re-mailing materials to those patients who had changed addresses within the study time frame.

RESULTS

"Why should a man's mind have been thrown into such close, sad, sensational, inexplicable relations with such a precarious object as his body?"

Thomas Hardy (1840-1928)

CHAPTER 10. IDENTIFICATION AND PREVALENCE OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS (PHASE-1)

This chapter outlines the findings from the identification process. Results from the ISD data will initially be presented, as this determined the case notes eligible for review. The GP case note data will then be presented in terms of the number of patients referred, specialties referred to and symptoms referred for. Finally this chapter will conclude with a prevalence estimate of FRMUS patients in primary care.

INFORMATION AND STATISTICS DIVISION DATA

Registered patients

ISD data indicated there were 39,562 patients registered with the five participating practices. The number of these patients who were aged 18-65 years from the five participating practices was 26,252 (66.4%).

Referred patients

Of patients in this age group, ISD data identified 14,034 (52.1%) as referred from the five practices 27,302 times (an average of 1.94 referrals per patient) during the study's five year time period. It was noted that 221 (1.6%) of the referred patients had died. This left 13,813 living patients, referred 26,572 times, as the study population from which to sample (an average of 1.92 referrals per patient).

Frequently referred (FR) patients

Of the patients aged 18-65, 2234 patients (of the 14034;15.9%) had been referred to any outpatient clinics three or more times from all five practices in a five year time frame. This group of patients accounted for a total of 9477 referrals (mean 4.24 referrals per patient).

The criterion of selected outpatient specialties was then applied. Of the 2234 patients referred three or more times, 1312 (58.7%) patients were identified as having been frequently referred 'FR' to selected specialties. These 1312 patients accounted for 5435 outpatient contacts (mean 4.14 referrals per patient, minimum 3 and maximum 15).

FR patients had a mean age of 47.05 years and 852 (64.9%) were women. Of the 1312 FR patients identified from ISD data: 259 (19.7%) were from Practice-1; 224 (17.1%) were from Practice-2; 235 (17.9%) were from Practice-3; 404 (30.8%) were from Practice-4; and 190 (14.5%) were from Practice-5.

Infrequently referred (IR) patients

There were 6848 patients referred once only to all hospital outpatient departments. Of these, 4505 (65.8%) had been referred to the selected specialties as outlined above for the FR group. Due to the large numbers, a final eligibility criterion of being referred in the last of the five year study period was applied to identify 898 (19.9%) 'IR' patients.

IR patients had a mean age of 40.75, and 54.0% (485) were women. Of the 898 IR patients identified from ISD data: 168 (18.7%) were from Practice-1; 201 (22.4%) were from Practice-2; 207 (23.1%) were from Practice-3; 154 (17.1%) were from Practice-4; and 168 (18.7%) were from Practice-5.

Basic comparisons between the FR and the IR groups, using the chi square statistic ($=^2$), indicated that FR patients tended to be older, had a greater proportion of women, and were more deprived (p=0.000). The practice in the most deprived residential area referred a higher proportion of patients, which is noteworthy given they had the second least number of registered patients of the five practices.

GP RECORDS AND CASE NOTE DATA

General Practitioners

Characteristics of GPs employed and the number of patients registered at the five participating practices are outlined in Table 1. below. Any differences between practices were not statistically significant, due to the small numbers working in each practice.

Table 1. Practice location deprivation score (DepCat), number of GPs employed (the number employed full-time, FT, and the number of females), mean years qualified as a GP, GP postgraduate qualifications, and the number of registered patients

	Practice	GPs				Patients	
	DepCat	n (FT)	(female)	mean yrs as a GP	Postgrad. quals	all ages	18-65 years
Practice-1	1	6 (4)	3	20.83	11	10,731	6,619
Practice-2					(13)		
A	2	1	0	34	4	2,078	1,408
B	2	1	0	29	3	2,131	1,680
C	2	3 (1)	2	19.7	3	3,360	2,652
D	2	1	0	37	3	1,767	1,411
Practice-3	5	8 (2)	4	20.75	24	5,206	3,695
Practice-4	6	5 (1)	2	30.2	10	5,838	3,755
Practice-5	1	5 (3)	2	23.4	7	8,451	5,033
Total study population		30 (14)	13		65	39,562	26,252

N.B. Deprivation categories (DepCat7) provided by ISD; a DepCat of '1' represents the highest score on the scale (most affluent) and '7' represents the lowest score on the scale (most deprived). Numbers were taken at the time practices agreed to participate in the study.

Half (15, 50.0%) of the 30 participating GPs worked full-time and 17 (57%) were male. The years qualified as a medical practitioner ranged from 1965-1996 (7 years to 38 years in practice as a GP). The mean total number of years qualified in medicine was 22.7 years (range 18.75 at Practice-3 to 27.80 at Practice-5).

Five (16%) GPs had post-graduate qualifications such as a Masters, MD or PhD. None of the GPs had specified further qualifications (i.e. diploma or certificate) in mental

health care. However, four GPs stated a special interest in mental health, and all GPs would have undertaken specific attachments in psychiatry for six months as part of their GP training scheme. Twenty three (76.7%) had membership with the Royal College of General Practitioners (MRCGP or FRCGP). There were no statistical differences in GP education or qualifications between the practices.

In terms of spread of deprivation for patients served by the five participating practices, further information from ISD demonstrated that these five were representative of general practices within the rest of Lothian. The proportion of patients registered with all general practices in Lothian categorised into the first three deprivation quintiles (the three least deprived of five) was 68.3%; 33.7% in quintile 1, 18.4% in quintile 2, and 16.2% in quintile 3 (see table in Appendix 2). The proportion of patients registered with Referral Study practices categorised in the first three quintiles was 73.7%; 54.5% in quintile 1, 12.9% in quintile 2, and 6.3% in quintile three. The percentage of Lothian primary care patients in the last two quintiles (i.e. most deprived) was 31.6% compared to the Referral Study's practice patients 26.4%. Comparison of these proportions was not statistically different (p=0.35) indicating that our practices provided a representative spread of primary care patients when compared to the rest of Lothian. This was not the case, however, compared to the total population of Scotland which had 59.7% of primary care patients in the three least deprived quintiles, and 40.2% of primary care patients in the two most deprived quintiles (p=0.035). As I was most interested in having a representative sample of the total primary care population of the region, i.e. Lothian, these findings are reassuring.

Availability of case notes

The general practice case notes of all 2210 patients (1312 FRs and 898 IRs) identified from the ISD data were sought for a retrospective review of the hospital correspondence section. From the FR group there was no record in the practice of 24 (1.8%) patients. Three had died, and 226 (17.2%) had left the practice. There was no record of 70 (7.8%) IR patients, one had died, and 197 (21.9%) had left the practice (deducted). Although this appears to be a high rate of patients deducted, practices reported their annual patient turnover to range from 3.4% in Practice-2 to 20.6% in Practice-3. The high patient turnover for Practice-3 was due to its location in the inner

city, as it serviced a very transient population of students, academics and temporary residents to Edinburgh.

There were 1059 (80.7%) FR patient case notes, and 630 (70.2%) IR patients' notes available for audit (1689 in total). Seven case notes (one IR and six FR) were incomplete. One of two volumes of notes was missing for six patients. One FR patient had left the country during the study period and documentation was incomplete. Referral data were collected from the available notes, but these patients were excluded further from the study.

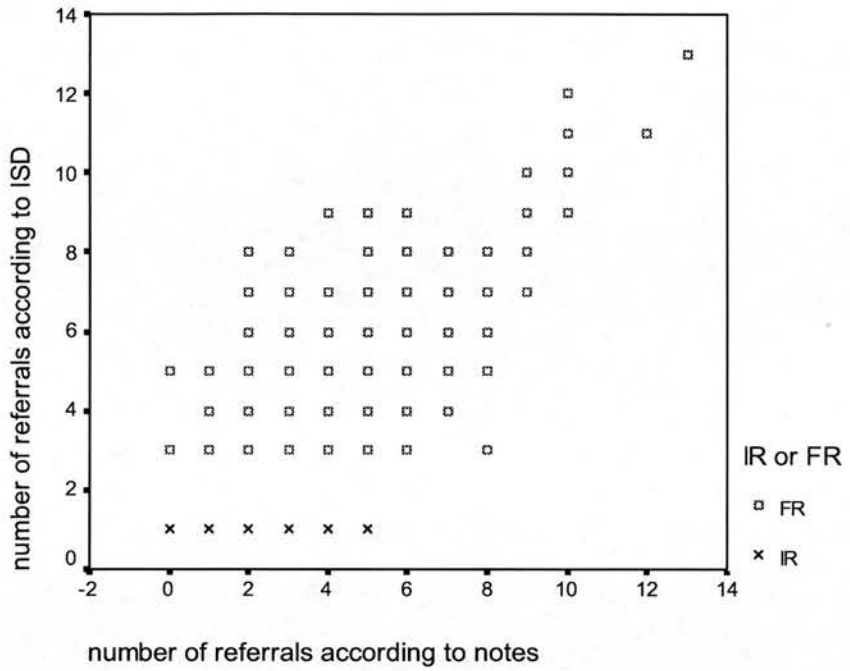
Information and Statistics Division data compared to case note referral data

From the case notes available for audit, a total of 5278 referral episodes were reviewed. The FR group accounted for 4445 referrals. There were 833 referrals noted for the IR group (given there were 630 IR case notes reviewed, some had been referred more than once and were ineligible; other reasons for ineligibility are listed on page 137).

Referral outcomes were unobtainable for 358 (8.1%) of the 4445 referrals from the FR group and 24 (2.9%) of the 833 referrals for the IR group. Reasons for this may have included patients defaulting, cancelling their appointment, yet to be seen by a specialist, or the absence of documentation in the GP records.

Figure 13. shows a scatter plot of ISD referrals against actual referrals documented in the case notes. Inspection of the graph suggests a good correlation. Statistical analysis of the correlation using Pearson's correlation for parametric variables found a coefficient of 0.87, significant at the 0.01 level (2-tailed). The pilot study found a similar correlation of 0.84. This finding further supports the effective use of ISD for identifying patients with a certain number of referrals to hospital outpatient departments.

Figure 13. Scatter plot of ISD referrals against those documented in GP case notes



Delays in data availability

There were time lags involved with each type of data collected for this study.

1. ISD takes six months to compile the previous year's complete secondary care data set.

2. The time between requesting and receiving the activity data from ISD took three months. This meant receiving 9 month old data.

3. There was a mean of 18 months delay from the last recorded ISD referral to the time of case note audit (range 3.02 to 33.35 months).

4. The case note audit for the first four practices took 10 months (i.e. approximately two months at each practice), and the fifth practice took two months to complete (one year in total).

DATA QUALITY CHECK OF RATINGS

A random selection of 20 case notes, from the 280 already reviewed by August 2003, were re-rated to ensure my application of the operationalised criteria had been reliable. Ten of these (50%) showed 100% agreement, seven (35%) had minor modifications to ratings so that no change to classification was required, and three (15%) were re-rated so that their classification was changed.

The consensus ratings between my supervisors and me were then conducted. Throughout the case note audit, a total of 61 patient summaries were rated by consensus. Issues raised and decisions made from these summaries were also able to be applied to referrals with similar complexities or problems.

The revision of the operationalised criteria in December 2003 involved reassessment of 980 patients' note summaries already performed. In this process there were no or minimal changes in the ratings for 966 (98.6%) of the patient case notes accounted for. However, 13 (1.3%) patients changed groupings as a result. Of the 13, seven (57.8%) were reclassified from ineligible, with one MUS episode, to eligible FRMUS cases. Four (30.8%) were re-classified to ineligible due to having only one MUS episode, and two (15.4%) were re-classified from FRMES to FRMUS.

Exclusions

Those referred for reasons other than symptoms (e.g. chronic disease reviews, abnormal blood results, medication advice, termination of pregnancy, fracture or wound care, etc.) made up 13.4% (142/1059) in the FR group. Practice-3 wished to give their patients the opportunity to 'opt out' of the study. Of 209 patients mailed a letter from their GP, 12 (5.7%) FR patients 'opted out'.

Of the 1312 FR patients identified from ISD data, 795(60.6%) did not meet the eligibility criteria (see Figure 14). These patients were determined to be ineligible for the study due to the following reasons:

- 226 (26.4%) had been deducted from the practice (i.e. left the practice; 3 had died)
- 142 (17.9%) were not referred for symptoms
- 125 (15.7%) had been referred for only one MUS episode (grey zone)
- 114 (14.3%) had no referrals in the final year of the study period
- 75 (9.4%) were not FR (i.e. had 0 or 2 referrals)
- 43 (5.4%) were aged 66 years or over
- 24 (3.0%) had no record in the general practice
- 19 (2.4%) had not been referred by a GP, only self referrals, A&E or other hospital specialist
- 12 (1.5%) patients from practice-3 opted out of the study
- 6 (0.8%) were unable to provide informed consent
- 3 had incomplete notes, and 3 were missing (0.8%)
- 3 (0.4%) were too ill to participate (i.e. had a recent diagnosis of cancer)

There were 636 of the identified 898 (70.8%) IR patients that were deemed ineligible for this study. No IR patients participated in the opt-out, and no IR patients were over the age of 65. In total, 1689 case notes were reviewed and 910 (54%) did not meet the eligibility criteria.

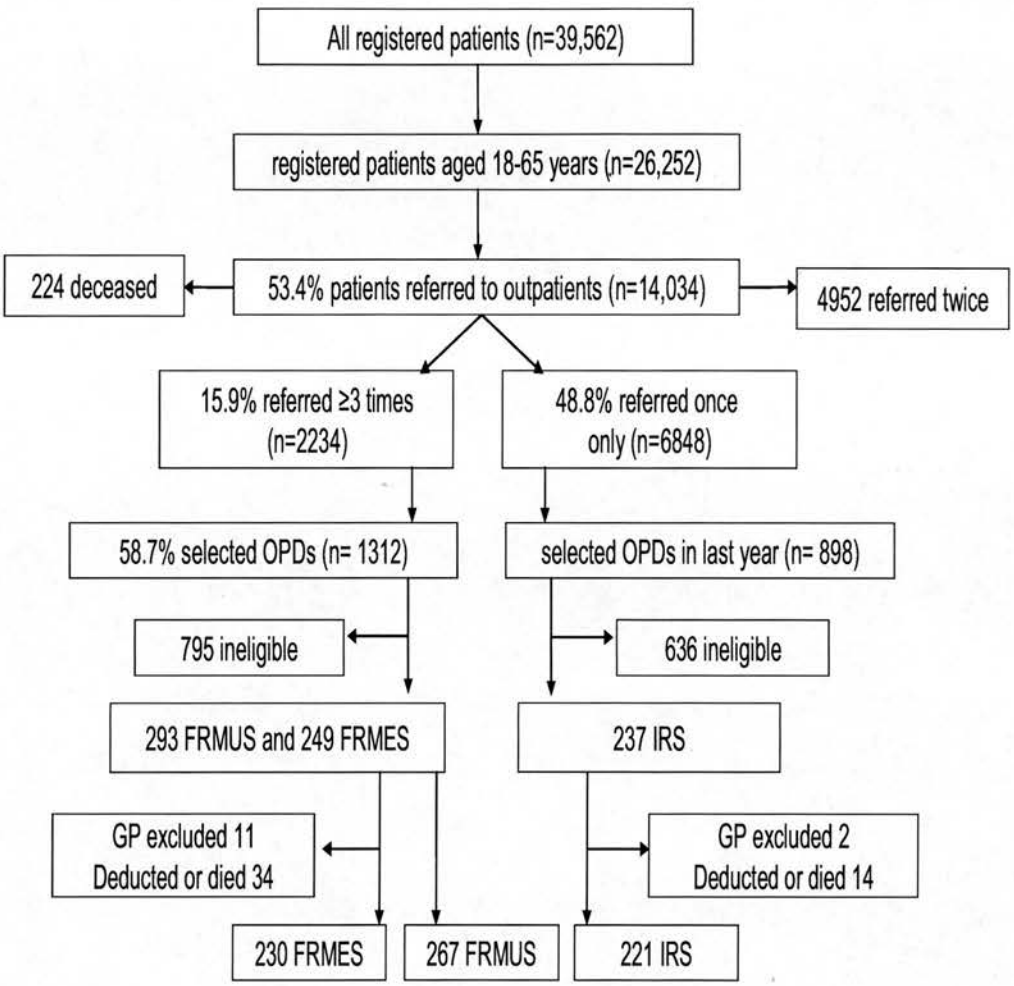
The 636 IR patients determined to be ineligible for this study were excluded for the following reasons:

- 197 had been deducted; one had died (31.0%)
- 147 (23.1%) were not referred for symptoms
- 5 (0.7%) had not been referred in the final year of the study period
- 147 (23.1%) were not IR (had been referred 0 or 2 times)
- 70 (11.0%) had no record in the practice
- 66 (10.4%) had not been referred by a GP
- 1 (0.2%) was unable to provide informed consent
- 1 (0.2%) patient's notes were missing
- 1 (0.2%) patient was too ill (due to cancer)

ELIGIBLE SUBJECTS

From the ISD derived FR group, application of the operationalised criteria to case note documented referrals identified 517 eligible patients; 284 FRMUS, 228 FRMES and five IRS. The ISD derived IR group consisted of 262 eligible patients, i.e. 232 IRS, 21 FRMES and 9 FRMUS. In total, 779 eligible patients were identified.

Figure 14. Flow diagram of the identification of FRMUS, FRMES and IRS patient groups from all five participating practices



Practice-4 contributed the most eligible FRMUS and FRMES subjects and the least IRS patients. Practice-5 had the least number of eligible patients. However, there were no statistical differences between practices. On visual inspection of the data, the two most deprived practices had the higher proportions of referrals. Given these two practices had the least registered patients, this finding is noteworthy. Table 2 below displays how many subjects were identified in each study group for each practice.

Table 2. Number (N) and percentage (%) of FRMUS cases, each of the two comparison groups (FRMES and IRS), those not eligible, and total number of patient case notes reviewed by study practice

	FRMUS N=293 (13.26)	**FRMES** N=249 (11.27)	**IRS** N=237 (10.72)	**Not eligible** N=1431 (64.75)	**Total** N=2210 (100.00)
Practice	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**N (%)**
1	58 (13.58)	50 (11.71)	51 (11.94)	268 (62.76)	427 (19.32)
2	47 (11.06)	37 (8.71)	50 (11.76)	291 (68.47)	425 (19.23)
3	43 (9.73)	34 (7.69)	50 (11.31)	315 (71.27)	442 (20.00)
4	90 (16.13)	65 (11.65)	32 (5.73)	371 (66.49)	558 (25.25)
5	55 (15.36)	63 (17.60)	54 (15.08)	186 (51.96)	358 (16.20)

PREVALENCE OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS

FRMUS patients, as defined in this study, accounted for 1.1% (293/26,252) of the primary care sample aged 18-65 years.

As a point of interest, 418 (1.6%) FR patients had at least one referral episode of MUS over the five year study time frame.

CHAPTER 11. REFERRALS AND SYMPTOMS REFERRED (PHASE-1)

This chapter describes the referrals made for FRMUS, with information about FRMES and IRS controls to contrast these findings. The outpatient specialties referred to, symptoms referred for, and symptoms deemed medically 'unexplained' will be presented.

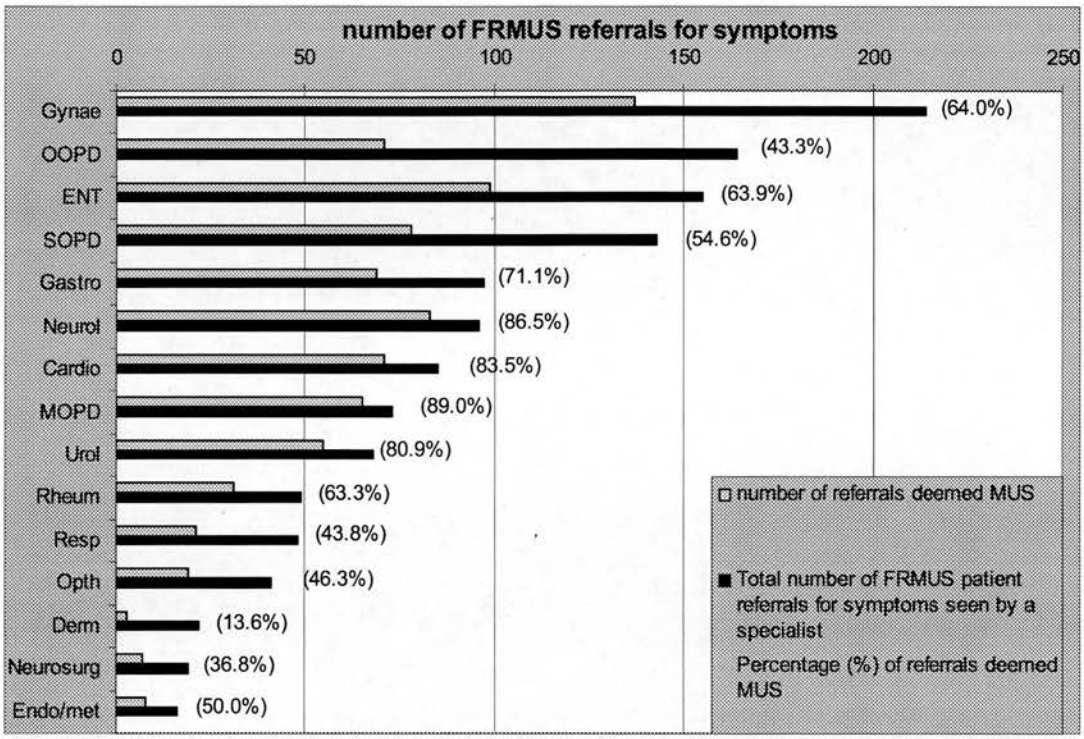
OUTPATIENT SPECIALTIES

Patients Frequently Referred with Medically Unexplained Symptoms (FRMUS)

A total of 1572 referrals had been made for this patient group according to the notes. Of these, 209 (13.3%) referrals were not for symptoms and 73 (4.6%) had no outcome as they had not been attended, been cancelled or there was no documentation. This left 1290 symptom specific referral episodes with specialist diagnoses documented in the case notes. The proportion of referrals and their outcomes are graphically represented in Figure 15. Of the 1290 referrals for symptoms, 817 (63.3%) were deemed to be 'somewhat' or 'not at all' explained by medical disease (MUS).

The specialties that had the highest proportion of referrals for MUS in the FRMUS group were General Medicine (65/73, 89.0%), Neurology (83/96, 86.5%), Cardiology (71/85, 83.5%), Urology (55/68, 80.9%), and Gastroenterology (69/97, 71.1%).

Figure 15. Total number of FRMUS patients' referrals for symptoms to each specialty, and the number and percentage (%) of referrals deemed 'somewhat' or 'not at all' explained by disease (MUS).



N.B. Black bars represent the total number of FRMUS patients' referrals for symptoms, and the grey bars represent the number of those referrals deemed MUS.

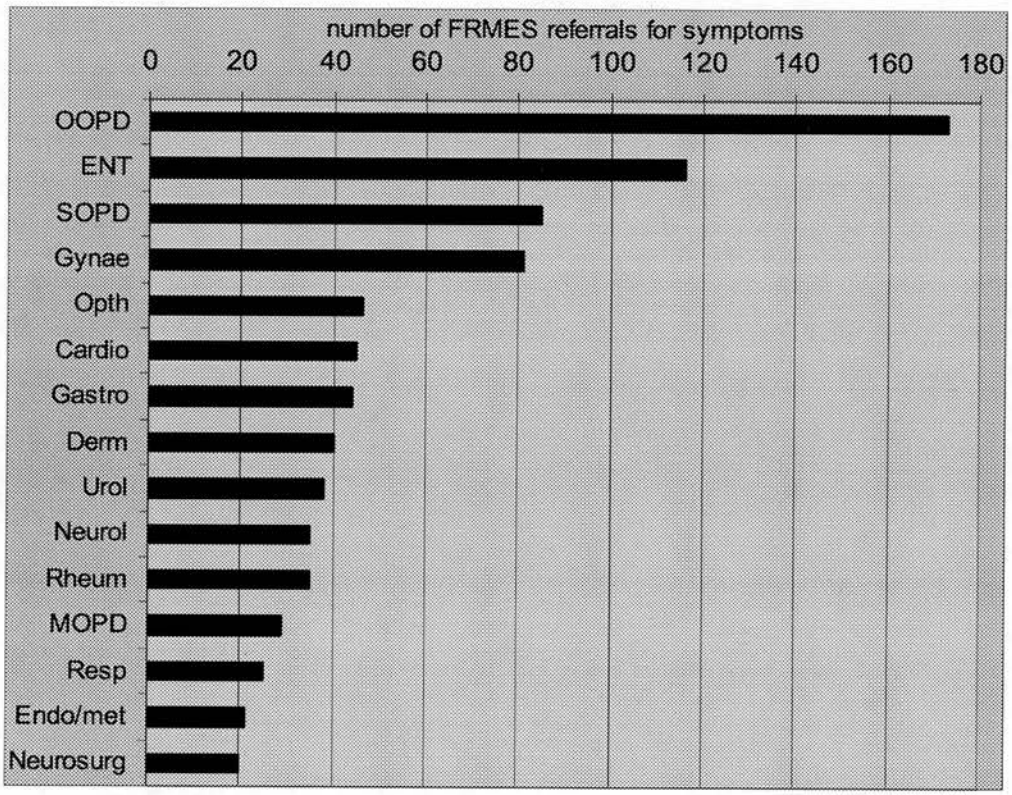
Investigations

Of the total number of investigations (N=3735) noted during the case note audit, FRMUS accounted for 2043 (54.7%). The most commonly performed tests for this group included blood tests, plain or barium x-rays, and histopathological tests. The number and outcome of investigations will be addressed in greater detail in the health economic chapter of the results section of this thesis (Chapter 15).

Patients Frequently Referred with Medically Explained Symptoms (FRMES)

This group accounted for 1137 referral episodes. As previously described, the FRMES patients were identified as controls as all symptoms referred were found to be caused by an objectively measurable physical condition or disease, i.e. they had no MUS referral episodes. Orthopaedics was the most common outpatient referral for this group (215/1137, 18.9%). Of the 1137, 833 (73.3%) referral episodes were for symptoms. Figure 16 presents the specialties FRMES controls were referred to for symptoms in order of those most commonly attended.

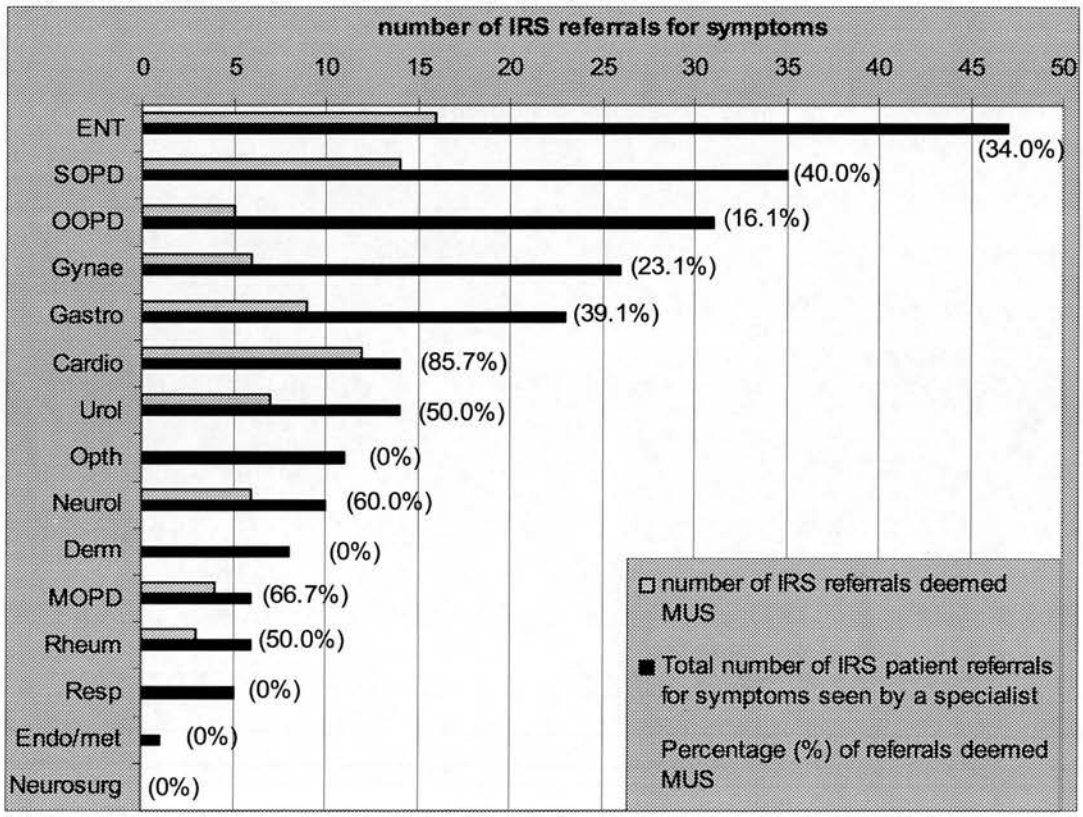
Figure 16. Number of FRMES patients' referrals for symptoms to selected specialties



Patients Infrequently Referred with Symptoms (IRS)

The 237 IRS accounted for 237 referral episodes for symptoms. The number and specialty that IRS patients were referred to are outlined in Figure 17 below. As displayed in the graph of referrals for IRS patients, Cardiology accounted for the greatest proportion of MUS (85.7%). Ophthalmology, Respiratory Medicine, Endocrinology, and Dermatology all had 100% explained referrals. There were no referrals to Neurosurgery for this group. Of the 237 referrals, 34.6% (82) were deemed to be 'somewhat' or 'not at all' explained by disease (MUS).

Figure 17. Number of IRS patients' referrals for symptoms to each specialty; number and percentage (%) of referrals deemed 'somewhat' or 'not at all' explained by disease (MUS).



N.B. Black bars represent the total number of IRS patients' referrals for symptoms, and the grey bars represent the number of those referrals deemed MUS.

SYMPTOMS REFERRED

Symptoms were the main reason for referral in over 80% of referrals made. There were 4694 symptoms documented from the referral letters of patients from all three study groups. Given there were 2360 referrals made for symptoms, this made an average of nearly two symptoms mentioned per referral. A list of 84 symptom categories was derived. Symptoms mentioned less than five times were put into a miscellaneous category.

Looking at the symptoms for the three groups combined, the most common symptoms to be referred included abdominal pain (205, 4.4%), joint pain (not including hip and knee; 198, 4.2%), back pain (169, 3.6%), and joint problems such as stiffness and locking (140, 3.0%).

Of all symptoms documented, 4524 (96.4%) had been assessed by a specialist. The other 3.6% had either not been attended by the patient or investigations were ongoing at the time of review.

Patients Frequently Referred with Medically Unexplained Symptoms (FRMUS)

Looking specifically at the FRMUS group, there was a total of 2736 symptoms referred (i.e. a mean of 2.12 symptoms were documented from each GP referral letter). The most often referred symptoms for this group included: abdominal pain, back pain, joint pains (other than hip or knee), and chest pain. FRMUS patients had 2736 documented symptoms referred, and a specialist diagnosis was available for 2626 (96.0%). Of these, 1753 (66.8%) symptoms were thought to be 'somewhat' or 'not at all' explained by disease (MUS).

Due to the size of the complete list of symptoms, the proportions of all symptoms deemed MUS for FRMUS cases are displayed in Appendix 4. Table 3 below displays the ten most commonly referred symptoms for FRMUS cases.

Table 3. List of the top ten most commonly referred symptoms for the FRMUS patient group, and the proportions deemed MUS by specialist opinion.

	totally explained (n=480)	largely explained (n=393)	somewhat explained *1 (n=626)	not at all explained *1 (n=1127)	MUS % (66.76)	total seen by specialist (n=2626)	no outcome*2 (n=110)	Total referrals made (N=2736)
abdominal pain	10	18	33	80	113/141 (80.14)	141	6	147
back pain	23	19	29	36	65/107 (60.75)	107	3	110
joint pain (other)	27	20	16	25	41/88 (46.59)	88	5	93
chest pain	8	9	22	48	70/87 (80.46)	87	1	88
headache	5	8	26	40	66/79 (83.54)	79	4	83
paraesthesia	15	7	18	30	48/70 (68.57)	70	9	79
fatigue	7	7	15	45	60/74 (81.08)	74	1	75
bladder problems	11	5	16	30	46/62 (74.19)	62	2	64
arm or leg pain	11	8	16	28	44/63 (69.84)	63	0	63
dizziness	2	7	21	31	52/61 (85.25)	61	1	62

*1. 'somewhat' and 'not at all' groupings were dichotomised as MUS in this table (For full list, see Appendix 4).

*2. 'No outcome' refers to referral made where they were seen by a specialist but investigations were still pending or the patient did not attend (DNA)

Patients Frequently Referred with Medically Explained Symptoms (FRMES)

A total of 1556 symptoms were given as reasons for referring FRMES patients (an average of 1.87 symptoms per referral for symptoms). By definition, FRMES patients had no MUS, and all of the symptoms were 'largely' or 'totally' explained by disease. Those ten most commonly referred symptoms for this group included:

1. joint pains (other than hip or knee)
2. joint problems (e.g. stiffness or locking)
3. back pain
4. breathing problems
5. abdominal pain
6. rash
7. lump
8. paraesthesia
9. knee pain
10. change in bowel habit

Patients Infrequently Referred with Symptoms (IRS)

The 237 IRS controls had a mean of 1.7 symptoms recorded in each GP referral letter. Of the 402 symptoms referred, 161 (40.1%) were assessed by a specialist to be MUS. Abdominal pain and mastalgia were the only symptoms in the list below with proportions of MUS over 50%. The ten symptoms most often referred for this group included:

1. hearing problems
2. lump
3. abdominal pain (11/15, 73% MUS)
4. mastalgia (breast pain; 7/13, 54% MUS)
5. dizziness
6. paraesthesia
7. epigastric pain
8. nausea
9. otalgia (ear pain)
10. joint pains (other than hip or knee)

Summary

Chapters 9 and 10 outlined the findings from the process of identifying cases and controls. Combining ISD activity data with case note data, identified 293 FRMUS patients, and this represented 1.1% of the primary care population sampled aged between 18-65 years. Specialties that received the most referrals from primary care for MUS included general medicine, gastroenterology and neurology. The most commonly referred symptoms for FRMUS patients where over 80% were deemed MUS included headache, fatigue, chest pain and abdominal pain.

CHAPTER 12. CHARACTERISTICS OF IDENTIFIED PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS

This chapter will focus on describing the characteristics of the 293 FRMUS patients identified as outlined in Chapter 10. The findings are presented according to each data source collected prior to mailing out the questionnaire, and these included:

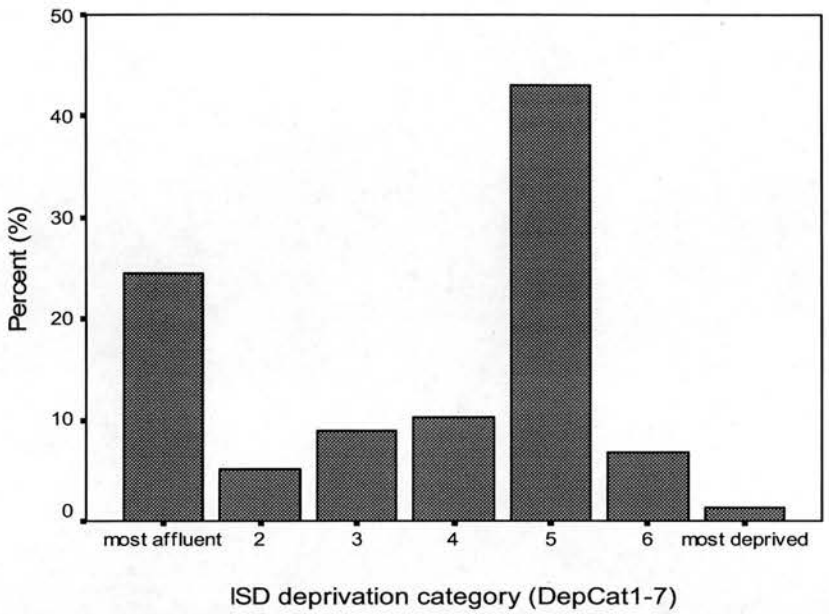
- ISD activity data
- GP case note data, and
- GP questionnaire.

DEMOGRAPHICS

Information and Statistics Division data

The 293 FRMUS patients had a mean age of 47.7 years and nearly three quarters were female 218 (74.4%). The majority of FRMUS patients (150, 51.2%) resided in deprived areas (i.e. DepCats 5 to 7). The spread of deprivation is displayed in Figure 18.

Figure 18. Percentage of FRMUS patients living in deprivation area codes 1-7 according to ISD



NB. Where DepCat 1 represents the lowest score for deprivation (i.e. most affluent), and DepCat 7 represents the highest score (i.e. most deprived).

HOSPITAL CONTACTS

Information and Statistics Division data

The mean number of new referrals made within the five year study period to selected outpatient clinics, according to ISD data, was 4.7 (range one[18] to 13).

Case note data

The mean number of new referrals documented in the case notes within the five year study period to selected specialties was five. A mean of three referrals were MUS according to the operational criteria (range two to eight referrals for MUS). The range of the total number of outpatient contacts (including reviews) was three to 85, with a

[18] Some FR patients had one referral according to ISD, so were reviewed as potential IR patients. However, on case note review, a small proportion of these patients had three or more referrals documented.

mean of 12.3 visits. A summary of FRMUS patient secondary health care contacts is outlined in Table 4.

Table 4. Mean number of secondary health care contacts for FRMUS patients

	FRMUS (N=293)
	mean
New NHS OPD contacts	4.98
Private OPD contacts	0.10
OPD reviews	7.10
Total number of OPD contacts	12.25
OPD consultations patient did not attend (DNA)	1.30
Days admitted as an inpatient	9.10
A&E visits	2.30

NB. Where 'OPD' refers to hospital outpatient departments

Of the new referrals for FRMUS patients, a substantial proportion (46.8%) was discharged back to their general practice, i.e. without further review or inter-hospital referral to another specialist. This patient group did not attend (DNA) a mean of 1.3 outpatient appointments (median 0), with a maximum of 18 DNAs for one patient. Reasons for non-attendance were not assessed in this study.

Accident and Emergency (A&E)

Patients had a mean of 2.3 visits to A&E during the five year review of their case notes. Case note review identified one patient who had visited A&E 41 times; the majority of these were for non-cardiac chest pain (with a substantial number referred by one of the GPs in the practice).

Inpatients

This group of patients had high levels of inpatient hospital care during the five years of study with a mean of nine days admitted. However, removing three outliers from the analysis (one for an extended admission for depression, and two for admission days of over 100 days), the mean number of days in hospital fell to 5.7 (median 3.0).

MEDICAL HISTORY

Almost half the study group (140, 48%) had smoking documented in their case notes, and 40% (117) were overweight. Fifty six patients (19%) were obese with a body mass index (BMI) of 30 or more.

Organic disease diagnoses (e.g. diabetes, asthma, arthritis, cardiac conditions and cancer) were noted for 84 (28.7%) FRMUS patients. Functional somatic syndromes (FSS), particularly irritable bowel syndrome (IBS) were documented for 139 (47.4%) FRMUS patients. Hysterectomy had been performed in one quarter of the FRMUS women (55/218, 25.2%).

MENTAL HEALTH

Psychiatric morbidity

Depression was documented in a third of FRMUS patients' case notes (see Table 5). Other psychiatric diagnoses, such as an eating disorder or history of self harm (mainly substance overdose), were recorded in 33 patients (11%). Drug and alcohol problems and abuse (i.e. domestic violence or child abuse) were noted for a minority of FRMUS patients.

Contacts with mental health care

Of the 293 FRMUS patients, 98 (33.4%) had at least one contact with a mental health professional (a mean of three contacts in five years[19]). In this thesis a mental health care professional was defined as a psychiatrist, clinical psychologist, or community psychiatric nurse (CPN).

Table 5. Number and percentage (%) of FRMUS patients with documented mental health problems, and mental health care received

	FRMUS (N=293) n (%)
Anxiety or panic	68 (23.2)
Depression	97 (33.1)
Other psychiatric diagnoses	33 (11.0)
Drugs or alcohol misuse	26 (9.0)
Abuse	16 (5.5)
Antidepressant prescribed at any time	166 (57%)
Current prescription of antidepressant	85 (29%)
Depression treatment according to guidelines	69/85 (81.2%)
mean number of contacts with a mental health professional	3 (in 5 years)

Over half (57%) the FRMUS patients had been prescribed an antidepressant at some time in their lives. At the time of case note review, 85 (29%) were receiving treatment for depression, and of the 85, 69 (81.2%) were according to recommended guidelines (as outlined in Chapter 8). This was an unexpected finding, as it indicated that the majority of FRMUS patients have adequate depression treatment.

[19] Excluding one woman who had an extended admission for depression

PRIMARY CARE CONTACTS

FRMUS patients had been registered with their general practice a mean of 12 years, and 81 (27.6%) had two or more volumes of notes (two patients were on their fifth). As a group they had a mean of 1.4 case note volumes. FRMUS patients contacted a GP out of hours (OOH) a mean of 3.13 times in five years.

Multiple doctors

FRMUS patients were more likely to consult, or be referred by, multiple doctors. It was often difficult to identify which GP was the main treating or referring GP. FRMUS patients had a mean of 2.5 doctors refer them to a hospital outpatient clinic over a five year period.

As there were a small number of doctors, and only five practices involved in the study, this information is more hypothesis generating in nature, and no meaningful analyses can be performed. There was high variation of GP referral patterns for MUS in this patient group. However, there is some indication that GP locums, registrars, assistants and solo practitioners refer higher proportions of MUS for this patient group.

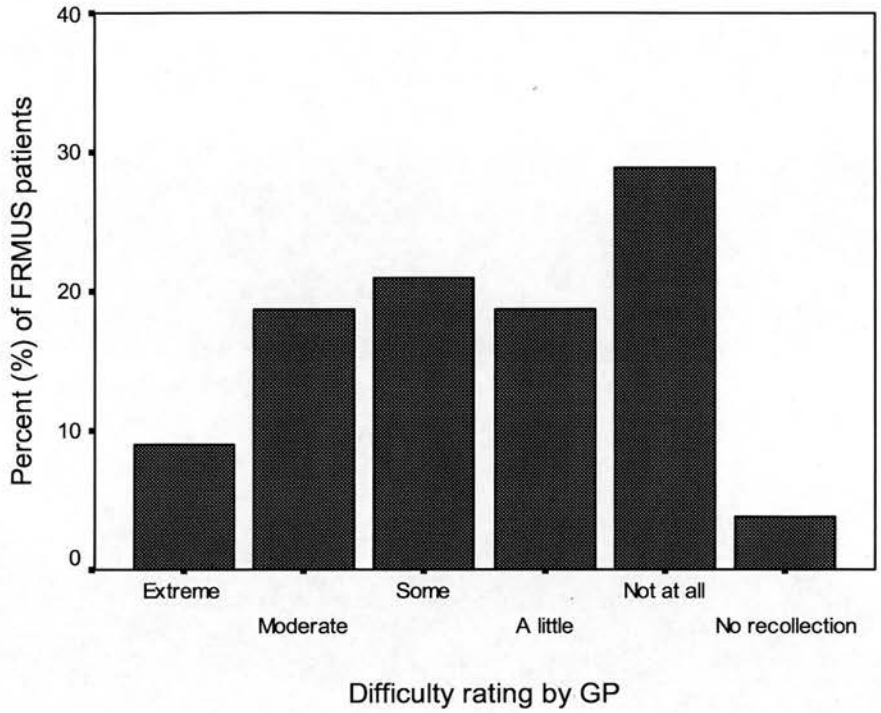
Of the referrals made by all three solo practitioners over 50% of each doctor's referrals were for MUS. Most GP registrars, assistants and locums, made over 50% of their FRMUS patient referrals for MUS.

Various out of hours (OOH) GPs made the least number of referrals for FRMUS patients, and only 20% of their referrals were for MUS. Hospital specialists actually made the most referrals to other hospital specialists for FRMUS patients. Approximately a third of inter-clinic referrals of FRMUS patients were for MUS.

General Practitioner difficulty ratings

When asked to rate how difficult these patients' problems were to manage in primary care, GPs found 180 (61.4%) patients to be at least a little difficult, with a quarter rated to be moderately or extremely difficult to manage (see Figure 19).

Figure 19. Ratings of how difficult problems of FRMUS patients were according to the GP who referred them most often (or if unclear, their registered GP)



SUMMARY

Three quarters of the FRMUS patients identified were female and lived in a deprived area of Lothian, Scotland. Indications of unhealthy lifestyles were evidenced by nearly 50% being current smokers or overweight. Nearly half had functional somatic syndromes and a quarter of the women had undergone a hysterectomy. Just under a third of the study group had some form of notable organic disease. Health care use in all medical settings was high and the majority of problems presented by FRMUS patients were found difficult to manage by their GP.

A third of FRMUS patients had depression documented in the GP notes and 166 (57%) had received an antidepressant at some time in their lives. Nearly a third were receiving an antidepressant at the time of case note review, and of those 81% (69/85) were receiving 'adequate treatment' for depression (according to the criteria outlined in Chapter 8).

CHAPTER 13. DESCRIPTION AND COMPARISON OF PARTICIPANTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS (PHASE-2)

This first section of chapter 12 deals with the results of piloting and administering the questionnaire to identified FRMUS, FRMES and IRS patients. Response rates to the questionnaire will follow and differences between responders and non-responders outlined. The second section provides the main findings from the case-control study.

PILOTING THE QUESTIONNAIRE FOR RESPONSE RATE

Of the 40 FR patients mailed the pilot study materials, 14 (35.0%) completed consent forms and questionnaires were returned unprompted. A further 8 questionnaires were completed after a mailed reminder (55.0 % cumulatively), and a final four after the second and final reminder mail out (65.0% response rate overall). Five patients (12.5%) had declined to participate and the rest were non-responders. Only one person gave a reason for declining and this was their reluctance to have their notes read by someone not directly involved in their care.

Of the 20 IRS patients mailed the study materials, only four came back unprompted (20.0%), and another four (40.0% cumulatively) were returned with a mailed reminder of all the study materials. A third and final mail out of all study materials brought back three completed questionnaires. A final response rate for the IRS pilot was 55.0%. Two patients (10.0%) returned their study materials blank as they had decided to decline participation, with no reason given. The remainder were non-responders. As a result of this pilot, ethics and CSO approval was sought and obtained to include financial incentives in the mail out for the main study.

PATIENT EXCLUSIONS

In preparing to mail out study materials to these patients, a further 61 of the 779 previously identified as eligible were excluded. Fifty (6.4%) of these patients had left their respective general practice. These patients had left during the period of time it took to complete the case note audit (for the original sample of 2210 patients) up until the questionnaires had been mailed out. Given the case note audit commenced at Practice-3 in June 2003, this ranged from a year for that practice to only one month time lag for Practice-5.

The other 11 (1.4%) became ineligible due to exclusion from the study by their main treating GP. The key reasons provided for exclusion included:

- the doctor's personal acquaintance with the patient,
- a pending complaint on the part of the patient about the GP or the practice, or
- the patient being too ill to participate in research.

A final sample of 718 patients remained eligible to invite: 267 FRMUS cases, 230 FRMES controls, and 221 IRS controls.

RESPONSE RATES

The first mail out involved mailing 551 questionnaires to eligible patients registered with Practices 1-4. Completed questionnaires were returned from 238 participants (43.2%) and 23 declined to participate.

A second reminder was mailed to 290 non-responders less than four weeks after the first mail out. This brought the participant response rate up to 60.1% (93 further returned questionnaires and 26 declining to participate).

Invitations were sent again to 16 patients in Practice-4 (non-responders who had changed addresses during the mail out period). Subsequently, a third mailed reminder was sent to 85 non-responders. This returned 33 completed questionnaires to make the response rate 66.1%.

Telephone reminders by practice staff prompted a number of varying requests from 17 patients who eventually completed the questionnaire:

- one asked to have a questionnaire left on his notes for their next consultation
- one wanted the questionnaire resent by fax
- three asked to have the questionnaire re-mailed
- two preferred the questionnaire to be resent by email, and
- ten went through the questionnaire with me over the phone.

Given these measures, the final response rate from the four practices was 69.1%. Although a near 70% response rate, the numbers of participants were below that required in each group to achieve power (i.e. 140 patients in each).

Practice-5 then joined the study and at the conclusion of the case note audit, 167 eligible patients were identified and mailed questionnaires. The first unprompted response was 54.5% (92 completed the questionnaire and seven declined). The second mail out of all study materials produced a return of 31 completed questionnaires (three declined). A final three questionnaires were obtained following the Practice Secretary contacting non-responders by phone.

The final response rate from Practice-5 was 75.4% (126/167), and this facilitated a final overall response rate of 70.6% (507/718) for all five practices. The numbers required to achieve power were exceeded in each patient group (see Table 6).

Table 6. Number of invited eligible patients, number of participants who completed the questionnaire and percentage (%) of invited patients who participated (response rates of the questionnaire study) by registered practice and study group

	FRMUS			FRMES			IRS			Overall response rate		
	invited	participated	(%)	invited	participated	(%)	invited	participated	(%)	invited	participated	(%)
Practice	**N=267**	**n=193**	**(72.3)**	**N=230**	**n=162**	**(70.4)**	**N=221**	**n=152**	**(68.8)**	**N=718**	**n=507**	**(70.6)**
Practice 1	55	46	(83.6)	46	37	(80.4)	50	41	(82.0)	151	124	(82.1)
Practice 2	44	33	(75.0)	33	23	(69.7)	42	31	(73.8)	119	87	(73.1)
Practice 3	35	27	(77.1)	30	22	(73.3)	45	23	(51.1)	110	72	(65.5)
Practice 4	83	49	(59.0)	58	35	(60.3)	30	14	(46.7)	171	98	(57.3)
Practice 5	50	38	(76.0)	63	45	(71.4)	54	43	(79.6)	167	126	(75.4)

Differences between responders and non-responders

There were no statistical differences (at the 0.05 level) between those who responded and those who did not for:

- registered general practice
- psychological problems such as anxiety or depression
- number of health care contacts
- GP difficulty
- organic disease diagnoses
- documented drug or alcohol abuse

However, there were some differences between responders and non-responders which should be considered. Table 7 summarises the statistically significant differences between responders and non-responders.

Table 7. Variables with a statistically significant difference comparing responders with non-responders

	Responders		Non-responders		
	N = 507		N = 211		p
Male (%)[1]	172	(33.9)	90	(42.7)	0.027
DepCat 5-7 (%)[1]	202	(39.8)	104	(49.3)	0.009
Mean age (mean difference, 95% C.I.)[2]	48.5		44.8	3.6 (5.47, 1.96)	0.000
Years registered with practice (mean, median)[3]	mean 12.6	median 10.0	mean 11.0	median 9.0	0.024
DNAs (mean, median)[3]	mean 0.70	median 0.0	mean 1.0	median 0.0	0.001

1. Calculated using the Chi square ($\chi 2$) statistic

2. Calculated using the student t-test (for parametric distributions)

3. P value calculated using Mann Whitney-U test (for non-parametric distributions)

The non-responders were more likely to be younger, male and reside in more deprived areas (i.e. DepCats 5-7). The mean number of years registered with a general practice was less for non-responders. Non-responders defaulted more often from outpatient departments than responders.

Within study group comparison, of responding FRMUS with non-responding FRMUS, non-responders were significantly younger (this was also the case for FRMES patients; $p \leq 0.027$). The IRS non-responders were more likely to be male ($p=0.024$) and registered with the practice for less time ($p=0.033$).

Data delays

The delays in data availability have already been outlined in Chapter 10. However, aside from delays in receiving the data, there were delays involved with the questionnaire data. The mean time from completing the case note audit to mailing out the first round of questionnaires to eligible patients was 4.08 months (range 2-12 months). The time from case note audit to questionnaire completion was a mean of 5.05 months (range 2-14 months). Due to delays in data, patients had not been referred for at least 16 months (range 16 to 38 months) at the point of being asked to complete the questionnaire.

CHARACTERISTICS OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS COMPARED WITH THE TWO OTHER COMPARISON PATIENT GROUPS

This section addresses how specific the findings of FRMUS patients were (as outlined in Chapter 12) by comparing the subset of 193 FRMUS questionnaire participants with the 162 FRMES and 152 IRS control participants respectively.

Findings are presented according to each hypothesis and each data source used to test it. The four sources of data presented for the case-control study include: ISD activity data; GP case note data; GP questionnaire; and patient self-report questionnaire.

Participant demographics

Information and Statistics Division data

FRMUS participants had a mean age of 49 years and over three quarters (75.6%) were female (see Table 8). Compared to the two comparison groups, FRMUS cases were more likely to reside in more deprived areas. Note that higher deprivation scores (i.e. Depcat5 scores of 4-5 and Depcat7 scores of 5-7) indicate greater deprivation.

Table 8. Differences in number (N) and percentage (%) for age, gender and deprivation between FRMUS patients and the FRMES and IRS control patient groups respectively

	FRMUS (N=193)	FRMES (N=162)		IRS (N=152)	
	n (%)	n (%)	p	n (%)	p
Mean age (years)[1]	49	51	0.100	45.5	0.002
Female[2]	146 (75.6)	144 (59.3)	0.001	93 (61.2)	0.004
Deprivation (DepCats 4-5)[2]	107 (55.5)	66 (40.7)	0.012	65 (42.8)	0.014
Deprivation (DepCats 5-7)[2]	93 (48.2)	67 (35.2)	0.014	52 (34.2)	0.020

1. Calculated using the student t-test comparing FRMUS with FRMES and IRS respectively.

2. Calculated using the Chi-squared statistic ($\chi 2$) comparing FRMUS with FRMES and IRS respectively.

As a point of interest, the demographic make-up of the two comparison groups was relatively similar. There were no statistical differences for deprivation scores or for gender. However, the IRS control group were significantly younger than the FRMES participants with a mean difference in age of 5.35 years (CI 2.94, 7.76).

Case note data

Over a quarter (26.4%) of the FRMUS participants had two or more volumes of case notes (two patients were on their fifth), and had extensive notes compared to the other two patient groups (see Table 9). There were no statistical associations between number of subjects in each patient group and the practice they were registered with.

Table 9. Mean number of years participants had been registered with their general practice; number and percentage (%) of participants with two or more volumes of case notes

	FRMUS (N=193)	FRMES (N=162)		IRS (N=152)	
			p		p
Mean number of years registered with practice[1]	12.57	13.12	0.708	12.21	0.141
Two volumes or more (n, %)[2]	51 (26.4)	18 (11.1)	0.003	2 (1.3)	0.000

1. P-value calculated using Mann-Whitney U for non-parametric distributions, comparing FRMUS with FRMES and IRS respectively.

2. P-value calculated using χ^2 comparing FRMUS with FRMES and IRS respectively.

Medical history

Case note data

FRMUS participants had substantially less organic disease than FRMES patients, but more than IRS controls (See Table 10). Nearly half of the FRMUS cases had one or more functional somatic syndrome (FSS) diagnoses, e.g. fibromyalgia or IBS. This is no surprise given the classifications set out in the operationalised criteria, and my definition of what constitutes an FRMUS 'case'.

A relatively high proportion of FRMUS participants had been prescribed opioid analgesics for pain, and this was slightly proportionately higher than for FRMES participants. Hysterectomies had been performed on nearly a third of the female FRMUS participants and this was more than either of the comparison groups.

A small percentage of patients from each study group had no weight or smoking status documented in their medical records. This averaged approximately five percent non-documentation of these clinical characteristics. Considerably more FRMUS cases were clinically overweight (80, 42%) and obese (37, 19.2%; with a BMI of 30 or more), compared to the FRMES controls (31% and 18% respectively, $p \geq 0.071$). This was double the prevalence of IRS control participants (24% and 7% respectively, $p=0.001$). There were similar levels of smoking found for all participants. Approximately 40% of each participant group were documented as current smokers.

Table 10. Number and percentage (%) of participants with medical diagnoses documented in the case notes

	FRMUS (N=193)	FRMES (N=162)			IRS (N=152)		
	n (%)	n (%)	χ2	p	n (%)	χ2	p
Organic disease diagnoses	84 (28.7)	109 (43.8)	13.42	0.000	28 (11.8)	13.46	0.000
Functional somatic syndrome (FSS)	99 (51.3)	28 (17.3)	44.22	0.000	11 (7.2)	75.78	0.000
Hysterectomy (female only)	43/146 (29.5)	17/96 (17.7)	4.27	0.039	11/93 (11.8)	10.05	0.002

NB. Statistics calculated using the Chi-square statistic (χ^2) to compare FRMUS cases with FRMES and IRS control groups respectively.

Patient self-report data

Compared with the two comparison groups, FRMUS participants were statistically more likely to have:

- had less education after the age of 16 years
- lived in rented or "other" accommodation
- had more time off from usual activities (See Table 11).

All differences in demographics between FRMUS and IRS participants were substantial and statistically significant. At the time of completing the questionnaire, and compared to the two comparison groups FRMUS participants had a higher proportion (but not statistically significant) who were:

- widowers or divorcees
- receiving some sort of social security benefit (most commonly the state pension, followed by incapacity benefit and disability living allowance, DLA).
- taking more time off paid work because of illness during the previous five years.

Table 11. Mean years of education; number and percentage (%) of participants for other self-reported demographics

	FRMUS (N=193)		FRMES (N=162)			IRS (N=152)		
	n	(%)	n	(%)	p	n	(%)	p
Mean years of education (after age 16) [1]	2.4	-	2.9	-	0.017	3.9	-	0.000
Renting or 'other' [2]	57	(29.5)	30	(18.5)	0.032	26	(17.1)	0.004
Widowed or divorced [2]	45	(23.3)	27	(16.7)	0.864	22	(14.5)	0.362
Currently in paid work [2]	101	(52.3)	90	(55.6)	0.454	120	(79.0)	0.000
Last 5yrs in paid work [2]	131	(67.9)	111	(68.5)	0.897	133	(87.5)	0.000
off work ≥6mths in 5yrs [2]	29	(22.1)	19	(17.1)	0.609	6	(4.5)	0.000
Benefits ≥6 months [2]	101	(52.3)	75	(46.3)	0.258	40	(26.3)	0.000
'a lot of time' off activity [2]	63	(33.3)	38	(23.6)	0.017	7	(4.6)	0.000

1. Calculated using the student t-test comparing FRMUS with FRMES and IRS respectively.

2. Calculated using the Chi-squared (X^2) statistic comparing FRMUS with FRMES and IRS respectively

The hypothesis that FRMUS cases would have more time off work than both control groups was not statistically supported (compared with FRMES controls). However, FRMUS cases had the lowest proportion of the three study groups in current or past five years employment, and had the highest proportion receiving benefits. Cases had statistically more time off usual activities compared to the two other patient groups.

HYPOTHESIS (1)

Patients frequently referred with medically unexplained symptoms (FRMUS) will have more anxiety and depression compared to comparison patient groups who are 1) frequently referred with medically explained symptoms (FRMES) and 2) infrequently referred with symptoms (IRS), respectively

Case note data

Substantially more anxiety and depression diagnoses were documented in the notes of FRMUS patients than both control groups (see Table 12). Other indicators of poor mental health, such as alcohol misuse (in some instances drug abuse), self harm (over dose), and other psychiatric disorders (i.e. eating disorder), were also more prevalent in the FRMUS group than the two comparison groups. However, the numbers of participants with psychiatric diagnoses, other than anxiety and depression, were small and validity of comparisons should be viewed with caution.

Table 12. Number and percentage (%) of participants with psychiatric diagnoses documented in the case notes

	FRMUS (N=193)	FRMES (N=162)			IRS (N=152)		
	n (%)	n (%)	χ2	p	n (%)	χ2	p
Anxiety or panic	44 (22.8)	7 (4.3)	24.372	0.000	15 (9.9)	9.998	0.002
Depression	67 (34.7)	31 (19.1)	10.666	0.001	24 (15.8)	15.638	0.000
Other Psych. diagnoses	19 (9.8)	2 (1.2)	11.698	0.001	6 (3.9)	4.387	0.036
Drugs/Alcohol	15 (7.8)	11 (6.8)	0.125	0.724	3 (2.0)	5.764	0.016
Self harm	19 (9.8)	7 (4.3)	3.948	0.047	2 (1.3)	10.789	0.001
Abuse	5 (2.6)	2 (1.2)	0.836	0.361	0 (0.0)	3.984	0.046

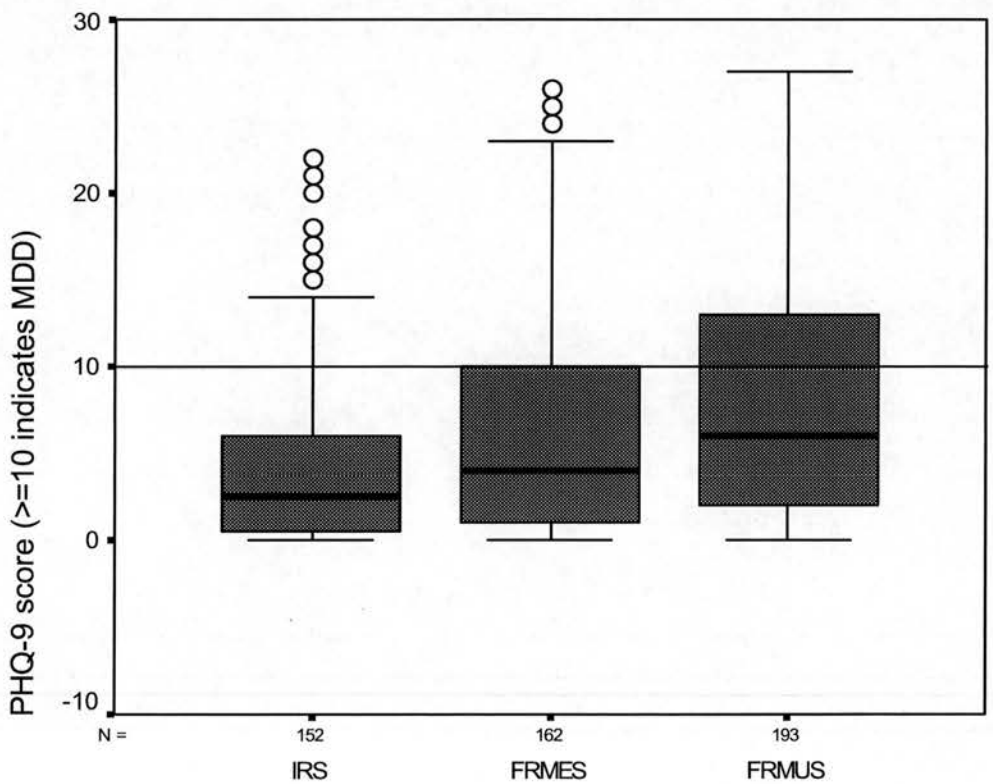
NB. Statistics calculated using the Chi-squared statistic (χ2) comparing FRMUS with FRMES and IRS respectively

Self-report data

Current depression

Calculating PHQ-9 scores gave an average mean of 8.1 (median 6) for FRMUS cases (below the score of 10 which represents clinical depression). FRMUS cases had statistically higher PHQ-9 scores for depressive symptoms than the FRMES (median 4) and IRS (median 2.5) comparison groups (p=0.000). Figure 20 shows that the majority of all participants scored below 10 as indicated by the line across the centre of the diagram. However, substantially more FRMUS patients scored above this marker.

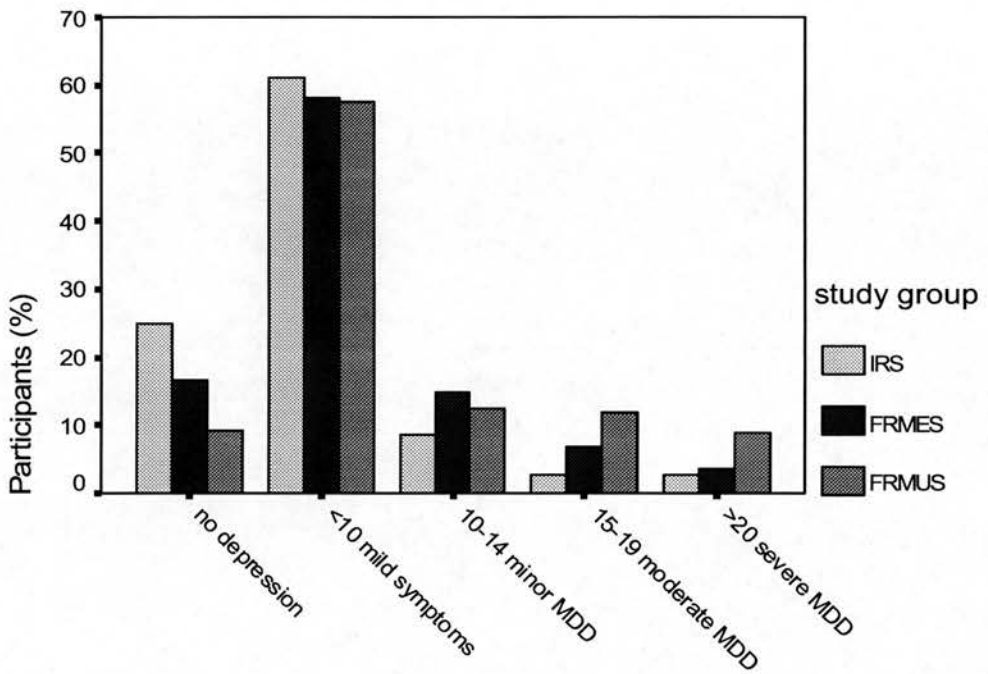
Figure 20. Box plot of PHQ-9 scores (0-27). A score of 10 or more represents major depressive disorder (MDD)



NB. The boxes represent the participant scores within the 95% confidence intervals. The dark black line represents the median scores for each group. The vertical lines represent the range of extreme scores, and the circles above are outlier scores. The horizontal line across the centre of the diagram represents a score of 10 (i.e. minimum PHQ-9 score for a diagnosis of MDD).

Figure 21 indicates that the majority of FRMUS participants had only mild symptoms of depression, and some had no depressive symptoms at all. This applied also to the two control patient groups. However, a third of cases (64/193, 33.2%) had MDD according to the PHQ-9. Of all participants who were depressed, a higher percentage of FRMUS cases, when compared to the two other patient groups, scored as 'moderate' or 'severe'.

Figure 21. Percentage (%) of participants with symptoms of depression and diagnosis of MDD according to the PHQ-9 (i.e. a score of 10 or more)



Current anxiety and panic

Nearly 40% (76/193) of FRMUS cases scored positively on the PHQ for an anxiety disorder (see Table 13). There were statistically significant differences in self reported anxiety between FRMUS cases and FRMES controls ($p=0.014$), and also compared to IRS controls ($p=0.000$). A third (65/193) of FRMUS cases reported symptoms of panic in a four week time frame. In this instance, there was a statistically significant difference ($p\leq0.001$) between the cases and the two control groups.

Table 13. Number and percentage (%) of participants with current diagnoses of anxiety, depression and panic

	FRMUS N=193		FRMES N=162				IRS N=152			
Current diagnosis	**n**	**(%)**	**n**	**(%)**	**X^2**	**p**	**n**	**(%)**	**X^2**	**p**
Anxiety	67	(34.7)	37	(22.8)	5.980	0.014	23	(15.1)	16.864	0.000
Depression	64	(33.2)	41	(25.3)	2.6	0.107	21	(13.8)	17.088	0.000
Panic	65	(33.7)	26	(16.0)	11.002	0.001	21	(13.8)	17.804	0.000

NB. Statistics calculated using the Chi-squared statistic ($\chi 2$) comparing FRMUS with FRMES and IRS respectively

Comorbid anxiety and depression

Table 14 demonstrates that there was some overlap of diagnoses, where a quarter of FRMUS participants had comorbid anxiety and depression (or 49/64, 76.6%). The majority of FRMUS patients (111/193, 57.5%) had no diagnoses of anxiety or depression according to the PHQ. However, a substantial proportion (82/193, 42.5%) had one or both disorders of anxiety and depression and this was statistically more than both control groups.

Table 14. Number and percentage (%) of current diagnoses of anxiety and depression according to the PHQ for the three study groups

	FRMUS N=193	%	FRMES N=162	%	p	IRS N=152	%	p
comorbid GAD and MDD	49	25.4	25	15.4		12	7.9	
GAD only	18	9.3	12	7.4		11	7.2	
MDD only	15	7.8	16	9.9		9	5.9	
(any disorder)	(82)	(42.5)	(53)	(32.7)		(32)	(21.0)	
no disorder	111	57.5	109	67.3	0.037	120	79.0	0.000

NB. Statistics calculated using the Chi-squared statistic ($\chi 2$) comparing FRMUS with FRMES and IRS respectively

Self-reported anxiety, depression and panic in the previous five years

The majority of FRMUS cases (119/193, 57%) reported depressive symptoms lasting two weeks or more at any time throughout the five years prior to completing the questionnaire (see Table 15). There were significant statistical differences for FRMUS self-reported anxiety, depression and panic when compared to FRMES and IRS controls. Although asked to provide an estimated number of episodes, patients tended to provide vague responses such as "all the time", "hundreds", "a lot" or "a few", and were invalid for analysis.

Table 15. Number and percentage (%) of participants reporting symptoms of anxiety, depression and panic in the past five years

	FRMUS N=193		FRMES N=162				IRS N=152			
Self-report (last 5 yrs)	**n**	**(%)**	**n**	**(%)**	**X^2**	***p***	**n**	**(%)**	**X^2**	***p***
Anxiety	64	(33.2)	34	(21.0)	6.512	0.011	30	(19.7)	7.707	0.005
Depression	110	(57.0)	67	(41.4)	8.590	0.003	69	(45.4)	4.570	0.033
Panic	71	(36.8)	34	(21.0)	10.526	0.001	25	(16.4)	17.466	0.000

NB. Calculated using the χ^2 statistic comparing FRMUS with FRMES and IRS participants respectively.

Possible confounding variables

A logistic regression was performed to assess for any confounding effect on the findings of anxiety according to the PHQ comparing FRMUS cases with FRMES control participants. Table 16. shows that area of residence (i.e. deprivation category) is a significant predictor, or confounding variable, on anxiety. However, it is worthy to note that the study group still remains a significant predictor to explain the difference in anxiety between FRMUS and FRMES patient groups.

Table 16. Logistic regression analyses for possible confounding effect of study group, age, gender and deprivation on anxiety according to the PHQ

Variables in the Equation	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
							Lower	Upper
study group	0.562	0.253	4.912	1	0.027	1.753	1.067	2.881
age	-0.021	0.012	3.172	1	0.075	0.979	0.956	1.002
gender	-0.457	0.262	3.043	1	0.081	0.633	0.379	1.058
depcat7	0.198	0.067	8.759	1	0.003	1.219	1.069	1.39
Constant	-1.201	0.991	1.470	1	0.225	0.301		

N.B. the dependent variable was a binary variable of whether a patient had anxiety or not according to scores on the PHQ; comparing FRMUS with FRMES patient groups only.

The Wald statistic and the corresponding significance level test the significance of each of the covariate and dummy independents in the model. The ratio of the logistic coefficient B to its standard error S.E., squared, equals the Wald statistic. If the Wald statistic is significant (i.e. less than 0.05) then the parameter is significant in the model. Thus study group and depcat7 are significant.

The "Exp(B)" column is the odds ratio of the row independent with the dependent. It is the predicted change in odds for a unit increase in the corresponding independent variable. Odds ratios less than 1 correspond to decreases and odds ratios more than 1.0 correspond to increases in odds. Odds ratios close to 1.0 indicate that unit changes in that independent variable do not affect the dependent variable.

Hypothesis (1) supported

Data extracted from case notes showed that FRMUS cases had more documented anxiety and depression disorders than the FRMES participants and IRS participants respectively. PHQ scores for symptoms of anxiety, panic and depression were statistically higher for FRMUS participants. One third of FRMUS had a depressive disorder. Overall, there were 82 of 193 (42.5%) FRMUS patients who had one or both diagnoses of anxiety or depression, and this was statistically significant compared with the other two control patient groups.

Self reported five year history of anxiety, panic and depression symptoms were statistically more common in FRMUS patients than the other two patient groups. An association between presence of an anxiety or depressive disorder and deprivation scores (i.e. area of residence) was found.

HYPOTHESIS (2)

Of those participants with depression, patients frequently referred with medically unexplained symptoms (FRMUS) would have inadequate treatment for their anxiety or depression compared to patients frequently referred with medically explained symptoms (FRMES) and patients infrequently referred with symptoms (IRS) respectively.

Depression

Antidepressants (General Practice records)

Of the 64 FRMUS participants who scored 10 or more on the PHQ-9 (i.e. had MDD), 44 (68.8%) were prescribed an antidepressant. Of those on an antidepressant, 86.4% (38/44) were on the minimum effective dose according to the BNF(397). Thus, of those with MDD, 59.4% (38/64) were receiving 'adequate' pharmacological treatment for their depression. However, over a third (25/64, 39%) were not receiving a therapeutic dose of an antidepressant (see Table 17). It should be noted that this was determined within a mean time of five months from case note audit (when antidepressant use was noted) to PHQ completion.

In absolute terms, this was a considerable proportion not receiving adequate treatment. However, relative to the two control groups with depression, they received substantially more ($p \leq 0.001$).

Table 17. Number and percentage (%) of participants with MDD who were receiving inadequate antidepressant treatment

	FRMUS N=64		FRMES N=41				IRS N=21			
	n	(%)	n	(%)	χ^2	p	n	(%)	χ^2	p
nil or sub-therapeutic antidepressant prescription	25	(39.1)	33	(80.5)	24.006	0.000	17	(81.0)	10.166	0.001

N.B. Calculated using the Chi-squared statistic ($\chi 2$) comparing FRMUS with FRMES and IRS participants respectively

Of the 129 FRMUS participants who did not have MDD according to the PHQ-9, over a quarter (35, 27.1%) were prescribed an antidepressant. Of the non-depressed control participants, antidepressants had been prescribed for 15 of 121 (12.4%) FRMES and 10 of 131 (7.6%) IRS patients at the time of case note review. Most doses were within the minimum therapeutic range, but received considerably less than non-depressed FRMUS participants ($p \leq 0.004$). Relatively, non-depressed FRMUS patients were receiving more antidepressant treatment than the two comparison groups.

Contacts with mental health professionals (case notes)

Over the five year time frame, 190 FRMUS participants had a mean number of 2.43 contacts (median 0; excluding three FRMUS outliers with admissions for depression totalling over 100 days). This was statistically significant when compared to a mean 1.2 for FRMES and a mean of 0.4 contacts for IRS over the five year time frame ($p=0.000$).

Looking only at the 64 FRMUS patients who scored positively for MDD on the PHQ, this sub group had a mean of 4.2 contacts with a mental health professional. This was not statistically different compared to FRMES (mean 3.1), and IRS (mean 2.2) control patients with MDD.

Contacts with mental health professionals (self-report data)

Of the 64 FRMUS participants with current MDD, 15 (23.4%) had consulted with a psychiatrist or psychological specialist in the previous year. This was not statistically significant compared to the two comparison groups. Of the 49 who had not, 14 (28.6%) felt they would benefit from seeing one.

To contrast, only four of the 40 FRMES (10%) with MDD had seen a mental health professional in the previous year. Of the 36 who had not, seven (19.4%) felt they would benefit from seeing one. Of the 21 IRS participants with MDD, two (9.5%) had seen a psychiatrist or psychological specialist in the previous year. Of the 19 who had not, two (10.5%) felt they would benefit from seeing one.

'Adequate treatment' for depression

Of the 64 FRMUS participants with depression, 43 (67.2%) were receiving treatment for their depression which was deemed to be the minimum effective or 'adequate'. Table 18 shows that a third (21/64, 32.8%) had no or suboptimal treatment (please refer back to Chapter 8 for the study definition of 'adequate treatment' for depression).

Table 18. Number and percentage (%) of participants with MDD who were receiving inadequate treatment for depression

	FRMUS N=64		FRMES N=41				IRS N=21			
	n	(%)	n	(%)	χ^2	p	n	(%)	χ^2	p
inadequate treatment for depression	21	(32.8)	31	(75.6)	18.136	0.000	16	(76.2)	11.961	0.001

N.B. Calculated using the Chi-squared statistic ($\chi 2$) comparing FRMUS with FRMES and IRS participants respectively

Relatively, FRMUS participants were receiving significantly more treatment for MDD ($p \leq 0.001$) than both the comparison patient groups (see Figure 22). Ten of the 41 FRMES with depression (24.4%), and five of the 21 IRS with depression (23.8%) had adequate treatment for depression. This meant that over three quarters of both the participants from the comparison groups had inadequate treatment for their depression.

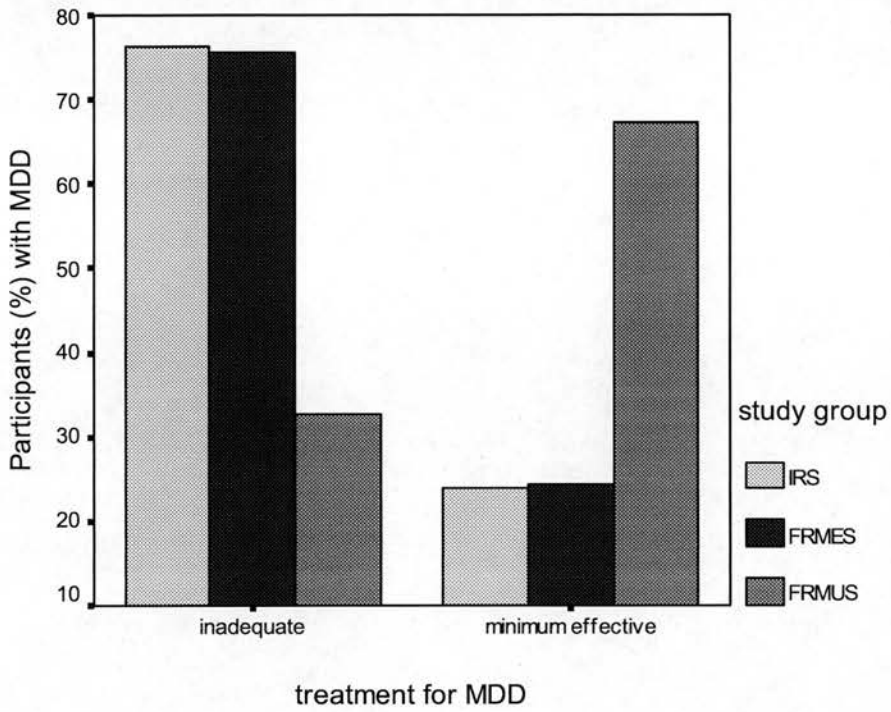
Anxiety

Pharmacological treatment (General Practice records)

Of the 67 FRMUS patients with a diagnosis of GAD according to the PHQ, 38 (56.7%) were receiving the minimum effective dose, and 7 (10.4%) were receiving a suboptimal dose, of an antidepressant or anxiolytic. Using the Chi-square statistic to compare FRMUS with FRMES, this was significant (p=0.000) as only six of the 37 (16.2%) FRMES patients with GAD were on an effective dose, and there were an additional three (8.1%) on a suboptimal dose. There were six IRS patients with GAD

(6/23, 26.1%) who had been prescribed a minimum effective dose of an antidepressant, and one (4%) who were prescribed a suboptimal dose (p=0.004).

Figure 22. Proportion of participants with MDD according to the PHQ who were receiving 'adequate treatment' for their depression at the time of the study



Contacts with mental health professionals (case notes)

Those 67 FRMUS patients with GAD had a mean 4.5 contacts with a mental health professional over the five year time frame. This was not statistically different to the mean 2.7 contacts made by the 37 FRMES patients, and mean 2.8 made by the 23 IRS patients.

Contacts with mental health professionals (self-report data)

Of the 67 FRMUS patients with GAD only or coexisting GAD and MDD, according to the PHQ, 15 (22.4%) had seen a mental health professional in the previous 12 months.

This was not statistically different compared to the five of 36 (13.9%) FRMES and two of 23 (8.7%) IRS patients with GAD at the p=0.05 level. However, the numbers are too small to be able to show a statistical difference.

'Adequate treatment' for anxiety

Using the definition as outlined in Chapter 8, adequate treatment for GAD was determined for 62% (41/67) of the FRMUS participants (see Table 19). There were 18 (27%) who were not receiving any treatment for anxiety and 8 (12%) receiving suboptimal treatment.

However, relatively, this was substantially more and statistically significant when compared to both of the comparison patient groups. Eight of the 37 FRMES participants (21.6%) were receiving the minimum effective treatment, and 24 (65%) were receiving no treatment at all. There were 8/23 IRS patients (34.8%) who were receiving 'adequate' treatment, and 13 (56.5%) who were receiving no pharmacological or behavioural therapy for their anxiety disorder.

Table 19. Number and percentage (%) of participants with GAD who were receiving no or suboptimal treatment for anxiety

	FRMUS N=67		FRMES N=37				IRS N=23			
	n	(%)	n	(%)	χ^2	p	n	(%)	χ^2	p
inadequate treatment for anxiety	26	(38.8)	29	(78.4)	12.253	0.000	15	(65.2)	7.328	0.007

N.B. Calculated using the Chi-squared statistic ($\chi 2$) statistic comparing FRMUS with FRMES and IRS respectively

Possible confounding variables

To assess if findings of 'adequate treatment' for anxiety and depression were associated with other confounding variables, a logistic regression was performed comparing FRMUS and FRMES using the independent variables of study group, age, gender, and deprivation scores (see Table 20). This found that the variables of study

group, deprivation and gender were significant predictor variables for 'adequate treatment' of anxiety and/or depression. Again, it is important to note that study group remains a significant predictor variable towards explaining adequate treatment for FR patients.

Table 20. Logistic regression analyses for possible confounding effect of study group, age, gender and deprivation on 'adequate' treatment for anxiety and depression

Variables in the Equation	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I. for EXP(B)	
							Lower	Upper
study group	1.364	0.306	19.921	1	0.000	3.911	2.149	7.119
age	-0.007	0.013	0.307	1	0.579	0.993	0.967	1.019
gender	0.732	0.325	5.078	1	0.024	2.079	1.1	3.929
depcat7	0.239	0.075	10.075	1	0.002	1.270	1.096	1.472
Constant	-6.486	1.271	26.047	1	0.000	0.002		

NB: The dependent variable was a binary variable as to whether anxiety or depression had been treated according to clinical guidelines; comparing FRMUS with FRMES patient groups only.

The Wald statistic and the corresponding significance level test the significance of each of the covariate and dummy independents in the model. The ratio of the logistic coefficient B to its standard error S.E., squared, equals the Wald statistic. If the Wald statistic is significant (i.e. less than 0.05) then the parameter is significant in the model. Thus study group, gender and depcat7 are significant.

The "Exp(B)" column is the odds ratio of the row independent with the dependent. It is the predicted change in odds for a unit increase in the corresponding independent variable. Odds ratios less than 1 correspond to decreases and odds ratios more than 1.0 correspond to increases in odds. Odds ratios close to 1.0 indicate that unit changes in that independent variable do not affect the dependent variable.

Hypothesis (2) not supported

A third of FRMUS cases with depression, according to the PHQ, were not receiving adequate treatment, and nearly 40% (47/67) of those with GAD were not receiving a therapeutic intervention for their anxiety. However, data extracted from case notes, as well as from patient self report, indicated that FRMUS cases received considerably more psychiatric and psychological treatment than the FRMES and IRS control groups. This was a statistically significant finding when comparing FRMUS with both control groups respectively.

SUBSIDIARY HYPOTHESES

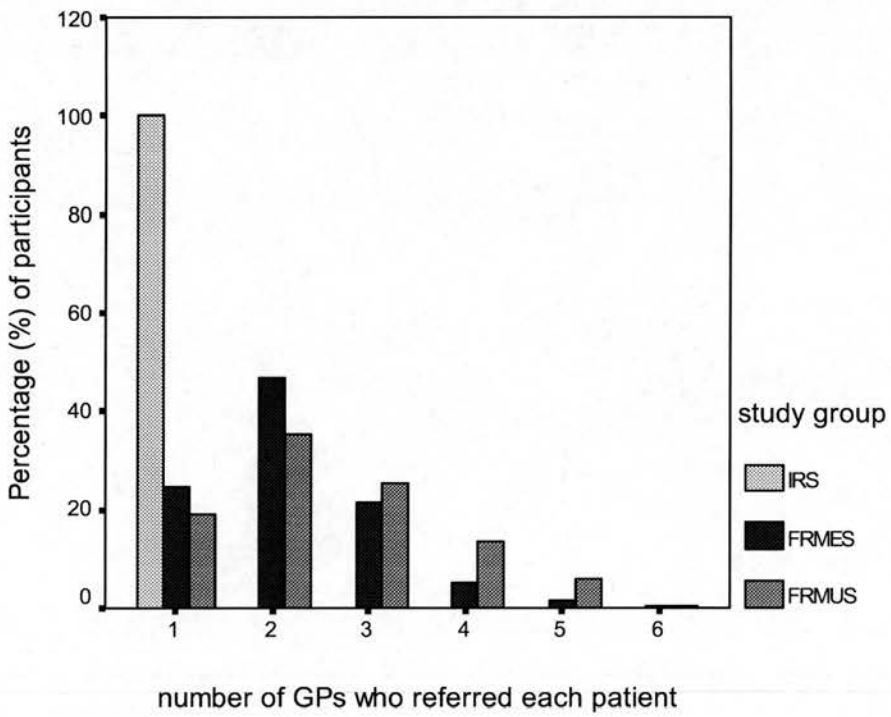
Use of health care services

Case note data

Primary care contacts

FRMUS participants were more likely to be referred by multiple doctors when compared to the other two comparison groups. This can be visualised in Figure 23 below.

Figure 23. Percentage (%) of participants who were referred by a number of different GPs during the five year time period.



Use of GP out of hours services (OOH) was higher among the FRMUS participants (see Table 21). GP contacts during business hours were not counted.

Table 21. Primary health care contacts of participants

	FRMUS N=193	FRMES N=162		IRS N=152	
	mean	mean	p	mean	p
Number of referring GPs	2.5	2.1	0.001	1.0	0.000
Number of out of hours (OOH) GP contacts	3.3	1.8	0.015	0.5	0.000

NB. Mann Whitney U statistic used to calculate p values when comparing FRMUS with FRMES and IRS respectively.

Researcher observations from conducting the case note reviews

It was not uncommon for GPs to mention doubtful likelihood of serious disease, anxious patient disposition, and patient depression in their referral letters to specialists. On rare occasions, even somatisation was mentioned. The following example is from a GP referral letter for an FRMUS patient made by a participating GP to gastroenterology for the symptom of abdominal pain:

> *"I am essentially requesting a second opinion to allay my patient's anxiety that she may have some serious pathology... a somatizing patient for many years... I am really seeking your opinion not because I believe there is any real pathology but in the hope that having seen you, her level of anxiety will be reduced and we can progress with helping her pain management..."*

However, regardless of the language and cues used by this referring GP, the patient was referred back to gastroenterology two years later by a GP locum. Within the same time frame, this patient was also referred to general surgery and orthopaedics by two different GPs for other symptoms. These other symptoms were also deemed MUS by the specialist.

My observation was that GPs used 'code' or cues for specialists in their referral letters. Common examples of this included *"this sensible woman"* to infer the symptoms may be serious in nature, or *"this anxious woman"* to infer the symptoms are not likely to be due to physical disease. However, specialists did not always decipher this code.

This second example was taken from a GP referral letter of an FRMUS patient to Ear, Nose and Throat (ENT) with a symptom of *"change in the voice"*. At the same time the GP flagged to the specialist that the patient had been:

> *"Seen by many specialists over the years with no substantial or serious illness being diagnosed."*

This patient was not only diagnosed with *"muscle spasm"* (MUS) by the ENT specialist, but was subsequently referred another seven times by four different GPs and one hospital specialist to six different specialties. Six of the seven referrals assessed by a specialist were deemed to be MUS.

Although these are anecdotal examples, a common theme from the case notes was that FRMUS patients consulted and were referred by multiple GPs to different hospital outpatient clinics. Here FRMUS patients saw several different hospital specialists and investigations were often performed. A lack of a single practitioner taking responsibility for coordinating a substantial number of FRMUS patients was evident.

Secondary care contacts

In terms of general health care utilisation, the FRMUS cases generally had high use of all health services determined from the case notes. The health economic costs associated with these contacts are outlined in Chapter 16. FRMUS cases had significantly more health care contacts than IRS controls (see Table 22 below). The FRMUS and FRMES study groups had similar patterns of health care use. FRMUS cases were more likely not to attend outpatient appointments that had been arranged for them.

Table 22. Mean number of secondary health care contacts of participants

	FRMUS N=193	FRMES N=162		IRS N=152	
	mean	mean	p	mean	p
A&E visits	2.4	1.8	0.130	0.5	0.000
New NHS OPD contacts	4.9	4.2	0.000	1.0	0.000
Private OPD contacts	0.2	0.4	0.025	0.01	0.004
OPD reviews	7.0	8.3	0.096	1.3	0.000
Total number of OPD contacts	12.1	12.9	0.376	2.3	0.000
OPD appointments not attended (DNA)	1.1	0.6	0.020	0.3	0.000
Days admitted as an inpatient	11.1	8.6	0.527	0.8	0.000

NB. The Mann Whitney U statistic was used to calculate p values comparing FRMUS with FRMES and IRS respectively.

OPD = outpatient department.

Patient self-report data (questionnaire)

Outpatient contacts

Participants were asked if they had seen a surgical or medical specialist within the year prior to completing the questionnaire. Of the FRMUS respondents 133 (69.1%) had seen a medical or surgical specialist in the 12 months prior to completing the questionnaire. Sixty five percent (105/162) of FRMES controls had seen a specialist in the previous year and this was not statistically different. Over a quarter of the IRS (43, 28.5%) controls stated having had a visit to a specialist in this time (p=0.000).

Of the 60 FRMUS participants who had not seen a specialist, a third (20, 33.3%) felt they would benefit from a consultation. Proportions of those participants who had not seen a specialist but felt they would benefit were 17/56 (30.4%) for FRMES and 30/109 (27.5%) for IRS control participants respectively. These were not statistically significant compared to FRMUS.

GP difficulty ratings

Some FRMUS patients had been referred by all of the doctors within the practice, including locums and registrars. It was often difficult to identify the main referring or treating GP for FRMUS participants to obtain the difficulty rating from. Nearly two thirds (65.3%) of FRMUS participants were considered to have problems that proved of some level of difficulty for the GP (see Table 23).

Table 23. Number and percentage (%) of participants according to the level of difficulty they present to the GP

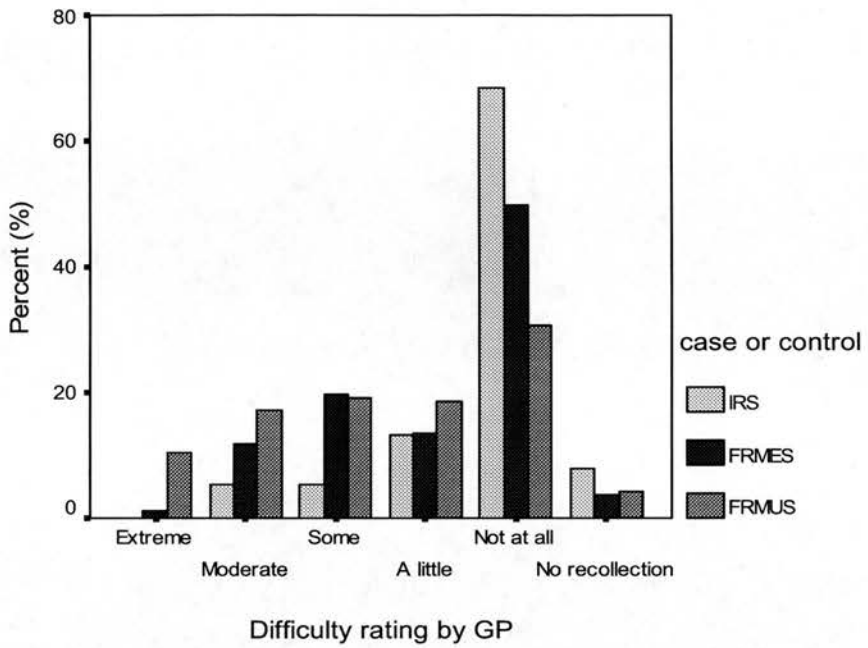
Difficulty rating	FRMUS (N=193		FRMES (N=162)		IRS (N=152)	
	n	(%)	n	(%)	n	(%)
Extreme	20	(10.4)	2	(1.2)	0	(0)
Moderate	33	(17.1)	19	(11.7)	8	(5.3)
Some	37	(19.2)	32	(19.8)	8	(5.3)
A little	36	(18.7)	22	(13.6)	20	(13.2)
Not at all	59	(30.6)	81	(50.0)	104	(68.4)
No recollection of patient	8	(4.2)	6	(3.7)	12	(7.9)

The majority of all patient groups were "not at all difficult", and for a small percentage of participants, GPs had "no recollection". Figure 24 below displays the spread of how difficult participants' problems were for their GP. One can see from this graph that FRMUS patients were more likely to pose some sort of difficulty to the GP compared to participants from the two other comparison groups.

FRMUS participants' problems were twice more likely to be considered "moderately" or "extremely" difficult than FRMES, and more than five times more difficult than IRS, participants. This was statistically significant ($p=0.000$) comparing ratings for FRMUS with both comparison groups respectively.

These associations were noted across all five practices ($p\leq0.05$). However, there was no statistically significant difference for difficulty ratings between the FRMES and FRMUS patients in Practice-4 (the practice in the most deprived residential area). There was some association with deprivation on a linear regression ($p=0.000$).

Figure 24. GP difficulty ratings in response to the question "To what extent do you feel this patient's problems are difficult to help?"



The hypothesis that FRMUS patients would be perceived as more difficult to manage by their GP was supported.

Free text comments from GPs

Given the opportunity to provide comments on the bottom of the difficulty rating forms, 190 (26.5%) GPs offered further information about the patient or their relationship with the patient. GPs were more likely to provide additional comments about those identified as FRMUS (97, 51.1%). Fewer comments were provided on FRMES (51, 27.0%) and about IRS (42, 22.2%) controls. This section will focus on the GP comments made about FRMUS patients. Quotes were chosen based on recurrent themes.

I was interested to note that a considerable number of GPs were aware of anxiety and depression impacting on their patients' presentations. Anxiety and depression had specifically been mentioned 32 times (33.3%) in reference to FRMUS participants. Examples of this are quoted below:

"Consults for very small problems - probably mostly because of anxiety disorder which I keep forgetting about"

"Morbidly anxious woman. Some of my partners find her impossible. One of the most difficult and time consuming patients I have"

"Neurotic depressive? Cancer fear. 'Multi doctors'."

"Her problem is severe, disabling anxiety; I support her"

GPs were aware that anxiety and depression were comorbid with diagnosed physical organic disease for some FRMUS patients. The anxiety and depression sometimes made the physical illness more difficult for the GP to manage. Examples of quotes include:

"Anxiety ++ after treatment for cancer"

"Endometriosis is a difficult to manage condition in an anxious woman with an unhappy marriage"

"Complex mix psychosocial and physical factors with many unaddressed issues still bubbling in background. Some progress"

"Took some while to reach equilibrium - she has a combination of real physical problems and sensitivity to symptoms"

GPs raised factors, other than anxiety and depression, which complicated the management of diagnosed physical illnesses. There was a high level of GP awareness of the personal difficulties that some of their patients were dealing with in daily life. The possible impact of these problems on their health was acknowledged. Examples of this theme included:

"Rather distressed and neurotic - I know she has severe problems with a drug abuser daughter and eight children that she cares for a lot as their father is an offender"

"I suspect she is a closet drinker with an unhappy marriage"

"Complicated by role as main carer to even more sick-role immersed wife. Tends to be fatalistic and poor at following health advice"

"Known for years. Defaults, chronically vaguely ill and off work for years. Suspect private house mortgage insurance makes work less attractive to her. I feel I have not really got to the root of her problems. ? V. angry"

In line with the quantitative results from the GP difficulty ratings, there was a sense from the GP comments of frustration and difficult doctor-patient relationships. GPs felt that some FRMUS cases had unusual illness beliefs and perspectives, or were just 'difficult' personalities to relate to. Examples of this theme include:

"Intractably fixed views held by patient about her health/illness"

"Very neurotic and under informed patient with strong (and odd) concepts of health"

"Long standing challenge in respect of illness behaviour. Relatively quiescent"

"Somewhat manipulative and non-complying with therapies"

"Rubs up all health professionals the wrong way including myself"

"Prickly customer"

Some GPs seemed to easily identify those patients who were prone to MUS. The level of awareness of patients who may be FRMUS seemed greater than I had expected. Varying terms such as 'MUS', 'somatising', 'functional', and 'minor illness' were used by GPs to describe FRMUS patients. Awareness of MUS was evident in the following quotes:

"Full blown MUS, somatising problems"

"Several functional problems in the past"

"Multiple presentations with minor illness. Very introspective"

"Presence of physical symptoms which specialists have said are not amenable to treatment dominates - difficult to move forward to look at psychological aspect but gradual progress"

"I recollect that he shows signs of somatising"

"Has cancer phobia with stress related somatic symptoms. Extremely difficult to get balance right of reassurance vs. not missing organic disease."

GPs indicated that FRMUS patients frequently presented with multiple problems. There was a sense in some instances where the involvement of specialists was more at the suggestion or will of the patient than the GP.

Perhaps shedding some light on the issue of 'frequent referral' were the comments that some GPs found it problematic to find a 'treatment' or management plan which suited the patient or effectively addressed their symptoms. The concept of unmet need perpetuating from the referral process was exemplified in some of the quotes below:

"Multiple problems straddling three or four specialist fields who didn't communicate properly"

"Multiple problems which prove difficult to treat or resolve. Never stops talking!"

"I think she wants a 'specialist' opinion"

"Difficult persisting problem causes genuine debility"

"Difficulty finding a treatment which will help"

"I have tried many avenues to help this man but it seems to make no difference!"

Similar themes of difficult consultations, anxiety and depression had been made by GPs about a small number of the IRS control participants. These may be examples of patients with 'FRMUS potential' who have been contained in the practice by the GP.

"Known for many years. She is neurotic, anxious and intelligent. Also English is her second language. Consultations are always long and dissonant."

"High anxiety levels and sometimes our optimistic expectations result in slightly more stressful consultations."

General Practice Assessment Survey (GPAS) satisfaction with health care items

Self-report data

The hypothesis that FRMUS patients would be less satisfied with their health care than FRMES and IRS controls was not supported as there was no statistical difference between the groups. The three groups had similar mean satisfaction scores of 29 indicating high levels of satisfaction (where the highest score possible was 35).

The final question relating to satisfaction asked patients to rate their overall satisfaction with the health care they had received. The majority of all respondents (78.7%) were satisfied with the health care they had received and Table 24 below indicates responses according to study patient group.

Table 24. Number (n) and percentage (%) of patients fairly or completely satisfied with health care services received

Overall satisfaction with health care services received	FRMUS N=193 n (%)	FRMES N=161* n (%)	χ^2	p	IRS N=152 n (%)	χ^2	p
fairly or completely satisfied	150 (77.7)	131 (81.3)	1.294	0.255	117 (76.9)	0.895	0.344

Calculated using the Chi-square statistic ($\chi 2$) comparing FRMUS with FRMES and IRS respectively.

* N.B. One FRMES patient did not complete the first page of the questionnaire

Medical Outcomes Study 12-Item Short-Form Health Survey (SF-12 v2)

Self-report data

The mean physical component score (PCS) for FRMUS patients was below the mean of 50, as was the mean PCS for FRMES controls, thus indicating poor physical health and perceived disability (see Table 25). The IRS control group scored above the mean PCS with 52.9; this was a statistically significant difference (p=0.000, 95% CI 8.56 - 13.03) compared to FRMUS patients.

An unexpected finding was that the mean mental component scores (MCS) for each of the three study groups, including IRS controls, were below the mean of 50 indicating poor mental health. Regardless of the low mean MCS of all the respondents, FRMUS cases had statistically poorer mental health scores than FRMES and IRS control patients.

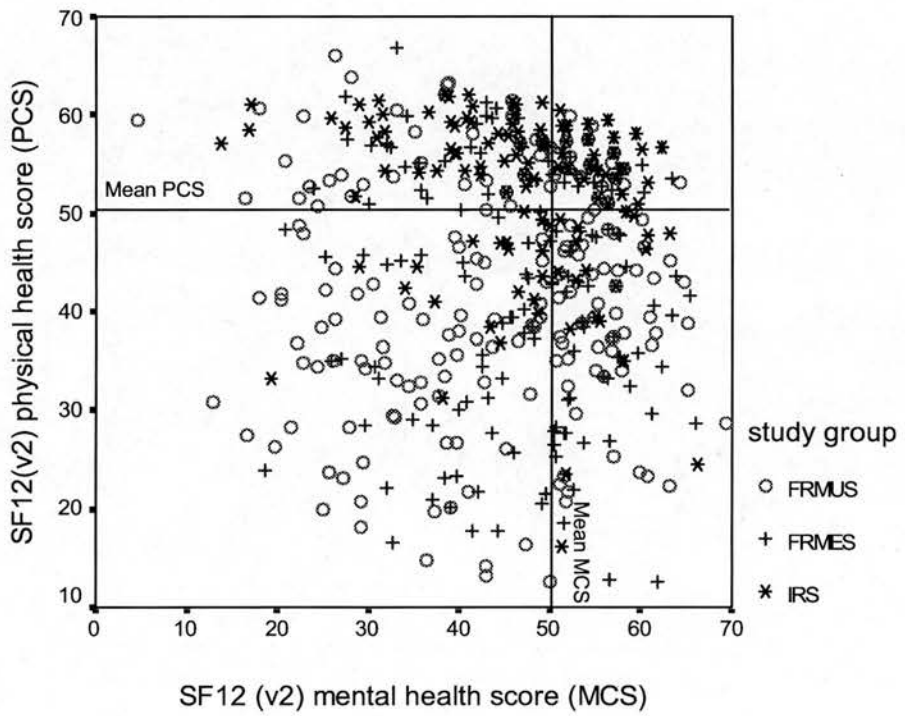
Table 25. Physical (PCS) and mental (MCS) component scores from the SF-12 (v2), where population mean scores are 50 for each; lower scores indicate poorer health

	FRMUS N=193		FRMES N=162			IRS N=152		
	mean	S.D.	mean	S.D.	p	mean	S.D.	p
PCS	42.09	12.14	43.11	12.82	0.313	52.89	7.86	0.000
MCS	43.78	13.29	47.47	10.18	0.023	48.22	9.99	0.005

NB. P value calculated using the Mann-Whitney U statistic to compare between FRMUS and FRMES and IRS respectively. S.D. stands for standard deviation.

A scatter plot of the SF-12 (v2) MCS and PCS of all participants is displayed below in Figure 25. It shows that the majority of scores for FRMUS cases were below the population mean of 50 for MCS and PCS (in the lower left quadrant). There were a considerable number of FRMES controls with PCS below the mean, but relatively higher scores for mental health functioning. The IRS participants generally rated higher on both component scores, and the majority can be seen clustering above the population mean indicating better self-reported physical and mental health in this group.

Figure 25. Scatter plot of SF-12 (v2) mental component scores (MCS) against physical component scores (PCS).



NB. A score of 50 represents the mean of the general population. The higher the score, the better participants perceive their health to be.

Possible confounding

For those participants under the age of 46 years, a linear regression (using the same four variables as before of age, gender, deprivation and study group) showed an association between MCS and PCS ($p \leq 0.026$) and deprivation. Subjects aged 46-65 years had an association with age and deprivation for PCS ($p \leq 0.010$), but not for MCS ($p=0.072$).

In summary, FRMUS participants had rated their physical health similarly to FRMES participants, which indicated similar perceptions of functional limitation and disability. However, their perceived mental health was statistically poorer than both FRMES and IRS control participants. The hypothesis that FRMUS patients would perceive their health to be worse, than the two comparison patient groups, was supported for mental health status, and clinically significant that health perceptions were equivalent for FRMUS and FRMES participants.

Illness Perception Questionnaire (IPQ) and Whitely Index items

Self-report data

A quarter of FRMUS participants stated stress or worry was the main cause of their health problems (see Table 26). However, this was statistically more than FRMES controls, and proportionately more than IRS controls. FRMUS and FRMES participants similarly perceived that health problems and symptoms had major consequences on their lives.

Possible confounding

A linear regression was conducted to determine if there was any effect of study group, age, gender and deprivation on IPQ3 answers. This showed that deprivation had a stronger association ($p=0.000$) than study group ($p=0.060$), i.e. the more deprived, the more stress and worry.

Table 26. Number and percentage (%) of patients and their illness perceptions (items from IPQ and Whitely Index)

Responded 'agree' or 'strongly agree' to the following statements:	**FRMUS (N = 193) n (%)**	**FRMES (N = 162)**			**IRS (N= 152)**		
		n (%)	**χ^2**	**p**	**n (%)**	**χ^2**	**p**
IPQ 1 - My health problems have major consequences on my life	108 (56.0)	87 (55.7)	0.767	0.381	37 (24.5)	44.029	0.000
IPQ 2 - Nothing I do will change these health problems	50 (26.0)	60 (37.0)	1.334	0.248	21 (13.9)	16.130	0.000
IPQ 3 - My health problems are largely caused by stress or worry	49 (25.4)	25 (15.4)	9.779	0.002	30 (19.9)	3.526	0.060
IPQ 4 - I worry a lot about my health	79 (41.0)	59 (36.4)	0.332	0.559	26 (17.2)	17.195	0.000
WI - I find that I am bothered by many different symptoms	93 (48.2)	74 (45.6)	1.972	0.160	27 (17.8)	43.864	0.000

NB. Statistics calculated using the Chi-square (χ^2) statistic comparing FRMUS with FRMES and IRS respectively

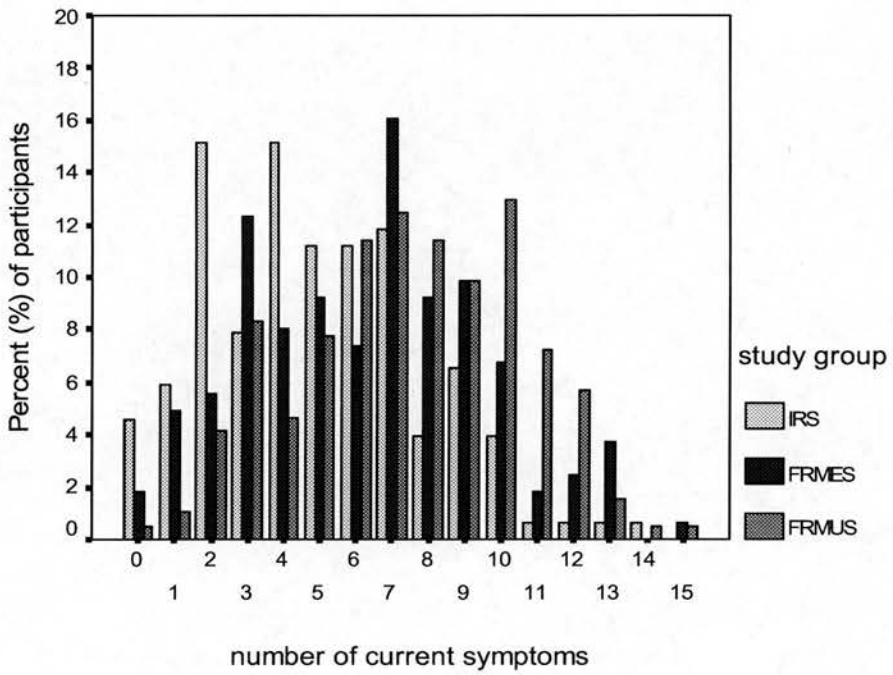
The hypothesis that FRMUS cases would be more worried about their health was not supported statistically when compared to the FRMES control patient group. However, there was a statistical difference between the IRS patients where there was a significant difference between the two patient groups. A higher percentage of FRMUS cases did report worry about their health and symptoms than both of the comparison groups, and proportionately more FRMUS patients felt their health problems were caused by stress or worry.

Patients Health Questionnaire current symptoms (PHQ-15)

Self-report data

FRMUS cases reported being bothered by more current symptoms (mean 7.4) than FRMES (mean 6.27, p=0.001) and IRS (mean 4.89, p=0.000) controls. Figure 26 indicates more of a skewed distribution of current symptoms to the right for FRMUS patients indicating more current symptoms than the two comparison patient groups.

Figure 26. Percentage (%) of participants and the number of symptoms they were bothered by at the time of questionnaire completion



With the exception of pain in the arms, legs or joints, FRMUS cases reported proportionately more of each of the 15 symptoms than the FRMES controls. There was a statistical difference in bothersome symptoms reported by FRMUS cases compared with both control participant groups for menstrual problems, headache, dizziness, palpitations and problems or pain during sex (dyspareunia). FRMUS participants were more likely to be bothered by each of the 15 symptoms listed than IRS controls and this was statistically significant (see Table 27 below).

Table 27. Number and percent (%) of participants bothered by 15 common symptoms at the time of questionnaire completion

PHQ-15 Symptoms	FRMUS N=193		FRMES N=162			IRS N=152		
	n	%	n	%	p	n	%	p
stomach pain	87	45.08	63	38.89	0.466	40	26.32	0.000
back pain	136	70.47	109	67.28	0.218	75	49.34	0.000
pain in arms, legs, joints	148	76.68	128	79.01	0.593	87	57.24	0.000
menstrual problems	43	22.28	22	13.58	0.002	33	21.71	0.013
headache	120	62.18	80	49.38	0.009	62	40.79	0.000
chest pain	54	27.98	39	24.07	0.654	25	16.45	0.032
dizziness	81	41.97	35	21.60	0.000	31	20.39	0.000
fainting spells	20	10.36	10	6.17	0.183	5	3.29	0.018
heart pound or race	87	45.08	43	26.54	0.001	32	21.05	0.000
short of breath	100	51.81	64	39.51	0.097	39	25.66	0.000
constipation, diarrhoea	110	56.99	91	56.17	0.224	55	36.18	0.000
nausea, gas, indigestion	115	59.59	82	50.62	0.075	65	42.76	0.000
pain, problems with sex	36	18.65	21	12.96	0.002	21	13.82	0.003
feeling tired, low energy	148	76.68	117	72.22	0.144	95	62.50	0.000
trouble sleeping	143	74.09	111	68.52	0.544	79	51.97	0.000

NB. Statistics calculated using the Chi square (χ^2) test comparing FRMUS with FRMES and IRS respectively

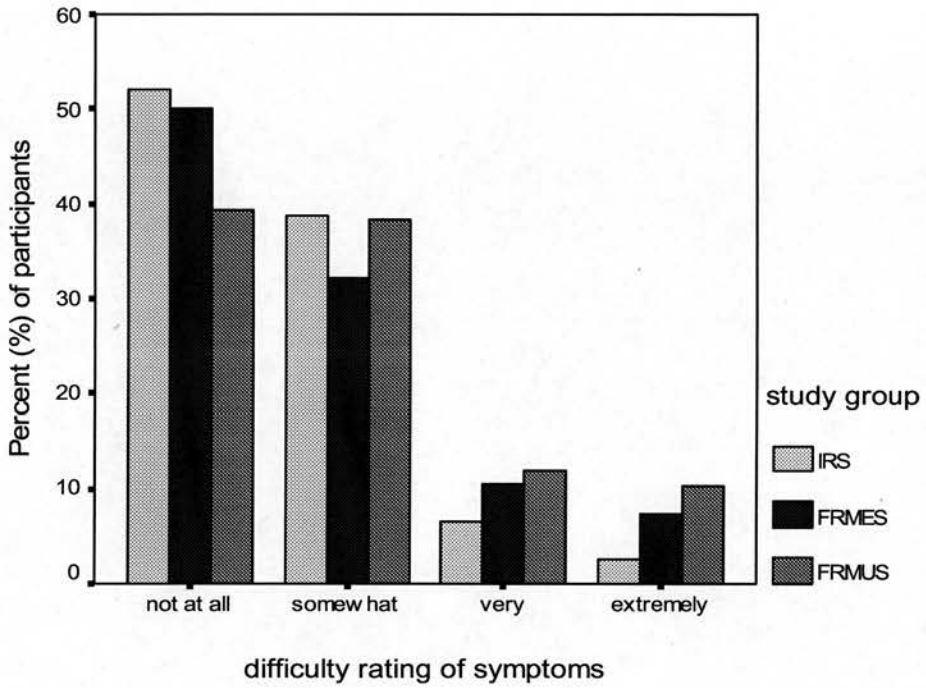
In terms of severity of symptoms, FRMUS scored a mean of 10.32 for how much they were bothered by their current symptoms. This was statistically more than FRMES (mean 8.61, p=0.002), and IRS participants (mean 5.94, p=0.000). A linear regression found an association between deprivation score and current symptoms (p=0.000).

The hypothesis that FRMUS cases would have more current symptoms than FRMES and IRS controls was supported.

Patient difficulty managing symptoms

The majority of participants reported that their symptoms were "not at all" or "somewhat" difficult to manage (see Figure 27 below). A substantial percentage (43/193, 22.3%) of FRMUS cases reported that their symptoms made life "very" or "extremely" difficult similar to the proportion of FRMES participants (19/162, 21.8%, p=0.075).

Figure 27. Patient reported difficulty with their physical and psychological symptoms



IRS controls were significantly less bothered by their symptoms than FRMUS cases. Only 9.2% (14/152) found them to be "very" or "extremely" difficult (χ^2 10.500, p=0.001). FRMUS cases had more current symptoms and found them more difficult to manage compared to FRMES and IRS controls.

Disclosure of problems to doctors

Self-report data

The majority of participants felt comfortable discussing physical problems with their GPs (see Table 28). All patients indicated less comfort talking with a hospital doctor than a GP, particularly for emotional problems. However, of the three study groups, FRMUS participants were the most comfortable discussing emotional problems than the other two comparison patient groups.

Table 28. Number and percentage (%) of participants who agreed or strongly agreed they felt comfortable disclosing physical and emotional problems with GPs and hospital specialists

comfort discussing physical problems with:	**FRMUS N=193 n (%)**	**FRMES N=161* n (%)**	**p**	**IRS N=152 n (%)**	**p**
GP	181 (93.8)	155 (96.3)	0.082	143 (94.1)	0.604
Hospital specialists	169 (87.6)	144 (89.4)	0.205	132 (86.8)	0.334
comfort discussing emotional problems with:					
GP	150 (77.7)	115 (71.4)	0.702	90 (59.2)	0.000
Hospital specialists	113 (58.5)	91 (56.9)	0.354	68 (44.7)	0.015

Calculated using Chi-square statistic ($\chi 2$) comparing FRMUS with FRMES and IRS respectively. * N.B. One FRMES patient did not complete the first page of the questionnaire

The hypothesis that FRMUS cases would report more discomfort in discussing emotional problems with doctors than the two comparison groups was not supported. A greater proportion of FRMUS participants, than FRMES and IRS participants, felt comfortable talking about their emotional problems with doctors. However, this was not statistically significant when comparing FRMUS with FRMES patients.

Free text comments from patient questionnaire

Upon completing the structured items of the questionnaire, 240 of the 507 respondents (47.3%) provided further written comments. This section presents examples of common themes provided by participants according to their study group.

The most common theme among all respondents (102/240, 42.5%) was a criticism of the long waiting times between the point of GP referral to actually being seen by a hospital specialist. Both FRMUS and FRMES patients expressed how they felt more anxious and their health deteriorated due to lengthy waiting periods. Examples of this theme are presented in the following quotes:

> *FRMUS - "The time taken from my first doctor visit to finally receive surgery - some 9 months - is disgraceful - and has resulted in myself being disabled for life. The services I received from GP, consultant and hospital were satisfactory. It was the time taken to achieve ACTION."*

> *FRMES - "General experience of being referred has been fine. My only complaint is that the time I waited between going to my GP and seeing a specialist was far too long, causing a great deal of stress and uncertainty."*

A third of participants found the referral process to be a positive one (82/240, 34.2%). Phrases such as *"no complaints"* or *"very satisfied"* were often used. Positive comments were more often directed towards their GP as the following quote indicates:

> *FRMUS - "The general practice is excellent, plus referral and once you get to the hospital the treatment is excellent. It's just the getting in the door i.e. the wait."*

There were a notable number of comments provided by FRMUS patients indicating that they hoped referral to hospital would provide them with a long-awaited diagnosis. The following quote provides an example of how FRMUS patients often mentioned not feeling listened to:

> *FRMUS - "I was happy to be referred to a hospital outpatient clinic by my GP because it meant that someone may be listening to me for once. And the pain I was experiencing was not just in my head. I now have to go for MRI scan which will take 4-6 months. And then have to wait for another outpatient appointment which will take 3-4 months. However, I really don't mind waiting. I just want them to confirm to me that I do have something wrong with me and it's not all in my HEAD!"*

When consulting with a specialist, patients often expressed feeling 'rushed' or having little time with the hospital doctor to discuss their problems in detail. The concept of being made to feel they were *'time wasting'* was raised by several FRMUS patients as the second quote exemplifies:

> *FRMUS - "I felt the doctor in the outpatient clinic was rushing me through the appointment. Because of the above, I felt I couldn't talk to the doctor about the other problems I was experiencing."*
>
> *FRMUS - "Made to feel you should not be there and time wasting."*
>
> *FRMUS - "GP was very good. Hospital doctor was unsympathetic, unfriendly and made me feel as if I was wasting her time!! I was referred to hospital the first time - was seen by this Dr. and told that I couldn't keep coming to hospital 'go back to your own doctor. I had waited over a year. My GP referred me again (another year!) I got the same doctor, same treatment. But finally she agreed to laparoscopy (?camera). After op. she was again very rude, explained nothing except saying 'Go back to your GP! You've probably got irritable bowel'. I have no symptoms of this. I have problems with pains in lower stomach at either side, extremely heavy periods and at times I am doubled over with the pain".*

Difficult doctor-patient interactions were often commented on by FRMUS participants. This patient group often expressed feeling belittled and patronised by hospital doctors and staff:

> *FRMUS - "Being patronised doesn't do my spirits any good at all! Being told 'there's nothing can be done, just plod along trial and error with pain killers' is very wearing."*
>
> *FRMUS – "Many, although by no means all medical professionals, treat specific symptoms while ignoring the person to whom they're attached. At times, I've experienced staff talking over me as if I'm not there and I find it particularly insulting when I'm not even told what they think the problem might be. Even worse is being treated as if you're a complete idiot."*
>
> *FRMUS - "The hospital doctor was good... at first but with so many times at being admitted and referred to him, has made him abrupt with me. It is very upsetting and makes me feel in the wrong. When in hospital the nursing staff are great but I have been in so often the doctor in charge just says 'you again' and I feel he may be a bit arrogant towards me. I do not wish to be there, but I am in so much pain it cannot be otherwise. I have no faith in the doctor I am under as he seems to influence the other doctors. He makes me feel awful. I have had 2 operations in 2002 and do not want another. I agree on that, but do I have to keep going through this pain?"*

Comments by some FRMUS patients provided indicators that their problems had been unaided by the process of being referred to hospital. The comment below also indicates that this patient's GP may also find frequently referring the patient unhelpful:

FRMUS - "I feel none of the hospital doctors I have seen have done anything to help me, but my GP always tries to think of someone else he can refer me to that will help me."

Some FRMUS patients made reference to a psychological or 'stress' component associated with their symptoms. However, patients provided varying reports as to their GPs' detection or willingness to engage in discussion of emotional problems:

FRMUS -"I have a tendency to attribute perceived physical complaints as symptoms of chronic illness, especially since having had a stroke in 1995 followed by anxiety and depression which led to early retirement because of health which I did not welcome. My GP has been very patient and has helped me gain a balanced view of my health problems."

FRMUS – "When I was referred to the outpatient clinic for investigation, I felt that it was necessary to make timely investigation re my bowel to eliminate any underlying illness. When the investigations revealed that my bowel was OK I felt relieved. Although the investigations were invasive and unpleasant…My second referral was for my eye. That again proved OK. With hind sight I felt it may have been caused by stress which on several occasions I told various GPs I saw at my GP surgery. I felt they paid scant attention."

Comments provided by some IRS participants highlighted the fact that they too had trouble with 'unexplained' symptoms. IRS participants provided varying degrees of insight into the connection between their emotional and physical health. The second example sheds light on why some IRS patients do not re-consult or get re-referred for their MUS. Because of disillusionment with the referral process, she had decided to self-medicate and deal with her symptoms herself:

IRS - "My initial appointment at the GP surgery I presented with a sore throat. However, I was experiencing depression - which I did not appreciate at the time. I think that GP should have asked questions relating to depression i.e. he failed to diagnose the problem. However, I made an appointment with a senior GP who I knew to have a sympathetic approach and was treated very well thereafter."

IRS - "I asked my GP to be referred to hospital so I can get to the bottom of the problem I had, but it made no difference. I'm still trying and testing other medications to treat the pain, but so far nothing is working nor knowing what the problem is."

In summary, recurring themes particularly from FRMUS patients emerged of long waiting times to see a hospital specialist and continued undiagnosed complaints. This patient group often reported feeling dismissed, not listened to and uncared for. The distress caused by the experience of physical and emotional problems was often raised by FRMUS participants. A representative comment of these themes is provided below:

FRMUS – "It was 9 months wait to see the respiratory doctor, that's no good. The longer you wait, the longer it takes to get well. Feel like the hospital doctors don't care, they just want to get rid of you (except the thyroid doctor, he is very nice). If I can't see my GP, then I don't go. The other doctors don't know me and I don't like to go over things. The doctors haven't been able to find out what's wrong with my hands and my periods. Now I have menopause. My health affects my emotions too; when I am stressed it's worse. Most of my problems are caused by stress. I have been given pain killers, which help, but they are not a cure so I don't use them. Things have been bad this year. Usually I can do things for myself. This year I can't help myself, I can't do anything. I feel anxious all the time. I don't know if the GP can give me anything to stop always feeling nervous and anxious. I can't relax. Even when I wake up I can't relax. I feel anxious all the time."

Summary

The key findings are summarised in Chapter 17 according to the main hypotheses. As a brief summary, FRMUS patients had more anxiety or depression than the other two patient groups, and this was statistically significant. However, the majority of FRMUS patients had neither an anxiety nor depressive disorder according to the PHQ. Of those with depression, the majority of FRMUS participants were receiving 'adequate' treatment for their depression, and considerably more treatment than the two comparison patient groups with depression.

There were many comparable characteristics shared by FRMUS cases and FRMES control patients. FRMUS patients perceived their physical and mental ill health as poor as the FRMES control patients. The majority of the FR participants felt comfortable talking about physical and emotional problems with their GPs. Both FR patient groups had equivalent high use of health care contacts. So although FRMUS patients had less disease or physical problems, they perceived their health similarly to patients who did. Most participants were satisfied with the health care they had received. However, FRMUS patients were more likely to DNA appointments.

Of the secondary hypotheses, statistically significant differences between FRMUS patients and the two other patient groups were that they: consulted with more doctors; presented problems which GPs considered to be more difficult; consultations were more often for symptoms; and had more time off their usual activities.

CHAPTER 14. LIFETIME MEDICAL HISTORIES

An international study by Simon and Gureje(247) assessed a random sample of 5447 from 25916 primary care patients using a structured psychiatric interview. All positive cases for somatisation disorder (SD) according to the interview and a random sample of non-cases were assessed again 12 months later (n= 3196). Only 74 patients were identified with SD at baseline and 70 at the follow-up a year later. Of these, only 21 cases were consistently identified at both assessments. The study found that of the lifetime MUS reported at baseline 61% were not detected during the interview at 12 months' follow-up. The researchers concluded that this could only represent inconsistent patient recall.

Although I was not assessing for SD in this study, I was interested to determine a lifetime pattern of consultations for symptoms by FRMUS patients. Basing this study in primary care provided access to a lifetime of documented symptoms and health care contacts for patients.

To further describe and compare the characteristics of FRMUS patients, a lifetime review of a random selection of patient case notes was conducted. As the first identification phase of the main study only looked at five years of referrals and other health care contacts for the three study patient groups, lifetime reviews were also conducted to determine how stable the 'classification' of being a FRMUS patient was over time.

Due to time and resource limitations, it was not possible to carry out lifetime reviews for all subjects identified. A random sample was selected for this purpose. Given the smaller denominator involved for this part of the study, compared to the numbers of the main study, the findings presented in this chapter can only be viewed as hypothesis generating. Thus I have presented the lifetime data in a separate chapter of its own.

METHODS

Number of lifetime case notes reviewed

An initial 10% random selection of the 193 FRMUS and 162 FRMES participants of the Referral Study questionnaire was generated for a lifetime case note review. The selection was drawn using the random number generator on Excel(376), and based on patient ISD allocated personal identification numbers (PINs). However, I was able to review a total of 47 FRMUS (24.4%) and 25 FRMES (15.4%) case notes for lifetime medical histories. The additional patient case notes reviewed were also drawn randomly from the Excel random number generator.

Four IRS participant lifetime case note reviews were conducted to ensure that there were no differences in medical history or health care use for this sub-sample which had gone undetected from the main study. All four IRS lifetime summaries took a maximum of 20 minutes, as opposed to some FR lifetime case notes taking up to five hours to summarise. IRS participants had only one thin volume of notes as opposed to some FR patients having three (a few FRMUS in the main case note audit had five volumes). It became evident that no new light would be shed from conducting any further IRS patient lifetime case notes, as they had significantly fewer health care contacts, investigations and subsequently far less health care costs. Only information relating to FRMUS cases and FRMES controls will be presented in this chapter.

Data collected

In addition to information collected from the five year review of case notes (outlined in Chapter 7), other information specific to lifetime data collection included:

- number of GP consultations
- all secondary health care contacts with all specialties
- number of allied health professional contacts e.g. physiotherapy
- age when the patient first experienced an episode of MUS (for FRMUS patients); i.e. the index MUS episode.

A first episode of MUS was defined for the purposes of this thesis as the first documented consultation with a doctor, who had assessed the patient, and could not find adequate disease to explain the patients' symptoms.

Analysis

The sub-sample of patients selected had different years of notes available for review. As such, counts of lifetime contacts were divided by the number of case note years available. This is limited by the fact that documents in case notes become less complete the older they are. Effectively, patients with more years of case notes may have fewer documented contacts per year using this method.

Data are presented as total number over the lifetime, and number per year of case notes available. Non-parametric tests were predominantly used to calculate p-values for the differences between FRMUS and FRMES patient groups. However, due to small numbers for some variables, median values are equal to zero and unhelpful to view differences between the groups, so I have also presented the mean. Results should be viewed with caution given small numbers and the potential confounding effect of years of case notes available.

RESULTS

Demographics of the sub-sample

This 'lifetime' sample consisted of 47 FRMUS and 25 FRMES participants selected randomly from the participants of the Referral Study questionnaire. There was an even representation of FRMUS cases and FRMES controls from each practice, except Practice-5 due to later involvement in the study. Years of notes available for review ranged from 11 to 56 years. Patients had a mean of 40.6 years of notes available for review. Other demographics are presented in Table 29.

Table 29. Mean age, years registered with the practice and years of notes available for review; number and percentage of gender and deprivation scores of the lifetime sample of the two study groups

	FRMUS N=47	FRMES N=25	p
Mean age	48.9	54.1	0.023
Mean years registered	13.5	14.3	0.771
Mean years of notes	40.4	41.1	0.805
Female	35 (74.5%)	10 (40.0%)	0.004
DepCat 5-7	24 (51.1%)	12 (48.0%)	0.468

Anxiety and depression

Symptoms of anxiety were mentioned often in FRMUS patients' notes. Depression, depressive symptoms or "low mood" were mentioned less often (see Table 31).

Treatment for anxiety and depression

FRMUS patients had a high number of contacts with mental health services (see Table 30). At the time of the case note review, 16 FRMUS (34%) patients and 5 FRMES (20%) controls were on antidepressants. At any one time in their lives, 26 (55.3%) FRMUS patients and 12 (48%) FRMES patients had documentation of an antidepressant prescription. The differences in proportions were not statistically significant.

Table 30. Mean lifetime, and per year of notes available, documentation of anxiety and depression by treating medical practitioners, and contacts with mental health care

	FRMUS (N=47)			FRMES (N=25)			
	Mean	Median	S.D.	Mean	Median	S.D.	p
Anxiety symptoms	3.77	3	3.53	0.56	0	0.65	0.000
Anxiety symptoms/year	0.11	0.08	0.10	0.02	0	0.03	0.000
Depression symptoms	2.47	1	2.70	0.72	0	1.31	0.002
Depression symptoms/ year	0.07	0.30	0.09	0.02	0	0.05	0.005
Mental health services (MHS)*	27.09	2	109.64	1.28	0	2.95	0.003
MHS contacts/year	0.72	0.04	2.94	0.04	0	0.10	0.004

* Mental health service (MHS) contacts included psychiatry, clinical psychology or community psychiatric services.

N.B. Calculated using the Mann Whitney U statistic, comparing FRMUS with FRMES.

Lifetime contacts with health care

General Practice

The average number of GP consultations per year in the UK population in 2003 was five for women and 3.5 for men, or 4.25 overall for those aged 16-65 years(405). The mean annual number of FRMUS patient consultations with a GP was seven (see Table 31). The range of GP visits per average year for FRMUS patients was one to 38, as opposed to one to 12 for FRMES patients. FRMUS patients had more consultations for symptoms than the FRMES comparison group.

A linear regression showed the difference in GP visits per year of notes available had some association with age (p=0.038) and years of notes available (p=0.000), as well as study group (p=0.046). The contacts with a GP out of hours (OOH) were substantially more for FRMUS patients than FRMES patients.

Table 31. Lifetime and average number of GP contacts per year of notes available.

	FRMUS (n=47)			FRMES (n=25)				95% C.I.	
	Mean	Median	S.D.	Mean	Median	S.D.	p	lower	upper
Total number of GP visits[1]	254.6	255.0	97.4	191.6	180.0	104.0	0.016	12.29	113.71
Ave. GP visits/year of notes [2]	7.1	6.5	5.3	4.9	4.6	2.7	0.012	-	-
Number of GP visits for symptoms [1]	44.7	44.1	13.9	30.3	30.9	10.4	0.000	8.01	20.68
Number of GP visits not attended [2]	7.0	4	8.1	4.4	3	5.2	0.276	-	-
Number of GP visits not attended/year of notes [2]	0.2	0.1	0.3	0.1	0.1	0.1	0.427	-	-
OOH GP contacts [2]	3.4	3	3.3	1.5	1.0	1.7	0.007	-	-
Ave. OOH GP contacts/year [2]	0.1	0.06	0.1	0.04	0.02	0.05	0.011	-	-

1. Calculated using the T-test for independent samples, comparing FRMUS with FRMES.

2. Calculated using the Mann-Whitney U statistical test for skewed distributions, comparing FRMUS with FRMES

Secondary care

FRMUS patients had an average of one new and one review outpatient appointment every two years; or an outpatient attendance every year (see Table 32). The number of outpatient contacts was statistically more than for the FRMES group. Equivalent high numbers of days admitted to hospital as well as surgical procedures and visits to the emergency department were documented for both patient groups.

Table 32. Mean, median and standard deviation (SD) of the total number, and number per year of notes available, of secondary care contacts.

	FRMUS (N=47)			FRMES (N=25)			
	Mean	**Median**	**S.D.**	**Mean**	**Median**	**S.D.**	**p**
New OPD contacts	17.00	15.00	6.61	12.64	12.00	6.10	0.008
New OPD/year	0.48	0.41	0.37	0.35	0.31	0.25	0.021
Total OPD contacts	38.49	39.00	19.94	28.68	29.00	17.06	0.031
Total OPD/year	1.05	0.89	0.77	0.74	0.71	0.44	0.076
Days admitted	69.51	32.00	157.17	29.24	22.00	26.13	0.098
Days admitted/year	1.81	0.80	4.22	0.67	0.52	0.55	0.057
A&E visits	7.36	5.00	7.23	5.64	4.00	5.29	0.341
A&E visits/year	0.20	0.15	0.22	0.15	0.10	0.15	0.411
AHP contacts	14.23	13.00	11.43	16.52	11.00	28.00	0.294
AHP contacts/year	0.38	0.33	0.34	0.42	0.27	0.71	0.232

NB. Calculated using the Mann-Whitney U statistic for skewed distributions, comparing FRMUS with FRMES

OPD = outpatient department, A&E = accident and emergency, AHP = allied health professional i.e. physiotherapist, dentist, optician, etc.

Investigations

FRMUS patients had rates of investigations, where 58.1% were negative or within normal range. In line with findings from the main study, FRMUS patients had substantially more investigations than the FRMES group. Examples of the tests performed more often are included in Table 33.

Table 33. Mean number and standard deviation (SD) of lifetime investigations, and number of selected tests conducted per year of notes available

	FRMUS		FRMES		
Tests	**Mean**	**S.D.**	**Mean**	**S.D.**	**p**
Blood tests	20.87	10.930	14.44	11.225	0.024
ECG	3.04	3.26	2.24	2.65	0.019
Endoscopy	3.70	3.72	1.72	1.99	0.000
Histological tests	20.57	14.48	9.52	8.15	0.010
X-ray	16.66	10.06	11.28	7.54	0.326
US	2.47	2.29	2.40	3.16	0.022
Total tests	75.79	32.688	44.04	29.680	0.000
Ave. tests/yr.	2.07	1.25	1.30	0.87	0.002

NB. P value calculated using the Mann-Whitney U statistic for skewed distributions, comparing FRMUS with FRMES

Symptoms

Throughout their lives, FRMUS patients consulted a doctor for a large and varied number of symptoms (see Table 34 below). They reported significantly more symptoms to their doctors than FRMES patients. Common symptoms that FRMUS patients consulted a doctor about included abdominal pain, back pain and joint problems. Pain was the symptom which brought both groups of patients to consult a doctor most often. The only symptoms documented more often in the notes of FRMES patients were joint pains.

Table 34. Lifetime symptoms commonly documented in the case notes, and per year of notes available

Symptoms documented	FRMUS (N=47)		FRMES (N=25)		
	Mean	S.D.	Mean	S.D.	p
Abdominal pain	5.49	5.22	1.28	1.86	0.000
Back pain	4.91	5.46	3.16	3.90	0.204
Bowel symptoms	3.72	3.60	1.68	3.12	0.001
Chest pain	3.20	3.60	1.56	2.29	0.041
Dizziness	1.77	2.13	1.12	1.72	0.025
Headache	3.66	4.64	1.52	1.83	0.036
Joint problems	4.81	4.76	5.40	5.96	0.028
Upper gastrointestinal symptoms	4.34	3.22	2.60	2.86	0.008
Urinary symptoms	3.62	4.72	1.40	1.87	0.000
All symptoms of pain	31.45	17.44	16.92	12.16	0.169
Consultation for symptoms/year	2.70	1.72	1.41	1.17	0.000

NB. Calculated using the Mann-Whitney U statistic for skewed distributions, comparing FRMUS with FRMES

Medically unexplained symptoms (MUS)

Table 35 below indicates that an average FRMUS patient would consult for what would be considered an 'unexplained' symptom approximately once every three years. The FRMUS patients had far more MUS than the FRMES group. There was evidence that some FRMES patients had consulted for MUS earlier in their lives. FRMUS patients were a mean age of 30.79 years when their first MUS episode was documented in the case notes.

Table 35. Total number of medically 'unexplained' symptom episodes, and per year of case notes available

	FRMUS (n=47)		FRMES (n=25)		
	Mean	**S.D.**	**Mean**	**S.D.**	**p**
MUS	9.79	6.88	1.88	2.42	0.000
MUS per year of notes	0.27	0.24	0.06	0.10	0.000

NB. Calculated using the Mann-Whitney U statistic for skewed distributions, comparing FRMUS with FRMES.

Summary

The findings presented in this chapter show that FRMUS can be a chronic state for some patients. High use of health care resources for MUS was evidenced for this group of patients from a mean of nearly 31 years of age. FRMUS patients had a lifetime history of multiple contacts with outpatient clinics, as well as high levels of contact with other health care services.

Lifetime health care use of GP services indicates a considerable number of FRMUS patients may also be frequent attenders at their general practice. The numbers of investigations performed were statistically and clinically greater for FRMUS patients than FRMES controls. Substantial proportions of investigations were negative, or within normal ranges, for the FRMUS sub-sample studied.

Symptoms of anxiety and depression were often noted for the FRMUS group. Mental health care treatment, in the form of prescribed antidepressants and contacts with mental health care professionals, were common.

CHAPTER 15. HEALTH ECONOMICS

This thesis has shown that a small proportion of the primary care population (1.1%) are frequently referred for MUS. However, their health care use is equivalent to, and for investigations greater than, patients who have been frequently referred for medically explained symptoms.

From a health services perspective, patients who consume a large amount of the health service budget are an important group of patients to study in order to try and reduce costs. However, there have been surprisingly few studies which have quantified the costs resulting from the health care use of patients with 'unexplained' symptoms.

THE HEALTH ECONOMICS OF MEDICALLY UNEXPLAINED SYMPTOMS IN THE LITERATURE

Studies have calculated the costs of patients with MUS in primary care(406;407). However, these are much less compared to patients who use secondary care services.

An earlier study by Shaw and Creed calculated the direct costs of a group of 52 patients with somatic symptoms who had been consecutively referred to a psychiatrist(62). Medical resources were determined from a review of each patient's hospital notes. Costs were calculated based on estimates provided by the hospital accountant. This study found wide variation in costs accumulated prior to the referral to a psychiatrist. The majority of costs arose from admissions and investigations. However, it was not made clear over what time period the health care costs were calculated for each patient. There was bias due to the fact that the study had no data on patients who did not attend their scheduled psychiatry appointment. No comparison group was used to determine how relative the calculated costs were. Shaw and Creed's study was also limited by the fact that their findings only applied to psychiatric patients.

A British study of consecutive attenders to cardiology, gastroenterology and neurology outpatient clinics at a large teaching hospital compared costs of investigation for those given a 'functional' diagnosis with those given an 'organic' diagnosis(45). Although the number of investigations performed was similar in both patient groups, the associated costs were substantially higher for those with an 'organic' diagnosis. However, the patient group under study were consecutive attenders, and the costs only included investigations, not number of outpatient and other health care contacts.

Ambulatory health care contacts (which American studies term 'outpatients', including physician services and laboratory procedures) were calculated in a study of patients with high scores of somatisation and health related anxiety according to self-report measures(63). The study found that this group of primary care patients had considerably higher health care contacts and costs than patients who did not somatise. Although it studied number of hospitalisations, the study did not cost these admissions, which generate the highest costs of medical care. Also costs were based on somatisation scores, and did not control for the most important variable in cost of health care, i.e. the cost of health care attendances.

In terms of calculating the costs of high users of health care, the Michigan study (as described in Chapter 5 of this thesis), calculated the costs of a group of 41 high users with a diagnosis of somatisation(64). This research group found that, compared to the estimated costs of the general population of America at the time, their high user subjects had more than six times the hospital inpatient use and costs, 14 times more physician charges, and a personal health care expenditure of nine times more.

The most relevant study to the current research was the London Study (also outlined in Chapter 5 of this thesis on pages 67-9) by Reid and colleagues(61). This was an important study as it estimated the costs of frequent attenders to a wide variety of secondary care outpatient clinics. The standardised costs of outpatient consultations were based on national data. A separate analysis of costs resulting from these consultations was also conducted. The 'somatising' frequent attenders (those with two or more MUS episodes) accounted for outpatient use and expenditure comparable with the other frequent attenders (patients with one or no MUS). However, in contrast to Hamilton and colleague's study(45), the use and cost of medical investigations in this group with MUS were significantly greater. The somatising frequent attenders had at least double the number of more expensive investigations than the other frequent

attenders. These included: computerised tomography (CT) of the brain (four times more), exercise ECG (double the rate), endoscopy (three times more), and abdominal ultrasound (nearly double).

What the London Study did not cost were hospital admissions, or indeed other relevant costs such as out of hours contacts with doctors (i.e. GP OOH or A&E contacts). There are no known studies which have quantified the number and cost of health care contacts of patients frequently referred to outpatient clinics.

This chapter shall present the associated costs of health care contacts resulting from being referred to a variety of hospital outpatient clinics from general practice for symptoms. The aim was to determine how much FRMUS patients cost, and how this cost compares with two other patient groups. The hypothesis, as stated in Chapter 7, was that FRMUS patients would have higher health care costs than the FRMES and IRS comparison patient groups.

METHODS

The direct health care costs of the original 293 identified FRMUS patients have been calculated. These expenses will be compared with the 249 FRMES and 237 IRS controls also originally identified as eligible for the study (see Chapter 10). A randomly selected sub-sample of the FRMUS and FRMES patients (as outlined in Chapter 15) also had an estimate of their lifetime health care costs calculated.

There are two key stages to working out the economic cost of patient health care contacts. These are:

1. *The measurement stage*, i.e. count the number of health care contacts, and
2. *The valuation stage*, i.e. apply a cost to them.

Data sources

A count and description of FRMUS outpatient contacts was outlined in Chapter 11, and other health care contacts and investigations performed were described in Chapter 12 of this thesis. Lifetime health care contacts were outlined in the previous chapter (Chapter 15). This health care data collected in phase-1 of the study formed the basis of a health economic analysis to further describe the characteristics of FRMUS study subjects.

The cost per unit of each type of resource use is usually obtained from health service management databases. For this study, cost data were obtained from a variety of sources. Scottish cost data were used where possible. However, when this was not available, cost data from England were assumed to provide an acceptable approximation. This method has been adapted by the Scottish Medicines Consortium (SMC) who provide advice about new medicines launched to NHS Boards and their Area Drug and Therapeutics Committees (ADTCs) across Scotland(408).

The cost of one day admitted as an inpatient is available for each hospital specialty from routine NHS Scotland data sources(409). However, because it was often unclear from the notes which specialty the patient had been admitted under, I only recorded a count of the total number of inpatient days. As such, a weighted average cost per inpatient day was calculated. This was done by using data from all acute hospital specialties on the number of cases and the average cost per day. The weighted average cost took account of each specialty's share of the work carried out in the acute sector. For example, general medicine accounts for 29% of the inpatient work of the hospital, whereas neurology only accounts for 0.5% so the weighted average cost would reflect this. As such, the calculated weighted average cost of one day as an inpatient amounted to £437.24 (see Appendix 10). Investigations performed during inpatient stays were factored into the average cost of each day admitted.

Outpatient costs were calculated in a similar way to inpatient costs. The weighted average cost of an outpatient department visit was £96.08 (see Appendix 11). I also noted the number of outpatient consultations that patients did not attend (DNA), and calculated an estimate of how much these non attendances cost the health service based on average outpatient attendance costs.

GP consultations were costed from the Personal Social Services Research Unit (www.pssru.ac.uk) which is an English dataset(410). The 2004 data available from this source quoted that a GP consultation in the surgery cost £21 (a phone call consultation cost £28, and a home visit by a GP amounted to £65). However, GP consultations were only counted during the lifetime case note reviews. A recent Scottish research study on GP out of hours (OOH) care provided estimates of these OOH costs(411).

Costs for specific investigations and procedures were harder to measure. In general, Scottish cost data are based on work carried out at the level of the hospital specialty. For example, there is a cost per case for orthopaedics but no costs for arthroscopy or DEXA scanning for bone mineral density(412). The second source was the English NHS Reference Costs compiled by the Department of Health in England from all hospitals(413). Where specific tests were still not obvious, ad hoc sources were used, including published research studies and tariffs for private patients(414).

As secondary care contacts cost considerably more than primary care visits, it is important to consider the costs associated with this resource use. Other secondary health care contact data collected for the five year study period included: accident and emergency (A&E) attendances, and mental health care service contacts (including psychiatry, clinical psychology and community psychiatric nursing).

Costs not accounted for

Costs that were not calculated in this economic analysis included:

- GP consultations during the five year period of the main study (but included in lifetime cost estimates)
- outpatient clinics not included in the identification process of phase-1, such as obstetrics or clinical genetics (but included in lifetime costs estimates)
- prescriptions
- other healthcare costs incurred privately by patients, such as alternative therapies

- costs to wider society, in terms of social security payments and lost productivity from work.

Given the methods outlined above, costs calculated are not entirely accurate. They are estimates calculated to provide an idea of the magnitude of health care costs, which could be compared between FRMUS patients and FRMES and IRS control patient groups respectively.

Statistics

Typically, economic evaluations have highly positively skewed distributions. Normally for skewed data, the median values and non-parametric statistical tests, such as the Mann-Whitney U test, would be conducted. However, for health economic data, this is not the case. The most informative measure of cost data is the arithmetic mean(415;416). Non-parametric measures do not provide information about the actual cost of treating patients, which is needed as the basis for making healthcare policy decisions.

Mean costs as well as 95% confidence intervals (95% C.I.) for the difference between mean costs of each study group were calculated. As such, both parametric and non-parametric tests were conducted to ensure similar outcomes. For completeness, the statistician assisted me to perform a non-parametric bootstrap, which involves repeated random sampled means from the observed data and calculating confidence intervals. The main differences in cost presented between FRMUS patients and the other two study groups were calculated using the student t-test.

HEALTH CARE COSTS

New outpatient contacts

Looking at the five year cost of new referrals to selected specialties alone, the cost for all 293 FRMUS patients totalled £152,328.00. Consultations which resulted in a diagnosis of MUS by the specialist represented 55% of the total cost, and equated to £83,554.00. The full list of outpatient contacts for FRMUS patients is attached as Appendix 12.

New outpatient contacts for all 249 FRMES patients totalled £103,442.00. This was £48,886 less overall than the FRMUS group over the five years assessed (p=0.000). The sum cost of the 237 referrals to outpatient departments for IRS patients totalled £21,705.00 (p=0.000). Of this, over a third (£8,137.00, 37.5%) was spent on referrals for MUS. The mean costs of new outpatient contacts are displayed below in Table 36. Mean differences between the cost of FRMUS patient outpatient contacts and that of the other two comparison groups were statistically significant (p=0.000).

Table 36. Mean costs (£) per patient and mean difference in cost between study groups of new outpatient contacts over the five year study period

	FRMUS N=293	FRMES N=249		IRS N=237	
	mean (£)	mean (£)	Mean difference between groups (95% CI)	mean (£)	Mean difference between groups (95% CI)
mean cost (£) of new OPD contacts	521.9	417.2	104.7 (74.1, 135.3)	91.99	429.9 (405.1, 454.7)

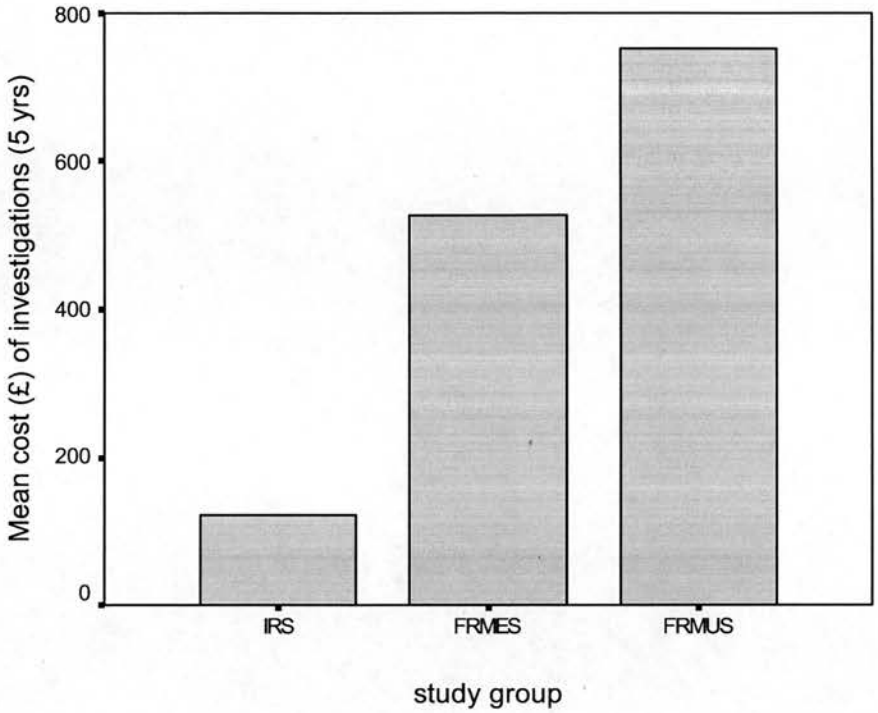
N.B. Calculated using t-test for independent samples comparing FRMUS with FRMES and IRS patients respectively. CI = confidence interval

Investigations resulting from new referrals

Of the investigations noted during the case note audit (N=3,735), FRMUS patients accounted for 2,043 (54.7%) of them. Five years of tests performed on the FRMUS group cost a total sum of £220,497. This was due to the large number of MRIs and invasive procedures such as laparoscopies, colonoscopies and sigmoidoscopies (see Table 37, with the full list in Appendix 13).

The 1394 tests performed for the FRMES group cost £131,551 over five years and £28,744 for the 311 IRS tests. The higher costs of investigations for the FRMUS patient group, compared to the other two patient groups, can clearly be visualised in Figure 28. below.

Figure 28. Mean five year costs (£) of investigations per patient for each of the three study groups



Although the most commonly ordered tests for all participants were blood tests and histopathology, the tests which amounted to the most expense included: magnetic resonance imaging (MRI), x-ray (plain and barium), laparoscopy, colonoscopy/ sigmoidoscopy, and CT scan. In the table below, I also included lumbar puncture given the invasive nature and cost associated with this procedure.

No formal statistical analyses are required in order to see in Table 37 that FRMUS patients near double the investigation use and cost for the FRMES patients. However, mean costs and mean differences in costs for investigations have been displayed in Table 39. For most investigations, FRMUS patients had ten times more performed than the IRS patients.

Table 37. Number and cost (£) of selected investigations for FRMUS patients and the two comparison groups over the five year study period

	Test Cost	FRMUS		FRMES		IRS	
	(£)	n	(£)	n	(£)	n	(£)
colonoscopy & sigmoidoscopy	171.00	95	16,245.0	47	8,037.0	15	2,565.0
CT scan	209.00	71	14,839.0	40	8,360.0	9	1,881.0
laparoscopy	683.00	28	19,124.0	3	2,049.0	0	0.0
lumbar puncture	680.00	10	6,800.0	3	2,040.0	1	680.0
MRI	309.63	103	31,891.9	53	16,410.4	10	3,096.3
x-ray (plain & barium)	55.62	399	22,192.4	308	17,131.0	44	2,447.3
Total		706	111,092.3	454	54,027.4	79	10,669.6

No formal statistical testing has been carried out on data specific to this table

Health care use

With the exception of total numbers of outpatient contacts, where FRMES patients had more contact, FRMUS patients had more contacts with the health care system than the two comparison groups overall (See Table 38). This group also had statistically more GP out of hours (OOH) contacts than the other two patient groups, and did not attend (DNA) a greater number of outpatient appointments.

Table 38. Mean number of health care contacts

	FRMUS N=293	FRMES N=249		IRS N=237	
	mean	mean	p	mean	p
Total number of OPD contacts	12.25	12.69	0.843	2.12	0.000
OPD consultations not attended (DNA)	1.30	0.90	0.050	0.28	0.000
Days admitted as an inpatient	9.10	8.50	0.292	0.70	0.000
Accident and Emergency (A&E) visits	2.30	2.00	0.330	0.48	0.000
Number of out of hours GP contacts	3.10	1.80	0.025	0.51	0.000

NB. Mann Whitney U statistic used to compare FRMUS with FRMES and IRS patients respectively. OPD = outpatient department

The main summary table of costs (Table 39) below show that FRMUS patients and FRMES patients had similar total health care costs overall. There were certain health care costs for FRMUS patients that were statistically greater than the FRMES patients, and these included the cost of:

- investigations
- GP OOH care, and
- outpatient appointments not attended

As stated in the methods of this chapter, the statistician assisted me in performing a non-parametric bootstrap, to compare those confidence intervals derived from calculating the mean costs. Interestingly, the confidence intervals for the non-parametric bootstrap analysis presented in Table 40 and those resulting from the parametric analysis presented in Table 39 were remarkably similar. However, the exception to this was mental health contacts, where the data were so skewed that the bootstrap analyses did make some difference, and the result was significant at $p<0.01$.

Lifetime health care costs

Over the lifetime of the sub-sample of 47 FRMUS patients, health care costs reached an estimated mean total of £48,373 (with a minimum sum of £6,413 and a maximum cost of £543,033). Given the years of notes available for each patient, this worked out to an annual mean cost of £1181.16 (see Table 41).

Table 39. Mean costs (£) per patient for five years of health care contacts, and mean difference in costs between the study groups

	FRMUS mean (£)	FRMES mean (£)	mean difference (95% CI)	p	IRS mean (£)	mean difference (95% CI)	p
OOH GP contacts	431.9	253.3	178.6 (59.8, 297.5)	0.00	71.0	360.9 (249.2, 472.5)	0.00
A&E contacts	159.9	139.4	20.5 (-17.7, 58.8)	0.29	33.2	126.7 (93.1, 160.3)	0.00
outpatient contacts	1205.9	1209.0	-3.0 (-148.0, 141.9)	0.97	199.8	1006.1 (894.0, 1118.2)	0.00
non-attended OPD appointments	127.2	90.2	37.0 (1.9, 72.1)	0.04	27.3	99.9 (68.4, 131.3)	0.00
inpatient days	3522.9	3712.2	-189.3 (-1810.9, 1432.4)	0.82	297.0	3225.9 (1768.7, 4683.0)	0.00
mental health service contacts	734.8	165.5	569.3 (-86.3, 1225.0)	0.09	55.8	679.0 (12.2, 1345.8)	0.05
investigations	752.6	528.3	224.2 (134.6, 313.9)	0.00	121.3	631.3 (552.6, 710.0)	0.00
all health care contacts and investigations	6935.2	6097.8	837.4 (-1352.1, 3026.9)	0.45	805.5	6129.7 (4090.0, 8169.4)	0.00

N.B. Calculated using t-test for independent samples comparing FRMUS with FRMES and IRS patients respectively. CI = confidence interval

Secondary care costs obtained from the Scottish Health Services Costs price index(409). A&E = accident and emergency department, OPD = outpatient departments. Average cost for a GP OOH contact was based on Scott and colleagues(411). OOH GP = out of hours GP contacts

Table 40. Non-parametric bootstrap of differences in costs (£) for five years of health care contacts between FRMUS and FRMES patients only

	95 % Confidence Intervals
OOH GP contacts	74.0, 297.3*
A&E contacts	-16.9, 59.4
outpatient contacts	-146.4, 144.6
non-attended OPD appointments	0.6, 72.5*
inpatient days	-1675.3, 1583.6
mental health service contacts	104.2, 1326.5*
investigations	136.0, 314.6 *
all health care contacts and investigations	-1064.5, 3108.1

NB. Where * indicates significant at the p≤0.05 level.

Table 41. Total lifetime health care contacts, followed by mean annual costs of health care contacts per patient, and the mean difference in costs between the two patient groups

	FRMUS n=47 Mean (£)	FRMES n=25 Mean (£)	Mean Difference	(95% CI)	p
total health care contacts	48372.9	23067.0	25305.8	(-9127.2, 59738.8)	0.147
GP/year	148.3	103.8	44.4	(-3.3, 92.2)	0.068
GP OOH/year	12.2	6.1	6.0	(0.8, 11.3)	0.026
all primary care/year	160.4	109.9	50.5	(1.3, 99.7)	0.044
allied health/year	11.5	12.6	-1.0	(-8.4, 6.3)	0.781
mental health services/year	98.9	5.2	93.7	(-68.2, 255.6)	0.252
A&E/year	13.7	10.6	3.0	(-3.7, 9.7)	0.371
OPD/year	101.0	71.4	29.6	(-2.3, 61.5)	0.069
investigations/year	103.4	58.4	45.1	(8.7, 81.4)	0.016
days admitted/year	791.1	294.1	497.0	(-244.3, 1238.2)	0.186
all secondary care/year	1016.2	394.0	622.2	(-282.7, 1527.2)	0.175
all health care contacts/year	1181.2	557.1	624.1	(-149.0, 1397.1)	0.112

N.B. Calculated using t-test for independent samples comparing FRMUS with FRMES and IRS patients respectively. CI = confidence interval

Secondary care costs obtained from the Scottish Health Services Costs price index(409). A&E = accident and emergency department, OPD = outpatient departments, mental health services = contacts with psychiatry, clinical psychology and community psychiatric services. All secondary care services included A&E, OPD, investigations, and days admitted.

Average cost for a GP OOH contact was based on Scott and colleagues(411). All primary care contacts included GP visits and GP OOH (out of hours contacts with a GP)

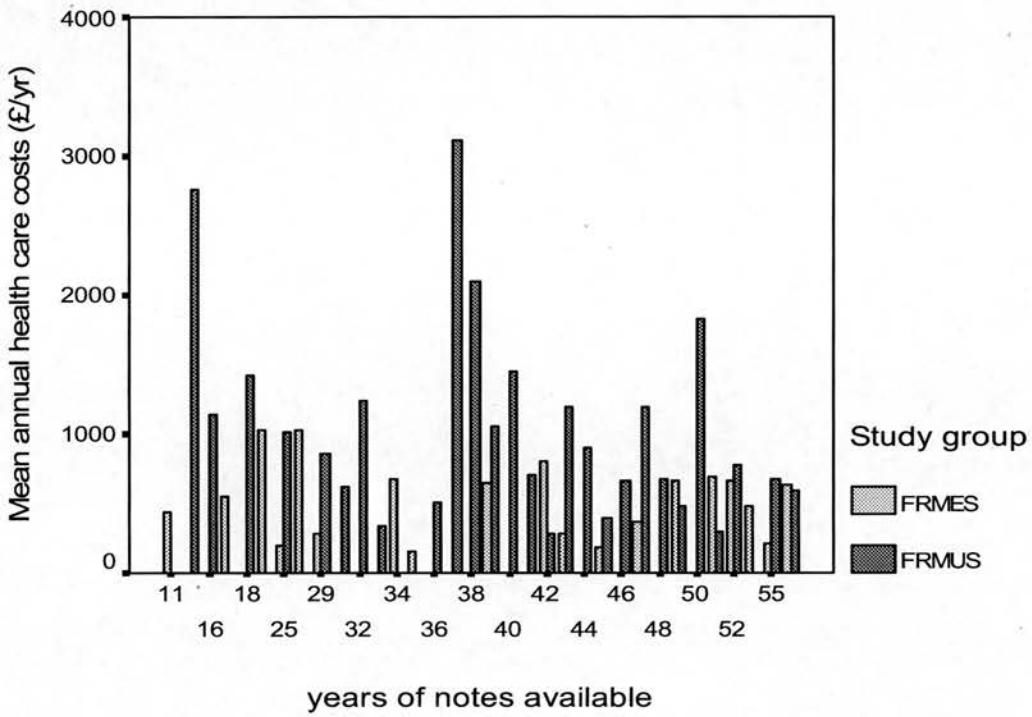
All health care contacts were calculated by adding 'all primary care' contacts with 'all secondary care contacts.

Looking at the table above, it is evident that annual primary care contacts, particularly GP out of hours (OOH) services, were contacted substantially more by FRMUS patients than the FRMES comparison group. There was also some association (p=0.000) between years of case notes available and annual mean primary care and investigation costs on a linear regression. However, there was no such effect on annual secondary health care costs, nor total costs calculated per year of notes available.

My initial concern with the analysis of the lifetime data costs was that the patients with more years of notes available would have less overall annual health care costs. This was due to the fact that documentation quality and quantity was poorer and less systematic for older records. However, Figure 29 shows that this was not necessarily

the case, as among those with the higher annual health care costs were patients (particularly FRMUS) with more years of case notes available.

Figure 29. Spread of annual mean health care costs per patient over number of years of case notes available for lifetime review



This lifetime health care cost data supports the five year cost data, which showed that FRMUS patients had equivalent high costs to FRMES patients. However, the numbers of investigations performed were considerably and statistically higher for FRMUS patients than FRMES patients. What this lifetime data added was that FRMUS patients were also more likely to have higher primary health care costs than FRMES patients. This provides further indication that there may be some overlap between the characteristics of FRMUS patients and frequent attenders to primary care.

It should be noted that these lifetime costs are not accurate patient costs. They are meant to provide an indication of the magnitude of health care use and costs for these patients. These estimated costs were based on 2004 prices, as health care expenses from the 1950s were not available. Costs and inflation rates over time were not calculated.

SUMMARY

The economic data presented in this chapter serve only as an indicator of health care costs for study subjects. Given the costs omitted as listed above in the methods of this chapter, the figures of the five year data are underestimates of total health care costs of these patients. Conversely the lifetime estimates are likely overestimates as there was no accounting for inflation and changes in costs over time. However, both five year and lifetime costs provide an estimate of cost, and indicate the magnitude of health service use and costs for these patients over the two time frames studied (five years and lifetime).

Medical investigations were ordered more regularly for the FRMUS patients, and were both statistically and substantially more expensive than the comparison groups. This was the case for both five year and lifetime costs calculated. These findings are in line with the costs of frequent outpatient attenders with somatisation compared to other frequent outpatient attenders studied by Reid and colleagues(61), and also for the cost differences in the outpatient patients studied by Hamilton and colleagues(45).

When totalling all health care contacts and investigations, the mean five year cost for 293 FRMUS patients equalled £6935.18 or an average of £1387.04 per average year. This was not substantially more than the FRMES patient group. However, in the context of how the money was spent for FRMUS patients, a considerable amount was spent on arguably unnecessary or ineffective medical care for medically 'unexplained' symptoms.

The lifetime costs for primary care contacts were considerably greater for FRMUS patients compared to FRMES patients, and this was also statistically significant. Totalling the health care costs of the 47 FRMUS sub-sample, these patients cost the health care system an estimated £2,373,484 over their lifetimes.

CHAPTER 16. KEY FINDINGS

MAIN HYPOTHESES TESTED

Hypothesis (1): A greater proportion of patients frequently referred with medically unexplained symptoms (FRMUS) will have symptoms and diagnoses of anxiety or depression compared to patients frequently referred with medically explained symptoms (FRMES) and patients infrequently referred with symptoms (IRS) respectively.

Hypothesis supported.

FRMUS patients had more diagnoses of anxiety and depressive disorders when compared to the two comparison patient groups. There were also a greater mean number of symptoms of anxiety, depression and panic reported by FRMUS patients than the FRMES and IRS patient groups. FRMUS patients had statistically more comorbid GAD and MDD according to the PHQ.

Hypothesis (2): A greater proportion of patients frequently referred with medically unexplained symptoms (FRMUS) with anxiety or depression diagnoses will have received inadequate treatment for these diagnoses compared to patients frequently referred with medically explained symptoms (FRMES) and patients infrequently referred with symptoms (IRS) respectively.

Hypothesis not supported.

Of the 64 FRMUS participants with a diagnosis of depression, 43 (67.2%) were receiving adequate treatment for this disorder. Nevertheless, a third (21/64, 32.8%) had no or suboptimal treatment.

Adequate treatment for anxiety was determined for 62% (41/67) of the FRMUS participants. There were 26/67 (39%) FRMUS patients who were receiving no or suboptimal treatment for their anxiety disorder.

Relatively, however, FRMUS patients received better treatment for their anxiety or depression than the other two patient groups. Over 81% of the other patient groups were untreated for depression, and this difference was highly statistically significant.

However, this 'adequate' treatment was arguably not effective as they continued to be more depressed and to be referred to hospital outpatient departments for symptoms.

SECONDARY HYPOTHESES TESTED

Compared to patients frequently referred with medically explained symptoms (FRMES) and patients infrequently referred with symptoms (IRS) respectively, patients frequently referred with medically unexplained symptoms (FRMUS) would:

1. ...be referred by a greater number of different General Practitioners

Hypothesis supported.

FRMUS patients were referred by a mean of 2.5 different GPs, and this was a greater number than the other two comparison groups. GP locums, registrars and assistants had among the highest proportions of MUS referrals for FRMUS patients. However, the latter statement was based on exploratory data and requires further investigation.

2. ...had problems regarded by General Practitioners as more difficult to help

Hypothesis supported.

There was a wide spectrum of GP difficulty ratings provided for FRMUS patients. More were rated as "moderately" or "extremely" difficult than the two comparison patients groups, and the difference was statistically significant. However, there was a small proportion of whom the GP could not recall. The other two comparison patient groups were perceived by GPs to be less difficult than FRMUS patients to manage in general practice.

3. ...have higher health care costs

Hypothesis supported.

FRMUS patients had equivalent total health care use and costs to FRMES patients (and for most costs, more than ten times the costs of IRS patients). More than half of the health care expenditure of FRMUS patients was for MUS. The number and costs of investigations for FRMUS patients were considerably more then both comparison groups. A statistically greater difference in lifetime use of primary care services was found for FRMUS compared to the FRMES patients. This indicated that some FRMUS patients may also be above average users of general practice services.

4. ... be more dissatisfied with health care received

Hypothesis not supported.

The majority of all participants from each of the three study groups were satisfied with the health care they had received. FRMUS patients were not significantly more or less satisfied with their health care than the other two patient groups.

5. ... perceive their general health to be worse

Hypothesis supported.

The self reported general physical health of FRMUS patients was equivalent to FRMES patients, and well below the standardised mean (indicating perceived poor physical health). FRMUS patients reported their physical health to be substantially worse than the IRS patients. However, the difference in FRMUS mental health scores compared with the other two patient groups were statistically lower (indicating perceived poor mental health).

6. ... have more current symptoms

Hypothesis supported.

FRMUS patients had been referred by the GP more often for symptoms, and self-reported more current symptoms than the other two patient groups. The symptoms which were statistically more often reported by FRMUS patients compared to both the other two patient groups included headache, dizziness and palpitations. For the female FRMUS patients, menstrual problems and pain or problems during sex were also more commonly reported symptoms. FRMUS patients tended to report more difficulty in the management of their symptoms than the other patient groups.

7. ... worry more about their health

Hypothesis supported (with qualification).

Three of the four IPQ items of FRMUS patients relating to their health problems were equivalent to FRMES patients. However, there were significant differences between the FRMUS and IRS patient groups, where FRMUS patients reported significantly more worry about their health. A quarter of FRMUS patients believed that stress or worry may be the cause of some of their health problems, and this was statistically greater than the FRMES patients. This finding should be viewed with caution given that on logistic regression, deprivation was considered to be a predictor variable for this item. There was no statistical difference in perceptions of stress and worry between the FRMUS and IRS patients. FRMUS patients reported considerably more burden by their health problems than the IRS patients.

8. ... state more discomfort in disclosing problems to doctors

Hypothesis not supported.

Of the three patient groups studied, FRMUS patients were more likely to feel comfortable disclosing both physical and emotional problems to doctors. As a general trend, all participants felt more comfortable disclosing physical problems than emotional problems, and discussing these issues with GPs rather than hospital doctors.

9. ... have more time off (a) work and (b) other activities

Hypothesis (a) not supported.

Nearly half of the FRMUS patients were not working. This was equivalent to the FRMES patients and was associated with age. However, of those who were working, one fifth had taken more than six months off from work over a five year period; again this was equivalent to FRMES patients but significantly more than IRS patients. Over one half of the FRMUS patients had collected benefits for a period of six months or more.

Hypothesis (b) supported.

The statistically significant finding was that FRMUS patients reported more time off from other usual activities than the two other patient groups.

OTHER FINDINGS OF INTEREST

Identification

This study showed that centralised referral activity data, such as that provided by ISD, can adequately identify patients who have been frequently referred to hospital outpatient clinics from general practice. In combination with GP case note data, patients frequently referred with MUS can be effectively identified using a set of operational criteria.

Referrals from general practice

Phase-1 of the study showed that the majority (14,034/26,252, 53.4%) of primary care patients were referred to a hospital clinic of any kind in a five year period. The mean number of referrals to secondary care over the five year study period for a primary care patient aged 18-65 years was 1.94; that equates to 0.39 per year or just over one referral every three years. Although this rate may seem high, data from the National Hospital Ambulatory Medical Care Surveys (NHAMCS), of visits to hospital

outpatient clinics, estimated patients attended a similar average of 0.31 times per year(391). The differences between the American and British health care systems are acknowledged, and these figures may not be directly comparable. However, this figure was separate from visits to private medical or surgical specialists where patients visited 1.2 times per person per year. Biggs' PhD research study found that a group of 151 participating consecutive attenders to outpatient clinics had attended a mean of 3.4 (or median 2) times to outpatient clinics and allied health practitioners (range 0-24 visits) over the 18 month study period (417).

Only 8.5% (2,234) were referred three or more times, and 5% (1312) of the primary care population were referred three or more times to selected outpatient clinics.

Prevalence of medically unexplained symptoms (MUS) and patients frequently referred with medically unexplained symptoms (FRMUS)

Nearly 32% of frequently referred patients identified had one or more referral episodes for MUS. FRMUS patients accounted for 1.1% of the primary care patient sample aged between 18 and 65 years. Over a third of the IRS patients were referred for MUS.

Specialties referred to for medically unexplained symptoms (MUS)

The hospital outpatient clinics which received the most referrals for MUS from GPs included general medicine, neurology, cardiology, urology, and gastroenterology.

The medically 'unexplained' symptoms (MUS)

Headache, fatigue, chest pain and abdominal pain were among the symptoms FRMUS patients were most often referred for by GPs. These were also among the symptoms most likely to be MUS according to the opinion of the assessing specialist.

The patients who were identified as frequently referred with medically unexplained symptoms (FRMUS)

Three quarters of the identified FRMUS patients were women and lived in deprived residential areas. FRMUS patient education levels were the lowest of the three patient groups. Considerable proportions smoked and were overweight according to their documented BMI. Not unexpectedly, nearly 50% of the FRMUS patients had a diagnosis of one or more functional somatic syndromes. Over a quarter of the women in this patient group had undergone surgery for a hysterectomy. These findings support the majority of literature published on the characteristics of patients with MUS(64;80;155;328;353;418).

This FRMUS patient group had high use of health care services and this was immediately evident from the size (i.e. volumes) of their case notes. Not only did they have high levels of hospital outpatient clinic contacts, but they also had high rates of admissions as inpatients, accident and emergency visits, and GP out of hours contacts. This group also had high non-attendance to outpatient appointments.

The lifetime data showed that FRMUS patients have a lifetime of high mental health and non-mental healthcare contacts in both primary and secondary care.

DISCUSSION AND CONCLUSIONS

"It is reasonable to expect the doctor to recognize that science may not have all the answers to problems of health and healing."

Norman Cousins (American Essayist and Editor, 1915-1990)

CHAPTER 17. STUDY LIMITATIONS

The findings presented in Chapter 17 must be viewed in light of some methodological limitations inherent in this study. Issues such as case definition and sampling methods, as well as measurements used to compare patient groups may have influenced my results(419). These, and other, potential limitations will be considered and discussed in this chapter. Some problems and complexities associated with the data will also be addressed.

THE CONCEPT OF PATIENTS FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS

Neal argued that using arbitrary cut-offs to define frequent attenders only identifies a "disparate group at the upper end of the consulting spectrum"(420). Some may view the identification of patients by the number of referrals, or number of symptoms (as is the case in Psychiatry) along similar lines. The problem with my approach, in terms of studying MUS, is that the majority of patients with MUS are not referred to hospital, and are not detected by this method. Arguably, patients who do not attend a doctor are less distressed about their symptoms, but there is no published evidence that this is the case. Certainly non-consulters are not seeking medical help for their symptoms, and they do not cost the health system a lot of money.

Schrire reasoned that frequently consulting a doctor is itself a sign of ill health needing treatment(421) and the FR approach adopts this assumption. The rationale for this approach has already been addressed in Chapter 5. The concept of MUS is fraught with enough confusion and debate. This study has offered a simple and practical operationalisation of a complex problem.

CASE-CONTROL STUDY DESIGN

Almost all studies have bias (factors which bring about a systematic deviation from the truth), but to varying degrees. Observational study designs, such as case-control studies, are more susceptible to bias than experimental study designs. However, the important question is whether or not the results (i.e. more anxiety or depression) are due more to bias than being frequently referred for MUS.

A case-control study, such as this, can be associated with a number of methodological problems and biases. The two main biases include sampling, or selection bias, and measurement bias. This encompasses:

- case and control group definition and selection
- definition and detection of the condition under study
- susceptibility of the study groups to the condition, and
- statistical considerations (particularly controlling for confounding variables).

SAMPLING BIAS

Participating general practices

Patients were sampled from a primary care population registered with five general practices. These practices were chosen to be representative of the Lothian primary care population. However, our sample had some limitations. There were no rural or remote practices, and although there were three single-handed practitioners involved, they shared the same facilities and staff and effectively worked together as one practice. As such, these findings are more generalisable to urban general practice.

It is acknowledged that the deprivation category allocated to each participating practice by ISD may not have accurately reflected the deprivation of the surrounding population registered and served by that practice. However, ISD data indicated that our sample was suitably representative of the socioeconomic status of the Lothian primary care population, but that they were significantly less deprived when compared

to the entire population of Scotland. In terms of generalisability to an even wider UK population, it is acknowledged that the findings of this study may not be generalisable to racially diverse areas of the UK, such as primary care populations from London or Manchester, for example. The findings of this study must be viewed in regards to possible biases introduced by patients' deprivation and ethnicity. Other measures of deprivation such as fewer years of education, unemployment, receipt of benefits and living arrangements corroborated the finding that FRMUS patients were likely to be more deprived.

Selected hospital outpatient specialties

These 15 outpatient specialties were chosen based on findings by Reid and colleagues(60) and the single practice pilot study(332) to be those most likely to receive referrals for MUS. This was a practical decision to minimise the number of unnecessary case notes for audit whilst maximising the likelihood of identifying most of the referrals for MUS. However, it is acknowledged that by implementing this eligibility criterion, this effectively lost 922 of 2234 (41.3%) FR patients from the study. There is no doubt that if all specialties had been included, the prevalence estimate of FRMUS patients would be greater than 1.1%. In this light, this prevalence estimate should be viewed as that for 15 outpatient specialties, and not necessarily an accurate estimate of FRMUS patients in all outpatient clinics.

The other specialties excluded from this study included: Clinical Genetics, Dentistry, Palliative Medicine, Transplantation Surgery, Obstetrics, Oncology, and Psychiatry. Given this study's definition of MUS as symptoms inadequately explained by disease, it is likely that patients referred to Dentistry, Obstetrics, Oncology, and even Palliative Medicine had symptoms out of proportion, or unrelated, to their disease or condition. There are very few studies which have looked at MUS in Obstetrics, and of those I managed to identify, patients were seen in a joint Obstetrics and Gynaecology clinic(381;422). To be clear, this study did assess referrals to joint Obstetrics and Gynaecology clinics, but excluded referrals specifically to Obstetrics for issues related to childbirth and fertility.

There is little evidence of MUS presentations in Oncology(199;423); certainly no systematic enquiry into prevalence. However, a recent study estimated 30-40% of

disease-free cancer patients are likely to have persisting, unexplained fatigue, and a significant proportion were aided by CBT when compared to control patients(424).

In terms of Dentistry (or Orthodontics), some MUS referral episodes which may not have been detected by this study include those for the functional somatic syndrome of temporomandibular joint dysfunction (TMJ). A British study found over one third of 301 unselected orthodontic referrals were found to exhibit at least one sign of TMJ, and two-thirds rated having mild to moderate dysfunction; although only five (1.7%) patients had severe dysfunction(425). Reassuringly, there is evidence that patients with TMJ also have high incidences of otologic complaints(426;427), and thus also likely to have been referred to Ear, Nose and Throat (ENT) outpatient clinics, where this study would likely have identified them. However, if patients had been referred once to Dentistry, once to ENT and once to Gastroenterology, for example, then this study would not have identified these patients from the ISD data, as this example would only count as two referrals to selected specialties.

Specialist opinions as 'gold standard'

It is acknowledged that specialist diagnoses are not always 100% correct, and therefore their use in this study as the 'gold standard' must be viewed with caution. The limitations of human processing and the inherent biases in using heuristics guarantee that human errors are inevitable. There is evidence in the literature of delayed diagnosis, or even misdiagnosis, of symptoms and certain medical conditions by specialist doctors. This not only impacts on the diagnoses of MUS, but also to the diagnoses of organic diseases. As such, the finding that 84 (28.7%) FRMUS patients had diagnoses of organic disease must be viewed with caution.

For example, there is a growing body of literature on the difficulties of diagnosis and diagnostic errors related to epilepsy. One study found that 26.1% (46/184) of patients studied with symptoms, such as seizures or loss of consciousness, had been misdiagnosed with epilepsy in a specialist clinic(428). In England and Wales, an estimated total of 92,000 people were misdiagnosed with epilepsy in 2002 at a calculated health economic cost of £316 per patient(429). A study of 100 diagnostic errors made by specialists of internal medicine, as identified by autopsy, found that specialists' failure to pursue reasonable alternatives after an initial diagnosis had been

made, was the most common cause of misdiagnosis(430). In some cases, only autopsy can provide the gold standard diagnosis, but clearly this is not a possibility when studying live patients!

Many conditions have diagnostic criteria which should be used as the gold standard to ensure the most accurate diagnosis, e.g. The International Headache Society Classification of Headache Disorders has been accepted widely(431). However, it is highlighted in the preface of these guidelines that these criteria are primarily based on expert medical opinion and experience in the absence of sufficient published evidence. It was often difficult to ascertain from case note audit the extent that doctors had followed these and other gold standard criteria, and impossible for me to have ensured diagnostic criteria had been met for all conditions as part of the case note audits.

Clinical guidelines aside, there are areas of both consensus and divergence among specialists with regard to diagnostic criteria; this includes specialists of the same and different medical specialties(432). This sometimes results in diagnostic disparities or disagreement between specialists(433). Partial explanation comes from patient symptoms and presentation. However, variability can also be explained by specialist age, level and type of training and years of medical experience(434). Specialist experience and years in practice could not be assessed in this study.

Study group definitions

Frequent Referral

This study defined frequently referred (FR) as three or more new referrals in a five year time frame. This threshold was chosen based on a practical need to identify greater numbers than identified from the single practice pilot study(332) which defined FR as five or more new outpatient contacts also in five years. Conceivably we have identified a group of patients who are at the less extreme end of high health care use. This approach did not address specialty specific attendance, i.e. three referrals in five years may not be that frequent for some clinics. Alternatively, selection could be based on patients in the top percentage of attendances for each clinic, such as the top 5% selected by Reid's study(60).

Patients frequently referred with medically unexplained symptoms (FRMUS)

At the conclusion of reviewing each patient's case notes, I counted the number of referral episodes rated MUS, i.e. "somewhat" or "not at all" explained by disease. Those with two or more MUS episodes were defined as FRMUS. Although chosen for practical reasons to achieve the desired numbers to study, three referrals and two MUS episodes were relatively arbitrary cut-off points. However, most studies of high users of health care have been based on arbitrary thresholds.

An alternative method would have been to provide each patient with a MUS score calculated by summing the ratings from the operational criteria (for example, a patient referred three times for episodes deemed by a specialist as 0 (explained) + 2 (somewhat explained) + 3 (not at all explained) would give this patient a score of 5). This would have provided a spectrum of severity of FRMUS, and could potentially include those with one MUS episode.

However, using the current procedure, FR patients were ineligible if they had only one referral episode for MUS. Arguably, this group of patients should have been included in the FRMUS category. Alternatively, perhaps it would have been more reasonable to have 'allowed' one MUS episode and considered these patients primarily FRMES. I argue that it is a strength of this study that the two FR patient groups are distinctively different from one another, and likely to increase sensitivity and specificity.

It may be worth revisiting the data of the FRs with one MUS referral episode. This would be to determine who these patients are and if their characteristics are more in line with FRMUS or FRMES patients. It is possible that these form a discrete group entity with transient or acute distress.

Patients infrequently referred with symptoms (IRS)

The findings of the IRS patient group do not necessarily represent characteristics of the general population. This is because they had contact with secondary care, when most of the population would have none at all within a five year time frame. Comparisons between FRMUS patients and a sample of the general population who had not been referred would have been preferable. However, the single practice pilot study found

that response rates of non-referred general practice patients were exceptionally low(332).

A high proportion of identified IR patients were ineligible for this study. A reason for this was that some had been referred again after the five year study period. Although ISD did not identify private referrals, I decided to take them into account during case identification if documented in the case notes. For example, I could not classify a patient as 'infrequently referred' (referred once only) when they had also seen a private gynaecologist and gastroenterologist.

Also, a substantial proportion of the ineligible patients had been registered with the practice less than the five year time frame, and had in fact been referred by their previous practice(s). Reflecting on Crimlisk's study that referrals often occurred after patients consulted new doctors(241), it is possible that some of the IR patients regularly changed practices and consulted multiple and new GPs. Future research may wish to study the referral patterns of this group of 'transient' patients, to see if they are associated with FRMUS patients. Given a different definition of IRS, which may have included use of alternative health services or a different time frame, some IRS patients may have become FR (MUS or MES) patients.

Patients frequently referred with medically explained symptoms (FRMES)

When conducting the lifetime case note reviews, I found limitations associated with reviewing notes for a five year time period. A series of single referral episodes which seemed explained by disease classified the patient as FRMES. However, for some patients, reviewing previous attendances created a different clinical picture. By reading further back in the notes, it was evident for some FRMES patients, that there had been past episodes of MUS. The problem with reviewing only five years of case notes was that I did not see a lifelong pattern of patient consultations for symptoms. A five year time frame provided a 'snap shot' for this period of time. Whereas the lifetime case note reviews provided a clearer picture of overall referral characteristics.

It was my impression that some FRMES patients may be more like FRMUS had the five year time frame changed. The lifetime case note reviews indicated that, in some instances, patients classified as FRMES had actually had MUS episodes prior to the

five year period. Surgery, or other medical procedures, for seemingly minor problems (e.g. hysterectomy for vaginal discharge) had resulted in complications which brought about objectively measurable physical problems, for example adhesions causing abdominal pain (i.e. iatrogenesis). If lifetime reviews and classifications had been implemented, it is possible that more FRMES identified patients would have been classified as cases. This may partly explain the similar levels of depression found in the FRMES group, and the higher than expected contacts with mental health care professionals.

General Practitioner exclusions

GPs excluded few patients from the study (less than 2% of those identified as eligible). It is unlikely that any bias has been introduced because of these exclusions. However, it is acknowledged that GP opinions and interpretations of patient suitability for research vary widely. Some GP exclusions may be inappropriate where patients are in fact eligible and potentially willing to participate. From the patients' perspective, these exclusions could be seen as paternalistic as it does not give them a chance to be involved in research that they may in fact be interested in participating in.

Response rates

Sample bias can be introduced by patient self-selection into a study. The differences between responders and non-responders to the study were outlined in Chapter 13 (see pages 158-60). Non-responders comprised more males, were younger, had been registered with the practice fewer years, and had more non attendances to outpatient departments. These differences have an impact on the generalisability of the data obtained from the questionnaire data. Non-response in the target population can reduce precision and may have biased estimates derived from the study.

Although two practices represented the more deprived patient population, the response rates from these two practices were the lowest of the five. This has likely brought about some deprivation bias in the results of this study. The study sample is possibly more representative of urban 'middle class' patients. This is mixed evidence on the

effect of socioeconomic status and consultations for MUS; some have found associations between unexplained symptoms and lower socioeconomic status(435;436), higher socioeconomic status(146), and others have found no association between MUS and deprivation(257). There is certainly evidence of depressive symptoms being more prevalent and persisting for those of lower socioeconomic status(437). Another measure of deprivation is level of education. A systematic review of studies on the characteristics of MUS found a consistent relationship with fewer years of education(353). This study provided further support for this common association where FRMUS patients had the least years of education.

Delays involved with receiving and processing patient data, meant that referrals had been made a mean of 27 months before a patient was contacted about the Referral Study. The elapsed time could have negatively affected questionnaire response rates. Anecdotally, several willing participants (particularly IRS) had to telephone me to ask what the referral was so that they could complete the questionnaire. A reason given on some unsigned consent forms for non-participation was that they could not recall having been referred. Conversely, a substantial proportion of patients (particularly FR) had documentation in their case notes of referrals yet to be detected by ISD. Although the most recent referrals made outside of the five year study period were not included in case identification, they could have positively affected response rates.

The ethnicity of this patient sample was not assessed, as according to recent Scottish Census data, only 2% of the population are from an ethnic minority background[20]. Therefore I can not comment on the differences between the responders and non-responders. However, it would be reasonable to suggest that the results of this study are more representative of patients from white backgrounds.

[20] See: http://www.scotpho.org.uk/web/site/home/Populationgroups/Ethnicminorities/ethnic_data/ethnic_popcomp.asp

MEASUREMENT BIAS

There were numerous sources of measurement bias throughout the conduct of this study. My own biases as researcher are acknowledged as well as biases inherent with the different methodologies and sources of data used.

Rater bias

The operationalised criteria used in this study had good inter-rater reliability according to the single practice pilot study(332). However, it is likely that my application of the operationalised criteria introduced a degree of bias by misclassification of some referral episodes, and possibly cases and controls. This provides added weight for the decision to exclude patients with one MUS episode, as possibly some were FRMUS and some were FRMES due to my potential misclassifications. As the classifications stand, I am confident in having identified two distinct patient groups.

Consensus meetings helped improve the validity of my ratings. However, these relied upon the quality of the data I extracted from the case notes and how I presented it to the other two raters.

Ratings were often difficult to make due to vague or incomplete descriptions outlined by specialists in their letters to GPs, this was particularly the case for Gynaecology and Urology where there are few definitive tests to 'prove' or 'disprove' disease. Some specialists imparted little information in their discharge letters which made ratings difficult. Applying the criteria often relied on my interpretation of laboratory investigations and the language used by specialists which may not have accurately reflected their opinion.

I was not 'blind' to other ratings and previous ratings may have affected how I rated subsequent ratings. It is possible that there were some MUS false positives (i.e. classified as MUS when in fact there was the possibility of a medical explanation). I may have biased my ratings in order to achieve the numbers required to power the study. However, to maximise objectivity, the operationalised criteria were applied to referral episodes as isolated events.

Data sources

Validity and utility of studies based on case note review are enhanced by inter-rater reliability and the use of supplementary data sources(438). A strength of this study is the combination of ISD and GP case note data to identify and describe patients. Other sources of information and study methods also strengthened the findings, such as ISD, case note, GP self-report, and patient self-report data. However, with each type of data lies bias and these shall be outlined for each data source listed below.

Information and Statistics Division data

The single practice pilot study found that outpatient contacts were sometimes over-counted in ISD data(332). This also applied for the current study. The main reason for this was that the data did not distinguish between attended and non-attended (DNA) consultations. However, an alternate explanation could be some breakdown in written communication somewhere between the outpatient assessment and documentation being filed in the patient primary care case notes. Some degree of under-counting was also noted. This may have been due to health care providers failing to report the contact to ISD.

Incorrect or mismatched names, dates of birth (DOB) and gender specified by ISD made identification of some patients in the practice problematic. Sources of referral and diagnoses were often missing and had to be obtained from the case notes. Of concern were patients identified by ISD who had no record of ever being registered in the designated general practice.

ISD data did not distinguish between new and review outpatient contacts. As such, there were high numbers of patients identified as 'FR' (i.e. three new referrals), and more case notes were audited than was actually necessary.

ISD data does not receive information about private referrals. Three of the participating practices estimated that 10% of their referrals were to private specialists. Some of these could have been identified through the practice records, but two of the practices did not record or monitor referrals on their computing system. I could have

sought access to individual specialist records, but the time and effort required did not match the small potential gain in patient numbers.

Case note data

Labour intensive

Reviewing large numbers of case notes is a labour intensive exercise. On an average day, 15 case notes were reviewed for five years of health care contacts, i.e. one set of case notes every half an hour. This may be reasonable from a research perspective, but clinicians do not have this amount of time to spend reviewing patient records. Although time to collect data from case notes is not a bias, if there are large numbers to extract data from, the exercise may bring about rater bias from 'case note fatigue'.

Unsystematic recording

Case note data may be subject to recording bias due to variation between institutions and practitioners in the documentation of care provided to patients. There is evidence that case note data generally underestimate care for common medical conditions(439). Busier doctors may do, or find, more than they write down; conversely good record keepers may not take a thorough medical history. This was evident in this study for weight and smoking status. Documentation of first registration with the practice and findings of physical examination or medical history from this consultation was often omitted from case notes.

Diagnoses may be made to enhance reimbursement for practitioners under contract. Patients less likely to adhere to treatment regimens may not be declared(440). Under-reporting of anxiety or depression in the case notes may in part be due to such contractual issues.

Other problems with case notes include missing laboratory or other reports. One study found that GPs often did not receive discharge letters from hospital doctors(441). Doctors' handwriting can be illegible and this was partly why GP consultations were not included in the main study.

Missing notes

What is documented or extracted from case notes becomes irrelevant if case notes can not be located. Nearly 20% of FR patients identified by ISD and nearly 30% of IR patient case notes could not be located. This was predominantly because patients had left the practice or there was no record of them ever having been registered at the practice. Classification could not be conducted on this group, but arguably they may be a group with substantial unmet needs. Reassuringly the case note return rate was similar to a recent study by Smith et al(442) who were able to review 85% of the primary care case notes of high utilising patients originally identified.

Although the biases mentioned above may have affected the identification and participation of eligible patients, this has been addressed in this study by involving a number of different practices and GPs.

General Practitioner difficulty ratings

GPs completed one rating per patient only. However, given my finding that a substantial proportion of FRMUS patients were not referred by one GP in particular, it was difficult to decide which GP should provide the rating. How one referring GP rated the patient may have been different to how another GP would have rated the patient. This was overcome in two of the practices by GPs completing the ratings as a group; if they were unfamiliar with the patient, they would ask for their colleagues' opinion. GPs from the other three practices completed the ratings individually. An alternative would have been to ask each referring GP to provide a rating for each patient they had ever referred and then to calculate the mean difficulty score.

Significant event related to the difficulty rating forms

Each practice manager, or in their absence the practice secretary, had been asked to collect and keep the completed GP difficulty ratings, and the signed letter of invitation to the patient. I would then check that the GP had agreed for each patient to be involved in the study, and mail off the study materials to each patient. Inadvertently, a practice staff member from practice-4 mailed three difficulty ratings to the patients.

This occurred when a GP had sent the completed forms and signed invitation letter to the practice secretary to keep for me to collect. However, forgetting our previous arrangement, and seeing a signed letter addressed to a patient, she mailed the signed letter along with the difficulty rating.

I was able to identify who the three women were by a process of elimination of the other ratings I had received from the practice. I contacted two of the three women, who had been mailed the ratings, and spoke to them personally about their concerns. I reassured them that whatever had been written was not personal, but more directed to how difficult the problems they presented with had been for their GP to manage in the practice setting. To my surprise, I managed to allay their concerns and they agreed to participate. Whether this incident influenced their answers is unclear. I was unable to contact the third patient, but I believe the GP managed to speak to her to apologise for any distress it may have caused.

Both the practice and I used this as a learning exercise. At the time these ratings were being completed by the GPs, I should have ensured that all practice staff clearly understood the procedure rather than relying on a busy and overstretched practice manager, practice secretary and GPs to oversee it. I had used a combination of email and personal contact with the practices prior to the event, but had not reiterated instructions to staff during the time of rating completion (which took approximately three weeks across all five practices to obtain all ratings and signed invitation letters). On top of each rating form, I should have ensured a sentence in bold writing that said something along the lines of **'THIS FORM IS NOT TO: 1) LEAVE THE PRACTICE; 2) BE MAILED TO THE PATIENT!'** This incident also provided an opportunity for the practice to review its confidentiality procedures, and for staff to be more aware of the materials they were sending out to patients.

Patient questionnaire data

Self-report data brings about its own problems such as recall bias, and response bias (in terms of how honestly and accurately the questions are answered). My choice of measures, including the title of the questionnaire, also may have had some affect on the validity of the results.

Patient Health Questionnaire (PHQ anxiety and depression modules)

The researchers who designed the PHQ asserted that it could validly diagnose conditions such as anxiety or depression in a primary care population which were comparable to the clinician-administered PRIME-MD(377). However, the PHQ has not been widely used in other UK studies. Whether this instrument is valid for a UK population is uncertain.

With respect to the Referral Study, it is possible that some participants became aware of the hypothesis, relating to anxiety and depression, from the questions in the survey. This may have altered participant answers to the PHQ by wanting to emphasise their physical problems over the emotional. Patients had admitted to me during interviews that they had not always filled in the answers to the PHQ and SF-12 truthfully as they wanted to come across as "Mrs. Cope it All" (to quote one woman). It is possible that the anxiety or depression detected in the FRMUS study group by the PHQ is an underestimate.

Another limitation of the PHQ relates to those patients on antidepressants or other treatment for anxiety or depression. If a respondent scored below 10 (no MDD), the PHQ would not differentiate between a patient on antidepressants whose therapy was working with a patient who did not have a depressive disorder at all. A substantial proportion of FRMUS participants were on antidepressants but had no depression according to the PHQ. Ultimately, I was looking to identify patients whose treatment for anxiety or depression was suboptimal, thus patients not scoring positively on the PHQ because they were receiving 'adequate' treatment are of less concern as they do not require any further intervention or help for their depression.

Past five-years of anxiety and depression

Self-reported past five year anxiety, depression and panic were subject to patient recall bias. Although questions were based on criteria from the DSM-IV for anxiety and depression, applying them to the past five years may not have been valid or reliable. Similarly, when asked to provide an estimated number of anxiety, depression and panic episodes, participants tended to provide vague responses such as 'hundreds', 'a lot' or 'a few'. These responses were considered invalid as no meaningful analysis

could be performed. This problem had gone undetected when piloting the questionnaire.

Non-validated measures

The items used to measure patient comfort in disclosure of problems to doctors were not from a validated questionnaire. However, piloting indicated the questions were easy to understand and responses were in keeping with group trends.

By combining different validated questionnaires, there was some duplication of items. These were removed to avoid repetition, and reduce the length of the questionnaire. However, reordering the items and their presentation may have affected validity.

The items used to determine time off work and usual activities did not measure a precise number of days, more a participants' estimation of the magnitude of time. The questions were not from a validated questionnaire. However, the measure did provide a sense of how patients perceived the impact of their illness. The answers were in keeping with anticipated study group trends indicating a good level of validity.

There is no one standardised measure to ascertain basic participant demographics such as education, employment, and deprivation. Pragmatism chiefly guided the choice of brief, concise and easily administered measures for this study. However, the Carstairs Index provided by the ISD was based on Scottish census data(443) and considered a benchmark measure for deprivation at the time(370).

Defining and measuring 'adequate' treatment

Defining 'adequate' treatment for anxiety or depression is problematic. The operational definitions used in this study have been outlined in Chapter 8. However, to treat anxiety or depression cost-effectively, patients would ideally be matched with therapies most appropriate for the individual. Patients have varying tolerance levels for medication due to individuals' metabolism, body mass index (BMI), stress, diet and interactions with other medications. Effectively, there is no 'one size fits all' treatment for anxiety or depression.

The definition of adequate treatment used by the current study was based on a number of assumptions. The following assumptions may have overestimated adequacy of anxiety or depression treatment:

1. the treating clinician prescribed the minimum recommended dose of an antidepressant which was at an appropriate level for the individual patient
2. patients adhered to the prescribed therapy
3. those patients who saw a mental health professional developed a therapeutic relationship with the practitioner
4. the practitioner was effective in their delivery of therapy.

Recent evidence has shown that patients initially seeing a psychiatrist were most likely to receive adequate treatment(440). Conversely, Bass and Murphy argued that chronic somatisers just see psychiatry as yet another health care service to consume(240).

In reality, the minimum recommended dose of an antidepressant or contact with particular mental health care professionals may not be adequate for some patients. The findings in this study support the fact that the treatment FRMUS patients were receiving was not adequate and was not meeting their needs. This was evidenced by the fact that they reported more symptoms of anxiety and depression, and most importantly, continued to be referred for MUS.

It is acknowledged that FRMUS patients were on a range of tricyclic and SSRI medications. Although three meta-analyses have shown improvement in symptoms following antidepressant treatment, these reviews mainly looked at studies of tricyclic antidepressants(166). There is less evidence on the effectiveness of SSRI antidepressants specifically for MUS, and in fact the review by O'Malley and colleagues(167) showed less efficacy for SSRIs than the tricyclics. Although a review of studies for the treatment of fibromyalgia found no differences between tricyclic antidepressants and SSRIs, the meta-analyses were limited by the paucity of trials of SSRIs(168). More recent evidence of benefits from SSRI therapy looks promising, but these studies tend to be pilot in nature(444-446). However, there is strong, systematically reviewed, evidence of benefit from SSRIs for premenstrual syndromes(447-449). Clearly further evidence, involving larger numbers of

participants and different unexplained syndromes, is required specifically on the efficacy of SSRIs for the treatment of MUS.

Pharmacological and psychological treatment for depression was assessed from the case notes prior to patients and GPs completing the study materials. However, this introduced a separate bias in that treatment was assessed at a different point in time to when patients rated their symptoms of anxiety and depression on the PHQ (a mean of five months before). It would have added more weight if participants were asked on the questionnaire if they were on antidepressants or treatment for anxiety and depression at that time.

LIFETIME MEDICAL HISTORIES

Sub-sample bias

It is possible that the process of randomly selecting a sub-sample of cases and controls for a lifetime case note review did not bring about a representative sample. Small numbers weaken quantitative findings, and make them less conclusive and generalisable than larger studies. However, the study was not powered on these findings, and this data merely served to provide further descriptive information about FRMUS patients.

Analysis of lifetime data

The lifetime medical history data was subject to the same measurement bias as outlined by the use of case notes, e.g. omitted data due to illegible doctors' handwriting and older hospital records. Of particular relevance was that each patient had a different number of years of notes available for review. Documentation between primary and secondary care was less complete the older it got, especially pre 1990s. Ideally, I should have reviewed (and analysed) the notes retrospectively according to time bands (e.g. five year) to account for these two limitations of the notes. Unfortunately, I had not recorded dates of GP consultations and was unable to do this.

To partially account for this, I divided the counts by the number of years of notes available, and adjusted the significant findings using a linear regression model. Some of the findings were at least partly explained by the number of case notes available for review. Findings from analysis of the lifetime data were strengthened by the fact that the two patient groups (FRMUS and FRMES) had a similar mean number of notes available for review.

HEALTH ECONOMIC ANALYSIS

The emphasis of the health economic analysis was pragmatism. For example, I did not count every single blood test during the case note audit, only the number of times blood tests were documented as ordered. It was also evident that many blood test results, particularly bloods taken at the hospital, were not in the GP notes. The actual number of blood tests has been under-reported in this study. However, these are the least costly of the tests measured.

Another example of my pragmatic approach was the calculation of certain tests (i.e. histopathology), as well as total outpatient and inpatient contacts, by weighted average costs. This was done to facilitate ease of analysis, but still produce a reliable estimate of the magnitude of patient costs. I did not include prescriptions or costs resulting from GP consultations. I did not calculate costs of inflation. As a result, costs calculated were not exact. The cost estimates provided in this thesis likely represent an underestimate of the actual costs.

I did not review handwritten GP records as they were often illegible and not part of the identification process. However, with hindsight and access to the records, a simple approximate count would have enabled a more complete health economic evaluation. A count of GP visits would have also more accurately informed if FRMUS patients were also frequent attenders in the practice. However, the lifetime case note reviews indicated that high use of primary care services may be a characteristic of FRMUS patients.

SUMMARY OF LIMITATIONS

The findings from this case-control study must be considered in the light of the limitations acknowledged in this chapter. Several issues with sampling bias and measurement bias have been identified at each stage of the study, and for each source of data, and these may have affected the findings.

However, a strength of this study is that it has employed a combination of methodologies (i.e. cross-sectional and case-control study designs) and data sources (i.e. ISD, case notes, GP records, GP and patient self report, as well as researcher observations) to test the main hypotheses and provide detailed information about FRMUS patients. The inclusion of two control groups also strengthens the findings of the associations found in the FRMUS patient group. This 'triangulation' of methods and data sources enhances the internal validity of the study.

CHAPTER 19. COMPARISONS WITH OTHER STUDIES

The findings from this study not only need to be considered in the light of its limitations and strengths. Comparisons with other related studies can provide an indication of the strength and generalisability of my findings.

No other study has used a combination of centralised health activity data and case note review to identify patients whom have been frequently referred from primary to secondary care for MUS. There is little in the way of other literature with which to directly compare my findings. However, aspects of the methodology employed in this study had been advised by a small number of published studies.

In this chapter, there are five key concepts I wish to discuss in terms of comparing my study with other published work:

1. Firstly, I shall compare key methods and findings from my study of frequently referred patients with two UK studies of frequent attenders (FA) to outpatients. The distinction between frequent attendance and frequent referral will be made.

2. I used a "hybrid approach", i.e. a combination of electronic and case note data, to identify patients frequently referred to outpatient departments. The two UK studies of FA outpatients also used this approach, and the merits and difficulties with this will be discussed.

3. There are a number of American studies which have addressed the concept of frequent attenders with MUS consulting between the primary care - secondary care interface. I have selected a couple of studies of interest (mostly outlined in Chapter 5) as they also used the hybrid approach to identify cases. However, these studies are difficult to make any meaningful comparisons with, due to differences between the UK and American health care systems. I shall briefly outline why in this section.

4. Although there are no other directly relevant studies, I wish to briefly mention more recent studies of high users of health care services published after the commencement of this research. These include high users of emergency care

and primary care to assess for any similar characteristics between FRMUS patients and these other high users of care.

5. Finally, I wish to briefly explore other concepts from the literature which may apply to the phenomenon of FRMUS. My findings show that untreated anxiety and depression do not necessarily apply to the majority of this group of patients. Anxiety and depression may explain an element of patient presentations, but perhaps less why patients are referred frequently. This will lead on to my final thesis chapter which will make some recommendations for future practice and research.

COMPARISONS BETWEEN THE REFERRAL STUDY AND TWO UK STUDIES OF FREQUENT OUTPATIENT ATTENDERS

Without reiterating my outline of these two studies from Chapter 5, I wish to direct the reader's attention to Table 42. This table summarises the key differences in methods and findings between the Referral Study and the two UK studies on frequent attender (FA) outpatient studies (i.e. The London Study(60) and the Oxford Study(59)). Referring to this table, I will briefly address the comparisons between the three studies.

Methods

Design

All three studies used a cohort observational design to identify the patient group under study. This is a useful study design for estimating the prevalence of a condition of interest. However, this design cannot provide any information on outcome relationships and how specific they are to the patient group of interest. As such, I identified two other comparison patient groups and employed a case-control study design to compare FRMUS cases with FRMES and IRS patients.

Table 42. Comparing methods and findings between the Referral Study and the two UK studies of frequent outpatient attenders (London Study and Oxford Study)

Study methods	Referral Study	London Study	Oxford Study
Main study design	Cohort and case-control	Cohort	Cohort
Study period	5 years	3 years	1 year
Population sampled	5 general practices	12 hospital trusts	3 gastroenterology clinics
Total population	14,034 referred patients	2,093,604 OPD attenders	2530 OPD attenders
Definition of 'frequent'	≥3 referrals in five years	top 5% of OPD attendances in three years	≥4 OPD attendances in one year
N frequent OPD attenders	1,312 (+898 IR)	61,232	762
Case note review	1,312 (GP case notes); 1059 reviewed [+630 IR]	Random sample of 400 (hospital case notes); 361 available for review	762 (assessed by gastroenterologist), 128 not assessed
Prevalence of at least one MUS in frequent outpatient attenders	418/1059 (39.5%) [+82/630 IR, 13%]	97/361 (27%)	159/634 (25%)
Cases identified	293 FRMUS (2 or more MUS episodes)	61 somatisers (2 or more MUS episodes)	50
Comparisons identified	249 FRMES (no MUS), 237 IRS (1 referral for symptoms)	219 'others' (1 MUS or fewer episodes)	nil
Participating cases	193 FRMUS (72.3%)	48 (78.7%)	48 (96%)
Measuring anxiety & depression	PHQ self-report questionnaire, case note documentation	SCAN psychiatric interview, HADS	SCID, Beck depression inventory
Diagnoses of anxiety & depression	64 depression (33%), 67 anxiety (39%), 65 panic (34%) anxiety or depressive disorder 82 (42.5%)	25 anxiety (52%) 20 depression (42%)	15 anxiety or panic (31%), 17 depression (35%)
Health economic analysis	all secondary care contacts, mental health care contacts, investigations in OPD, OOH GP contacts, lifetime total health care contacts (sub-sample only)	OPD contacts, investigations in OPD, indirect costs of illness	nil

Study period

My study collected data on the study groups for the longest period of time of the three studies (i.e. five years). This was more likely to have identified more chronic frequently referred patients as opposed to the more acute episodes of frequent attendance that the Oxford Study was more likely to have identified.

Study sample

All three studies used a "hybrid" method to identify patients using computer data to identify outpatient contacts and specialist opinions for diagnoses of MUS. The London Study and my study both used national NHS data to identify outpatient contacts. The outpatient attendances identified by the Oxford Study were derived from the local hospital system. The secondary care studies identified a heterogeneous group of patients who had come to attend outpatient clinics by all possible means (e.g. GP, self, community, A&E, other hospital specialists, etc.). The main sampling difference between the FA outpatient studies and the Referral Study was the setting. By identifying FA outpatients from secondary care, they do not inform us about frequent referrals for MUS from primary care.

Frequent referral versus frequent attendance

At this point it is important to clarify the key difference between the study of FR patients and the study of FA patients. By definition, frequent referral involves the patient consulting a GP and the GP referring the patient to an outpatient clinic and the specialist providing an opinion to both patient and GP (whether this is the same, or interpreted similarly, is unclear). FR is not solely a patient driven phenomenon, and any future intervention informed by the results of the study would not only target the patient, but also the GP, and perhaps even the specialist. Frequent attendance to an outpatient clinic may be more patient driven by accident and emergency attendances or calls to out of hours services such as NHS 24. Alternatively, frequent attendance can be specialist driven by asking for the patient to return for review, or for the GP to refer again if required. Effectively, the FR group may be more homogenous in terms of

their access to outpatient clinics. However, these differently identified patient groups may share similar characteristics.

Case definition

'Frequent'

Each of the three studies adopted a different definition or threshold for what constituted 'frequent'. For all three studies, the reasons why these definitions were chosen were based on:

- identifying patients with above average outpatient use
- obtaining patient numbers required to achieve power
- pragmatic grounds that only a certain number of patients can be managed effectively in one research project given the resources allocated to the project.

Medically unexplained symptoms (MUS)

My operationalised criteria were similar to the London Study. 'Unexplained' symptoms were determined if a specialist had documented no, or inadequate, physical cause for patient symptoms. The strength of the Oxford Study was that a specialist actually assessed the patient as part of the study and directly provided their clinical opinion. Reid and I interpreted and extracted the specialists' opinions from the case notes which likely introduced some rater bias.

Cases

The Oxford Study defined cases as those patients who had four outpatient attendances within a year and one MUS outpatient attendance within the following 11 months. This definition was more likely to identify acute attendances for MUS rather than repeat or persistent attendances for MUS. However, their 50 cases were recruited from the 159 cases with MUS (31%) as being the first 50 to be diagnosed with MUS, rather

than by random selection of the entire FAMUS sample. This may have introduced selection bias.

The London Study defined cases as a random sample of the top 5% attenders of those who had attended at least one outpatient appointment in 1993, with two or more subsequent outpatient attendances for MUS. I identified patients who had been referred three or more times in five years and where at least two of the referral episodes were for MUS. These two studies were more likely to have identified more chronic FR/FA patients who were consulting outpatient specialists for MUS over a longer period of time.

Prevalence of medically unexplained symptoms

Due to the difference in operational definitions, the prevalence of MUS in these three groups is difficult to compare. Even so, the London and Oxford studies both showed that approximately a quarter of their FA outpatients attended for MUS. The FR patients were referred for a higher proportion (nearly 40%) of outpatient consultations that were deemed by a specialist to be MUS. This raises the question as to whether GP referrals bring a greater number of outpatient attendances for MUS compared to other means of accessing outpatient services (as previously outlined).

My estimation of the prevalence of FRMUS came to 1.1% of the primary care population aged 18-65 years. This cannot be directly compared as there are no other studies of this group of patients. Interestingly, this is exactly the same proportion found by Brown's pilot study(19). Kirmayer and Robbins' study found a prevalence of 1% somatisation disorder in their Canadian primary care population(253).

Comparison groups

Mine was the only case-control study of the three. As previously described, and indicated in Table 42, there were two control groups: 1) a frequently referred control group of patients with medically explained symptoms (FRMES) to control for the fact of being ill, and 2) an infrequently referred control group of patients with symptoms (IRS) to control for being frequently referred. The FRMES comparison group in the

Referral Study had all explained symptoms according to specialist assessment, and the IRS comparison group had only been referred once in the five years, so the three study groups were distinct.

Although the London Study used the other FAs to act as a comparison group, the definitions of patients were not distinct enough to provide adequate comparisons(61), as the 'others' included patients with one MUS episode. I excluded FR patients with only one MUS episode. The merit with my approach was that there was a clear difference between cases and controls. However, the limitation was that questionnaire data of a larger number of patients was effectively lost.

The Oxford Study of the 50 FAs with MUS(328) was a descriptive study only to identify cases for potential intervention. There were no comparison patients in this study.

Specialties and symptoms

Particularly compared to the London Study, both FA and FR patient groups consulted for similar symptoms (i.e. abdominal pain, back pain, chest pain, and headache) and these were among the highest proportions classified as 'unexplained'. Similar specialties (i.e. gastroenterology and neurology) received high proportions of referrals for MUS in these studies. This shows that these groups share similar characteristics. There is likely to be some overlap between FAMUS and FRMUS. Other similarities included the high proportions of women and similarly reported poor physical and mental health according to the respective general health measures used in each study.

Anxiety and depression

The London Study(208) administered the Hospital Anxiety and Depression Scale (HADS)(331) and Schedules for Clinical Assessment in Neuropsychiatry (SCAN, a structured interview schedule including the Present State Examination or PSE)(330) to diagnose psychiatric disorders. The Structured Clinical Interview for the DSM (SCID) (324) was administered by the Oxford Study. This is a strength of these two studies as psychiatric interviews are considered 'gold standard' psychiatric diagnoses. The

weakness from a research perspective is that it limits the number of patients one researcher can interview at one time.

Although high levels of anxiety and depression were found in the FA patients, there were no comparisons made with the other frequent attenders. If other patients without MUS also have anxiety and depression, then the assumption that this contributes to their FAMUS status is flawed. There was also no assessment of treatment for these psychiatric diagnoses. Both issues are important when considering how the findings inform future alternative management.

I assessed contacts with mental health care services. In finding that the majority of FRMUS patients with anxiety or depressive disorders had high levels of psychiatric and psychological treatment (substantially more than the two comparison groups), any intended future intervention would not solely be directed at the patient. More, it would be aimed at the general practice or outpatient clinic. For example, GP reattribution training as studied by Richard Morris, Linda Gask and colleagues(450-452).

Costs

The 'somatizers' (cases) of the London Study had comparable health care use and costs to the 'other' FAs studied, but medical investigations were far higher and more expensive among the somatizers(61). My findings supported this, in that the difference in number and cost of investigations ordered for FRMUS patients was statistically greater compared to those ordered for FRMES patients. GP out of hours contacts and costs were also considerably greater for the FRMUS patients compared to the other patient groups.

The strengths of the London Study analysis were that the cost of outpatient consultations were determined by speciality and based upon national data. Although the health contacts included in this economic analysis were relatively few, it had good accuracy including an element to reflect the cost of capital and support services. Social care services, time taken off work due to illness, personal expenditure and informal care were also costed. The inclusion of social costs is rarely studied, but is useful from a wider population perspective. In my opinion such costs warrant greater

attention for future studies. The London Study provided no indication as to whether other FA patients might also be receiving high levels of social services and benefits.

In contrast, the Referral Study also used national data to cost a more comprehensive range of health care contacts including: inpatient admissions, A&E attendances, mental health contacts, all investigations conducted in the outpatient clinics, as well as GP OOH care. I used weighted inpatient and outpatient costs rather than outpatient specific costs. My study provided an estimate of the magnitude of all secondary care costs over five years of a larger study sample; the lifetime costs provided an estimate of how much health care resource some FRMUS patients have used. My study indicated that both FRMUS and FRMES patients had high level of benefits received from the government.

No costs were assessed by the Oxford Study.

General Practitioner opinions

Of interest was that 93% of GPs, surveyed by Reid and colleagues, stated that MUS were difficult to manage in general practice(25). Although 84% agreed their role was to act as a gatekeeper to prevent inappropriate investigation, 64% said they would likely refer patients for further investigation. This was in line with the Referral Study where 61% of FRMUS patients were considered to have problems which posed at least a little difficulty to GPs, with a quarter rated to be 'moderately' or 'extremely' difficult to manage. This was considerably and statistically more than the two comparison groups.

Summary of comparisons between the studies

Strengths

There were several strengths of the FA outpatient studies which included:

- direct specialist opinions of MUS in the Oxford Study
- good inter-rater reliability of the operationalised criteria used in the London Study for case note reviews(329)
- use of 'gold standard' psychiatric interviews enabling accurate DSM-IV diagnoses of anxiety, depression and somatoform disorders (I did not assess for the latter)
- good response rates of over 70%
- measurement of indirect costs in the London Study

Weaknesses

There were several weaknesses of both the FA studies. These were that they:

- were observational cohort studies
- assessed small numbers (48 in each study)
- had no or inadequate comparison groups to determine if their findings were specific to the group they were studying, so the findings were inconclusive and more hypothesis generating in nature
- confounding variables had not been assessed as a source of bias, e.g. how did the patient end up attending the outpatient clinics (self, GP, specialist, other), or what might the influence of deprivation on these findings have been?
- extracted information from hospital records, which often do not have documentation from other hospitals, or health care organisations. The benefit of basing my study in primary care was that GP case notes had documentation

of all health care contacts from a range of health services and organisations for each patient.

Finally, specifically to the London Study, the economic analysis did not include hospital admissions or other substantial secondary care costs. This meant the most substantial expense was not accounted for. Costs were further underestimated by excluding health resources used out-with the hospitals under study during the same time frame. Although Reid's survey of GPs about MUS was interesting, it did not ask GPs about specific patients.

Unanswered questions answered by the Referral Study

Anxiety and depression

Although substantial anxiety and depression was diagnosed in the cases of the two FAMUS outpatient studies, these studies failed to account for the fact that the other frequent attenders may also have been anxious and depressed. The Referral Study has shown that FRMUS patients have more anxiety or depression than FRMES or IRS patients.

So does this mean that inadequate treatment of anxiety or depression in patients with MUS is a key contributing factor to high outpatient contacts? The Referral Study found that this was not the case for the majority of FRMUS patients, as over 61% of depressed or anxious patients were receiving 'adequate' treatment for anxiety or depression.

Health care use and costs

The London Study calculated an accurate estimate of the use and costs of outpatient attendances and investigations. The Referral Study was able to support these findings, and further provide estimates of inpatient costs and some primary care costs (particularly for the lifetime sample). I was able to address the issue of acute and chronic outpatient contacts for MUS, not only by the longer five year study period, but

also by conducting a lifetime case note review to show that the majority of FRMUS patients had a long history of consulting doctors for MUS. This showed FRMUS was a chronic problem for some patients and was not being adequately addressed as evidenced by frequent referral and high levels of other health care contacts for MUS.

COMPARISONS BETWEEN THE REFERRAL STUDY AND STUDIES OF FREQUENT ATTENDERS TO PRIMARY CARE

The lifetime data for the Referral Study indicated that some FRMUS patients may also frequently attend general practice. There are no other known UK studies, or studies conducted in health care systems similar to the UK, which have looked at the interface between primary care and secondary care for patients with high health care contacts in both settings. There have been several conducted in America. However, as emphasised previously in Chapter 5, American studies of high users to both primary and secondary care services are difficult to compare with FRMUS patients in the UK, as patient attendance to secondary care in America is often more patient driven. Issues of insurance and patient access confound patient attendance and number of health care contacts. In spite of the differences, the following studies raised some interesting findings which may have some relevance to the Referral Study.

The Seattle Study

My findings contrasted with those of Katon and colleagues(321) (as described in Chapter 5), who found that their 'distressed high utilizer' primary care patients with MUS were more likely to have inadequately treated anxiety or depression. Once these 'distressed high utilizers' had been identified, 'adequate' treatment for their anxiety and depression disorders were commenced by this research group and this included starting therapeutic doses of antidepressants(453), or the provision of an in-depth psychiatric consultation and recommendations for the GP(454). However, although the prescription and use of antidepressants increased, there were no significant differences between the distressed high utilizing intervention patients and the control

patients at six and 12 months in terms of distress, functional disability, or number of attendances with ambulatory health care services.

With reference to the patients studied in the Referral Study, even if my second hypothesis had been supported (i.e. anxiety and depression had been inadequately treated), Katon and colleagues suggest that improved treatment of anxiety and depressive disorders would not necessarily reduce the number of health care contacts. The Seattle and Referral studies suggest that adequate patient treatment for anxiety and depression does not reduce frequent referral for MUS. There are other factors to be considered which perpetuate high use of health care and frequent referral from general practice to outpatient clinics for MUS.

The Michigan Study

For completeness, I will briefly mention the study of 'high utilizing somatizing patients' by Smith and colleagues (previously referred to as the Michigan Study in Chapter 5). The similarity between the Michigan Study and the Referral Study was the concept of identifying a patient group with MUS using the "hybrid" method. The Michigan Study identified patients by high numbers of contacts recorded in health maintenance organization (HMO) computer data and applied a complex set of rules to case note review(318). Since the earlier publication, Smith and colleagues have published two more recent papers about their method for rating case notes to identify high users of ambulatory health care with MUS(258;367).

However, there were several shortcomings the Michigan Study. The operationalised criteria applied to the case notes were extremely detailed and involved a series of scoring rules. Some of the diagnoses included as 'non-organic' were questionable e.g. migraine, gastritis and duodenitis. Specificity was poor and there was a high false positive rate of MUS. The ratings were only conducted for a one year period, which was unlikely to have differentiated chronic from acute presentations.

The greatest flaw with the Michigan Study was that it made no contact with the patient, or other physician, to confirm 'somatisation' as identified from the case note ratings. Anxiety, depression and somatoform diagnoses made from this study relied not only on documentation of symptoms in the case notes, but also the duration of

symptoms (which from my experience was unusual). It is likely this method missed a considerable number of patients with diagnoses of anxiety, depression and somatisation.

In summary, it is difficult to contrast my findings with the American studies for the reasons previously given. Nevertheless, I am satisfied that my method of identifying FRMUS patients missed very few eligible patients, and that those who were identified were accurately categorised using criteria with good inter-rater reliability. The Michigan Study can not be so assured.

The Seattle Study and the Referral Study have shown that adequate treatment of anxiety and depression for primary care patients with MUS does not necessarily reduce the number of health care contacts. Further research is required on the basis of these two studies to determine what further can be done to reduce the health care contacts of patients with MUS.

Reviews of other frequent attenders to primary care studies

There are numerous other primary care studies relating to FA for MUS which I could cite. However, the body of literature about the prevalence and characteristics of frequent attenders to primary care clinics is extremely large and not of specific relevance to this thesis. I have outlined some of the key relevant studies in Chapter 5, as well as summary points from a review conducted by Gill and Sharpe in 1999(174).

Since the 1999 review, an update was published by Vedsted and Christensen in 2005(455), with a particular focus on methodological considerations. Similar findings to the 1999 review were found, where frequent attendance to general practice was associated with chronic physical conditions. Although the strongest association with frequent primary care attendance was psychological conditions, they discussed how a combination of physical, psychological and social problems brought a patient to see a GP. The majority of frequent attenders in the studies reviewed were women, but gender was not necessarily associated with frequent attendance.

My interest in this review was the fact that they could find no generally accepted definition of 'frequent attendance' (in general practice). They proposed that future

research should adopt a common, transparent and operational definition of frequent attendance which should include:

- the period of counting
- the threshold used and the denominator (population, listed patients or attenders)
- an exact description of the contacts counted, and
- controls which are sampled similarly, but distinctly different for the variable under measure.

My study ticks all of these boxes.

Regardless of the large body of literature about frequent attenders to primary care, the reviewers summarised that identification and classification remains unsystematic and care inconsistent across medical settings. They acknowledged that it may not be possible to have the same definition of frequent attendance in different healthcare systems. This observation could bring into question the generalisability of findings for this, and other, studies of 'frequent' health care contacts.

STUDIES OF FREQUENT ATTENDERS TO EMERGENCY DEPARTMENTS

Acknowledging that patients attending emergency departments (ED) generally present as a result of self referral, I was still interested to contrast the characteristics of the FRMUS patient group with those of frequent attenders (FA) to ED. Reviewing the literature, MUS in these studies was rarely specifically addressed. Although the FAED patients were also high users of primary and other secondary care services for symptoms, there were indicators suggesting that these frequent attenders were a distinct group from FRMUS patients. In the FAED groups there were high proportions of males, high rates of alcohol abuse, and the prevalence of other frank and often severe psychiatric diagnoses was also high(456;457). My FRMUS group were predominantly women, were excluded from this study if severe mental illness was present, and did not have particularly high rates of alcohol misuse. Hansagi and

colleague's study showed that ED attendance was more often due to chronic ill health and frequent attender mortality was high(67).

On the surface, the FAED studies provided no complementary information about the phenomenon of FRMUS. However, I would add that it was more a comment made by Williams and colleagues(456) which I found of particular interest. Their study found no evidence of a coordinated response to the FAED patients. Despite the high use of most health care services, the GPs, mental health practitioners, other specialists and ED doctors providing health care to these FAED patients had no direct communication or systematic sharing of health care information between them. Could this lack of information sharing between GPs, specialists and FRMUS patients partially explain the phenomenon?

OTHER POSSIBLE FACTORS THAT MAY CONTRIBUTE TO THE PHENOMENON OF BEING FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS

Childhood adversity

I documented childhood abuse or neglect if available from the case notes. However, I did not specifically study this issue. Evidence from the case notes showed that there was more documented abuse in the records of FRMUS compared to the other two patient groups. However, this was likely an underestimate for all study groups as patients may not disclose this, or ask doctors not to document it. I wondered if this might have been a factor worth exploring further as (one of many) contributing factors for FRMUS.

I have already outlined 'the Manchester Study' in chapter six of this thesis (see page 76) which quantified high health care contacts for those identified to have suffered childhood adversity. However, a later study, also conducted by Francis Creed's team in Manchester, was undertaken to determine psychological mediators of the relationship between childhood adversity and frequent primary and secondary care medical consultations(336). This study identified consecutive attenders to neurology, cardiology and gastroenterology outpatient clinics and asked them to complete the

Hospital, Anxiety and Depression Scale (HADS(331)) and other instruments relating to illness beliefs and general health. Their case notes were reviewed for 18 months of medical consultations, and operationalised criteria to identify MUS were applied. Participants were also interviewed using the CECA (Childhood Experience of Care and Abuse) interview schedule.

The response rate was 129/211 (61%), which for such a sensitive topic was very good. Of note was the fact that approximately 60% of participants had been referred from primary care. The study tested a series of somewhat complex hypotheses, but the three of interest to this thesis were as follows:

1. *Outpatients reporting childhood adversity would have a greater number of medical consultations* (defined as outpatient, emergency, and primary care visits), *than outpatients who did not.* This was supported where cases had a median of 16 visits with a specialist, ED doctor or GP, compared to 10 in the other group.

2. *Anxiety or depression would be associated with childhood adversity.* This was supported as childhood adversity was correlated with depression, health anxiety, and a greater number of symptoms.

3. *Childhood adversity and medical consultations would be mediated by depression and health anxiety and present only in those outpatients with MUS.* The study found a clear excess of childhood adversity in patients with MUS compared to those with symptoms related to organic disease. Depression and the number of symptoms attributed to illness mediated the relationship between childhood problems and frequency of medical consultations.

The study concluded that frequent consultation, particularly in outpatient clinic services, can be predicted by a complex model. This includes childhood adversity, depressive symptoms, multiple MUS and attributing symptoms to illness. Although the study group asserted that antidepressants and CBT would help these patients, they did not assess the treatment these patients were already receiving. A third of FRMUS patients had depression, but substantially more had depressive symptoms. My assessment of FRMUS patients IPQ scores indicated that they also perceived their symptoms as similar to those patients with organic disease. I think this study has the right idea that consultation and MUS cannot be 'explained' by any one answer. A

series of complex interwoven factors apply to a heterogeneous group of people with MUS.

General Practitioner perceived patient pressure for referral

Trying to shed some light on the interaction between patient and GP prior to referral, Little and colleagues(458) assessed 847 consecutive primary care patients before their consultation with the GP, and the GP recorded medical need and the outcome of the consultation. Patients were asked their reasons for consultation, and if they were expecting an examination, prescription, investigation and referral. The strongest predictor of whether any of the four actions were taken during the consultation was the GP's perception of medical need. However, 27/125 (22%) patients with no or slight medical need were referred to a hospital specialist, and nearly half (99/216, 46%) of the investigations ordered during this study were for no or slight medical need according to the GP.

This study concluded that, although GP behaviour is strongly associated with their own perception of the patient's medical need, a considerable minority of referrals and half of investigations were more due to perceived patient pressure. This supports Ring and colleague's findings(459) that only a third of patients attending a GP with MUS requested a somatic intervention, including referral. There was evidence that patients had tried to engage GPs in conversation about the reality of their distress, but GPs responded symptomatically. What patients describe and how they describe their symptoms can be interpreted in many different ways by their GP. Salmon and colleagues found that primary care doctors were more likely to offer medical care to patients' with symptom presentations rather than the patients pressurising GPs for medical care(460).

Lost in translation

The above assumption made by Little and colleague's study leads to my final conjecture for this chapter of the thesis. That is, that the language or communication between patients, GPs and specialists, changes, or gets translated differently as the

patient moves between the community to the primary and secondary care settings; a form of 'Chinese whispers' if you will.

A study of GP referrals to gynaecology outpatient clinics of women with menstrual problems by Warner and colleagues(42) found that 38% of women attending their GP reported excessive menstrual bleeding. Yet, 60% reported it as the reason for attending an outpatient clinic, and 76% of GPs gave it as the reason for referral. Second only to failure to attend, hysterectomy was the most likely outcome from a GP referral to the gynaecology outpatient clinic. Dysfunctional uterine bleeding was diagnosed by a specialist for a third of the women who neither reported very heavy or excessive bleeding as a severe problem nor gave bleeding as reason for attending the clinic. In those referred by their GP for something other than excessive bleeding, dysfunctional uterine bleeding was nevertheless diagnosed for 29%. This study found discordance from what the patient originally consulted the GP for and the rationale for referral of women to gynaecology clinics. In over a quarter of cases, the patient and GP disagreed as to whether excessive menstruation was a reason, with the doctor four times more likely to be the only one citing this. This is an interesting study considering my findings that one quarter of the FRMUS women had surgery for a hysterectomy.

A dissonance in reason for consultation and referral between patient, GP and specialist may partially contribute to why patients return to the GP, and get referred again to a specialist. Perhaps for a proportion of patients, there is a lay understanding of what might be regarded by doctors as a valid reason for attendance at a clinic. Alternatively, the problem may lie more in a communication breakdown between what the patient feels and says, and the GP and specialist hear and interpret. This misunderstanding between the three (patient, GP and specialist) may be a contributing factor to perpetuating more GP consultations, more referrals and more reviews for a small percentage of patients whose needs were not originally understood or met.

CHAPTER 20. IMPLICATIONS OF THE REFERRAL STUDY

As a result of conducting this research, and finding out more about the characteristics of this group of FRMUS patients, I am left with more questions than answers. However, I have learned a great deal more about general practice at the coal face. General practice is a busy setting where one GP can be responsible for thousands of patients. Yet, the GPs I spoke to knew a great deal about their patients' physical, emotional and social problems, and I was impressed by how much was already being done for FRMUS patients both in general practice and by other allied health and community services. It still does not seem adequate, and this study has shown that FRMUS patients continue to be referred to hospital for symptoms that cannot be treated effectively in a hospital setting (MUS).

Perhaps any interventions we try to implement for this patient group may never be enough. There seem to be a multitude of reasons which might contribute to the frequent referral of a small proportion of primary care patients for MUS. One intervention or medication is unlikely to solve the problem. Nevertheless, by collecting the data and speaking to patients and GPs, I have become aware of some limitations in the current health care system. Specialists were not directly involved in this study. However, I think this would be an important inclusion in a future study to determine the perspectives of all three involved in the FRMUS phenomenon (i.e. patient, GP and specialist).

Some practical recommendations for clinical practice are suggested in this section including raising the awareness of FRMUS and management of patients in primary care. Future research recommendations are outlined in this chapter including intervention studies and early detection of patients developing a pattern of FRMUS. These practical and future research recommendations will be outlined in this chapter.

RECOMMENDATIONS FOR CLINICAL PRACTICE

Firstly, I wish to begin this section with a list of system factors that I assert contribute to the phenomenon of FRMUS. This combination of observations and hypotheses are listed in Figure 30 below.

Figure 30. Systemic factors contributing to frequent referral for MUS

- Patients can register with one or more practice rather than one GP
- Patients often consult and are subsequently referred by several different GPs
- Consultations are time limited
- There is no systematic recording of referrals or their outcomes in GP computing systems or patient records
- Summaries in GP records are often not up to date and tend not to record referrals and negative investigations deemed MUS
- Patients often see different hospital specialists in different outpatient clinics
- There is no systematic recording of investigations or referral episode outcomes in hospital computing systems
- Doctors do not routinely ask patients if they have consulted other doctors or been referred to other specialties in recent times
- There is often no one responsible coordinator of FRMUS patients' care
- There is no centralised patient record accessible for both GPs and specialists to use

Raising awareness of patients frequently referred with medically unexplained symptoms

The difficulty ratings and lifetime data indicated that some FRMUS patients may also be frequent attenders to general practice. It is no longer my belief that GPs are not aware of these patients. However, I would suggest that GPs are not aware of exactly how frequently a patient has been referred or what the outcomes of these referrals have been. Conversely, although I did not speak to specialists as part of this research, it was my impression from reading specialist accounts of outpatient consultations that

hospital doctors knew FRMUS patients, and their history of MUS, less well, if at all. For example, specialist registrars move placements as part of their continuing training on average every six months.

FRMUS patients often consulted and were referred by a number of different GPs. When reaching hospital outpatients, the specialists involved in these patients care did not seem to be aware of the others' involvement. A similar observation of chronic somatising patients had been made by Bass and Murphy(240). The findings from this study suggest there is a need to heighten the awareness of referrals, particularly frequent referrals, for MUS. There is also a need to raise awareness of how many doctors and other allied health practitioners are involved in one person's care.

However, new or expensive interventions may not be necessary when there are resources currently in place which could be used more effectively. I have a number of practical suggestions which may help raise practitioners' awareness of FRMUS in both primary and secondary care settings.

Consistent and standardised case note summaries

Although 'paper-lite' and 'paper free' patient records are being phased into general practice, this will take a very long time and there is no evidence of it in four of the five practices that participated in this research. Until this comes into full operation, many GPs rely on the medical history summary at the front of the patient's paper case notes, especially if the file is thick or more than one volume. An up to date summary of patient's health care contacts and outcomes is essential, as otherwise documents such as referral and discharge letters get filed and buried in the notes. However, summaries are not often up to date due to practice resource restraints. Summary information is also inconsistent as to what and how it is recorded across the practices.

High users of health care can have several different medical records in general practice, hospitals and other health care settings. This might become even more of an issue if the Department of Health proposal goes forward for patients to be able to register with more than one practice.

Asking the right questions

A full case note review is not often possible before each patient consultation. Summaries in the notes are often not up to date and rarely include the number, or outcomes resulting from, contacts with other health care professionals. Getting relevant information for a consultation with a patient involves asking the right questions(394). A simple solution would be for doctors to consider including a simple question with each medical consultation as follows: *"Have you seen or been referred to any other doctor recently?"* Identifying all practitioners involved in the patient's current care might bring about better coordination of patient care.

Previous studies have also recommended that GPs include questions about emotional, social and family factors with each consultation; a biopsychosocial approach(461-466). A consultation should ensure to ask patients about their main physical problem and also enquire about current problems at home, work, or social life(393). Robinson and Roter found that if GPs asked, most psychologically distressed or somatically presenting patients would disclose their psychosocial problems(393).

An automatic system to flag patients

Referrals and outcomes

GPs are inundated with paper copies of various guidelines, let alone notes, piling up on their desks. Doctors are human, and it is also easy to forget previous consultations and management plans for individual patients. As such, it is likely that the most useful future aids for identifying referrals will involve information technology in the form of data management systems[21].

Although GP detection and treatment of anxiety and depression was higher for FRMUS patients in this study, doctors may be less aware of exactly *how* frequently patients have been referred, and the outcomes of those (i.e. MUS). This may be in part due to patients consulting different GPs and seeing different doctors in the hospital system. Currently however, other than by going through volumes of case notes, there

[21] Anecdotally, in presenting this work to GPs, they stated that they did not want any more clinical guidelines about patient management of MUS. Their desks are already full to overflowing with paperwork, and another set of guidelines would likely be forgotten at the bottom of the pile!

is no easily obtainable data for doctors to review total referrals and outcomes for each patient.

A system operating in both general practice and hospital computing systems to automatically record these patients would help busy doctors keep track of patient referrals and outcomes. A similar suggestion was put forward in 1999 by Bass and colleagues as a result of their study of frequent attenders to gastroenterology clinics(59;328).

Once identified, retrieval of the patient's case notes may be warranted for review of their referrals and management. Given the finding that a third of FRMUS patients and the majority of FRMES patients were receiving inadequate treatment for their anxiety or depression, identification of all FR patients would also enable screening for any disorders of anxiety or depression. In general practice, quick and simple measures such as the PHQ or HADS could be administered.

This principal of 'automated flagging' could also be applied to other factors of interest. For FRMUS patients, indicators such as non-attendances to outpatient clinics, and numbers and outcomes of particular investigations (such as MRI and endoscopy), could be recorded in patient records. Patients with a certain number of these tests or a certain number of non-attendances could be flagged and their notes reviewed.

Negative investigations

Previous studies have suggested that negative investigations may play a role in reassuring patients with MUS(467-469). A recent randomised controlled trial by Howard and colleagues showed a significant reduction in health care use and costs for those patients with chronic daily headache offered a scan compared to those who were not(470). Conversely, Dowrick and colleagues found patients were not necessarily reassured by negative test results, and preferred an explanation from their doctor(471). In fact another study found that some patients had their beliefs of disease confirmed by the mere fact of having an investigation and misinterpreting what the doctors said to them about the result (negative or not)(472). Limiting the use of investigations to specific indications and avoiding repeated and invasive investigation should be the aim, along with avoiding referral elsewhere unless clearly necessary.

Non-attendance to outpatient appointments

Few studies have researched reasons why patients do not attend (DNA) their appointments, and which patients tend to do this most often. FRMUS patients were more likely to DNA their outpatient appointment than the other two patient groups. Ideally any non-attendance at an outpatient clinic should be flagged for a patient case note review and follow-up. However, I acknowledge the limited resources to be able to do this in practice. As such, general practices and hospital clinics could again set a certain number of DNAs over a period of time to flag up the patient for review. These patients who are unable to make their appointments for what ever reason may in fact be a group of patients with unmet need.

How this might be done in General Practice

General Practice computer records

As described in Chapter 8, page 93, the majority of general practices in Scotland use the GPASS general practice computing system, or equivalent. There are two functions already built in to this system which have the ability to flag referrals but are inconsistently used in general practice.

1. A 'referral' tab in the 'history' section of GPASS enables direct entry of referrals made from the practice. If this data were collected, using this function would enable quick retrieval of the number, nature and outcome of referrals for each patient registered with the practice. This could then be linked to ISD secondary care data. However, of the five participating practices, only two of the five systematically used this function, one only used it for some referrals. Two did not use the 'referral' function at all. This is important basic information to identify FRMUS patients in the practice.

2. 'Second Opinion' software is installed on most general practice computing systems. This software creates referral letters drawn from existing data on GPASS (and includes information such as CHI, past medical history, and current medication). Referral letters can take one minute to create as all GPs have to enter is the reason for referral. By using Second Opinion, referrals are sent electronically direct to outpatient clinics, as well as being automatically recorded

with ISD (as SMR0 data). Practices also receive email confirmation when the referral letter had gone through.

As of 2003, 10 of 15 (67%) health boards in Scotland had Second Opinion and all practices had received training. However, only 20% of practices were actually using it(362). This is primarily due to the fact that there is no link or transfer of information from Second Opinion back to GPASS. If there was some way of linking between the two, more practices would likely use it, and more referrals would be systematically recorded to enable the flagging system of referrals.

Ideally, all patient health care contacts and outcomes would be linked to a centralised medical record which automatically updates patient information. It seems logical that an institution such as ISD might be in a position to develop this system. However, this still relies on dedicated and systematic data entry.

Previous government suggestions of patients carrying their medical health care records on a "smart card" might be a solution to coordinating patient health care contacts (but a radical and expensive one, some might argue). These smart cards have been in limited use in Europe and the United States since 1982, and several barriers including lack of infrastructure, low patient confidence, competing standards, and cost continue to thwart the progress of this concept(473).

Management in General Practice

GPs are well placed to play a crucial role as coordinators responsible for patient care. Alternatively this role could also be fulfilled by a nurse practitioner, practice manager or even a GPASS data manager who could note when the referral threshold had been reached and flag the patient for a review.

I am not suggesting that a potentially difficult patient should just see one GP, as this many not be therapeutic for the GP or the patient. (This may partially contribute to why single-handed GPs were observed to have high proportions of referrals for MUS). What I am suggesting is that someone in the practice needs to be aware of the contacts

and coordinate them more effectively, to minimise future unnecessary referrals and investigations.

Other approaches to minimise secondary care contact for patients with MUS and maintain the patient in general practice may include:

- for those not on antidepressants, prescribing them might be the first line of treatment if the patient was willing. Research has shown that patients with 'unexplained' symptoms are willing to try psychological treatments for their symptoms(474).
- special status or extended consultations for frequent attenders(475).
- regularly scheduled consultations with the GP or practice nurse to review the patient's progress.
- in-house referrals to GP colleagues for second opinions before referring patients to secondary care(476)
- specialist clinics run by GPs (GPSI) or nurse practitioners with an interest in MUS to review and manage the needs of FRMUS patients. This could include triage of outpatient referrals(477). However, the evidence for this in primary care is almost non-existent and would require further research into clinical effectiveness and patient satisfaction(478).

Multidisciplinary management of patients frequently referred with medically unexplained symptoms

For those FRMUS patients already trialled and unaided by different doses and types of antidepressants, and indeed, for the 57.5% of FRMUS patients with no anxiety and depression, alternatives need to be considered. GPs, practice nurses and practice staff require training and further resources to bring about effective management of MUS in primary care. Although GPs are probably in the best place to coordinate the care of FRMUS patients, they must be supported.

For the patients with anxiety and depression, there needs to be improved access for GPs to liaison psychiatry and other mental health care services(479). An innovative

approach suggested by Mayou and Sharpe was to use specifically developed clinics for the management of MUS in which physicians work closely with psychiatrists and psychologists(480). This format of specialist outpatient clinic would provide a multidisciplinary approach to the management of MUS, regardless of the speciality to which the patient initially presents.

A non-randomised study which analysed the cost effectiveness of referral to a behavioural medicine clinic showed that the costs of health care for the participating somatising patients had reduced by approximately 25%(481). Further preliminary work in Israel showed a multidisciplinary referral clinic for primary care frequent attenders was able to modify patients' illness behaviour, decrease the number of consultations, referrals, hospitalizations and the costs of medical investigations(482). The members of the clinic team comprised a GP with psychotherapy skills, and a social worker, with a supervising senior psychiatrist who had no direct patient contact. The intervention commenced with a detailed medical and psychosocial interview, a physical examination, team discussion (including the patient and family doctor) and reframing of symptoms in the context of the patient's current or lifetime stressful events. This was administered over 10 visits of one hour duration and included a combination of pharmacological and psychological therapies tailored to suit each patient. Patients had a case manager coordinating their care. As a result of completing the 'contract' of care, patient costs reduced from US$4035 per year to US$1161 the following year, indicating a reduction in health care contacts, especially number of investigations. GP satisfaction with the doctor-patient relationship also markedly improved as a result of the intervention.

However, these studies of multidisciplinary clinics were not randomised controlled trials (RCTs) and further work is required. This leads on to the next section of this thesis, which is to outline ideas and suggestions for future research in this field.

RECOMMENDATIONS FOR FUTURE RESEARCH

Intervention studies

The Referral Study has indicated that FRMUS is not just a specific patient problem or characteristic. Although some interventions may be directed at the patient to improve their mental and physical health, there also needs to be a more strategic approach to tackle some of the inadequacies of the current health care system.

My first recommendation would be to trial some of the above suggestions regarding change in clinical practice. To summarise, this would involve studies to test my hypotheses that FRMUS patients:

1. could be identified through an automatic flagging system, and that this detection would result in reduced inappropriate referrals to secondary care and lower costs (this could involve a randomised trial of the intervention in a selection of representative general practices)

2. referred to another GP, or specialist nurse within the practice, rather than to an outpatient specialist, would be equally satisfied and have similar, if not better outcomes than those patients with MUS who still get referred to hospital.

3. would have fewer referrals for MUS if given scheduled, extended and problem focussed primary care consultations with a GP, GPSI, or nurse practitioner (along the lines of similar projects looking at the role of nurse practitioners currently underway in Michigan, America(483), and another in the Netherlands(484)). By problem focussed, I not only refer to physical and mental health problems, but wider social, environmental and economic problems the patient may be grappling with. This is perhaps more along the lines of the multidisciplinary clinics previously mentioned.

There is evidence that strategies are available which can reduce high levels of health care use and costs for patients with MUS. A series of studies in Arkansas(485;486) indicated that identifying patients with somatisation disorder to their GPs led to significant reductions in treatment costs. The intervention in these randomised controlled trials consisted of a phone call and consultation letter, following a

standardised psychiatric consultation, which instructed GPs to make four to six weekly appointments with patients and to take their symptoms seriously. They were also told to avoid unnecessary investigations, procedures and referrals. This intervention resulted in improved patient reports of physical functioning and reduced annual median costs of patient's medical care by 33%(487).

Alternative identification of patients frequently referred with medically unexplained symptoms

General Practitioners

Anecdotally, GPs in this study often asked if a particular patient was 'on my list'. The patients they named tended to be frequent attenders to the practice, and not necessarily to secondary care. However, in one instance, a frequent attender to selected outpatients was named by a GP, but this patient had not met the selection criteria due to having one MUS referral episode during the study period. On discussing this case, the GP felt that the specialist had 'medicalised' the patient's problems, and that more referrals had been for MUS. Although several GPs had offered, I did not directly seek their opinion as to who the FRMUS patients were in their practice. It would have made for an interesting exercise to compare GP identification of FRMUS with those identified by ISD and case notes. Although there is a large body of research indicating poor GP detection of depression(148;151;161;488-491), there is little which has assessed GP's awareness of patients with MUS(18;137;347), and none as far as I am aware of frequently referred patients with MUS.

Costs

A recent German study of high utilising inpatients identified their sample by two year inpatient and outpatient health care costs(341). Based on average per capita expenditures of approximately €700 (£471) for outpatient attendances and €1400 (£943) for hospital care, the study defined high users as those who consumed ≥ €2500 (£1684) of inpatient and outpatient services over two years. The FRMUS patients

described in the current study cost a mean of £946 per year (thus £1892 for two years for inpatient and outpatient costs only).

High medical costs have also shown success in identifying high utilising patients with depression in primary care(492). Cost may well be an efficient means to operationalise identification of frequently referred patients. An organisation with centralised activity data, similar to ISD, would be the ideal provider of such costs. This would certainly be feasible for American studies given the country's emphasis on insurance claims and payments.

Primary care contacts

Demers and colleagues found that patients who consulted a greater number of GPs, received more specialist care and had 10 times more medical services and costs than the general population(239). My lifetime data supported this. However, it would be interesting to count the number of GP consultations a patient had attended before being referred.

Of interest was the observation that FRMUS patients had considerably higher levels of GP out of hours (OOH) contacts than the other two comparison groups. However, of the referrals made for FRMUS patients, OOH GPs made the least, and only 20% of them were for MUS. Hildebrandt and colleagues offered evidence that 'frequent callers' of out of hours GP services have high levels of psychiatric disorders and are high users of hospital services(493). There may be lessons to be learned from an analysis of FRMUS patient interactions with GP OOH services.

There are hundreds of success stories where GPs have contained the management of patients with MUS to general practice. However, these achievements do not tend to be heralded. GPs able to maintain patients in primary care should be acknowledged and rewarded for their sound clinical judgments. Their strategies and skills in managing MUS should be used to educate other GPs who struggle with the uncertainty.

The latter point reminds me of the seminar concept initiated by Michael Balint held regularly for small groups of GPs. The GPs would present and discuss interactions between themselves and their patients during consultations. These and similar groups

could encourage doctors to reflect on their style of relating to patients and help gain a deeper understanding of their patients' and the GPs' own needs in dealing with difficult situations or uncertainty(465).

There is growing evidence that GP awareness raising and training about management of MUS in primary care has improved GP attitudes and job satisfaction as well as patient outcomes(345;450;451;494-496). However, studies have shown conflicting results regarding the effect of GP training on GP initiated health care use or patient care(497;498). Further research into GP group meetings as suggested above may be warranted. This may provide the opportunity for second opinion referrals to a colleague rather than hospital services as suggested previously.

Lessons from the infrequently referred

A search of the literature in PubMed indicates there is a scarcity of research into those who infrequently attend a doctor. Studying attributes of infrequent consulters, or in this case infrequently referred patients) may help advise interventions for frequent attenders or those frequently referred(499). Although this infrequently referred group does not cost the health care service much now, the cost may come further down the line from untreated physical and emotional problems.

The characteristics of the IRS population described in this thesis match the demographic characteristics of low attenders (LAs) to general practice from a 1989 UK study(500). This group had long standing physical, psychological and social problems. Murray and Corney found LA patients felt it was inappropriate to consult a doctor for stress related illnesses. Notably, the LA patient group had previously been more frequent consulters, but had been dissatisfied with the outcome of referrals to specialist services or advice from their GPs, so no longer chose to consult. Although our IRS patients were predominantly satisfied with health care, a quarter were not; and among those who chose not to participate these may be an 'inconspicuously at risk' group.

In the current study, a higher proportion of infrequently referred patients identified by ISD had left their general practice than the frequently referred patients. Perhaps these patients were more dissatisfied with their care and sought care elsewhere, such as

alternative therapists or homeopathic remedies. This study did not set out to assess this. A future study to follow the course of deducted patients and their health care utilisation patterns would provide useful information for both health care providers and policy makers. Along these lines, a study of patient use of alternative therapies for MUS could be quite illuminating in terms of health care sought and total care costs.

There were a number of IRS outliers who sat outside the normal trend of low PHQ and high SF-12 scores. It may be worth studying in more detail the IRS patients with high depression and symptoms scores, and their GPs, to determine why this group of patients have not been referred as often as the FRMUS and FRMES group. Are there lessons to be learned from these patients and their infrequently referring GPs?

Waiting times

Data from the case notes, and comments from the patient self report questionnaire, indicated that waiting lists were generally long and unacceptable. Some patients mentioned that the time they had to wait from being referred by the GP to actually being seen by a hospital doctor actually made them anxious, and in some cases more disabled. Do waiting lists make people (more) sick or (more) anxious? Is this a contributing factor to the FRMUS phenomenon? Further research is required.

'Adequate' treatment of anxiety and depression

A third of FRMUS patients who were not deemed depressed by the PHQ, had been prescribed antidepressants. Further exploration is required to determine why antidepressants had been prescribed for patients who were not clinically depressed. There is evidence that antidepressants are effective in the treatment of FSS such as fibromyalgia, IBS, and other unexplained symptoms, even in those without anxiety or depressive diagnoses(166). However, as previously mentioned in the limitations section of this thesis (see page 247), these reviews mainly included studies assessing the efficacy of tricyclic antidepressants. Further evidence is required specifically on the efficacy of SSRIs for the treatment of MUS.

I would be interested to know if my findings were simply due to the effectiveness of the antidepressant, or if GPs prescribed antidepressants in the hope that they may relieve patients' physical symptoms, or was it that patients were not completely truthful when answering the PHQ, and actually had MDD?

These questions aside, 'adequate' doses of antidepressants or contacts with mental health professionals may not be adequate for FRMUS patients. This group continued to have referrals for MUS, and some had long histories of high medical care contacts, anxiety and depression. A recent study by Chung looked at the effect of different types and doses of antidepressants on health care use(501). He found that, compared with tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs) reduced overall outpatient visits and other prescription drugs. A reanalysis of my antidepressant data may be able to add weight to this finding. Further research is required to determine what defines adequate treatment for FRMUS patients.

One suggestion is to identify frequently referred patients who have never been on, or are not currently, prescribed antidepressants. Once prescribed a therapeutic dose of antidepressant, it would be interesting to determine the effect on the patient's symptoms, PHQ score and number of referrals and other health care contacts. An alternative intervention using a similar methodology may involve cognitive behavioural therapy, or a combination of both problem solving and pharmacological therapies. The key question is what kind of patient responds best to what kind of treatment?

The findings from this study suggest that the issue of FRMUS relates more to a problem with the health care system, and less about detection and treatment of depression. There is a mismatch between what specialist services can provide and what FRMUS patients need. It may be that interactions between GPs and specialist doctors, and/or doctors and patients, require a targeted intervention.

Treatment of anxiety and depression for patients frequently referred with medically explained symptoms and patients infrequently referred with symptoms

Unexpectedly, the FRMES patient group and IRS patients, with depression according to the PHQ, had proportionately far less treatment for their depression than the

depressed FRMUS patients. This is in line, however, with findings of two primary care studies which showed that patients with serious physical disease were up to five times more likely not to be recognized and treated as depressed by their GP than those without physical disease(502;503). Katon and colleagues also found similar outcomes for diabetes patients with undetected or under treated depression(504).

However, there is no similar evidence for the IRS patients. The lower number of contacts with doctors possibly provides fewer opportunities for detection in this group. Future research and clinical resources need to be directed towards those patients who have comorbid chronic medical diseases with depression, and those patients who present less often.

Doctors who frequently refer for medically unexplained symptoms

Three British studies have provided conflicting results as to whether it is pressure from patients that brings about some GP referrals, or somatic treatments, for patients with MUS(458;505), or whether in fact the GPs are the ones initiating medical approaches when the patient is not necessarily expecting them(459;460).

Further study of the referral patterns of solo practitioners would be of interest. There is conflicting evidence about the relationship between practice size and variation in referral rates. One UK study found no difference in referral rates between single-handed GPs and those in partnerships(506), where as another found a significant association between single-handed practices and high referral rates(38). Although, single practitioners tend to be of mature age, have years of experience, and know their patients well, they may have fewer resources available to them than larger practices. Referrals to hospital for MUS may be a support mechanism for solo practitioners to share the burden of 'difficult' patients.

Few studies have looked at the role of the specialist in the management of MUS, and none for the phenomenon of FRMUS. Perhaps in a proportion of the cases, FR is a result of specialists asking the GP to send the patient back to the clinic should certain clinical symptoms or signs arise, or for the patient to reattend for review. In this study I applied a set of operationalised criteria to identify frequently referred patients with MUS. However, an alternative view point would be to develop operationalised criteria

to identify frequently referring GPs or hospital specialists for MUS, i.e. criteria to identify: FRMUS patients, FRMUS GPs and FRMUS hospital doctors.

Prospective longitudinal studies

Available longitudinal studies that have followed the course of MUS provide conflicting findings(17;58;208;304;507). One most recently published by Jackson and colleagues showed a third of symptoms remained unexplained after five years(508). Anxiety and depression were not associated with MUS or worse outcomes. A prospective study of this patient group would not only be able to determine referral outcomes, but also be better able to assess what is going on at the primary-secondary care interface. Why do these patients continue to be referred?

Measures

Patient Health Questionnaire (PHQ)

There is no consensus of standardised measures to detect anxiety and depression in patients with MUS, let alone high health care users with MUS. This continues to limit research in this field. The validity of the PHQ for determining anxiety and depression in British primary care participants has not been tested. It is an instrument that was developed in the United States. However, the language is not overtly 'American', and there is increasing evidence that the PHQ has provided valid diagnoses in other countries such as Belgium, Germany, Saudi Arabia and Spain(378;382;491;509-512).

More importantly, further study is required to determine whether the PHQ is appropriate for high utilising or FRMUS patients. Although Spitzer and colleagues purport patients feel 'comfortable' completing the questionnaire(377), it is my supposition that high users of health care services are less inclined to report or admit depressive symptoms on the PHQ. The results of an intervention study which is using the PHQ to measure psychological problems in frequent attenders is awaited with interest(484).

A standardised measure of demographic characteristics

Aside from diagnostic and general research measures, I would like to see a set of simple, standardised and validated items to measure basic demographic information such as education, employment status, deprivation, etc. These could be included in all health services research to develop population norms and comparisons across similar, study populations.

Further use of centralised activity data

There is a shortage of rigorous studies looking at MUS in patients admitted to hospital. A similar methodology to that described in this thesis could be applied to identify and describe patients frequently admitted to hospital with MUS using ISD inpatient or other centralised activity data. Similar methodology was conducted over 10 years ago on a small number of patients in Denmark using the Danish National Patient Register(48;68). Per Fink's work and findings from the current study may inform a larger study of the more extreme end of health care users with MUS.

Deprivation

Patient deprivation (the Carstairs Scottish Deprivation Categories determined by postcode for this study) often showed some association with FRMUS when linear or logistic regressions (depending on variable) were performed to test for confounding on other variables of interest. Although I did not set out to test the effect of deprivation on FRMUS, this study adds weight to numerous other studies which suggest that deprivation plays a part in high health care use and poor health outcomes (37;281;369;437). A UK study found that socio-economic factors acted as predictors of frequent attendance to general practice(513). Further work is required to explore the extent that deprivation plays a part in frequent referrals to outpatient clinics for MUS.

Larger health economic analysis

The total cost of all health care contacts measured in this study was equivalent to those of FRMES patients. However, FRMUS patients' health care costs reached more than ten times those of the IRS patient group. These findings are in line with a ten year old study, by Labott and colleagues, which found somatisers identified from a pulmonary clinic had comparable costs to asthmatics and far greater compared to other patients registered with the health maintenance organisation (HMO)(44).

Similar to Reid's findings, the frequent attenders with MUS accounted for levels of service use and expenditure comparable with other frequent attenders, but the use and cost of medical investigations in this group were significantly greater(61).

A larger study with a precise and complete health economic focus would be extremely valuable to determine the true cost of the problem from a health services perspective. Total care contacts and care would need to be collected and this should encompass:

- all secondary care costs, including investigations
- all primary care costs, including prescriptions
- personal costs (e.g. alternative therapies), and
- the wider social (i.e. unemployment, benefits, etc.) costs of frequently referred patients with MUS, which is sorely lacking in the literature.

CHAPTER 21. CONCLUSIONS

A COMMON LANGUAGE

We continue to strive for clarification and shared meaning about MUS. Since the commencement of the Referral Study further reviews of the evidence have been conducted(102;105;348;353;354;514-524). The key view points about MUS are that they are:

1. 'hidden psychiatric morbidity', an 'idiom of distress', i.e. somatisation
2. a collection of symptoms which form a 'functional somatic syndrome' (FSS)
3. a product of the interaction between doctor and patient
4. a complex interaction of physiological and cognitive processes in the context of patients' personal lives

All four are correct to a certain extent. The concept remains multi-dimensional and consensus eludes us. Different researchers have different perspectives about what constitutes 'unexplained' symptoms. It is unlikely that we are ever going to be able to find one common term or one common classification. However, the findings of the Referral Study showed that less than half of the FRMUS patients had diagnoses of anxiety or depression and less than half had a functional syndrome. The latter two dot points above may better explain the FRMUS phenomenon for the majority of this patient group.

Fink and colleagues recently proposed a new classification system for identifying somatisation in primary care(525). A recommendation from this paper was that clinicians adopt a "common language", where an appropriate and comprehensive system could be shared by all physicians. A simplistic definition which could be shared by all health care services is the number of times a patient has had contact with them. This study suggests that accurate and dedicated information about the number, type and outcome of health care contacts could help identify patients with unmet needs. Centralised health care activity data, such as that collected by ISD, enables this

method to be used in all health care settings. Centralised data has the potential for cross-referencing between settings so that high use of other health care services can be identified and patient outcomes better monitored and coordinated. This is useful to identify patients with MUS, as well as FRMES patients whose anxiety and depression needs treating.

Recording the number of health care contacts, and the number of outcomes for MUS, could potentially benefit all involved. It would enable early identification of patients developing a pattern of FRMUS. Patient care could then be reviewed to find out what their needs are and how to better meet them with alternative management strategies. This would free up outpatient clinic time to be able to spend more time with the patients who may benefit more from hospital treatment.

This assertion is supported by new UK government initiatives (as stated in the soon to be published white paper) which support better monitoring of chronically ill people in general practice to minimise their need to go to hospital(526). If these proposed government plans go ahead, there will be fewer outpatient appointments for patients to attend, and alternatives need to be sought for FRMUS patients regardless. This strengthens the importance of the roles of the GP, GPSIs and specialist nurse practitioners in primary care.

The outpatient system has reached critical mass. Because of high demand and limited resources, there is currently a quick turnover of patients through hospital outpatient clinics. Doctors are rushed to get through their daily clinic patient load. Patients feel hurried through the clinic. Consultations are limited in time and symptom focussed.

Care provided by the NHS is episode-based. Multiple providers look for the problems they can attend to in the time they have while neglecting others. Some MUS can be chronic illnesses which require unified, and often long-term management arrangements. This study throws caution to the proposal made by the Department of Health that patients should be able to register not just with one GP, not even with one general practice, but with more than one general practice. Although this would give the general population greater flexibility and access to primary care services, it would likely amplify the problem of FRMUS.

THE IMPORTANCE OF THE GENERALIST

The nature of British general practice has changed and continues to change into the 21st century. There are growing GP workloads, but the resources to meet this rising demand do not necessarily reflect this(527). Contracts involve more, and more challenging, targets in order to achieve financial reimbursement. This seems to be resulting in a shift of emphasis from a 'doctor-patient relationship' to more immediate day to day consultation management(528).

Although I have emphasised the importance of identifying FRMUS as early as possible to minimise patient iatrogenic harm and high health care costs, this study has shown that FRMUS patients represent only 1.1% of the primary care population (aged 18-65 years). This figure indicates that the majority of GPs are already doing a good job! Most primary care patients with MUS are maintained in primary care or may be referred infrequently. Referral seems to be a last resort in a combination of strategies that GPs use to manage FRMUS patients in primary care.

Less than half of the FRMUS patients identified in this study had an anxiety or depressive disorder. Of those that did, the majority were receiving treatment for it. The actual therapeutic value of the levels of treatment may be questioned. However, it indicates that doctors are aware and are trying to treat their patients' anxiety and depression. This research suggests that undetected anxiety and depression by the GP is not the main reason behind the frequent referral of a small group of patients for MUS.

THE PHENOMENON OF PATIENTS BEING FREQUENTLY REFERRED WITH MEDICALLY UNEXPLAINED SYMPTOMS

This study has shown that there are spectrums of MUS, and I have targeted a group of patients affected by their symptoms enough to be referred often to hospital for them. Some of these patients have had more severe and prolonged episodes than others.

Symptoms experienced by FRMUS patients may be partially explained by:

- manifestations of anxiety, depression and panic
- acute or chronic stress
- issues around lifestyle (weight, diet, smoking)
- area of residence (i.e. deprivation, financial worries, education, etc.)
- disease, substance or change in the body
- illness perceptions
- life events
- childhood neglect
- abuse

In an ideal world, wider actions to tackle the deprivation and inequalities of health in Scotland may prove more effective than any intervention we could offer within primary care(513). Two questions posed by Ferrer and colleagues(529) may help us to ponder how we might better address the problem of FRMUS:

> "Firstly, how can we make the benefits of basic health care widely accessible to all people within a society? Second, how can needs and services best be matched so that we neither neglect necessary care nor deliver unnecessary care?"

The phenomenon of FRMUS itself may be due to a communication mismatch. This communication problem applies to the interaction between doctors and patients, as extensive work by Salmon, Dowrick and colleagues has shown(277;278;358;459;462;471;530-532). However, there is also a communication problem at the primary and secondary care interface.

These 'unexplained' symptoms are not homogeneous. Neither are the patients who experience them or the doctors that care for them. FRMUS is a multifactorial problem, and I assert that these are multifactorial symptoms. However, we need to stop wasting

health care resources by chasing a 'label' and direct our attentions to dedicated and automated recording of patient contacts with the health care system. Patients identified as having high, and poor outcomes, from contacts with health services could then be more readily identified in order to adopt a more coordinated, efficient and holistic patient care approach.

Reference List

1. Olesen F, Dickinson J, Jortdahl P. General practice---time for a new definition. BMJ 2000;320(7231):354-7.

2. Zalidis S. A General Practitioner, his Patients and their Feelings: Exploring the Emotions Behind Physical Symptoms. Free Association Books; 2001.

3. The Oxford Paperback Dictionary, Thesaurus, and Wordpower Guide. Oxford, U.K.: Oxford University Press; 2001.

4. Eaton WW, Holzer CE, Von Korff M, Anthony JC, Helzer L, George L et al. The design of the Epidemiologic Catchment Area surveys. The control and measurement of error. Arch Gen Psychiatry 1984;41:942-8.

5. Kroenke K, Price R. Symptoms in the community: Prevalence, classification, and psychiatric comorbidity. Arch Intern Med 1993;153(21):2474-80.

6. Boardman HF, Thomas E, Croft PR, Millson DS. Headache experiences and medication use in primary care. Int J Pharm Pract 2001;9(suppl):R34.

7. Office for National Statistics, Social Survey Division. ONS Omnibus Survey, April 1998. UK Data Archive . 2001. Office for National Statistics. 15-5-2003.
Ref Type: Electronic Citation

8. Drossman DA, Li Z, Andruzzi E, Temple RD, Tallry NJ, Thompson WG et al. U.S. householder survey of functional gastrointestinal disorders. Prevalence, sociodemography, and health impact. Dig Dis Sci 1993;38:1569-80.

9. Stanghellini V. Three-month prevalence rates of gastrointestinal symptoms and the influence of demographic factors: results from the Domestic/International Gastroenterology Surveillance Study (DIGEST). Scan J Gastroenterol 1999;231(Suppl):20-8.

10. Sloane PD, Coeytaux RR, Beck RS, Dallara J. Dizziness: state of the science. Ann Intern Med 2001;134(9 (Pt 2)):823-32.

11. Kroenke K, Price RK. Symptoms in the community. Prevalence, classification, and psychiatric comorbidity. Arch Intern Med 1993;153(21):2474-80.

12. Nylenna M. Why do our patients see us? A study of reasons for encounter in general practice. Scand J Prim Health Care 1985;3(3):155-62.

13. Schappert SM. Ambulatory care visits to physician offices, hospital outpatient departments, and emergency departments: United States, 1997. Vital Health Stat 1999;13(143):i-39.

14. Cherry DK, Burt CW, Woodwell DA. National Ambulatory Medical Care Survey: 2001 summary. Adv Data 2003;337:1-44.

15. Kroenke K, Spitzer RL, De Gruy FV, Hahn SR, Linzer M, Williams JB et al. Multisomatoform disorder. An alternative to undifferentiated somatoform disorder for the somatizing patient in primary care. Arch Gen Psychiatry 1997;54(4):352-8.

16. Kroenke K, Spitzer RL, Williams JB. The PHQ-15: validity of a new measure for evaluating the severity of somatic symptoms. Psychosom Med 2002;64(2):258-66.

17. Kroenke K, Mangelsdorff AD. Common symptoms in ambulatory care: incidence, evaluation, therapy, and outcome. Am J Med 1989;86(3):262-6.

18. Fink P, Sorensen L, Engberg M, Holm M, Munk-Jorgensen P. Somatization in primary care. Prevalence, health care utilization, and general practitioner recognition. Psychosomatics 1999;40(4):330-8.

19. Brown TM. Somatising Disorders in an Edinburgh General Practice [dissertation]. University of Edinburgh; 1988.

20. Weich S, Lewis G, Donmall R, Mann A. Somatic Presentation of Psychiatric Morbidity in General Practice. BJGP 1995;45(392):143-7.

21. Peveler R, Kilkenny L, Kinmonth AL. Medically unexplained physical symptoms in primary care: a comparison of self-report screening questionnaires and clinical opinion. J Psychosom Res 1997;42(3):245-52.

22. Kroenke K, Price R. Symptoms in the community: Prevalence, classification, and psychiatric comorbidity. Arch Intern Med 1993;153(21):2474-80.

23. Nylenna M, Bruusgaard D. Symptomatic and non-symptomatic reasons for encounter in general practice. Scand J Prim Health Care 1987;5(4):221-4.

24. Morris CJ, Cantrill JA, Weiss MC. GPs' attitudes to minor ailments. Fam Pract 2001;18(6):581-5.

25. Reid S, Whooley D, Crayford T, Hotopf M. Medically unexplained symptoms--GPs' attitudes towards their cause and management. Fam Pract 2001;18(5):519-23.

26. Gladman LM, Gorard DA. General practitioner and hospital specialist attitudes to functional gastrointestinal disorders. Alim Pharmacol Therapeut 2003;17(5):651-4.

27. Grumbach K, Selby J, Damberg C, Bindman AB, Quesenberry C, Truman A et al. Resolving the gatekeeper conundrum: what patients value in primary care and referrals to specialists. JAMA 1999;282(3):261-6.

28. Laine C, Turner BJ. The Good (Gatekeeper), the Bad (Gatekeeper), and the Ugly (Situation). J Gen Intern Med 1999;14(5):320-1.

29. Goldberg D, Bridges K. Somatic presentations of psychiatric illness in primary care setting. J Psychosom Res 1988;32(2):137-44.

30. Forrest CB, Nutting PA, Starfield B, von Schrader S. Family physicians' referral decisions: results from the ASPN referral study. J Fam Pract 2002;51(3):215-22.

31. Thompson WG, Heaton KW, Smyth GT, Smyth C. Irritable bowel syndrome in general practice: prevalence, characteristics, and referral. Gut 2000;46(1):78-82.

32. Carson AJ, Ringbauer B, Stone J, McKenzie L, Warlow C, Sharpe M. Do medically unexplained symptoms matter? A prospective cohort study of 300 new referrals to neurology outpatient clinics. J Neurol Neurosurg Psychiatry 2000;68(2):207-10.

33. Wilkin D, Smith A. Explaining variation in general practitioner referrals to hospital. Fam Pract 1987;4(3):160-9.

34. Baker R. Monitoring of general practitioners' outpatient referral rates by Family Health Services Authorities: how practical? Health Trends 1990;22(2):53-5.

35. Garcia OL, Abraira V, Gervas J, Otero A, Perez FM. Variability in GPs' referral rates in Spain. Fam Pract 1995;12(2):159-62.

36. Langley GR, Minkin S, Till JE. Regional variation in nonmedical factors affecting family physicians' decisions about referral for consultation. CMAJ 1997;157(3):265-72.

37. Hippisley-Cox J, Hardy C, Pringle M, Fielding K, Carlisle R, Chilvers C. The effect of deprivation on variations in general practitioners' referral rates: a cross sectional study on computerised data on new medical and surgical outpatient referrals in Nottinghamshire. BMJ 1997;314(7092):1458-61.

38. O'Donnell CA. Variation in GP referral rates: what can we learn from the literature? Fam.Pract. 2000;17(6):462-71.

39. Starfield B, Forrest CB, Nutting PA, von Schrader S. Variability in physician referral decisions. J Am Board Fam Pract 2002;15(6):473-80.

40. Coulter A, Noone A, Goldacre M. General practitioners' referrals to specialist outpatient clinics. I. Why general practitioners refer patients to specialist outpatient clinics. BMJ 1989;299(6694):304-6.

41. Bowling A, Redfern J. The process of outpatient referral and care: the experiences and views of patients, their General Practitioners and Specialists. BJGP 2000;50:116-20.

42. Warner P, Critchley HO, Lumsden MA, Campbell-Brown M, Douglas A, Murray G. Referral for menstrual problems: cross sectional survey of symptoms, reasons for referral, and management. BMJ 2001;323(7303):24-8.

43. Zoccolillo MS, Cloninger CR. Excess medical care of women with somatization disorder. South Med J 1986;79(5):532-5.

44. Labott SM, Preisman RC, Popovich J, Jr., Iannuzzi MC. Health care utilization of somatizing patients in a pulmonary subspecialty clinic. Psychosomatics 1995;36(2):122-8.

45. Hamilton J, Campos R, Creed F. Anxiety, depression and management of medically unexplained symptoms in medical clinics. J R Coll Physicians Lond 1996;30(1):18-20.

46. Stone J, Sharpe M, Rothwell PM, Warlow CP. The 12 year prognosis of unilateral functional weakness and sensory disturbance. J Neurol Neurosurg Psychiatry 2003;74(5):591-6.

47. Grol R. To Heal or to Harm: The Prevention of Somatic Fixation in General Practice. Thirded. London: The Royal College of General Practitioners; 1983.

48. Fink P. Surgery and medical treatment in persistent somatizing patients. J Psychosom Res 1992;36(5):439-47.

49. Kouyanou K, Pither CE, Wessely S. Iatrogenic factors and chronic pain. Psychosom Med 1997;59(6):597-604.

50. Kouyanou K, Pither CE, Rabe-Hesketh S, Wessely S. A comparative study of iatrogenesis, medication abuse, and psychiatric morbidity in chronic pain patients with and without medically explained symptoms. Pain 1998;76(3):417-26.

51. Biderman A, Yeheskel A, Herman J. Somatic fixation: the harm of healing. Soc Sci Med 2003;56(5):1135-8.

52. Van Hemert AM, Hengeveld MW, Bolk JH, Rooijmans HG, Vandenbroucke JP. Psychiatric disorders in relation to medical illness among patients of a general medical out-patient clinic. Psychol Med 1993;23(1):167-73.

53. De Gruy FV, Crider J, Hashimi DK, Dickinson P, Mullins HC, Troncale J. Somatization in a university hospital. J Fam Pract 1987;25(6):579-84.

54. Creed F, Firth D, Timol M, Metcalfe R, Pollock S. Somatization and illness behaviour in a neurology ward. J Psychosom Res 1990;34(4):427-37.

55. Ewald H, Rogne T, Ewald K, Fink P. Somatization in patients newly admitted to a neurological department. Acta Psychiatr Scand 1994;89(3):174-9.

56. Fink P. Physical disorders associated with mental illness: a register investigation. Psychol Med 1990;20(4):829-34.

57. Fink P. Physical complaints and symptoms of somatizing patients. J Psychosom Res 1992;36(2):125-36.

58. Crimlisk HL, Bhatia K, Cope H, David A, Marsden CD, Ron MA. Slater revisited: 6 year follow up study of patients with medically unexplained motor symptoms. BMJ 1998;316(7131):582-6.

59. Bass C, Hyde G, Bond A, Sharpe M. A survey of frequent attenders at a gastroenterology clinic. J Psychosom Res 2001;50(2):107-9.

60. Reid S, Wessely S, Crayford T, Hotopf M. Medically unexplained symptoms in frequent attenders of secondary health care: retrospective cohort study. BMJ 2001;322(7289):767-70.

61. Reid S, Wessely S, Crayford T, Hotopf M. Frequent attenders with medically unexplained symptoms: service use and costs in secondary care. Br J Psychiatry 2002;180:248-53.

62. Shaw J, Creed F. The cost of somatization. J Psychosom Res 1991;35(2-3):307-12.

63. Barsky AJ, Ettner SL, Horsky J, Bates DW. Resource utilization of patients with hypochondriacal health anxiety and somatization. Med Care 2001;39(7):705-15.

64. Smith GR, Monson RA, Ray DC. Patients with multiple unexplained symptoms: Their characteristics, functional health, and health care utilization. Arch Intern Med 1986;146(1):69-72.

65. Berki SE, Lepkowski JN, Wyszewianski L, Landis JR, Magilavy ML, McLaughlin CG et al. High-volume and low-volume users of health services: United States, 1980. Natl Med Care Util Expend Surv C 1985(2):1-88.

66. Freeborn DK, Pope CR, Mullooly JP, McFarland BH. Consistently high users of medical care among the elderly. Med Care 1990;28(6):527-40.

67. Hansagi H, Olsson M, Sjoberg S, Tomson Y, Goransson S. Frequent use of the hospital emergency department is indicative of high use of other health care services. Ann Emerg Med 2001;37(6):561-7.

68. Fink P. The use of hospitalizations by persistent somatizing patients. Psychol Med 1992;22(1):173-80.

69. Wright JP. Hysteria and Mechanical Man. J Hist Ideas 1980;41(2):233-47.

70. Psyche and Soma: physicians and metaphysicians on the mind-body problem from Antiquity to the Enlightenment. Oxford: Clarendon Press; 2000.

71. Boss JM. The seventeenth-century transformation of the hysteric affection, and Sydenham's Baconian medicine. Psychol Med 1979;9(2):221-34.

72. Scheper-Hughes N, Lock MM. The Mindful Body: A Prolegomenon to Future Work in Medical Anthropology. Med Anthropol Q 1987;1(1):6-41.

73. Mattsson B, Mattsson M. The concept of "psychosomatic" in general practice. Reflections on body language and a tentative model for understanding. Scand J Prim Health Care 2002;20(3):135-8.

74. Martin RD. The somatoform conundrum: a question of nosological values. Gen Hosp Psychiatry 1999;21(3):177-86.

75. Pilowsky I. Abnormal illness behaviour. Br J Med Psychol 1969;42(4):347-51.

76. Taylor GJ, Bagby RM, Parker JDA. Disorders of Affect Regulation: Alexithymia in Medical and Psychiatric Illness. Cambridge, U.K.: Cambridge University Press; 1997.

77. Guze SB. Studies in hysteria. Can J Psychiatry 1983;28(6):434-7.

78. Sharpe M, Carson A. "Unexplained" somatic symptoms, functional syndromes, and somatization: do we need a paradigm shift? Ann Intern Med 2001;134(9 (Pt 2)):926-30.

79. Trimble MR. Functional diseases. BMJ 1982;285(6357):1768-70.

80. Wessely S, Nimnuan C, Sharpe M. Functional somatic syndromes: one or many? Lancet 1999;354(9182):936-9.

81. Simon GE, Gureje O, Fullerton C. Course of hypochondriasis in an international primary care study. Gen Hosp Psychiatry 2001;23(2):51-5.

82. Richmond C. Myalgic encephalomyelitis, Princess Aurora, and the wandering womb. BMJ 1989;298(6683):1295-6.

83. Miller E. Conversion Hysteria: Is it a Viable Concept? Cog Neuropsychiatry 1999;4(3):181-91.

84. Engel CC, Jr., Liu X, Hoge C, Smith S. Multiple idiopathic physical symptoms in the ECA study: competing-risks analysis of 1-year incidence, mortality, and resolution. (Epidemiological Catchment Area). Am J Psychiatry 2002;159(6):998-1004.

85. World Health Organisation. The Tenth Revision of the International Classification of Diseases and Related Health Problems (ICD-10). Geneva: World Health Organisation; 1992.

86. Shorter E. From paralysis to fatigue: A history of psychosomatic illness in the modern era. New York: The Free Press; 1995.

87. Mayou R, Bass C, Sharpe M. Overview of epidemiology, classification, and aetiology. In: Mayou R, Bass C, Sharpe M, editors. Treatment of Functional Somatic Symptoms. Oxford: Oxford University Press; 1995. p. 42-65.

88. PURTELL JJ, ROBINS E, COHEN ME. Observations on clinical aspects of hysteria; a quantitative study of 50 hysteria patients and 156 control subjects. J Am Med Assoc 1951;146(10):902-9.

89. Guze SB. The role of follow-up studies: their contribution to diagnostic classification as applied to hysteria. Semin Psychiatry 1970;2(4):392-402.

90. Steckel W. The Interpretation of Dreams. New York: Liveright; 1943.

91. Lipowski ZJ. Review of consultation psychiatry and psychosomatic medicine. Psychosom Med 1968;30:395-422.

92. Lipowski ZJ. Somatization: a borderland between medicine and psychiatry. CMAJ 1986;135(6):609-14.

93. Lipowski ZJ. Somatization - the concept and its clinical application. Am J Psychiatry 1988;145(11):1358-68.

94. American Psychiatric Association. Somatoform Disorders. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Fourth ed. Washington, D.C.: American Psychiatric Association; 1994. p. 445-69.

95. Sharpe M, Mayou R, Bass C. Concepts, theories, and terminology. In: Mayou R, Bass C, Sharpe M, editors. Treatment of functional somatic symptoms. Oxford: Oxford University Press; 1995. p. 3-16.

96. Sharpe M. Rethinking somatization. Adv Mind Body Med 2001;17(4):260-3.

97. van Vliet KP, Everaerd W, van Zuuren FJ, Lammes FB, Briet M, Kleiverda G et al. Symptom perception: psychological correlates of symptom reporting and illness behavior of women with medically unexplained gynecological symptoms. J Psychosom Obstet Gynaecol 1994;15(3):171-81.

98. Fink P, Rosendal M, Toft T. Assessment and treatment of functional disorders in general practice: the extended reattribution and management model--an advanced educational program for nonpsychiatric doctors. Psychosomatics 2002;43(2):93-131.

99. Smith RC, Gardiner JC, Lyles JS, Johnson M, Rost K, Luo Z et al. Minor acute illness: a preliminary research report on the "worried well". J Fam Pract 2002;51(1):24-9.

100. Kipen HM, Fiedler N. The role of environmental factors in medically unexplained symptoms and related syndromes: conference summary and recommendations. Environ Health Perspect 2002;110(Suppl 4):591-5.

101. Kipen H, Fiedler N. Environmental factors in medically unexplained symptoms and related syndromes: the evidence and the challenge. Environ Health Perspect 2002;110(Suppl 4):597-9.

102. Burton C. Beyond somatisation: a review of the understanding and treatment of medically unexplained physical symptoms (MUPS). Br J Gen Pract 2003;53(488):231-9.

103. Mayou R. Medically Unexplained Physical Symptoms. BMJ 1991;303(6802):534-5.

104. Ehlert U, Gaab J, Heinrichs M. Psychoneuroendocrinological contributions to the etiology of depression, posttraumatic stress disorder, and stress-related bodily disorders: the role of the hypothalamus-pituitary-adrenal axis. Biol Psychol 2001;57(1-3):141-52.

105. Henningsen P. The body in the brain: towards a representational neurobiology of somatoform disorders. Acta Neuropsychiatrica 2003;15(4):157-60.

106. Bonne O, Grillon C, Vythilingam M, Neumeister A, Charney DS. Adaptive and maladaptive psychobiological responses to severe psychological stress: implications for the discovery of novel pharmacotherapy. Neurosci Biobehav Rev 2004;28(1):65-94.

107. Kellner R. The Significance of Somatization. Homeostasis Health Dis 1991;33(1-2):2-6.

108. Sharpe M. Medically unexplained symptoms and syndromes. Clin Med 2002;2(6):501-4.

109. Kroenke K, Price R. Symptoms in the community: Prevalence, classification, and psychiatric comorbidity. Arch Intern Med 1993;153(21):2474-80.

110. Kroenke K, Spitzer RL, Williams JB, Linzer M, Hahn SR, De Gruy FV et al. Physical symptoms in primary care. Predictors of psychiatric disorders and functional impairment. Arch Fam Med 1994;3(9):774-9.

111. Gerber PD, Barrett JE, Barrett J, Oxman T, Manheimer E, Smith R et al. The relationship of presenting physical complaints to depressive symptoms in primary care patients. J Gen Intern Med 1992;7(2):170-3.

112. Kroenke K, Lucas C, Rosenberg M, Scherokman B. Psychiatric disorders and functional impairment in patients with persistent dizziness. J Gen Intern Med 1993;8(10):530-5.

113. Clark MR, Sullivan MD, Fischl M, Katon W, Russo JE, Dobie RA et al. Symptoms as a clue to otologic and psychiatric diagnosis in patients with dizziness. J Psychosom Res 1994;38(5):461-70.

114. Coyne JC, Fechner-Bates S, Schwenk TL. Prevalence, nature, and comorbidity of depressive disorders in primary care. Gen Hosp Psychiatry 1994;16(4):267-76.

115. Feightner JW, Worrall G. Early detection of depression by primary care physicians. CMAJ 1990;142(11):1215-20.

116. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. IVed. Washington, DC: American Psychiatric Association; 1994.

117. Nelson JC. Synergistic effects of serotonin and noradrenaline reuptake inhibition. Depress Anxiety 1998;7(Suppl 1):5-6.

118. Bao Y, Sturm R, Croghan TW. A national study of the effect of chronic pain on the use of health care by depressed persons. Psychiatr Serv 2003;54:693-7.

119. Peveler R, Carson A, Rodin G. Depression in medical patients. BMJ 2002;325(7356):149-52.

120. Addington AM, Gallo JJ, Ford DE, Eaton WW. Epidemiology of unexplained fatigue and major depression in the community: the Baltimore ECA follow-up, 1981-1994. Psychol Med 2001;31(6):1037-44.

121. Ohayon MM, Schatzberg AF. Using chronic pain to predict depressive morbidity in the general population. Arch Gen Psychiatry 2003;60:39-47.

122. Gelder M, Gath D, Mayou R, Cowen P. Anxiety, obsessive-compulsive and dissociative disorders. Oxford Textbook of Psychiatry. Third ed. Oxford: Oxford University Press; 1996. p. 160-96.

123. Kooiman C, Bolk J, Brand R, Trijsburg R, Rooijmans H. Is Alexithymia a risk factor for unexplained physical symptoms in general medical outpatients? Psychosom Med 2000;62(6):768-78.

124. Lieb R, Zimmermann P, Friis RH, Hofler M, Tholen S, Wittchen HU. The natural course of DSM-IV somatoform disorders and syndromes among adolescents and young adults: a prospective-longitudinal community study. Eur Psychiatry 2002;17(6):321-31.

125. Kouakam C, Lacroix D, Klug D, Baux P, Marquie C, Kacet S. Prevalence and prognostic significance of psychiatric disorders in patients evaluated for recurrent unexplained syncope. Am J Cardiol 2002;89(5):530-5.

126. Fink P. Psychiatric illness in patients with persistent somatization. Br J Psychiatry 1995;166:93-9.

127. Rief W, Hiller W. Toward empirically based criteria for the classification of somatoform disorders. J Psychosom Res 1999;46(6):507-18.

128. Andrews G, Jenkins R. Managing mental disorders. UKed. Sydney: World Health Organization Collaborating Centre for Mental Health and Substance Abuse; 1999.

129. Katon W. Panic disorder and somatization. Review of 55 cases. Am J Med 1984;77(1):101-6.

130. Katon W. Panic disorder: relationship to high medical utilization, unexplained physical symptoms, and medical costs. J Clin Psychiatry 1996;57 Suppl 10:11-8.

131. Katon W, Von Korff M, Lin E. Panic disorder: relationship to high medical utilization. Am J Med 1992;92(1A):7S-11S.

132. Katon W. Depression: relationship to somatization and chronic medical illness. J Clin Psychiatry 1984;45(3:Pt 2):4-12.

133. Roy-Byrne P, Stein MB, Russo J, Mercier E, Thomas R, McQuaid J et al. Panic disorder in the primary care setting: comorbidity, disability, service utilization, and treatment. J Clin Psychiatry 1999;60(7):492-9.

134. Katon W, Russo J. Somatic Symptoms and Depression. J Fam Pract 1989;29(1):65-9.

135. Ormel J, Van Den BW, Koeter MW, Giel R, Van Der MK, Van De WG et al. Recognition, management and outcome of psychological disorders in primary care: a naturalistic follow-up study. Psychol Med 1990;20(4):909-23.

136. Bowers PJ. Selections from current literature: psychiatric disorders in primary care. Fam Pract 1993;10(2):231-7.

137. Kirmayer LJ, Robbins JM, Dworkind M, Yaffe MJ. Somatization and the recognition of depression and anxiety in primary care. Am J Psychiatry 1993;150(5):734-41.

138. Ormel J, VonKorff M, Ustun TB, Pini S, Korten A, Oldehinkel T. Common mental disorders and disability across cultures. Results from the WHO Collaborative Study on Psychological Problems in General Health Care. JAMA 1994;272(22):1741-8.

139. Spitzer RL, Williams JB, Kroenke K, Linzer M, De Gruy FV, Hahn SR et al. Utility of a new procedure for diagnosing mental disorders in primary care. The PRIME-MD 1000 study. JAMA 1994;272(22):1749-56.

140. Betrus PA, Elmore SK, Hamilton PA. Women and somatization: unrecognized depression. Health Care Women Int 1995;16(4):287-97.

141. Ballenger JC. Comorbidity of panic and depression: implications for clinical management. Int Clin Psychopharmacol 1998;13(Suppl):13-7.

142. Weiller E, Bisserbe JC, Maier W, Lecrubier Y. Prevalence and recognition of anxiety syndromes in five European primary care settings. A report from the WHO study on Psychological Problems in General Health Care. Br J Psychiatry 1998;Suppl(34):18-23.

143. Kessler D, Lloyd K, Lewis G, Gray DP. Cross sectional study of symptom attribution and recognition of depression and anxiety in primary care. BMJ 1999;318(7181):436-9.

144. Upton MW, Evans M, Goldberg D, Sharp DJ. Evaluation of ICD-10 PHC mental health guidelines in detecting and managing depression within primary care. Br J Psychiatry 1999;175:476-82.

145. Zamorski MA, Ward RK. Social anxiety disorder: common, disabling, and treatable. J.Am.Board Fam.Pract. 2000;13(4):251-60.

146. Feder A, Olfson M, Gameroff M, Fuentes M, Shea S, Lantigua RA et al. Medically unexplained symptoms in an urban general medicine practice. Psychosomatics 2001;42(3):261-8.

147. Wells KB, Stewart A, Hays RD, Burnam MA, Rogers W, Daniels M et al. The functioning and well-being of depressed patients. Results from the Medical Outcomes Study. JAMA 1989;262(7):914-9.

148. Rost K, Zhang M, Fortney J, Smith J, Coyne JC, Smith R. Persistently poor outcomes of undetected major depression in primary care. Gen Hosp Psychiatry 1998;20:12-20.

149. Bridges K, Goldberg D. Somatic presentation of DSM III psychiatric disorders in primary care. J Psychosom Res 1985;29(6):563-9.

150. Rosenberg E, Lussier MT, Beaudoin C, Kirmayer LJ, Dufort GG. Determinants of the diagnosis of psychological problems by primary care physicians in patients with normal GHQ-28 scores. Gen Hosp Psychiatry 2002;24(5):322-7.

151. Kessler D, Bennewith O, Lewis G, Sharp D. Detection of depression and anxiety in primary care: follow up study. BMJ 2002;325:1016-7.

152. Paykel E, Hart D, Priest RG. Changes in public attitudes to depression during the Defeat Depression Campaign. Br J Psychiatry 1998;173:519-22.

153. Roeloffs C, Sherbourne C, Unutzer J, Fink A, Tang L, Wells KB. Stigma and depression among primary care patients. Gen Hosp Psychiatry 2003;25(5):311-5.

154. Lydeard S, Jones R. Factors affecting the decision to consult with dyspepsia: comparison of consulters and non-consulters. J R Coll Gen Pract 1989;39(329):495-8.

155. Barsky AJ, Borus JF. Functional somatic syndromes. Ann Intern Med 1999;130(11):910-21.

156. Roy-Byrne P. Generalized anxiety and mixed anxiety-depression: association with disability and health care utilization. J Clin Psychiatry 1996;57(Suppl 7):86-91.

157. Bower P, West R, Tylee A, Hann M. Symptom attribution and the recognition of psychiatric morbidity. J.Psychosom.Res. 2000;48(2):157-60.

158. Fritzsche K, Sandholzer H, Werner J, Brucks U, Cierpka M, Deter HC et al. Psychosocial care in general practice - Results of a demonstration project on quality management in psychosocial primary care. Psychotherapie Psychosomatik Medizinische Psychologie 2000;50(6):240-6.

159. Tylee A. Depression in the community: physician and patient perspective. J Clin Psychiatry 1999;60(Suppl 7):12-8.

160. Simon GE, VonKorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. N Engl J Med 1999;341(18):1329-35.

161. Coyne JC, Schwenk TL, Fechner-Bates S. Nondetection of depression by primary care physicians reconsidered. Gen Hosp Psychiatry 1995;17(1):3-12.

162. Tiemens BG, Ormel J, Simon GE. Occurrence, recognition, and outcome of psychological disorders in primary care. Am.J Psychiatry 1996;153(5):636-44.

163. Pini S, Berardi D, Rucci P, Piccinelli M, Neri C, Tansella M et al. Identification of psychiatric distress by primary care physicians. Gen Hosp Psychiatry 1997;19(6):411-8.

164. Howe A. Detecting psychological distress: can general practitioners improve their own performance? Br J Gen Pract 1996;46(408):407-10.

165. Kroenke K, Taylor-Vaisey A, Dietrich A, Oxman T. Interventions to improve provider diagnosis and treatment of mental disorders in primary care: a critical review of the literature. Psychosomatics 2000;41(1):39-52.

166. Jackson JL, O'Malley PG, Tomkins G, Balden E, Santoro J, Kroenke K. Treatment of functional gastrointestinal disorders with antidepressant medications: a meta-analysis. Am J Med 2000;108(1):65-72.

167. O'Malley PG, Jackson JL, Santoro J, Tomkins G, Balden E, Kroenke K. Antidepressant therapy for unexplained symptoms and symptom syndromes. J Fam Pract 1999;48(12):980-90.

168. O'Malley PG, Balden E, Tomkins G, Santoro J, Kroenke K, Jackson JL. Treatment of fibromyalgia with antidepressants: a meta-analysis. J Gen Intern Med 2000;15(9):659-66.

169. Varia I, Logue E, O'Connor C, Newby K, Wagner R, Davenport C et al. Randomized trial of sertraline in patients with unexplained chest pain of noncardiac origin. Am Heart J 2000;140:367-72.

170. Kroenke K, Swindle R. Cognitive-behavioral therapy for somatization and symptom syndromes: a critical review of controlled clinical trials. Psychother Psychosom 2000;69(4):205-15.

171. Raine R, Haines A, Sensky T, Hutchings A, Larkin K, Lack N. Systematic review of mental health interventions for patients with common somatic symptoms: can research evidence from secondary care be extrapolated to primary care? BMJ 2002;325(7372):1082.

172. Dimmock PW, Wyatt KM, Jones PW, O'Brien PM. Efficacy of selective serotonin re-uptake inhibitors in premenstrual syndrome: a systematic review. Lancet 2000;356:1131-6.

173. Green CA, Pope CR. Gender, psychosocial factors and the use of medical services: a longitudinal analysis. Soc Sci Med 1999;48(10):1363-72.

174. Gill D, Sharpe M. Frequent consulters in general practice: A systematic review of studies of prevalence, associations and outcome. J Psychosom Res 1999;47(2):115-30.

175. Vanwijk CMTG, Kolk AM. Sex differences in physical symptoms: The contribution of symptom perception theory. Soc Sci Med 1997;45(2):231-46.

176. Barsky AJ, Peekna HM, Borus JF. Somatic symptom reporting in women and men. J Gen Intern Med 2001;16(4):266-75.

177. Kolk AM, Hanewald GJ, Schagen S, Gushers van Wijk CMT. A symptom perception approach to common physical symptoms. Soc Sci Med 2003;57(12):2343-54.

178. Swartz M, Landerman R, Blazer D, George L. Somatization symptoms in the community: a rural/urban comparison. Psychosomatics 1989;30(1):44-53.

179. Verhaak PF. Determinants of the help-seeking process: Goldberg and Huxley's first level and first filter. Psychol Med 1995;25(1):95-104.

180. Ladwig KH, Marten-Mittag B, Erazo N, Gundel H. Identifying somatization disorder in a population-based health examination survey - Psychosocial burden and gender differences. Psychosomatics 2001;42(6):511-8.

181. Adamson J, Ben Shlomo Y, Chaturvedi N, Donovan J. Ethnicity, socio-economic position and gender--do they affect reported health--care seeking behaviour? Soc Sci Med 2003;57(5):895-904.

182. Drossman DA, Leserman J, Nachman G, Li Z, Gluck H, Toomey TC et al. Sexual and physical abuse in women with functional or organic gastrointestinal disorders. Ann Intern Med 1990;113(11):828-33.

183. Rosenberg DA, Krugman RD. Epidemiology and outcome of child abuse. Ann Rev Med 1991;42:217-44.

184. Butler DJ, Qualheim K, Turkal N, Wissing M. Men sexually abused in childhood. Sequelae and implications for the family physician. Arch Fam Med 1993;2(1):29-33.

185. Drossman DA. Sexual and physical abuse and gastrointestinal illness. Scand J Gastroenterol 1995;208(Suppl):90-6.

186. Walker EA, Gelfand AN, Gelfand MD, Koss MP, Katon WJ. Medical and psychiatric symptoms in female gastroenterology clinic patients with histories of sexual victimization. Gen Hosp Psychiatry 1995;17(2):85-92.

187. Leserman J, Drossman DA, Li Z, Toomey TC, Nachman G, Glogau L. Sexual and physical abuse history in gastroenterology practice: how types of abuse impact health status. Psychosom Med 1996;58(1):4-15.

188. Roberts SJ. The sequelae of childhood sexual abuse: a primary care focus for adult female survivors. Nurse Pract 1996;21(12 Pt 1):42-52.

189. Salmon P, Calderbank S. The relationship of childhood physical and sexual abuse to adult illness behavior. J.Psychosom.Res. 1996;40(3):329-36.

190. Jamieson DJ, Steege JF. The association of sexual abuse with pelvic pain complaints in a primary care population. Am J Obstet Gynecol 1997;177(6):1408-12.

191. Reilly J, Baker GA, Rhodes J, Salmon P. The association of sexual and physical abuse with somatization: characteristics of patients presenting with irritable bowel syndrome and non-epileptic attack disorder. Psychol Med 1999;29(2):399-406.

192. Hulme PA. Symptomatology and health care utilization of women primary care patients who experienced childhood sexual abuse. Child Abuse Negl 2000;24(11):1471-84.

193. Kovac SH, Klapow JC, Kroenke K, Spitzer RL, Williams JB. Differing symptoms of abused versus nonabused women in obstetric-gynecology settings. Am J Obstet Gynecol 2003;188(3):707-13.

194. Spertus IL, Yehuda R, Wong CM, Halligan S, Seremetis SV. Childhood emotional abuse and neglect as predictors of psychological and physical symptoms in women presenting to a primary care practice. Child Abuse Negl 2003;27(11):1247-58.

195. Robbins JM, Kirmayer LJ. Attributions of common somatic symptoms. Psychol Med 1991;21(4):1029-45.

196. Cope H, David A, Mann A. 'Maybe it's a virus?': beliefs about viruses, symptom attributional style and psychological health. J Psychosom Res 1994;38(2):89-98.

197. Petrie KJ, Sivertsen B, Hysing M, Broadbent E, Moss-Morris R, Eriksen HR et al. Thoroughly modern worries: The relationship of worries about modernity to reported symptoms, health and medical care utilization. J Psychosom Res 2001;51(1):395-401.

198. Woloshynowych M, Valori R, Salmon P. General practice patients' beliefs about their symptoms. Br J Gen Pract 1998;48(426):885-9.

199. Chaturvedi SK, Hopwood P, Maguire P. Nonorganic Somatic Symptoms in Cancer. Eur J Cancer 1993;29A(7):1006-8.

200. Perkins DO, Leserman J, Stern RA, Baum SF, Liao D, Golden RN et al. Somatic symptoms and HIV infection: relationship to depressive symptoms and indicators of HIV disease. Am J Psychiatry 1995;152(12):1776-81.

201. Kelly RH, Russo J, Katon W. Somatic complaints among pregnant women cared for in obstetrics: normal pregnancy or depressive and anxiety symptom amplification revisited? Gen Hosp Psychiatry 2001;23(3):107-13.

202. Ciechanowski PS, Katon W, Russo JE, Dwight-Johnson MM. Association of attachment style to lifetime medically unexplained symptoms in patients with hepatitis C. Psychosomatics 2002;43(3):206-12.

203. Stansfeld SA. Commentary: The problem with stress: minds, hearts and disease. Int J Epidemiol 2002;31(6):1113-6.

204. Ruo B, Rumsfeld JS, Hlatky MA, Liu H, Browner WS, Whooley MA. Depressive symptoms and health-related quality of life: the Heart and Soul Study. JAMA 2003;290(2):215-21.

205. Rodin G, Voshart K. Depressive symptoms and functional impairment in the medically ill. Gen Hosp Psychiatry 1987;9(4):251-8.

206. Dennis M, O'Rourke S, Lewis S, Sharpe M, Warlow C. Emotional outcomes after stroke: factors associated with poor outcome. J Neurol Neurosurg Psychiatry 2000;68(1):47-52.

207. Tew R, Guthrie E, Creed F, Cotter L, Kisely S, Tomenson B. A long-term follow-up study of patients with ischaemic heart disease versus patients with nonspecific chest pain. J Psychosom Res 1995;39(8):977-85.

208. Reid S, Crayford T, Patel A, Wessely S, Hotopf M. Frequent attenders in secondary care: a 3-year follow-up study of patients with medically unexplained symptoms. Psychol Med 2003;33(3):519-24.

209. Mayou R, Bryant B, Forfar C, Clark D. Non-cardiac chest pain and benign palpitations in the cardiac clinic. Br Heart J 1994;72(6):548-53.

210. Carson AJ, Best S, Postma K, Stone J, Warlow C, Sharpe M. The outcome of neurology outpatients with medically unexplained symptoms: a prospective cohort study. J Neurol Neurosurg Psychiatry 2003;74(7):897-900.

211. Kroenke K, Lucas CA, Rosenberg ML, Scherokman B. Psychiatric disorders and functional impairment in patients with persistent dizziness. JGIM 1993;8(10):530-5.

212. Hahn SR, Kroenke K, Spitzer RL, Brody D, Williams JB, Linzer M et al. The difficult patient: prevalence, psychopathology, and functional impairment. Ann Intern Med 1996;11(1):1-8.

213. Walker EA, Keegan D, Gardner G, Sullivan M, Katon W, Bernstein D. Psychosocial factors in fibromyalgia compared with rheumatoid arthritis: I. Psychiatric diagnoses and functional disability. Psychosom Med 1997;59(6):565-71.

214. Gureje O, Ustun TB, Simon GE. The syndrome of hypochondriasis: a cross-national study in primary care. Psychol Med 1997;27(5):1001-10.

215. Escobar JI, Gara MA, Waitzkin H, Silver RC, Holman A, Compton W. DSM-IV hypochondriasis in primary care. Gen Hosp Psychiatry 1998;20(3):155-9.

216. Carson AJ, Ringbauer B, MacKenzie L, Warlow C, Sharpe M. Neurological disease, emotional disorder, and disability: they are related: a study of 300 consecutive new referrals to a neurology outpatient department. J Neurol Neurosurg Psychiatry 2000;68(2):202-6.

217. Connelly JE, Wofford AB, Philbrick JT. Healthy patients who perceive poor health: why are they worried sick? Am J Med Sci 2000;320(1):36-42.

218. Hiller W, Rief W, Fichter MM. How disabled are patients with somatoform disorders? Gen Hosp Psychiatry 1997;19(6):432-8.

219. Thompson C, Ostler K, Peveler R, Baker N, Kinmonth AL. Dimensional perspective on the recognition of depressive symptoms in primary care: The Hampshire Depression Project 3. Br J Psychiatry 2001;179:317-23.

220. Jackson JL, Kroenke K, Chamberlin J. Effects of physician awareness of symptom-related expectations and mental disorders. A controlled trial. Arch Fam Med 1999;8(2):135-42.

221. Jackson JL, Kroenke K. The effect of unmet expectations among adults presenting with physical symptoms. Ann Intern Med 2001;134(9 (Pt 2)):889-97.

222. Jackson JL, Chamberlin J, Kroenke K. Predictors of patient satisfaction. Soc Sci Med 2001;52(4):609-20.

223. Salmon P, Peters S, Stanley I. Patients' perceptions of medical explanations for somatisation disorders: qualitative analysis. BMJ 1999;318(7180):372-6.

224. Malcolm R, Foster HK, Smith C. The problem patient as perceived by family physicians. J Fam Pract 1977;5(3):361-4.

225. Deighton CM. Problem Patients in General-Practice - Identifying Young-Women with Recurrent Abnormal Illness Behavior. J R Coll Gen Pract 1985;35(279):466-70.

226. Hahn SR, Thompson KS, Wills TA, Stern V, Budner NS. The difficult doctor-patient relationship: somatization, personality and psychopathology. J Clin Epidemiol 1994;47(6):647-57.

227. Sharpe M, Mayou R, Seagroatt V, Surawy C, Warwick H, Bulstrode C et al. Why do doctors find some patients difficult to help? Q J Med 1994;87(3):187-93.

228. Jackson JL, Kroenke K. Difficult patient encounters in the ambulatory clinic: clinical predictors and outcomes. Arch Intern Med 1999;159(10):1069-75.

229. Hahn SR. Physical symptoms and physician-experienced difficulty in the physician-patient relationship. Ann Intern Med 2001;134(9 (Pt 2)):897-904.

230. Hartz AJ, Noyes R, Bentler SE, Damiano PC, Willard JC, Momany ET. Unexplained symptoms in primary care: perspectives of doctors and patients. Gen Hosp Psychiatry 2000;22(3):144-52.

231. Allaz AF, Vannotti M, Desmeules J, Piguet V, Celik Y, Pyroth O et al. Use of the label "litigation neurosis" in patients with somatoform pain disorder. Gen Hosp Psychiatry 1998;20(2):91-7.

232. Scott S, Deary IJ, Pelosi AJ. General practitioners' attitudes to patients with a self diagnosis of myalgic encephalomyelitis. BMJ 1995;310(6978):508.

233. Steven ID, McGrath B, Qureshi F, Wong C, Chern I, Pearn-Rowe B. General practitioners' beliefs, attitudes and reported actions towards chronic fatigue syndrome. Aust Fam Physician 2000;29(1):80-5.

234. Williamson P, Beitman BD, Katon W. Beliefs that foster physician avoidance of psychosocial aspects of health care. J Fam Pract 1981;13(7):999-1003.

235. Ferrari R, Kwan O. The no-fault flavor of disability syndromes. Med Hypoth 2001;56(1):77-84.

236. Christopoulos KA. The Sick Role in Literature and Society. JAMA 2001;285(1):93.

237. Steinmetz D, Tabenkin H. The difficult patient' as perceived by family physicians. Fam Pract 2001;18(5):495-500.

238. Neal R, Heywood PL, Morley S. Frequent attenders' consulting patterns with general practitioners. BJGP 2000;50(461):972-6.

239. Demers M. Frequent users of ambulatory health care in Quebec: the case of doctor-shoppers. CMAJ 1995;153(1):37-42.

240. Bass C, Murphy M. The chronic somatizer and the Government White Paper. J R Soc Med 1990;83:203-5.

241. Crimlisk HL, Bhatia K, Cope H, David AS, Marsden D, Ron MA. Patterns of referral in patients with medically unexplained motor symptoms. J Psychosom Res 2000;49(3):217-9.

242. Tomasson K, Kent D, Coryell W. Comparison of four diagnostic systems for the diagnosis of somatization disorder. Acta Psychiatr Scand 1993;88(5):311-5.

243. Rief W, Heuser J, Mayrhuber E, Stelzer I, Hiller W, Fichter MM. The classification of multiple somatoform symptoms. J Nerv Ment Dis 1996;184(11):680-7.

244. Escobar JI, Hoyos-Nervi C, Gara MA. Medically unexplained physical symptoms in medical practice: a psychiatric perspective. Environ Health Perspect 2002;110(Suppl 4):631-6.

245. Kroenke K, Spitzer RL, De Gruy FV, Swindle R. A symptom checklist to screen for somatoform disorders in primary care. Psychosomatics 1998;39(3):263-72.

246. Lynch D, McGrady A, Nagel R, Zsembik C. Somatization in Family Practice: Comparing 5 Methods of Classification. Prim Care Companion J Clin Psychiatry 1999;1(3):85-9.

247. Simon GE, Gureje O. Stability of somatization disorder and somatization symptoms among primary care patients. Arch Gen Psychiatry 1999;56(1):90-5.

248. Ustun TB, Bridges-Weeb C, Cooper J, Goldberg D, Sartorius N. A new classification for mental disorders with management guidelines for use in primary care: the ICD-10 PHC. Cas Lek Cesk 1994;133(21):660-4.

249. Parnanen H, Kumpusalo EA, Takala J. Primary health care ICD--a tool for general practice research. Int J Health Plann Manage. 2000;15(2):133-48.

250. Escobar JI, Burnam MA, Karno M, Forsythe A, Golding JM. Somatization in the community. Arch Gen Psychiatry 1987;44(8):713-8.

251. Escobar JI, Golding JM, Hough RL, Karno M, Burnam MA, Wells KB. Somatization in the community: relationship to disability and use of services. Am J Public Health 1987;77(7):837-40.

252. Escobar JI, Waitzkin H, Silver RC, Gara MA, Holman A. Abridged somatization: a study in primary care. Psychosom Med 1998;60(4):466-72.

253. Kirmayer LJ, Robbins JM. Three forms of somatization in primary care: prevalence, co-occurrence, and sociodemographic characteristics. J Nerv Ment Dis 1991;179(11):647-55.

254. Hiller W, Rief W, Fichter MM. Further Evidence for A Broader Concept of Somatization Disorder Using the Somatic Symptom Index. Psychosomatics 1995;36(3):285-94.

255. Labott SM, Preisman RC, Torosian T, Popovich J, Jr., Iannuzzi MC. Screening for somatizing patients in the pulmonary subspecialty clinic. Psychosomatics 1996;37(4):327-38.

256. Sullivan M, Clark MR, Katon W, Fischl M, Russo J, Dobie RA et al. Psychiatric and otologic diagnoses in patients complaining of dizziness. Arch Intern Med 1993;153(12):1479-84.

257. Gureje O, Simon GE, Ustun TB, Goldberg D. Somatization in cross-cultural perspective: a World Health Organization study in primary care. Am J Psychiatry 1997;154(7):989-95.

258. Smith RC, Gardiner JC, Lyles JS, Sirbu C, Dwamena FC, Hodges AM et al. Exploration of DSM-IV criteria in primary care patients with medically unexplained symptoms. Psychosom Med 2005;67(1):123-9.

259. Dickinson WP, Dickinson LM, De Gruy FV, Candib LM, Main DS, Libby AM et al. The somatization in primary care study: a tale of three diagnoses. Gen Hosp Psychiatry 2003;25(1):7-Feb.

260. Pincus HA, Vettorello NE, McQueen LE, First MB, Wise TN, Zarin D et al. Bridging the gap between psychiatry and primary care. The DSM-IV-PC. Psychosomatics 1995;36(4):328-35.

261. Pingitore D, Sansone RA. Using DSM-IV primary care version: a guide to psychiatric diagnosis in primary care. Am Fam Phys 1998;58(6):1347-52.

262. WHO. International Statistical Classification of Diseases and Related Health Problems (10th Edition). 1994. Geneva, World Health Organisation (WHO). 10th Edition.
Ref Type: Report

263. Mayou R, Hawton K. Psychiatric disorder in the general hospital. Br J Psychiatry 1986;149:172-90.

264. Kroenke K, Jackson JL, Chamberlin J. Depressive and anxiety disorders in patients presenting with physical complaints: clinical predictors and outcome. Am J Med 1997;103(5):339-47.

265. Deary IJ. A taxonomy of medically unexplained symptoms. J Psychosom Res 1999;47(1):51-9.

266. Vanner SJ, Depew WT, Paterson WG, DaCosta LR, Groll AG, Simon JB et al. Predictive value of the Rome criteria for diagnosing the irritable bowel syndrome. Am J Gastroenterol 1999;94(10):2912-7.

267. Wilkie, A and Wessely, S. Patients with medically unexplained symptoms. British Journal of Hospital Medicine 51(8), 421-427. 1994.
Ref Type: Generic

268. White K, Speechley M, Harth M, Òstbye T. Coexistence of chronic fatigue syndrome with fibromyalgia syndrome in the general population: A controlled study. Scand J Rheum 2000;29(1):44-51.

269. Stanley IM, Peters S, Salmon P. A primary care perspective on prevailing assumptions about persistent medically unexplained physical symptoms. Int J Psychiatry Med 2002;32(2):125-40.

270. Nimnuan C, Rabe-Hesketh S, Wessely S, Hotopf M. How many functional somatic syndromes? J Psychosom Res 2001;51(4):549-57.

271. Aaron LA, Buchwald D. A review of the evidence for overlap among unexplained clinical conditions. Ann Intern Med 2001;134(9 Pt 2):868-81.

272. Slater ET. What is hysteria? New Psychiatry 1976;3:714-5.

273. Malterud K. Illness and disease in female patients. I. Pitfalls and inadequacies of primary health care classification systems--a theoretical review. Scand J Prim Health Care 1987;5(4):205-9.

274. McDaniel SH, Campbell TL, Seaburn DB. Integrating the mind-body split: a biopsychosocial approach to somatic fixation. Family Oriented Primary Care. New York: Springer-Verlag; 1990. p. 248-62.

275. Usherwood T. Somatization and somatic fixation. Understanding the consultation : evidence, theory and practice. Buckingham: Open University Press; 1999. p. 97-131.

276. Wileman L, May C, Chew-Graham CA. Medically unexplained symptoms and the problem of power in the primary care consultation: a qualitative study. Fam Pract 2002;19(2):178-82.

277. Marchant-Haycox S, Salmon P. Patients' and doctors' strategies in consultations with unexplained symptoms. Interactions of gynecologists with women presenting menstrual problems. Psychosomatics 1997;38(5):440-50.

278. Salmon P. Patients who present physical symptoms in the absence of physical pathology: a challenge to existing models of doctor-patient interaction. Patient Educ Couns 2000;39(1):105-13.

279. Mechanic D. Health and illness behavior and patient-practitioner relationships. Soc Sci Med 1992;34(12):1345-50.

280. Gask L, Usherwood T. ABC of Psychological Medicine: The consultation. BMJ 2002;324:1567-9.

281. Stirling AM, Wilson P, McConnachie A. Deprivation, psychological distress and consultation length in general practice. BJGP 2001;51:456-60.

282. Hjortdahl P. The influence of general practitioners' knowledge about their patients on the clinical decision-making process. Scand J Prim Health Care 1992;10(4):290-4.

283. Page LA, Wessely S. Medically unexplained symptoms: exacerbating factors in the doctor-patient encounter. J R Soc Med 2003;96(5):223-7.

284. Biggs AM, Aziz Q, Tomenson B, Creed F. Do Childhood Adversity and Recent Social Stress Predict Health Care Use in Patients Presenting With Upper Abdominal or Chest Pain? Psychosom Med 2003;65(6):1020-8.

285. Lipsitt DR. Challenges of somatization: diagnostic, therapeutic and economic. Psychiatr Med 1992;10(3):1-12.

286. Wilkie A, Wessely S. Patients with medically unexplained symptoms. Br J Hosp Med 1994;51(8):421-7.

287. Escobar JI. Overview of somatization: diagnosis, epidemiology, and management. Psychopharmacol Bull 1996;32(4):589-96.

288. Peveler R. Understanding medically unexplained physical symptoms: faster progress in the next century than in this? J Psychosom Res 1998;45(2):93-7.

289. Sack M, Loew T, Scheidt CE. Diagnosis and treatment of somatization disorder and undifferentiated somatization disorder - a literature review. Z Psychosom Med Psychoanal 1998;44(3):214-32.

290. Khouzam HR, Field S. Somatization Disorder: Clinical Presentation and Treatment in Primary Care. Hosp Phys 1999;35(4):20-1-24+45.

291. Kroenke K. Symptoms are sufficient: refining our concept of somatization. Adv Mind Body Med 2001;17(4):244-9.

292. Kipen HM, Fiedler N. Environmental factors in medically unexplained symptoms and related syndromes: the evidence and the challenge. Environ Health Perspect 2002;110(Suppl 4):597-9.

293. De Gucht V, Fischler B. Somatization: A critical review of conceptual and methodological issues. Psychosomatics 2002;43(1):1-9.

294. Garcia-Campayo J, Lobo A, Perez-Echeverria MJ, Campos R. Three forms of somatization presenting in primary care settings in Spain. J Nerv Ment Dis 1998;186(9):554-60.

295. Holder-Perkins V, Wise T, Williams DE. The somatizing patient. Curr Psychiatry Rep 2000;2(3):234-40.

296. Cox, J., Rayner, C., Tylee, A., and Hancock, C. WHO Guide to Mental Health in Primary Care. Goldberg, D., Gask, L., Jenkins, R., Lewis, B., Paton, J., Sharp, D., and Tylee, A. http://cebmh.warne.ox.ac.uk/cebmh/whoguidemhpcuk/pdf/index.html . 12-4-2000. This edition published by the Royal Society of Medicine Press Ltd, 1 Wimpole Street, London W1M 8AE, UK. Website designed and maintained by CEBMH Copyright © 1998-2001 World Health Organization . 7-5-2003.
Ref Type: Electronic Citation

297. Kroenke K, Spitzer R, Williams J, Linzer M, Hahn S, De Gruy F et al. Physical symptoms in primary care: predictors of psychiatric disorders and functional impairment. Arch Fam Med 1994;3(9):774-9.

298. Kroenke K. Symptoms in medical patients: an untended field. Am J Med 1992;92(1A):3S-6S.

299. Lynch D, McGrady A, Nagel R, Zsembik C. Somatization in family practice - comparing 5 methods of classification. Prim Care Companion J Clin Psychiatry 1999;1(3):85-9.

300. Jyvasjarvi S, Keinanen-Kiukaanniemi S, Vaisanen E, Larivaara P, Kivela S. Frequent attenders in a Finnish health centre: morbidity and reasons for encounter. Scand J Prim Health Care 1998;16(3):141-8.

301. Heywood PL, Blackie GC, Cameron IH, Dowell AC. An assessment of the attributes of frequent attenders to general practice. Fam Pract 1998;15(3):198-204.

302. Robinson JO, Granfield AJ. The frequent consulter in primary medical care. J Psychosom Res 1986;30(5):589-600.

303. Barsky AJ, Wyshak G, Klerman GL. Medical and psychiatric determinants of outpatient medical utilization. Med Care 1986;24(6):548-60.

304. Speckens AE, Van Hemert AM, Bolk JH, Rooijmans HG, Hengeveld MW. Unexplained physical symptoms: outcome, utilization of medical care and associated factors. Psychol Med 1996;26(4):745-52.

305. Escobar JI, Golding JM, Hough RL, Karno M, Burnam MA, Wells KB. Somatization in the community: relationship to disability and use of services. Am J Public Health 1987;77(7):837-40.

306. Jyvasjarvi S, Joukamaa M, Vaisanen E, Larivaara P, Kivela S, Keinanen-Kiukaanniemi S. Somatizing frequent attenders in primary health care. J Psychosom Res 2001;50(4):185-92.

307. Haas LJ, Spendlove DC, Silver MP, Holmberg TC. Psychopathology and emotional distress among older high-utilizing health maintenance organization patients. J Gerontol A Biol Sci Med Sci 1999;54(11):M577-M582.

308. Vedsted, P., Fink, P., Olesen, F., Munk-Jorgensen, P., and Holm, M. The prediction of frequent attendance in general practice based on measurements of psychological distress. Poster . 23-6-2000.
Ref Type: Abstract

309. Little P, Somerville J, Williamson I, Warner G, Moore M, Wiles R et al. Psychosocial, lifestyle, and health status variables in predicting high attendance among adults. Br J Gen Pract 2001;51(473):987-94.

310. Vedsted P, Fink P, Olesen F, Munk-Jorgensen P. Psychological distress as a predictor of frequent attendance in family practice: a cohort study. Psychosomatics 2001;42(5):416-22.

311. Dowrick CF, Bellon JA, Gomez MJ. GP frequent attendance in Liverpool and Granada: the impact of depressive symptoms. Br J Gen Pract 2000;50(454):361-5.

312. Tessler R, Mechanic D, Dimond M. The effect of psychological distress on physician utilization: a prospective study. J Health Soc Behav. 1976;17(4):353-64.

313. Gortmaker SL, Eckenrode J, Gore S. Stress and the utilization of health services: a time series and cross-sectional analysis. J Health Soc Behav 1982;23(1):25-38.

314. Bellon JA, Delgado A, Luna JD, Lardelli P. Psychosocial and health belief variables associated with frequent attendance in primary care. Psychol Med 1999;29(6):1347-57.

315. Brown TM. Somatizing disorders in an Edinburgh general practice [dissertation]. University of Edinburgh; 1988.

316. De Lusignan S, Valentin T, Chan T, Hague N, Wood O, van Vlymen J et al. Problems with primary care data quality: osteoporosis as an exemplar. Inform Prim Care 2004;12(3):147-56.

317. Hamilton WT, Round AP, Sharp D, Peters TJ. The quality of record keeping in primary care: a comparison of computerised, paper and hybrid systems. Br J Gen Pract 2003;53(497):929-33.

318. Smith RC, Gardiner JC, Armatti S, Johnson M, Lyles JS, Given CW et al. Screening for high utilizing somatizing patients using a prediction rule derived from the management information system of an HMO - A preliminary study. Med Care 2001;39(9):968-78.

319. Neal R, Dowell AC, Heywood P, Morley S. Frequent Attenders: Who needs treatment? BJGP 1996(March):131-2.

320. Smith GR, Monson RA, Ray DC. Psychiatric consultation in somatization disorder. A randomized controlled study. New Eng J Med 1986;314(22):1407-13.

321. Katon W, Von Korff M, Lin E, Lipscomb P, Russo J, Wagner E et al. Distressed high utilizers of medical care. DSM-III-R diagnoses and treatment needs. Gen Hosp Psychiatry 1990;12(6):355-62.

322. Robins L, Helzer J, Weissman M, Orvaschel H, Gruenberg E, Burke J, Jr. et al. Lifetime prevalence of specific psychiatric disorders in three sites. Arch Gen Psychiatry 1984;41(10):949-58.

323. Pearson SD, Katzelnick DJ, Simon GE, Manning WG, Helstad CP, Henk HJ. Depression Among High Utilizers of Medical Care. J Gen Intern Med 1999;14(8):461-8.

324. First MB, Spitzer R, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition. (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

325. Fink P. Admission Patterns of Persistent Somatization Patients. Gen Hosp Psychiatry 1993;15(4):211-8.

326. Fink P. Psychiatric-Illness in Patients with Persistent Somatization. Br J Psychiatry 1995;166:93-9.

327. Stedman's Concise Medical Dictionary for the Health Professions. 4th Editioned. Lippincott Williams & Wilkins; 2001.

328. Bass C, Bond A, Gill D, Sharpe M. Frequent attenders without organic disease in a gastroenterology clinic. Patient characteristics and health care use. Gen Hosp Psychiatry 1999;21(1):30-8.

329. Reid S, Crayford T, Richards S, Nimnuan C, Hotopf M. Recognition of medically unexplained symptoms--do doctors agree? J Psychosom Res 1999;47(5):483-5.

330. Wing JK, Babor T, Brugha T, Burke J, Cooper JE, Giel R et al. SCAN. Schedules for Clinical Assessment in Neuropsychiatry. Arch Gen Psychiatry 1990;47(6):589-93.

331. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67(6):361-70.

332. Smith B. Patients Referred to Hospital from Primary Care with Medically Unexplained Symptoms: A Primary Care Perspective - MPhil Thesis. MPhil Thesis 2003:1-132.

333. Verhaak PF, Meijer SA, Visser AP, Wolters G. Persistent presentation of medically unexplained symptoms in general practice. Fam Pract 2006;23(4):414-20.

334. Robbins JM, Kirmayer LJ, Hemami S. Latent variable models of functional somatic distress. J Nerv Ment Dis 1997;185(10):606-15.

335. Spiegel BM, Kanwal F, Naliboff B, Mayer E. The impact of somatization on the use of gastrointestinal health-care resources in patients with irritable bowel syndrome. Am J Gastroenterol 2005;100(10):2262-73.

336. Fiddler M, Jackson J, Kapur N, Wells A, Creed F. Childhood adversity and frequent medical consultations. Gen Hosp Psychiatry 2004;26(5):367-77.

337. Barsky AJ, Orav EJ, Bates DW. Somatization Increases Medical Utilization and Costs Independent of Psychiatric and Medical Comorbidity. Arch Gen Psychiatry 2005;62(8):903-10.

338. Barsky AJ, Orav EJ, Bates DW. Distinctive patterns of medical care utilization in patients who somatize. Med Care 2006;44(9):803-11.

339. Ford JD, Trestman RL, Tennen H, Allen S. Relationship of anxiety, depression and alcohol use disorders to persistent high utilization and potentially problematic under-utilization of primary medical care. Soc Sci Med 2005;61(7):1618-25.

340. Ford JD, Trestman RL, Steinberg K, Tennen H, Allen S. Prospective association of anxiety, depressive, and addictive disorders with high utilization of primary, specialty and emergency medical care. Soc Sci Med 2004;58(11):2145-8.

341. Hiller W, Fichter MM. High utilizers of medical care: A crucial subgroup among somatizing patients. J Psychosom Res 2004;56(4):437-43.

342. Hiller W, Fichter MM, Rief W. A controlled treatment study of somatoform disorders including analysis of healthcare utilization and cost-effectiveness. J Psychosom Res 2003;54(4):369-80.

343. Bleichhardt G, Timmer B, Rief W. Cognitive-behavioural therapy for patients with multiple somatoform symptoms--a randomised controlled trial in tertiary care. J Psychosom Res 2004;56(4):449-54.

344. Kolk AM, Schagen S, Hanewald GJ. Multiple medically unexplained physical symptoms and health care utilization: outcome of psychological intervention and patient-related predictors of change. J Psychosom Res 2004;57(4):379-89.

345. Rosendal M, Bro F, Sokolowski I, Fink P, Toft T, Olesen F. A randomised controlled trial of brief training in assessment and treatment of somatisation: effects on GPs' attitudes. Fam Pract 2005;22(4):419-27.

346. Frostholm L, Fink P, Oernboel E, Christensen KS, Toft T, Olesen F et al. The uncertain consultation and patient satisfaction: the impact of patients' illness perceptions and a randomized controlled trial on the training of physicians' communication skills. Psychosom Med 2005;67(6):897-905.

347. Rosendal M, Bro F, Fink P, Christensen KS, Olesen F. Diagnosis of somatisation: effect of an educational intervention in a cluster randomised controlled trial. Br J Gen Pract 2003;53(497):917-22.

348. Mayou R, Kirmayer LJ, Simon G, Kroenke K, Sharpe M. Somatoform Disorders: Time for a New Approach in DSM-V. Am J Psychiatry 2005;162(5):847-55.

349. Talley NJ, Spiller RC. Irritable bowel syndrome: a little understood organic bowel disease? Lancet 2002;360(9332):555-64.

350. Kellner R. Functional Somatic Symptoms and Hypochondriasis - A Survey of Empirical-Studies. Arch Gen Psychiatry 1985;42(8):821-33.

351. Sharpe M, Peveler R, Mayou R. The psychological treatment of patients with functional somatic symptoms: a practical guide. J Psychosom Res 1992;36(6):515-29.

352. Guo Y, Kuroki T, Koizumi S. Abnormal illness behavior of patients with functional somatic symptoms: relation to psychiatric disorders. Gen Hosp Psychiatry 2001;23(4):223-9.

353. Creed F, Barsky A. A systematic review of the epidemiology of somatisation disorder and hypochondriasis. J Psychosom Res 2004;56(4):391-408.

354. Henningsen P, Zimmermann T, Sattel H. Medically Unexplained Physical Symptoms, Anxiety, and Depression: A Meta-Analytic Review. Psychosom Med 2003;65(4):528-33.

355. Nimnuan C, Hotopf M, Wessely S. Medically unexplained symptoms: An epidemiological study in seven specialities. J Psychosom Res 2001;51(1):361-7.

356. Maiden NL, Hurst NP, Lochhead A, Carson AJ, Sharpe M. Medically unexplained symptoms in patients referred to a specialist rheumatology service: prevalence and associations. Rheumatology 2003;42(1):108-12.

357. Salmon P. The potentially somatizing effect of clinical consultation. CNS Spectr 2006;11(3):190-200.

358. Ring A, Dowrick CF, Humphris GM, Davies J, Salmon P. The somatising effect of clinical consultation: What patients and doctors say and do not say when patients present medically unexplained physical symptoms. Soc Sci Med 2005;61(7):1505-15.

359. Cropley M, Steptoe A. Social support, life events and physical symptoms: A prospective study of chronic and recent life stress in men and women. Psychol Health Med 2005;10(4):317-25.

360. Kirmayer LJ, Groleau D, Looper KJ, Dao MD. Explaining medically unexplained symptoms. Can J Psychiatry 2004;49(10):663-72.

361. Hulley SB, Cummings SR, Browner WS, Grady D, Hearst N, Newman TB. Designing Clinical Research: An Epidemiological Approach (Second Edition). Philadelphia: Lippincott Williams and Wilkins; 2001.

362. Donald, J. Referrals from primary care in Lothian. 15-4-2003.
Ref Type: Personal Communication

363. Taylor MW, Milne R, Taylor RJ, Duncan R. The state of general practice computing in Scotland and the characteristics of computerised practices: a survey of 948 practices. Health Bull (Edinb.) 1991;49(4):250-8.

364. Whitelaw FG, Nevin SL, Milne RM, Taylor RJ, Taylor MW, Watt AH. Completeness and accuracy of morbidity and repeat prescribing records held on general practice computers in Scotland. Br J Gen Pract 1996;46(404):181-6.

365. Coggon D, Martyn C, Palmer KT, Evanoff B. Assessing case definitions in the absence of a diagnostic gold standard. Int J Epidemiol 2005;34(4):949-52.

366. Knotterus JA, Van Weel C, Muris JWM. Evidence base of clinical diagnosis: Evaluation of diagnostic procedures. BMJ 2002;324(7335):477-80.

367. Smith RC, Korban E, Kanj M, Haddad R, Lyles JS, Lein C et al. A method for rating charts to identify and classify patients with medically unexplained symptoms. Psychother Psychosom 2004;73(1):36-42.

368. Townsend P. Deprivation. J Soc Policy 1987;16(2):125-46.

369. Carstairs V, Morris R. Deprivation: explaining differences in mortality between Scotland and England and Wales. BMJ 1989;299(6704):886-9.

370. Morris R, Carstairs V. Which deprivation? A comparison of selected deprivation indexes. J Public Health Med 1991;13(4):318-26.

371. Jarman B. Identification of underprivileged areas. BMJ 1983;286(6379):1705-9.

372. Cassell J, Young A. Why we should not seek individual informed consent for participation in health services research. J Med Ethics 2002;28(5):313-7.

373. Willison DJ, Keshavjee K, Nair K, Goldsmith C, Holbrook AM. Patients' consent preferences for research uses of information in electronic medical records: interview and survey data. BMJ 2003;326(7385):373.

374. Microsoft Corporation. Microsoft (R) Access 2002. (10.6501.6735). 2002. Ref Type: Computer Program

375. Willison DJ, Keshavjee K, Nair K, Goldsmith C, Holbrook AM. Patients' consent preferences for research uses of information in electronic medical records: interview and survey data. BMJ 2003;326(7385):373.

376. Microsoft Corporation. Microsoft Excel (R) 2002. (10.6501.6735). 2002. Ref Type: Computer Program

377. Spitzer RL, Kroenke K, Williams JB. Validation and utility of a self-report version of PRIME-MD: the PHQ primary care study. Primary Care Evaluation of Mental Disorders. Patient Health Questionnaire. JAMA 1999;282(18):1737-44.

378. Becker S, Al Zaid K, Al Faris E. Screening for somatization and depression in Saudi Arabia: a validation study of the PHQ in primary care. Int J Psychiatry Med 2002;32(3):271-83.

379. Olfson M, Shea S, Feder A, Fuentes M, Nomura Y, Gameroff M et al. Prevalence of anxiety, depression, and substance use disorders in an urban general medicine practice. Arch Fam Med 2000;9(9):876-83.

380. Klapow JC, Kroenke K, Horton T, Schmidt S, Spitzer R, Williams JB. Psychological disorders and distress in older primary care patients: a comparison of older and younger samples. Psychosom Med 2002;64(4):635-43.

381. Spitzer RL, Williams JB, Kroenke K, Hornyak R, McMurray J. Validity and utility of the PRIME-MD patient health questionnaire in assessment of 3000 obstetric-gynecologic patients: the PRIME-MD Patient Health Questionnaire Obstetrics-Gynecology Study. Am J Obstet Gynecol 2000;183(3):759-69.

382. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. JGIM 2001;16(9):606-13.

383. Stein MB, Roy-Byrne P, McQuaid J, Laffaye C, Russo J, McCahill M et al. Development of a Brief Diagnostic Screen for Panic Disorder in Primary Care. Psychosom Med 1999;61(3):359-64.

384. Ware J, Jr., Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34(3):220-33.

385. Jenkinson C, Layte R, Jenkinson D, Lawrence K, Petersen S, Paice C et al. A shorter form health survey: can the SF-12 replicate results from the SF-36 in longitudinal studies? J Pub Health 1997;19(2):179-86.

386. Ware JE, Kosinski M, Turner-Bowker DM, Gandek B. How to score version 2 of the SF-12 health survey (with a supplement documenting version 1). Lincoln, RI: Quality Metric Incorporated; 2002.

387. Johnson JA, Coons SJ. Comparison of the EQ-5D and SF-12 in an adult US sample. Qual.Life Res 1998;7(2):155-66.

388. Ramsay J, Campbell JL, Schroter S, Green J, Roland M. The General Practice Assessment Survey (GPAS): tests of data quality and measurement properties. Fam Pract 2000;17(5):372-9.

389. Weinman J, Petrie KJ, Moss-Morris R, Horne R. The Illness Perception Questionnaire: A new method for assessing the cognitive representation of illness. Psychol Health 1996;11(3):431-45.

390. Pilowsky I. Dimensions of hypochondriasis. Br J Psychiatry 1967;113(494):89-93.

391. Fink P, Ewald H, Jensen J, Sorensen L, Engberg M, Holm M et al. Screening for somatization and hypochondriasis in primary care and neurological in-patients: a seven-item scale for hypochondriasis and somatization. J Psychosom Res 1999;46(3):261-73.

392. Gulbrandsen P, Fugelli P, Hjortdahl P. Psychosocial problems presented by patients with somatic reasons for encounter: tip of the iceberg? Fam Pract 1998;15(1):1-8.

393. Robinson JW, Roter DL. Psychosocial problem disclosure by primary care patients. Soc Sci Med 1999;48(10):1353-62.

394. Lang F, Floyd MR, Beine KL, Buck P. Sequenced questioning to elicit the patient's perspective on illness: Effects on information disclosure, patient satisfaction, and time expenditure. Fam Med 2002;34(5):325-30.

395. National Centre for Social Research. National Health Survey of NHS Patients. 2002. Middlesex, Department of Health.
Ref Type: Generic

396. Lang F, Floyd MR, Beine KL, Buck P. Sequenced questioning to elicit the patient's perspective on illness: Effects on information disclosure, patient satisfaction, and time expenditure. Fam Med 2002;34(5):325-30.

397. British Medical Association, Royal Pharmaceutical Society of Great Britain. Central Nervous System. British National Formulary. 50 ed. London: BMJ Publishing Group Ltd. and Royal Pharmaceutical Society of Great Britain; 2005. p. 174-265.

398. Office for National Statistics, Social Survey Division. ONS Omnibus Survey, April 1998. UK Data Archive . 2001. Office for National Statistics. 15-5-2003.
Ref Type: Electronic Citation

399. Taylor D, McConnell D, Abel K. Treatment of Affective Illness. In: Kerwin R, editor. The Bethlem and Maudsley NHS Trust Prescribing Guidelines. 5th ed. London: Martin Dunitz Ltd.; 1999. p. 40-62.

400. Edwards P, Roberts I, Larke M, Iguiseppi C, Ratap S, Entz R et al. Increasing response rates to postal questionnaires: systematic review. BMJ 2002;324(7347):1183.

401. Gibson PJ, Koespell TD, Diehr P, Hale C. Increasing response rates for mailed surveys of Medicaid clients and other low-income populations. Am J Epidemiol 1999;149(11):1057-62.

402. Shaw MJ, Beebe TJ, Jensen HL, Adis SA. The use of monetary incentives in a community survey: impact on response rates, data quality and cost. Health Serv Res 2001;35(6):1339-46.

403. SPSS, Inc. SPSS for Windows: Standard Version. (11.5.0). 6-9-2002.
Ref Type: Computer Program

404. Jewell NP. Statistics for Epidemiology. Chapman & Hall / CRC; 2004.

405. Office for National Statistics (ONS). Average number of NHS GP consultations per person per year by sex and age: 1972 to 2003: GHS 2003. 29-3-2005. ONS.
Ref Type: Data File

406. Ciechanowski PS, Walker EA, Katon W, Russo JE. Attachment theory: a model for health care utilization and somatization. Psychosom Med 2002;64(4):660-7.

407. De Gruy FV, Columbia L, Dickinson P. Somatization disorder in a family practice. J Fam Pract 1987;25(1):45-51.

408. Scottish Medicines Consortium (SMC). http://www.scottishmedicines.org.uk/ . 2005. 19-11-2005.
Ref Type: Electronic Citation

409. Information and Statistics Division. Scottish Health Service Costs, Year Ended 31st March 2004. 2005. Edinburgh, National Health Service Scotland.
Ref Type: Report

410. Curtis, L. and Netten, A. Unit Costs of Health and Social Care 2004. 2004. PSSRU, University of Kent at Canterbury.
Ref Type: Report

411. Scott A, Simoens S, Heaney D, O'Donnell CA, Thomson H, Moffat KJ et al. What Does GP Out Of Hours Care Cost? An Analysis Of Different Models Of Out Of Hours Care In Scotland. Scott Med J 2003;49(1):61-6.

412. Information and Statistics Division. Scottish Health Service Costs, Year Ended 31st March 2004. 2005. Edinburgh, National Health Service Scotland.
Ref Type: Report

413. Department of Health. Reference Costs 2004. 7-3-2005.
Ref Type: Report

414. West Dorset General Hospitals NHS Trust. Private Patients 2005/2006 Tariff. 1-54. 2005. Dorchester, Dorset.
Ref Type: Report

415. Thompson SG, Barber JA. How should cost data in pragmatic randomised trials be analysed? BMJ 2000;320(7243):1197-200.

416. Nixon RM, Thompson SG. TI - Parametric modelling of cost data in medical studies. Stat Med 2004;23(8):1311-31.

417. Biggs AM. Current symptoms, life adversity and health care use in medical outpatients [dissertation]. UNIVERSITY OF MANCHESTER; 2002.

418. Bass C, May S. Chronic multiple functional somatic symptoms. BMJ 2002;325(7359):323-6.

419. Information and Statistics Division. Scottish Health Service Costs, Year Ended 31st March 2004. 2005. Edinburgh, National Health Service Scotland.
Ref Type: Report

420. Neal R. Frequent Attenders. Fam.Pract. 1995;12(3):370.

421. Shrire S. Frequent attenders - a review. Fam Pract 1986;3:272-5.

422. Johnson JG, Spitzer RL, Williams JB. Health problems, impairment and illnesses associated with bulimia nervosa and binge eating disorder among primary care and obstetric gynaecology patients. Psychol Med 2001;31(8):1455-66.

423. Novy D, Berry MP, Palmer JL, Mensing C, Willey J, Bruera E. Somatic Symptoms in Patients with Chronic Non-Cancer-Related and Cancer-Related Pain. J Pain Symptom Manage 2005;29(6):603-12.

424. Gielissen MF, Verhagen S, Witjes F, Bleijenberg G. Effects of cognitive behavior therapy in severely fatigued disease-free cancer patients compared with patients waiting for cognitive behavior therapy: a randomized controlled trial. J Clin Oncol 2006;24(30):4882-7.

425. Morrant DG, Taylor GS. The prevalence of temporomandibular disorder in patients referred for orthodontic assessment. Br J Orthod 1996;23(3):261-5.

426. Tuz HH, Onder EM, Kisnisci RS. Prevalence of otologic complaints in patients with temporomandibular disorder. Am J Orthod Dentofacial Orthop 2003;123(6):620-3.

427. Chole RA, Parker WS. Tinnitus and vertigo in patients with temporomandibular disorder. Arch Otolaryngol Head Neck Surg 1992;118(8):817-21.

428. Smith D, Defalla BA, Chadwick DW. The misdiagnosis of epilepsy and the management of refractory epilepsy in a specialist clinic. Q J Med 1999;92(1):15-23.

429. Juarez-Garcia A, Stokes T, Shaw B, Camosso-Stefinovic J, Baker R. The costs of epilepsy misdiagnosis in England and Wales. Seizure 2006;15(8):598-605.

430. Graber ML, Franklin N, Gordon R. Diagnostic error in internal medicine. Arch Intern Med 2005;165(13):1493-9.

431. Headache Classification Subcommittee of the International Headache Society. The International Headache Society Classification of Headache Disorders, 2nd Edition. Cephalgia 2004;24(Suppl 1):9-160.

432. Hagemeister J, Schneider CA, Barabas S, Schadt R, Wassmer G, Mager G et al. Hypertension guidelines and their limitations--the impact of physicians' compliance as evaluated by guideline awareness. J Hypertens 2001;19(11):2079-86.

433. Baker KM, Brand DA, Hen J, Jr. Classifying asthma: disagreement among specialists. Chest 2003;124(6):2156-63.

434. Kalf AJ, Spruijt-Metz D. Variation in diagnoses: influence of specialists' training on selecting and ranking relevant information in geriatric case vignettes. Soc Sci Med 1996;42(5):705-12.

435. Smith GR, Monson RA, Livingston R. Somatization disorder in men. Gen Hosp Psych 1985;7(1):4-8.

436. Curtis SE. Use of survey data and small area statistics to assess the link between individual morbidity and neighbourhood deprivation. J Epidemiol Community Health 1990;44(1):62-8.

437. Ostler K, Thompson C, Kinmonth AL, Peveler R, Stevens L, Stevens A. Influence of socio-economic deprivation on the prevalence and outcome of depression in primary care: the Hampshire Depression Project. Br J Psychiatry 2001;178(1):12-7.

438. Wu L, Ashton CM. Chart review. A need for reappraisal. Eval Health Prof 1997;20(2):146-63.

439. Luck J, Peabody JW, Dresselhaus TR, Lee M, Glassman P. How well does chart abstraction measure quality? A prospective comparison of standardized patients with the medical record. Am J Med 2000;108(8):642-9.

440. Kniesner TJ, Powers RH, Croghan TW. Provider type and depression treatment adequacy. Health Policy 2005;72(3):321-32.

441. Haikio JP, Linden K, Kvist M. Outcomes of referrals from general practice. Scand J Prim Health Care 1995;13(4):287-93.

442. Luck J, Peabody JW, Dresselhaus TR, Lee M, Glassman P. How well does chart abstraction measure quality? A prospective comparison of standardized patients with the medical record. Am J Med 2000;108(8):642-9.

443. Carstairs V, Morris R. Deprivation and mortality: an alternative to social class? Community Med 1989;11(3):210-9.

444. Staab JP, Ruckenstein MJ, Amsterdam JD. A prospective trial of sertraline for chronic subjective dizziness. Laryngoscope 2004;2004 Sep;114(9):1637-41.

445. Masand PS, Schwartz TL, Virk S, Hameed A, Kaplan DS. Open-label treatment with citalopram in patients with irritable bowel syndrome: a pilot study. Prim Care Companion J Clin Psychiatry 2005;2005;7(4):162-6.

446. Freeman EW. Effects of antidepressants on quality of life in women with premenstrual dysphoric disorder. Pharmacoeconomics 2005;2005;23(5):433-44.

447. Wyatt KM FAU, Dimmock PW FAU, O'Brien PM. Selective serotonin reuptake inhibitors for premenstrual syndrome. Cochrane Database Syst Rev 2002(4):CD001396.

448. Pearlstein T. Selective serotonin reuptake inhibitors for premenstrual dysphoric disorder: the emerging gold standard? Drugs 2002;62(13):1869-85.

449. Dimmock PW FAU, Wyatt KM FAU, Jones PW FAU, O'Brien PM. Efficacy of selective serotonin-reuptake inhibitors in premenstrual syndrome: a systematic review. Lancet 2000;356(9236):1131-6.

450. Morriss R, Gask L, Ronalds C, Downes-Grainger E, Thompson H, Leese B et al. Cost-effectiveness of a new treatment for somatized mental disorder taught to GPs. Fam Pract 1998;15(2):119-25.

451. Morriss R, Gask L, Ronalds C, Downes-Grainger E, Thompson H, Goldberg D. Clinical and patient satisfaction outcomes of a new treatment for somatized mental disorder taught to general practitioners. BJGP 1999;49(441):263-7.

452. First MB, Spitzer R, Gibbon M, Williams JBW. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Non-patient Edition. (SCID-I/NP). New York: Biometrics Research, New York State Psychiatric Institute; 2002.

453. Katon W, Von Korff M, Lin E, Bush T, Ormel J. Adequacy and duration of antidepressant treatment in primary care. Med Care 1992;30(1):67-76.

454. Reid S, Crayford T, Richards S, Nimnuan C, Hotopf M. Recognition of medically unexplained symptoms--do doctors agree? J Psychosom Res 1999;47(5):483-5.

455. Smith RC, Korban E, Kanj M, Haddad R, Lyles JS, Lein C et al. A method for rating charts to identify and classify patients with medically unexplained symptoms. Psychother Psychosom 2004;73(1):36-42.

456. Williams ERL, Guthrie E, Mackway-Jones K, James M, Tomenson B, Eastham J et al. Psychiatric status, somatisation, and health care utilization of frequent attenders at the emergency department: a comparison with routine attenders. J Psychosom Res 2001;50(3):161-7.

457. Byrne M, Murphy AW, Plunkett PK, McGee HM, Murray A, Bury G. Frequent attenders to an emergency department: A study of primary health care use, medical profile, and psychosocial characteristics. Ann Emerg Med 2003;41(3):309-18.

458. Little P, Dorward M, Warner G, Stephens K, Senior J, Moore M. Importance of patient pressure and perceived pressure and perceived medical need for investigations, referral, and prescribing in primary care: nested observational study. BMJ 2004;328(7437):444-0.

459. Ring A, Dowrick C, Humphris G, Salmon P. Do patients with unexplained physical symptoms pressurise general practitioners for somatic treatment? A qualitative study. BMJ 2004;328(7447):1057-0.

460. Salmon P, Humphris GM, Ring A, Davies JC, Dowrick CF. Why do primary care physicians propose medical care to patients with medically unexplained symptoms? A new method of sequence analysis to test theories of patient pressure. Psychosom Med 2006;68(4):570-7.

461. Like R, Reeb KG. Clinical hypothesis testing in family practice: a biopsychosocial perspective. J Fam Pract 1984;19(4):517-23.

462. Dowrick C. Why do the O'Sheas consult so often? An exploration of complex family illness behaviour. Soc Sci Med 1992;34(5):491-7.

463. Baez K, Aiarzaguena J, Grandes G, Pedrero E, Aranguren J, Retolaza A. Understanding patient-initiated frequent attendance in primary care: a case-control study. Br J Gen Pract 1998;48:1824-7.

464. Oken D. Multiaxial Diagnosis and the Psychosomatic Model of Disease. Psychosom Med 2000;62(2):171-5.

465. Clarke D, Coleman J. Balint groups - examining the doctor-patient relationship. Aust Fam Phys 2002;31(1):41-4.

466. Vedsted P, Fink P, Sorensen HT, Olesen F. Physical, mental and social factors associated with frequent attendance in Danish general practice. A population-based cross-sectional study. Soc Sci Med 2004;59(4):813-23.

467. Sox HC, Jr., Margulies I, Sox CH. Psychologically mediated effects of diagnostic tests. Ann Int Med 1981;95:680-5.

468. Potts SG, Bass CM. Psychosocial outcome and use of medical resources in patients with chest pain and normal or near normal coronary arteries: a long-term follow-up study. Quart J Med 1993;86:583-93.

469. Howard LM, Wessely S. Reappraising reassurance - the role of investigations. J Psychosom Res 1996;41:307-11.

470. Howard L, Wessely S, Leese M, Page L, McCrone P, Husain K et al. Are investigations anxiolytic or anxiogenic? A randomised controlled trial of neuroimaging to provide reassurance in chronic daily headache. JNNP 2005;76(11):1558-64.

471. Dowrick CF, Ring A, Humphris GM, Salmon P. Normalisation of unexplained symptoms by general practitioners: a functional typology. Br J Gen Pract 2004;54(500):165-70.

472. Beitman B, Kushner MG, Basha I, et al. Follow-up status of patients with angiographically normal coronary arteries and panic disorder. JAMA 1991;265:1545-9.

473. Dowrick CF, Ring A, Humphris GM, Salmon P. Normalisation of unexplained symptoms by general practitioners: a functional typology. Br J Gen Pract 2004;54(500):165-70.

474. Speckens AE, Van Hemert AM, Bolk JH, Hawton K, Rooijmans HG. The acceptability of psychological treatment in patients with medically unexplained physical symptoms. J Psychosom Res 1995;39(7):855-63.

475. Vedsted P, Christensen MB, Sorensen HT, Fink P, Olesen F. Special status consultation for frequent attenders. Who are the candidates? J Pub Health Med 2002;24(1):53-7.

476. Kinnersley P, Rapport FM, Owen P, Stott N. In-house referral: a primary care alternative to immediate secondary care referral? Fam Pract 1999;16(6):558-61.

477. Speckens AE, Van Hemert AM, Bolk JH, Hawton K, Rooijmans HG. The acceptability of psychological treatment in patients with medically unexplained physical symptoms. J Psychosom Res 1995;39(7):855-63.

478. Vedsted P, Christensen MB, Sorensen HT, Fink P, Olesen F. Special status consultation for frequent attenders. Who are the candidates? J Pub Health Med 2002;24(1):53-7.

479. Phongsavan P, Ward JE, Oldenburg BF, Gordon JJ. Mental health care practices and educational needs of general practitioners. Med J Aust 1995;162(3):139-42.

480. Mayou R, Sharpe M. Treating medically unexplained physical symptoms. BMJ 1997;315(7108):561-2.

481. Locke SE, Ford P, McLaughlin T. A comparative cost analysis of participating versus non-participating somatizing patients referred to a behavioral medicine group in a health maintenance organization. Dis Man Health Outcomes 2003;11(5):327-35.

482. Matalon A, Nahmani T, Rabin S, Maoz B, Hart J. A short-term intervention in a multidisciplinary referral clinic for primary care frequent attenders: description of the model, patient characteristics and their use of medical resources. Fam Pract 2002;19(3):251-6.

483. Lyles JS, Hodges AM, Collins C, Lein C, Given CW, Given B et al. Using nurse practitioners to implement an intervention in primary care for high-utilizing patients with medically unexplained symptoms. Gen Hosp Psychiatry 2003;25(2):63-73.

484. Schreuders B, Van Oppen P, Van Marwijk HWJ, Smit JH, Stalman WA. Frequent attenders in general practice: problem solving treatment provided by nurses. BMC Fam Pract 2005;6(42).

485. Kashner TM, Rost K, Smith GR, Lewis S. An analysis of panel data. The impact of a psychiatric consultation letter on the expenditures and outcomes of care for patients with somatization disorder. Med Care 1992;30(9):811-21.

486. Rost K, Kashner TM, Smith RG. Effectiveness of psychiatric intervention with somatization disorder patients: improved outcomes at reduced costs. Gen Hosp Psychiatry 1994;16(6):381-7.

487. Smith GR, Jr., Rost K, Kashner TM. A trial of the effect of a standardized psychiatric consultation on health outcomes and costs in somatizing patients. Arch Gen Psychiatry 1995;52(3):238-43.

488. Fisch RZ. Masked depression: its interrelations with somatization, hypochondriasis and conversion. Int J Psychiatry Med 1987;17(4):367-79.

489. Badger LW, De Gruy FV, Hartman J, Plant MA, Leeper J, Anderson R et al. Patient presentation, interview content, and the detection of depression by primary care physicians. Psychosom Med 1994;56(2):128-35.

490. Wittchen HU, Hofler M, Meister W. Prevalence and recognition of depressive syndromes in German primary care settings: poorly recognized and treated? Int Clin Psychopharmacol 2001;16(3):121-35.

491. Lowe B, Spitzer RL, Grafe K, Kroenke K, Quenter A, Zipfel S et al. Comparative validity of three screening questionnaires for DSM-IV depressive disorders and physicians' diagnoses. J Affect Disord 2004;78(2):131-40.

492. Henk HJ, Katzelnick DJ, Kobak KA, Greist JH, Jefferson JW. Medical costs attributed to depression among patients with a history of high medical expenses in a health maintenance organization. Arch Gen Psychiatry 1996;53(10):899-904.

493. Hildebrandt DE, Westfall JM, Nicholas RA, Smith PC, Stern J. Are frequent callers to family physicians high utilizers. Ann Fam Med 2004;2(6):546-8.

494. Blankenstein AH, van der Horst HE, Schilte AF, De Vries D, Zaat JO, Andre KJ et al. Development and feasibility of a modified reattribution model for somatising patients, applied by their own general practitioners. Patient Educ Couns 2002;47(3):229-35.

495. Fink P, Rosendal M, Toft T. Assessment and treatment of functional disorders in general practice: The extended reattribution and management model - An advanced educational program for nonpsychiatric doctors. Psychosomatics 2002;43(2):93-131.

496. Kaaya S, Goldberg D, Gask L. Management of Somatic Presentations of Psychiatric-Illness in General Medical Settings - Evaluation of A New Training Course for General-Practitioners. Med Educ 1992;26(2):138-44.

497. Lin E, Katon W, Simon GE, Von Korff M, Bush TM, Rutter C et al. Achieving guidelines for the treatment of depression in primary care: is physician education enough? Med Care 1995;35(8):831-42.

498. Morriss R, Gask L. Treatment of Patients With Somatized Mental Disorder: Effects of Reattribution Training on Outcomes Under the Direct Control of the Family Doctor. Psychosomatics 2002;43(5):394-9.

499. Egan KJ, Beaton R. Response to symptoms in healthy low utilisers of the health care system. J Psychiatr Res 1987;31(1):11-21.

500. Murray J, Corney R. Not a medical problem? An intensive study of the attitudes and illness behaviour of low attenders with psychosocial difficulties. Soc Psychiatry Psychiatr Epidemiol 1990;25(3):159-64.

501. Chung S. Does the Use of SSRIs Reduce Medical Care Utilization and Expenditures? J Ment Health Policy Econ 2005;8(3):119-29.

502. Broadhead WE, Clapp-Channing N, Finch JN, Copeland JA. Effects of medical illness and somatic symptoms on treatment of depression in a family medicine residency practice. Gen Hosp Psychiatry 1989;11(3):194-200; discussion 216-21.

503. Tylee AT, Freeling P, Kerry S. Why do general practitioners recognize major depression in one woman patient yet miss it in another? BJGP 1993;43(373):327-30.

504. Katon WJ, Simon G, Russo J, Von Korff M, Lin EH, Ludman E et al. Quality of depression care in a population-based sample of patients with diabetes and major depression. Med Care 2004;42(12):1222-9.

505. Armstrong D, Fry J, Armstrong P. Doctors' perceptions of pressure from patients for referral. BMJ 1991;302(6786):1186-8.

506. Jones E, Stott NC. Avoidable referrals? Analysis of 170 consecutive referrals to secondary care. BMJ 1994;309(6954):576-8.

507. Craig TK, Boardman AP, Mills K, Daly-Jones O, Drake H. The South London Somatisation Study. I: Longitudinal course and the influence of early life experiences. Br J Psychiatry 1993;163:579-88.

508. Jackson JL, Passamonti M. The Outcomes Among Patients Presenting in Primary Care with a Physical Symptom at 5 Years. J Gen Intern Med 2005;20(11):1032-7.

509. Diez-Quevedo C, Rangil T, Sanchez-Planell L, Kroenke K, Spitzer RL. Validation and utility of the patient health questionnaire in diagnosing mental disorders in 1003 general hospital Spanish inpatients. Psychosom Med 2001;63(4):679-86.

510. Persoons P, Luyckx K, Desloovere C, Vandenberghe J, Fischler B. Anxiety and mood disorders in otorhinolaryngology outpatients presenting with dizziness: validation of the self-administered PRIME-MD Patient Health Questionnaire and epidemiology. Gen Hosp Psychiatry 2003;25(5):316-23.

511. Lowe B, Grafe K, Zipfel S, Spitzer RL, Herrmann-Lingen C, Witte S et al. Detecting panic disorder in medical and psychosomatic outpatients: comparative validation of the Hospital Anxiety and Depression Scale, the Patient Health Questionnaire, a screening question, and physicians' diagnosis. J Psychosom Res 2003;55(6):515-9.

512. Lowe B, Unutzer J, Callahan CM, Perkins AJ, Kroenke K. Monitoring depression treatment outcomes with the patient health questionnaire-9. Med Care 2004;42(12):1194-201.

513. Scaife B, Gill P, Heywood P, Neal R. Socio-economic characteristics of adult frequent attenders in general practice: secondary analysis of data. Fam Pract 2000;17(4):298-304.

514. Ballas CA, Staab JP. Medically unexplained physical symptoms: toward an alternative paradigm for diagnosis and treatment. CNS Spectr 2003;8(12 Suppl 3):20-6.

515. Binder LM, Campbell KA. Medically unexplained symptoms and neuropsychological assessment. J Clin Exp Neuropsychol 2004;26(3):369-92.

516. Brown RJ. Psychological mechanisms of medically unexplained symptoms: an integrative conceptual model. Psychol Bull 2004;130(5):793-812.

517. Heinrich TW. Medically unexplained symptoms and the concept of somatization. WMJ 2004;103(6):83-7.

518. Hurwitz TA. Somatization and conversion disorder. Can J Psychiatry 2004;49(3):172-8.

519. Merskey H. Somatization, hysteria, or incompletely explained symptoms? Can J Psychiatry 2004;49(10):649-51.

520. Mai F. Somatization disorder: a practical review. Can J Psychiatry 2004;49(10):652-62.

521. Sharpe M, Mayou R. Somatoform disorders: a help or hindrance to good patient care? Br J Psychiatry 2004;184:465-7.

522. Wessely S, White PD. There is only one functional somatic syndrome. Br J Psychiatry 2004;185(2):95-6.

523. Reuber M, Mitchell AJ, Howlett SJ, Crimlisk HL, Grunewald RA. Functional symptoms in neurology: questions and answers. Journal of Neurology, Neurosurgery, and Psychiatry 2005;76(3):307-14.

524. Smith RC, Gardiner JC, Lyles JS, Sirbu C, Dwamena FC, Hodges AM et al. Exploration of DSM-IV Criteria in Primary Care Patients With Medically Unexplained Symptoms. Psychosom Med 2005;67(1):123-9.

525. Fink P, Rosendal M, Olesen F. Classification of somatization and functional somatic symptoms in primary care. Aust N Z J Psychiatry 2005;39:772-81.

526. Hinsliff, G. Plan to cut outpatient numbers by 1m. http://observer.guardian.co.uk/uk_news/story/0,,1697410,00.html . 29-1-2006. 29-1-2006.
Ref Type: Electronic Citation

527. Gill D, Dawes M, Sharpe M, Mayou R. GP frequent consulters: their prevalence, natural history, and contribution to rising workload. Br J Gen Pract 1998;48(437):1856-7.

528. Dowrick C. Rethinking the doctor-patient relationship in general practice. Health Soc Care Community 1997;5(1):11-4.

529. Ferrer R, Hambidge S, Maly R. The essential role of generalists in health care systems. Ann Intern Med 2005;142(8):691-9.

530. Salmon P, May CR. Patients' influence on doctors' behavior: a case study of patient strategies in somatization. Int J Psychiatry Med 1995;25(4):319-29.

531. Echlin D, Garden AS, Salmon P. Listening to patients with unexplained menstrual symptoms: what do they tell the gynaecologist? BJOG. 2002;109(12):1335-40.

532. Salmon P, Dowrick CF, Ring A, Humphris GM. Voiced but unheard agendas: qualitative analysis of the psychosocial cues that patients with unexplained symptoms present to general practitioners. Br J Gen Pract 2004;54(500):171-6.

Appendices

Appendix 1. Single practice pilot study's operationalised criteria

Single Practice Pilot Study Operationalised Criteria

The core of the operationalised criteria:
1. The patient is referred with a symptom the cause of which is not known
2. How explained the symptom is, based on the specialist's opinion

Referrals for complaints fall into several categories:

- **referrals for patient's subjective symptoms**
- referrals for clear positive findings e.g. abnormal LFTs or FBC
- referrals for patient's subjective symptoms accompanied by ***relevant*** positive GP findings e.g. dysuria and positive urinalysis.
- referrals for advice
- referrals for follow up of "explained" condition (cancer, sarcoidosis, diabetes, haemophilia)
- referrals for specific pain management (even if pain unexplained)

For referrals not outlined in bold, the referral will *not* be considered for an unexplained symptom. These will be classified under *different headings* so that the *proportion* of subjective symptoms unexplained after secondary care consultation can be analysed separately.

Determining MUS from case notes

The following criteria will be applied to each consultation episode;

1. The patient presents with subjective physical symptoms.
2. A history is taken by a specialist and/or clinical examination(s) and/or investigations are done.
3. The specialist completes all planned investigations and sends a letter to the GP

MUS are elicited when:

There is an absence of evidence that a defined organic disease caused the symptom. This is possible when;

- The final diagnosis suggests doubt surrounding the cause of symptom
- The final diagnosis is a recognised medically unexplained (functional) syndrome.
- The investigations performed were normal or, if abnormal, was felt by the specialist to be an incidental finding or unlikely to account for the severity of the presenting symptom.

In all cases, the underlying opinion ***of the specialist*** should be interpreted from the case notes and we should not attempt to second-guess this opinion.

Unexplained symptom scale

Each consultation episode for a symptom will be scored using the scale below:

0. Explained
1. *Largely* explained *(Somewhat* unexplained)
2. *Largely* unexplained
3. *Completely* unexplained

Completely *medically unexplained*

- Evidence of a thorough investigation of the symptoms, all of which were negative;
  OR
- Diagnosis was made of a medically unexplained syndrome (e.g. fibromyalgia, irritable bowel syndrome, chronic fatigue syndrome, tension headache, ME);
  OR
- Conclusion that "no organic basis" for presenting symptoms;
  OR
- A psychosocial "diagnosis" is made e.g. anxiety, depression, and problems at home.

***Medically Explained* (Not at all *medically unexplained*)**

A clear connection exists between positive findings from clinical examination/investigations and presenting symptom(s) leading to diagnosis.

Intermediate categories

- Used when there is an absence of clear evidence that a defined organic disease caused the presenting symptom(s);
  OR
- Diagnostic uncertainty is expressed;
  OR
- Investigations are inconclusive.

***Largely* medically explained *(Somewhat* medically unexplained)**

- When there are positive investigations/examination findings which are, in the opinion of the specialist or reviewer, likely ("probably") to be pertinent to the aetiology of the presenting symptom but insufficient evidence to make a more certain diagnosis;
  OR
- When a diagnosis of an "organic condition" is described as a "probability" but history/examination/investigations do not allow specialist to be more definitive.

***Largely* medically unexplained**

- The physician *suggests* a functional syndrome or other diagnosis which implies MUS (IBS, atypical chest pain, chronic fatigue syndrome);
  OR
- Positive investigations/examination findings are unlikely to be pertinent to the aetiology *of the presenting symptom, unless* specialist states that findings *are* relevant; OR
- Positive investigations/examination findings appear to be pertinent to the presenting symptom but the specialist or the case note reviewer considers the response to the symptom to be *out of proportion* to the positive findings and apparent severity of any underlying "organic" condition for example, lower back pain and associated disability; OR
- Suggests a diagnosis but expresses doubts about its likelihood or considers it only to be a "possibility" and makes no further attempts to clarify.

Appendix 2. Table of deprivation quintiles for the five participating practices and comparisons with other general practices in Lothian and the rest of Scotland

Practice	Population Quintile 1	(%)	Population Quintile 2	(%)	Population Quintile 3	(%)	Population Quintile 4	(%)	Population Quintile 5	(%)	Population Total
Practice 1	8,957	(84.9)	776	(7.4)	244	(2.3)	159	(1.5)	418	(4.0)	10,554
Practice 2a	1,093	(57.8)	329	(17.4)	145	(7.7)	195	(10.3)	128	(6.8)	1,890
Practice 2b	1,054	(59.1)	311	(17.4)	154	(8.6)	204	(11.4)	61	(3.4)	1,784
Practice 2c	3,311	(57.9)	985	(17.2)	368	(6.4)	786	(13.8)	266	(4.7)	5,716
Practice 2d	1,054	(59.1)	311	(17.4)	154	(8.6)	204	(11.4)	61	(3.4)	1,784
Practice 3	789	(15.7)	646	(12.9)	331	(6.6)	2,289	(45.6)	960	(19.1)	5,015
Practice 4	514	(9.2)	623	(11.2)	295	(5.3)	598	(10.7)	3,544	(63.6)	5,574
Practice 5	7,823	(92.0)	180	(2.1)	376	(4.4)	90	(1.1)	30	(0.4)	8,499
N average (%)	24,595	(54.5)	4,161	(12.9)	2,067	(6.3)	4,525	(13.2)	5,468	(13.2)	40,816
All Lothian	282,973	(33.7)	154,390	(18.4)	136,147	(16.2)	172,825	(20.6)	92,432	(11.0)	838,767
All Scotland	1,065,195	(19.8)	1,073,199	(20.0)	1,070,971	(19.9)	1,075,059	(20.0)	1,086,640	(20.2)	5,371,064

N.B. This data, based on 2004 Scottish Index of Multiple Deprivation (SIMD) data, was obtained from ISD when seeking to clarify examiners' questions resulting from my thesis defense on 9th October 2006. Thus, the numbers for the practices are different to those outlined in the main text of the thesis. Regardless of the year differences, this table demonstrates the proportions of patient deprivation served by the five participating practices in comparison to the rest of the Lothian and Scottish primary care populations.

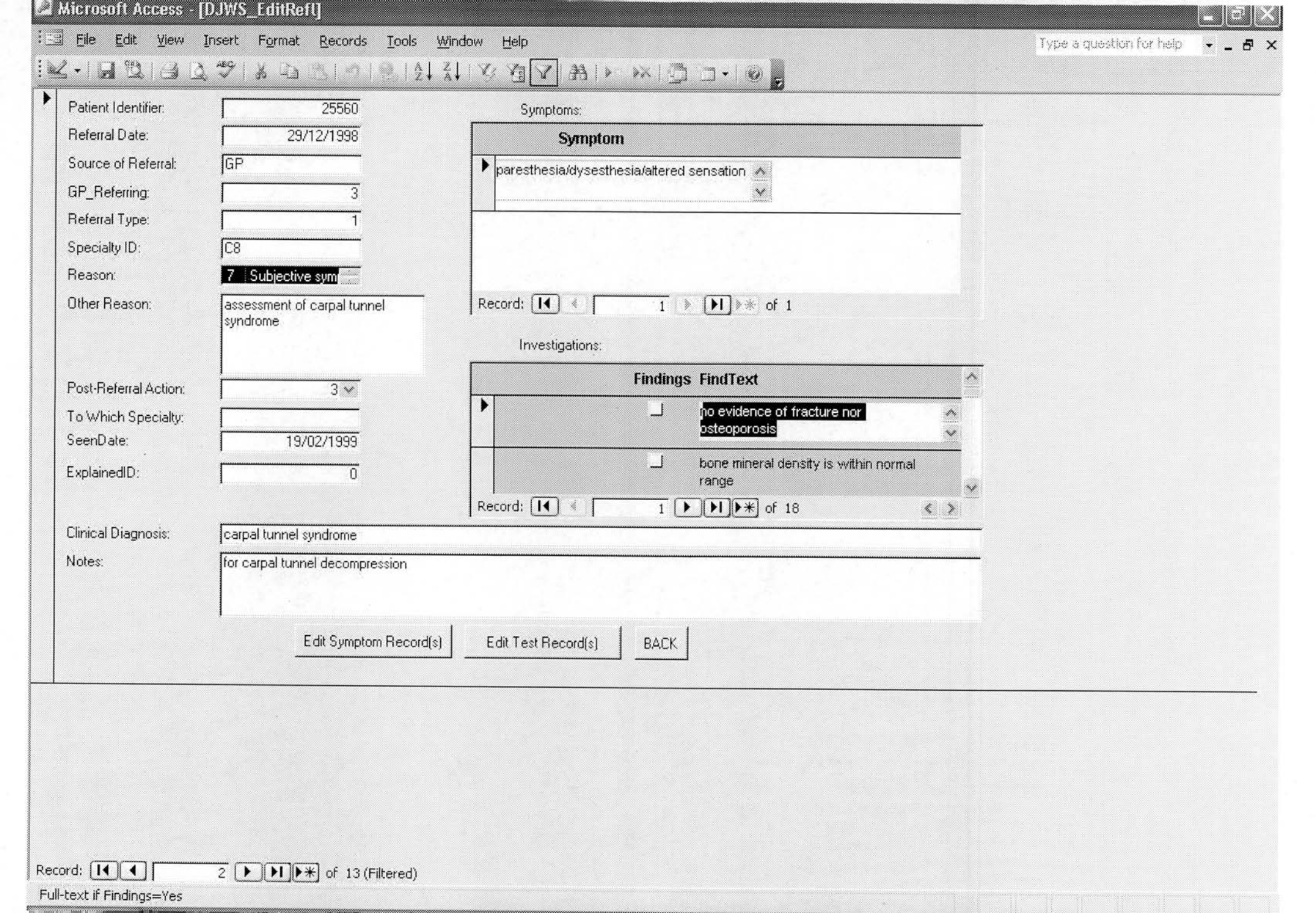
Appendix 3. Screen views of Microsoft Access data entry forms for case note audit

File Edit View Insert Format Records Tools Window Help

Type a question for help

Patient Identifier:
Surname:
Forname:
Previous surname:
Date Registered:
Address:
City:
Postcode:
Telephone:
CHI:
Sex:
Registered GP:
PracticeID:
Deducted:
Auditdate:
Current ADs:
Casenote volumes:
Smoker?
No. of ISD Refs:
Date of birth:
Title:
Date Deducted:
Past ADs:
CBT:
Overweight?
DNAs:
Current Antideps:
Past Antideps:
Year last Ad:
IR/FR:
GP Refs:
Hospref:
Private:
Allrefs:
NumMUS
DOHs:
A and E:
Reviews:
Admit days:
MH days:
Current opioids:
Current Opioid
Past opioids:
Past Opioid:
Medical Condition1:
Medical Condition2:
Medical Condition3:
Medical Condition4:
Medical Condition5:
Medical Condition6:
Medical Condition7:
Medical Condition8:
Other Medical Conditions:
BACK
Edit Referral Record(s)
Case or Contro ?
Control / FR
Control / FRMES
Case / FRMUS
Not Eligible
Reason NE:
Retest?
Opted Out:
Opt Out reason:
Reviewer rating:
Retestdat:
NOTES:

Record:


Microsoft Access - [DJWS_EditRef]
File Edit View Insert Format Records Tools Window Help
Type a question for help
Patient Identifier: 25560
Referral Date: 29/12/1998
Source of Referral: GP
GP_Referring: 3
Referral Type: 1
Specialty ID: C8
Reason: 7 Subjective sym
Other Reason: assessment of carpal tunnel syndrome
Post-Referral Action: 3
To Which Specialty:
SeenDate: 19/02/1999
ExplainedID: 0
Symptoms:
Symptom
paresthesia/dysesthesia/altered sensation
Record: 1 of 1
Investigations:
Findings FindText
no evidence of fracture nor osteoporosis
bone mineral density is within normal range
Record: 1 of 18
Clinical Diagnosis: carpal tunnel syndrome
Notes: for carpal tunnel decompression
Edit Symptom Record(s)
Edit Test Record(s)
BACK
Record: 2 of 13 (Filtered)
Full-text if Findings=Yes

Appendix 4. List of all symptoms referred for FRMUS, and the proportions deemed MUS.

Explanation	totally (n=480)	largely (n=393)	*somewhat (n=626)*	*not at all (n=1127)*	MUS % (66.76)	seen (n=2626)	no outcome (n=110)	Total (N=2736)
abdo. pain	10	18	33	80	80.14	141	6	147
back pain	23	19	29	36	60.75	107	3	110
joint pain (other)	27	20	16	25	46.59	88	5	93
chest pain	8	9	22	48	80.46	87	1	88
headache	5	8	26	40	83.54	79	4	83
paraesthesia	15	7	18	30	68.57	70	9	79
fatigue	7	7	15	45	81.08	74	1	75
bladder problems	11	5	16	30	74.19	62	2	64
arm/leg pain	11	8	16	28	69.84	63	0	63
dizziness	2	7	21	31	85.25	61	1	62
lump	41	7	8	4	20.00	60	2	62
breathing	11	6	11	27	69.09	55	1	56
joint probs.	17	12	9	16	46.30	54	2	56
epigastric pain	8	6	10	24	70.83	48	4	52
mastalgia	6	9	12	21	68.75	48	3	51
nausea	3	3	16	21	86.05	43	3	46
PR bleed	16	6	10	11	48.84	43	2	45
cough	7	8	13	14	64.29	42	2	44
pelvic pain	6	5	10	21	73.81	42	1	43
visual blurring	4	5	9	22	77.50	40	2	42
knee pain	6	12	10	10	52.63	38	3	41
altered bowel habit	4	2	8	21	82.86	35	5	40
menorrhagia	2	8	19	11	75.00	40	0	40
incontinent	5	5	13	13	72.22	36	2	38
constipation	9	4	8	16	64.86	37	1	38
neck pain	4	3	10	18	80.00	35	2	37
nasal/sinus	16	6	6	7	37.14	35	2	37
rash	17	8	2	5	21.88	32	5	37
diarrhoea	5	2	10	18	80.00	35	0	35
hand/foot pain	14	8	4	5	29.03	31	4	35
dysphonia	4	6	9	14	69.70	33	0	33
itch	14	6	3	5	28.57	28	5	33
bloating	3	5	8	16	75.00	32	0	32
indigestion	7	4	6	13	63.33	30	2	32
IMB/PCB	4	5	10	12	70.97	31	0	31
misc. neuro.	4	4	5	19	75.00	32	0	32
raynauds phenomenon	0	1	0	1	50.00	2	0	2
irregular periods	1	9	8	12	66.67	30	0	30
weakness	4	3	5	13	72.00	25	2	27
faint	1	3	5	15	83.33	24	2	26
throat pain	5	1	4	16	76.92	26	0	26
swallowing problems	3	4	4	14	72.00	25	1	26
vomit	2	5	5	13	72.00	25	0	25
palpitations	1	6	3	11	66.67	21	2	23
pain with sex (dyspareunia)	3	6	7	6	59.09	22	0	22
hearing	4	6	7	4	52.38	21	1	22

Explanation	totally (n=480)	largely (n=393)	*somewhat (n=626)*	*not at all (n=1127)*	MUS % (66.76)	seen (n=2626)	no outcome (n=110)	Total (N=2736)
pain (other)	11	0	3	7	47.62	21	1	22
genital pain	2	7	7	5	57.14	21	0	21
facial pain	6	3	1	10	55.00	20	1	21
sweating	0	3	7	10	85.00	20	0	20
tinnitus	2	5	4	8	63.16	19	1	20
tenesmus (trouble defaecating)	6	2	3	9	60.00	20	0	20
discharge	8	6	3	3	30.00	20	0	20
groin pain	2	2	5	10	78.95	19	0	19
otalgia	4	2	4	9	68.42	19	0	19
retention	5	1	7	6	68.42	19	0	19
vision loss	6	3	3	5	47.06	17	2	19
pain (vague)	1	1	4	11	88.24	17	0	17
dysuria	1	1	5	8	86.67	15	1	16
anal pain	4	2	1	8	60.00	15	1	16
vasomotor symptoms	3	4	2	7	56.25	16	0	16
'stuck in throat'	1	0	5	8	92.86	14	0	14
sleep probs.	2	0	4	8	85.71	14	0	14
sex problems	0	4	3	6	69.23	13	1	14
period pain	0	1	5	7	92.31	13	0	13
Post-menopausal bleeding	1	6	4	2	46.15	13	0	13
excess wind	1	1	0	8	80.00	10	2	12
weight loss	2	1	1	6	70.00	10	2	12
wheeze	2	0	3	4	77.78	9	2	11
eye pain	1	3	1	6	63.64	11	0	11
hip pain	2	3	1	5	54.55	11	0	11
erectile dysfunction	0	1	2	6	88.89	9	1	10
loss of appetite	0	0	3	6	100.00	9	0	9
'something coming down'	5	0	2	2	44.44	9	0	9
fits	0	2	2	3	71.43	7	1	8
amenorrhoea	0	3	4	0	57.14	7	0	7
altered sense (taste/smell)	0	0	0	6	100.00	6	0	6
faecal probs.	1	0	2	3	83.33	6	0	6
tremor	1	1	3	1	66.67	6	0	6
snoring	4	2	0	0	0.00	6	0	6
Gynae(other)	0	3	1	1	40.00	5	0	5
eye problems	1	2	1	0	25.00	4	0	4
thirst	2	0	0	1	33.33	3	0	3
speech probs.	0	0	0	1	100.00	1	0	1
misc. symptoms	13	12	21	40	70.93	86	1	87

Appendix 5. GP difficulty rating form

The Referral Study

Principal Investigators: Dr. Michael Sharpe & Prof. David Weller

Research Nurse & Contact: Ms. Kelly McGorm

Patient ID: **CHI:** **ID:**

Today's Date: / /200

Dear Dr.

Thank you for being part of this study and filling out this form about the above patient. We are trying to obtain a sense of how you feel re managing this patient and the problems they present with.

Please note that the PHC Trust have stated they will reimburse participating GPs for their time towards this study. Be assured that your responses remain strictly ***confidential***. When complete, please leave this form with {practice manager's name}. I will be visiting the practice weekly and collect it then.

If you wish to provide other comments either use the section provided below or the back of this page. Do not hesitate to contact me by telephone (0131) **650 9464, 07932 565018** or email kelly.mcgorm@ed.ac.uk if you have queries or concerns about any aspect of the Referral Study.

	Extreme Difficulty	Moderate Difficulty	Some Difficulty	A little difficulty	No difficulty at all
To what extent do you feel you have difficulties helping this patient and the problems they present with?	❑	❑	❑	❑	❑
Comment:					

With kind regards and many thanks for your time

Kelly McGorm
Research Nurse, General Practice, University of Edinburgh

Appendix 6. GP invitation letter to the patient

{Practice Letter Head}

Dear {Patient name}

Our practice is participating in a research study of referrals to hospital for patients who have presented with various symptoms common to General Practice. **'The Referral Study'** is being conducted by the University of Edinburgh and funded by the Scottish Chief Scientist's Office. The aim of this study is to provide information to help the NHS better meet the needs of patients referred to hospital.

As you have been referred to hospital services in the last few years, we hope that you will participate. We are aware that some patients are referred more than others; some only the once in their lifetime. As such, we are inviting patients from the practice that have been referred once or more in order to obtain a range of perspectives and experiences.

I encourage you to read the information sheet enclosed with this letter as it provides more information about what is involved. If you are willing to participate, please check and sign the consent form, complete the questionnaire enclosed and return these two documents in the enclosed reply-paid envelope. This may take about 20 minutes.

If you decide not to take part in the study, please return the enclosed consent form leaving it blank. The number on the form will ensure that we do not contact you any further about this. It would be helpful if you can tell us why you prefer not to participate, but you do not have to do this. Please be assured that your decision will not affect your care with this practice in any way.

If you have any questions or require further information, call Kelly McGorm (the Research Nurse running the study) on 0131 650 9461 or contact me via the practice.

Yours sincerely and thank you for your time,

Dr. {GP name}

Appendix 7. Patient information sheet

THE REFERRAL STUDY

Contact Person
Kelly McGorm, Research Nurse
(0131) 650 9461

Principal Investigators
Prof. Michael Sharpe
Prof. David Weller

Patient Information Sheet
10 May 2004

This is information for you to keep in case you have any questions about the study in the future.

Introduction

You are being invited to take part in a research study. Before you make the decision to participate, it is important for you to understand why the research is being done and what it will involve. Please take your time to read the following information carefully and discuss it with others if you wish. Feel free to contact us if there is anything that is not clear or if you would like more information.

What is the aim of the study?

We are carrying out a study with the General Practitioners (GPs) at your practice. Patients are referred to hospital by their GPs for many different reasons. We would like to learn more about these reasons and your experience of being referred. Our particular interest involves the symptoms patients present with.

Our overall aim is to learn more about what it is like to be referred to hospital outpatient departments and how helpful it is for patients. The results of this study will help advise the NHS in order to improve the care of future patients.

Why have I been chosen?

We are inviting patients who have been referred to hospital outpatient clinics by their GP one or more times within the last five years.

Do I have to take part?

Taking part in this research is voluntary. It is up to you to decide whether or not to take part. If you do decide to participate you will be asked to sign the enclosed consent form and return it in the stamped, self-addressed envelope. If you do decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw, or not to take part, will not affect your care with your doctors or the NHS in any way.

What would I have to do?

If you do agree to take part, we ask that you fill out the enclosed questionnaire. This should take approximately 20 minutes to complete. The questionnaire asks general questions about your health and medical history. It would be helpful if you could answer <u>all</u> the questions. You have the option to contact the Research Nurse at any time and discuss the questions, or other aspects of the study, if you have any queries or comments.

Should you be referred to a hospital outpatient clinic again before August 2005, the Research Nurse would like to talk to you about your latest experience and will invite you for a brief interview either over the phone or in person (which ever is most convenient for you). The researcher would also like to talk to the GP that referred you to understand the reasons why you were referred.

THE REFERRAL STUDY

Contact Person
Kelly McGorm, Research Nurse
(0131) 650 9461

Principal Investigators
Prof. Michael Sharpe
Prof. David Weller

Will it be confidential?
All information collected about you during the course of the research will be kept strictly confidential. The Research Nurse will review your case notes for study purposes only, and no identifying information will be removed from the practice. Any information about you which does leave the practice will have your name and address removed so that you cannot be recognised from it.

Your GP will be notified of your participation in the study. If we find out important clinical information during the study which is relevant to your medical care we may inform your doctor after discussing it with you first.

What are the possible disadvantages and risks of taking part?
There are no foreseeable risks from being involved in this study.

What are the possible benefits of taking part?
There is no direct clinical benefit to you from taking part in the study. The information gained from your involvement in this study may better help us understand and meet the needs of future patients referred to hospital outpatient clinics by their GP.

What will happen to the results of the research study?
It will take one to two years to complete this study. The results of the study are likely to be published in 2005-2006. If you are interested in receiving a copy of the results, please indicate this on the questionnaire by ticking the appropriate box, and we will send out a summary to you. You will not be identified in any report or publication.

Who is funding the research?
The Chief Scientist Office (CSO) of the Scottish Executive has funded this study for three years.

Who has reviewed the study?
This study has been reviewed and approved by a Lothian Research Ethics Committee.

Any questions?
Kelly McGorm, the Research Nurse, is happy to be contacted at any time should you have any questions about the study. Her contact number is (0131) 650 9461. If you get the answering machine, please leave your name and number and she will get back to you as quickly as possible.

If you would like to speak to someone who knows about the project but is *independent* from it, you can contact Dr. Christine Campbell in the Department of General Practice, University of Edinburgh on (0131) 650 9252.

Thank you for taking the time to read this information.

Appendix 8. Patient consent form

THE REFERRAL STUDY

Contact Person
Kelly McGorm, Research Nurse
(0131) 650 9461

Principal Investigators
Prof. Michael Sharpe
Prof. David Weller

CONSENT FORM

10 May 2004

ID no. «patient_identifier»

Title of Project: **The Referral Study**
Name of Researcher: **Kelly McGorm**
Principal Investigators: **Prof. Michael Sharpe and Prof. David Weller**

1. I confirm that I have read and understand the information sheet dated 10 May 2004 for the above named study.
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
3. I understand that sections of my medical notes may be examined in confidence by the Research Nurse where it is relevant to my taking part in this research. I give permission for the Research Nurse to have access to my medical records.
4. I understand that clinically important information may be communicated to my General Practitioner.
5. I agree to the above. ☐ Please initial each box
6. I agree to any information about future hospital referrals being confidentially reviewed by the Research Nurse. ☐ Please initial each box
7. I agree to the Research Nurse contacting me by letter or telephone in the event that I am referred to a hospital outpatient clinic for the purposes of this study. ☐ Please initial each box
8. There is a possibility that another project may result from this study. I am willing for a researcher to contact me in the future to provide me with information about this. ☐ Please initial each box

Name (please print) **Today's Date** **Signature**

I DO NOT WANT TO PARTICIPATE IN THE STUDY AND DO NOT WISH TO BE CONTACTED AGAIN – TICK THIS BOX AND PROVIDE YOUR NAME (NO SIGNATURE NECESSARY) ☐

Although you are not obliged, it would help us to know why you have or have not decided to participate. Please tell us using the space below.

PLEASE KEEP A COPY OF THE CONSENT FORM FOR YOUR OWN USE AND RETURN THE SIGNED CONSENT FORM IN THE ACCOMPANYING STAMPED ADDRESSED ENVELOPE WITH THE QUESTIONNAIRE. THANK YOU

Appendix 9. Patient baseline questionnaire

The Referral Study Questionnaire

Principal Investigators: ***Prof. Michael Sharpe***
Prof. David Weller
Research Nurse & Contact: ***Ms. Kelly McGorm***

Dear Participant,

Thank you for being part of 'The Referral Study' and filling out this questionnaire. We hope the results of this study will help advise the NHS to improve services of patients referred to hospital. The 'participant number' on each page is to ensure that you cannot be identified by name. Your responses will be kept strictly ***anonymous***.

Please check that you have ***answered all of the required questions.*** When you have finished, return the questionnaire in the self-addressed reply-paid envelope supplied.

Should you have any problems or concerns about answering any of the questions, feel free to contact me by telephone (0131) **650 9461** or email kelly.mcgorm@ed.ac.uk .

Wishing you well!

Kelly McGorm

Research Nurse, General Practice, University of Edinburgh

The following is a sample of how to complete most of the questions. The questions for you to answer begin on page 2 under the heading: 'Referral from General Practice to Hospital Outpatient Clinics'.

Please complete each question by putting a clear mark (i.e. either colour in the circle, ✔ or X) in one circle for each line. Try to keep your mark the same throughout so that we know exactly what your answer is.

For example: *How* strongly do you agree or disagree with each of the following statements?

	Strongly agree	Agree	Uncertain	Disagree	Strongly Disagree
a) I enjoy listening to music.	●	❑	❑	❑	❑
Or					
b) I enjoy reading magazines.	❑	❑	☒	❑	❑

What is today's date? ____ / ____ / 200__

Referral from General Practice to Hospital Outpatient Clinics

The following questions ask you about your experience of being referred by your GP to hospital outpatient clinics. If you have seen more than one GP or hospital doctor, try to give an *overall answer*. There are no right or wrong answers. Your answers are confidential and will not be seen by your doctors.

1. Thinking about your *most recent referral* to a hospital outpatient clinic, please rate the following statements:	**Completely dissatisfied**	**Fairly dissatisfied**	**Neither satisfied or dissatisfied**	**Fairly satisfied**	**Completely satisfied**
a) The examination and/or tests the GP did before referring you to hospital	❑	❑	❑	❑	❑
b) Explanation from the GP about why you were referred	❑	❑	❑	❑	❑
c) Your overall satisfaction with your registered General Practice	❑	❑	❑	❑	❑
d) The time it took from the GP referring you to the time you actually saw the hospital doctor	❑	❑	❑	❑	❑
e) Access to the outpatient clinic i.e. distance from your home, transport etc.	❑	❑	❑	❑	❑
f) Information given to you by the hospital doctor about the problem you were referred for	❑	❑	❑	❑	❑
g) Your overall satisfaction with hospital outpatient services received	❑	❑	❑	❑	❑
h) If you would like to make comments about being referred *by your GP* to hospital outpatient clinics, please write them here.....					

2. Please rate the following statements:	**Strongly disagree**	**Disagree**	**Don't know**	**Agree**	**Strongly agree**
a) I think my health may benefit from seeing a medical or surgical specialist	❑	❑	❑	❑	❑
b) I have seen a medical or surgical specialist in the **last 12 months**:				**Yes** ❑	**No** ❑
c) I think my health may benefit from seeing a psychological or psychiatric specialist	❑	❑	❑	❑	❑
d) I have seen a psychological or psychiatric specialist in the **last 12 months**:				**Yes** ❑	**No** ❑

3. I feel comfortable discussing:	**Strongly disagree**	**Disagree**	**Don't know**	**Agree**	**Strongly agree**
a) Physical problems with my GP	❑	❑	❑	❑	❑
b) Emotional problems with my GP	❑	❑	❑	❑	❑
c) Physical problems with hospital doctors	❑	❑	❑	❑	❑
d) Emotional problems with hospital doctors	❑	❑	❑	❑	❑

General Health

Health has physical and emotional aspects; for example, experiencing pain can be upsetting and frustrating. The next few questions ask about your physical and emotional health and will help us understand how you have been feeling, and how well you have been able to do your usual activities.

	Excellent	Very good	Good	Fair	Poor
4. In general, would you say your health is:	❑	❑	❑	❑	❑

5. The following questions are about activities you might do during a typical day. Does **your health now limit you** in these activities? If so, how much? *Please tick only one box for each line*

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a) **Moderate activities,** such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	❑	❑	❑
b) Climbing **several** flights of stairs	❑	❑	❑

6. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities as a *result* of your **physical health**?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) **Accomplished less** than you would like	❑	❑	❑	❑	❑
b) Were limited in the **kind** of work or other activities	❑	❑	❑	❑	❑

7. During the **past 4 weeks**, how much of the time have you had any of the following problems with your work or other regular daily activities as a *result* of any **emotional problems** (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) **Accomplished less** than you would like	❑	❑	❑	❑	❑
b) Didn't do work or other activities as **carefully** as usual	❑	❑	❑	❑	❑

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including both work outside the home and housework)?

Not at all	A little bit	Moderately	Quite a bit	Extremely
❑	❑	❑	❑	❑

For each of the following questions (a, b and c), please give one answer that comes closest to the way you have been feeling recently.

9. How much of the time during the **past 4 weeks**...

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Have you felt calm and peaceful?	❑	❑	❑	❑	❑
b) Did you have a lot of energy?	❑	❑	❑	❑	❑
c) Have you felt downhearted and depressed?	❑	❑	❑	❑	❑

10. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
❑	❑	❑	❑	❑

11. Thinking about the health problems you have been referred to hospital outpatient clinics for, please indicate how much you agree or disagree with each of the five following statements (a, b, c, d, and e) by ticking the appropriate box.

	Strongly disagree	Disagree	Don't know	Agree	Strongly agree
a) My health problems have major consequences on my life	❑	❑	❑	❑	❑
b) Nothing I do will change these health problems	❑	❑	❑	❑	❑
c) My health problems are largely caused by stress or worry	❑	❑	❑	❑	❑
d) I worry a lot about my health	❑	❑	❑	❑	❑
e) I find that I am bothered by many different symptoms	❑	❑	❑	❑	❑

Symptoms

This section of the questionnaire asks about any **physical symptoms** that you may have experienced recently. Please answer each question unless you are requested to skip one.

12. During the **last 4 weeks,** how much have you been bothered by any of the following problems?

	Not bothered	Bothered a little	Bothered a lot
a) Stomach pain	❑	❑	❑
b) Back pain	❑	❑	❑
c) Pain in your arms, legs, or joints (knees, hips, etc.)	❑	❑	❑
d) Pain or problems during sexual intercourse	❑	❑	❑
e) Headaches	❑	❑	❑
f) Chest pain	❑	❑	❑
(Q 12 continued) **Symptoms** over the **last 4 weeks**	**Not bothered**	**Bothered a little**	**Bothered a lot**
g) Dizziness	❑	❑	❑

h) Fainting spells		❑	❑	❑
i) Feeling your heart pound or race		❑	❑	❑
j) Shortness of breath		❑	❑	❑
k) Constipation, loose bowels, or diarrhea		❑	❑	❑
l) Nausea, gas, or indigestion		❑	❑	❑
m) Menstrual cramps or other problems with your periods	❑ N/A (male)	❑	❑	❑
n) Please use this space to list any other symptoms…				

13. Over the **last 2 weeks**, how often have you been bothered by any of the following problems?

	Not at all	Several days	More than half the days	Nearly every day
a) Little interest or pleasure in doing things	❑	❑	❑	❑
b) Feeling down, depressed, or hopeless	❑	❑	❑	❑
c) Trouble falling or staying asleep, or sleeping too much	❑	❑	❑	❑
d) Feeling tired or having little energy	❑	❑	❑	❑
e) Poor appetite or overeating	❑	❑	❑	❑
f) Feeling bad about yourself, or that you are a failure, or have let yourself or your family down	❑	❑	❑	❑
g) Trouble concentrating on things, such as reading the newspaper or watching television	❑	❑	❑	❑
h) Moving or speaking so slowly that other people could have noticed. *Or the opposite* - Being so fidgety or restless that you have been moving around a lot more than usual	❑	❑	❑	❑
i) Thoughts that you would be better off dead or of hurting yourself in some way	❑	❑	❑	❑

	Yes	No
14. a) Thinking back over the **last 5 years**, do you remember any periods *lasting 2 weeks or more* where you felt down, depressed, or lost interest or pleasure in doing things?	❑	❑
14. b) If you answered "Yes", please <u>estimate</u> **how many episodes**:	episodes	N/A ❑

15. Over the **last 4 weeks**, how often have you been bothered by any of the following problems:

	Not at all	Several days	More than half the days
a) Feeling nervous, anxious, on edge, or worrying a lot about different things	❑	❑	❑
b) Feeling restless so that it is hard to sit still	❑	❑	❑
c) Becoming easily annoyed or irritable	❑	❑	❑

	Yes	No
16. During the **last 5 years**, have you felt nervous, anxious, on edge, or worrying a lot about different things more days than not? And has this lasted for a period *lasting 6 months or more*?	❑	❑
16. a) If you answered "Yes", please estimate **how many episodes** *lasting 6 months or more* you have had within the **last 5 years**:	episodes	N/A ❑

	Not at all	Several days	More than half the days
17. Over the **last 4 weeks**, have you had a **sudden** spell or attack (e.g. feeling frightened, anxious, uneasy, your heart race, faint, or unable to catch your breath)?	❑	❑	❑
17. a) If you have, please estimate **how many episodes** you have had over the **last 5 years**:	episodes		N/A ❑
17. b) Has this caused you a lot of worry or to change what you would usually do in anyway for a period ***lasting 1 month*** *or more*?	Yes ❑	No ❑	N/A ❑

18. If you checked off any problems in this section (*question 12 onwards*), how **difficult** have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
❑	❑	❑	❑

About You

Finally, we would like to ask you some basic details about your self so that we are able to determine the characteristics of participants in this study.

19. What is your **marital status?** *(Mark the best answer that applies to you)*

Single/Never Married	Living with a partner	Married	Divorced/separated	Widowed
❑	❑	❑	❑	❑

(Please mark one box)	Owned, occupied or mortgaged	Rented from a private landlord	Rented from a local authority or housing association	Other arrangements
20. Is your home:	❑	❑	❑	❑

21. How many years of education have you completed from the age of 16 years onwards? _____ years

22. Do you *currently* receive any of the following benefits? *(please tick all boxes that apply)*

N/A	Attendance allowance	Disability living allowance	Housing benefit	Incapacity benefit	Income support	Job seeker's allowance	Pension	Statutory sick pay
❑	❑	❑	❑	❑	❑	❑	❑	❑

22. a) Have you ever received any of these benefits for a period **lasting 6 months** or more? **Yes** ❑ **No** ❑

23. Which statement **best describes** your current situation? *(Please mark only one box)*

❑ Unemployed and looking for work	❑ Looking after the home and/or family full-time
❑ Intending to look for work but prevented by temporary sickness or injury	❑ Studying
❑ Permanently sick or disabled and not able to work	❑ Doing paid work or self-employed – full-time *
❑ Retired	❑ Doing paid work or self-employed – part-time *
23. a) * **If you work,** please tell us what you do …	

24. In the **last 5 years**,

a) Have you had any **paid employment**?	**Yes**	**No**	**N/A**	
	❑	❑	❑	
b) If 'Yes' has illness caused you to take **time off** from paid employment? *	**Less than 1 month**	**1 – 6 months**	**6 – 12 months**	**Over 12 months**
	❑	❑	❑	❑
*** If you have had to take more than 6 months time off work, please tell us what the problem was?**				
c) Has illness caused you to take time off from your **usual activities** other than paid work? *e.g. unable to for your usual Sunday walk due to pain*	**Not at all**	**A little time**	**A lot of time**	
	❑	❑	❑	

25. Please provide any other comments you would like to make about your experiences of being referred to hospital clinics from General Practice (e.g. what was good or not so good about being referred) Use the back of this page or enclose a separate piece of paper if you need to.

Comments:

Please check that you have answered each question.
When you have finished, return the questionnaire in the self-addressed reply-paid envelope supplied.
Thank you for your time and involvement in 'The Referral Study'

Appendix 10. Calculation of the weighted average cost of one day in hospital

In-Patient	Cases	Average length of stay	Cost/case	Cost/day	Share of cases	Weighted average cost
A&E	11,721	0.9	£480	£533	1.4%	£7.46
Acute other	363	8.3	£2,646	£319	0.0%	£0.14
Cardiac surgery	5,437	7.2	£8,288	£1,151	0.6%	£7.47
Cardiology	18,927	4.5	£1,958	£435	2.3%	£9.83
CCU	18,494	2.6	£1,444	£555	2.2%	£12.26
Communicable disease	5,900	6.8	£2,874	£423	0.7%	£2.98
Dental	87	1.1	£4,002	£3,638	0.0%	£0.38
Dermatology	2,363	14.6	£3,509	£240	0.3%	£0.68
ENT	25,486	2.2	£1,316	£598	3.0%	£18.19
Gastroenterology	6,179	6.7	£2,464	£368	0.7%	£2.71
General medicine	240,176	4.6	£1,264	£275	28.7%	£78.74
General surgery	135,612	4.5	£1,896	£421	16.2%	£68.17
GP	21,212	15.6	£3,118	£200	2.5%	£5.06
Gynaecology	30,883	2.7	£1,602	£593	3.7%	£21.86
Haematology	9,092	7.3	£3,060	£419	1.1%	£4.55
HDU	12,999	3.2	£1,781	£557	1.6%	£8.63
ICU	10,793	5.1	£7,422	£1,455	1.3%	£18.74
Medical oncology	6,736	4.4	£2,381	£541	0.8%	£4.35
Medical other	2,917	8.9	£3,201	£360	0.3%	£1.25
Nephrology	7,099	8.6	£3,418	£397	0.8%	£3.37
Neurology	4,225	6	£2,772	£462	0.5%	£2.33
Neurosurgery	7,436	6.4	£3,977	£621	0.9%	£5.51
Obstetrics GP	2,604	2.5	£1,629	£652	0.3%	£2.02
Obstetrics specialist	88,016	2.3	£1,298	£564	10.5%	£59.27
Ophthalmology	8,427	2.4	£1,844	£768	1.0%	£7.73
Oral surgery & medicine	4,828	2.6	£1,813	£697	0.6%	£4.02
Orthopaedics	66,593	6.5	£2,998	£461	7.9%	£36.65
Plastic surgery	11,714	3.4	£1,813	£533	1.4%	£7.45
Radiotherapy	11,142	5.7	£2,803	£492	1.3%	£6.54
Rehab medicine	2,900	39.2	£8,472	£216	0.3%	£0.75
Respiratory medicine	14,671	6.9	£1,738	£252	1.8%	£4.41
Rheumatology	2,004	10.3	£3,470	£337	0.2%	£0.81
Spinal paralysis	315	50.6	£20,336	£402	0.0%	£0.15
Thoracic surgery	4,004	5.1	£4,052	£795	0.5%	£3.80
Urology	30,740	3.4	£1,503	£442	3.7%	£16.21
Vascular surgery	6,014	7.6	£2,963	£390	0.7%	£2.80
	838,109		Average weighted inpatient cost			**£437.24**
(General psychiatry	20,985	157065	£1,485	£212)		

With thanks to Dr. Andrew Walker using NHS Scotland data, 2005

Appendix 11. Calculation of the weighted average cost of an outpatient consultation

Out-patient	Attendances	Cost per attend	Share of cases	Calc weighted ave. cost
A&E	0	0	0.0%	£0.00
Acute other	13,020	146	0.3%	£0.48
Cardiac surgery	6,389	344	0.2%	£0.55
Cardiology	120,325	145	3.0%	£4.38
CCU	0	0	0.0%	£0.00
Clinical genetics	4,571	291	0.1%	£0.33
Communicable disease	19,554	371	0.5%	£1.82
Dental	237,504	100	6.0%	£5.96
Dermatology	273,158	76	6.9%	£5.21
ENT	200,098	75	5.0%	£3.77
Gastroenterology	72,882	111	1.8%	£2.03
General medicine	299,909	112	7.5%	£8.43
General surgery	343,635	73	8.6%	£6.30
GP	6,465	41	0.2%	£0.07
Gynaecology	195,807	108	4.9%	£5.31
Haematology	199,677	114	5.0%	£5.71
HDU	0	0	0.0%	£0.00
ICU	0	0	0.0%	£0.00
Medical oncology	39,148	192	1.0%	£1.89
Medical other	134,183	97	3.4%	£3.27
Nephrology	58,476	90	1.5%	£1.32
Neurology	49,252	150	1.2%	£1.85
Neurosurgery	13,378	140	0.3%	£0.47
Obstetrics GP	943	77	0.0%	£0.02
Obstetrics specialist	193,828	104	4.9%	£5.06
Ophthalmology	404,565	65	10.2%	£6.60
Oral surgery & medicine	112,395	78	2.8%	£2.20
Orthopaedics	483,841	82	12.1%	£9.96
Pain relief	17,080	126	0.4%	£0.54
Plastic surgery	74,046	70	1.9%	£1.30
Radiotherapy	68,437	169	1.7%	£2.90
Rehab medicine	14,467	270	0.4%	£0.98
Respiratory medicine	79,950	110	2.0%	£2.21
Rheumatology	83,008	94	2.1%	£1.96
Spinal paralysis	0	0	0.0%	£0.00
Thoracic surgery	5,329	146	0.1%	£0.20
Urology	125,920	74	3.2%	£2.34
Vascular surgery	33,033	81	0.8%	£0.67
	3,984,273		Average weighted outpatient cost	**£96.08**

Appendix 12. Number and cost of new outpatient consultations for FRMUS patients (over a five year period) in order of proportion of cost for MUS

Outpatient Clinic	Cost/visit	All Referrals	Total cost (£)	Referrals for MUS	MUS cost (£)	MUS (%)
Total	(£)	**N = 1572**	**152328.00**	**n = 817**	**83554.00**	**54.9**
General Medicine	112.00	83	9296.00	65	7280.00	78.31
Cardiology	145.00	94	13630.00	71	10295.00	75.53
Neurology and neurosurgery	145.00	122	17690.00	90	13050.00	73.77
Urology	74.00	79	5846.00	55	4070.00	69.62
Gastroenterology	111.00	107	11877.00	69	7659.00	64.49
Rheumatology	94.00	52	4888.00	31	2914.00	59.62
ENT	75.00	167	12525.00	99	7425.00	59.28
Gynaecology	108.00	260	28080.00	137	14796.00	52.69
General Surgery	73.00	190	13870.00	78	5694.00	41.05
Respiratory Medicine	110.00	53	5830.00	21	2310.00	39.62
Orthopaedics	82.00	202	16564.00	71	5822.00	35.15
Endocrinology	97.00	24	2328.00	8	776.00	33.33
Opthalmology	65.00	60	3900.00	19	1235.00	31.67
Dermatology	76.00	79	6004.00	3	228.00	3.80

NB. The 1572 also includes the referrals which were not for symptoms during the five year time frame.

Appendix 13. Number of tests resulting from new outpatient consultations for FRMUS patients (over a five year period) in order of greatest expense

Test	Test cost	FRMUS (n=2043)	£220497.25	FRMES (n=1394)	£131550.54	IRS (n=311)	£28744.21
MRI	309.63	103	31891.89	53	16410.39	10	3096.30
X-Ray	55.62	355	19745.10	276	15351.12	36	2002.32
Laparoscopy	683.00	28	19124.00	3	2049.00	1	683.00
Colonoscopy/ Sigmoidoscopy	171.00	95	16245.00	47	8037.00	15	2565.00
CT Scan	209.00	71	14839.00	40	8360.00	9	1881.00
Cystoscopy	351.00	38	13338.00	19	6669.00	4	1404.00
Endoscopy	163.00	75	12225.00	55	8965.00	20	3260.00
US (Ultrasound)	59.36	187	11100.32	123	7301.28	27	1602.72
Angiogram	688.00	12	8256.00	11	7568.00	2	1376.00
Hysteroscopy/ Colposcopy	139.50	57	7951.50	35	4882.50	1	139.50
Lumbar Puncture	680.00	10	6800.00	2	1360.00	1	680.00
Manometry	397.00	17	6749.00	14	5558.00	0	0.00
Audiogram	95.00	47	4465.00	45	4275.00	36	3420.00
Laryngoscopy	139.00	32	4448.00	10	1390.00	3	417.00
Urodynamic Studies	130.00	33	4290.00	19	2470.00	1	130.00
EUA (Exam under anaesthetic)	567.00	7	3969.00	6	3402.00	0	0.00
Lung Function Tests/ Spirometry	86.00	43	3698.00	22	1892.00	4	344.00
Sleep Study	422.00	8	3376.00	13	5486.00	2	844.00
Biopsy	19.56	153	2992.68	145	2836.20	29	567.24
ETT (Exercise tolerance test)	66.22	44	2913.68	18	1191.96	6	397.32
ECG (Electrocardiogram)	29.48	93	2741.64	51	1503.48	17	501.16
EEG (Electro-encephalogram)	112.00	23	2576.00	1	112.00	0	0.00
Bronchoscopy	408.00	6	2448.00	1	408.00	0	0.00
Arthroscopy	767.00	3	2301.00	5	3835.00	1	767.00
Echocardiogram	64.85	30	1945.50	21	1361.85	7	453.95
Skin Testing	123.00	15	1845.00	16	1968.00	4	492.00
Mammogram	31.67	44	1393.48	34	1076.78	9	285.03

Test	Test cost	FRMUS (n=2043)	£220497.25	FRMES (n=1394)	£131550.54	IRS (n=311)	£28744.21
ECG (24 hour)	86.00	13	1118.00	2	172.00	3	258.00
FNA (Fine needle aspirate)	133.00	8	1064.00	18	2394.00	4	532.00
Blood Tests	3.26	268	873.68	206	671.56	42	136.92
ENG (Electro-nystagmography)	97.00	8	776.00	0	0.00	0	0.00
NCS (Nerve conduction studies)	83.00	9	747.00	10	830.00	3	249.00
Cytology	9.64	68	655.52	37	356.68	5	48.20
BP (24 hour)	86.00	6	516.00	2	172.00	2	172.00
Sleep Study (Home)	88.81	5	444.05	6	532.86	0	0.00
Dexa Scan	34.00	9	306.00	14	476.00	0	0.00
EMG (Electromyogram)	83.00	3	249.00	2	166.00	0	0.00
Helicobacter/ Hpylori	7.09	9	63.81	7	49.63	5	35.45
FOBT (faecal occult blood test)	2.05	8	16.40	5	10.25	2	4.10