THE INCIDENCE OF DEPRESSION, AND ITS EFFECTS UPON OUTCOME, IN FOUR LIFE-THREATENING ILLNESSES

M.D. THESIS (LONDON) 1989

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SUMMARY:

The M.D. Thesis study was an attempt to test the hypothesis that inpatients with medical illness who are depressed have worse outcomes, in terms of morbidity and mortality, than similar patients who are not depressed. This hypothesis was tested in four groups of patients who presented with life-threatening illness; myocardial infarction (n=100); sub-arachnoid haemorrhage (n=41); pulmonary embolism (n=40); and acute upper gastro-intestinal bleeding (n=30).

The patients entered into the trial underwent initial cognitive examination using the Mini-Mental State examination (MMS), to exclude patients with cognitive deficeits. This was followed by the Montgomery-Asberg Rating Scale for depression (MARS). These tests were repeated on alternate days until discharge, or 21 days post admission, whichever occurred sooner. The degree of pain experienced by the various groups of patients was measured using a simple Pain Rating Scale. The severity of illness for each individual patient was also computed, using currently available prognostic indicators. Four different cut-off points on the MARS were then used to determine the presence of depression. These cut-off points were 7, 14, 21 and 7 when the somatic components of the MARS were excluded (7-SCE).

The results showed that the depressed patients were not more seriously ill than the non-depressed group, regardless of the cut-off point used. There were also no significant diffences in age, sex, or pain experienced. Despite this equal prognosis for both the depressed and non-depressed groups, the former did significantly worse in all four conditionsn both in terms of morbidity and mortality. The most significant findings however, were when the patient populations were combined. Of the 211 patients, 55% were depressed when the cut-off point was 7, 41% when it was 14, 18% when it was 21 and 33% when it was 7-SCE. The 7-SCE group also consistently showed the most statistically significant differences between depressed and non-depressed patients in terms of outcome in all groups. In the 7-SCE group 46% had a poor outcome and 22% died, compared with 10% who did poorly and <2% who died in the non depressed group.

In studying the individual items of the MARS in patients who scored less than 14, then 80% of their score was due to somatic items which were likely to reflect the underlying illness. In the other cut-off points for depression this was approximately 50%. This risk of bias is inherent when using rating scales validated in the psychiatrically ill to detect depression in those with physical problems. The 7-SCE group is that in which the least likelihood of being affected by bias occurs.

The results also showed that the depressed patients experienced more pain, although this difference was not statistically significant. A further finding was the possibility that aneurysms of the right internal carotid artery were particularly associated with depression in those patients presenting with sub-arachnoid haemorrhage.

It was also clear from the change in the MARS over time that the phenomenon outlined above could more accurately be termed an adjustment reaction with depression rather than depressive illness.

INTRODUCTION:

This study tests the hypothesis that depressed patients with life-threatening medical illness do worse, in terms of mortality and morbidity, than similar patients who are not depressed. This hypothesis was tested in four life-threatening conditions, myocardial infarction, sub-arachnoid haemorrhage, upper gastro-intestinal haemorrhage, and pulmonary embolism.

The study was started after the author, in common with many predecessors, made an observation that patients under his care who appeared depressed, or to have lost "the will to live", seemed to do worse than patients whose illness appeared more severe, yet were not depressed.The influence of psychological factors upon 'physical' illness has long been recognized, and ranges from observations of increased numbers of admissions for appendicectomy following life events, to increased mortality in widowers in the first six months following bereavement (Murray Parkes 1969). The problem was how to test the original hypothesis in a group of hospitalised medical patients. It was clearly important that any conditions studied were not only life-threatening but that enough patients were likely to die so as to make any statistical analysis of mortality valid. Secondly, any mortality should be likely to occur during the relatively short period of hospital admission. The patients

must also be accessible to psychological testing. To meet these criteria, four groups of patients were selected, patients who were post myocardial infarction, post sub-arachnoid haemorrhage, post upper gastro-intestinal haemorrhage, and post pulmonary embolism. These four groups of patients had two other advantages, firstly, that they were all due to either obstruction or rupture of an artery and secondly, they were all accessible to the author.

Once the groups of patients were decided upon there were several potential confounding factors that might invalidate any results, and which the study must be designed to overcome. The first, and potentially most serious, was that patients who were noted to be depressed might simply be those patients with the most severe illness. Strenuous efforts were made to overcome this, with careful note being made of prognostic indicators available for each group of patients. A full record of these indicators was then made and kept for subsequent analysis on each patient. For example in myocardial infarction cardiac enzyme analysis and electrocardiographic changes can indicate the size and severity of an infarction, and thus probable prognosis. Therefore a record was kept of these results for each patient with subsequent reanalysis of the electrocardiographic changes after the psychological ratings were completed.

A second potential confounding factor was that some patients might have cognitive deficits affecting their ability to participate in the study. This was particularly likely with elderly patients and those with sub-arachnoid haemorrhage. Therefore a measure of cognitive performance was included in the study, and this will be discussed in more detail subsequently. The third potential problem was that depressed patients might have experienced more pain than non-depressed patients, and therefore a pain rating scale was incorporated into the study protocol. This is also discussed in more detail in the methodology section.

From the original hypothesis further questions arose; if depressed patients did worse what happened to their depression over time. Previous studies have looked at patients on only one occasion during the acute stage of the illness, and it was felt more appropriate that patients should be repeatedly assessed. Thus they were repeatedly interviewed from the first day of admission until discharge or 21 days, whichever occured first. Secondly, if depressed patients did worse, in what way did this affect them? Was it only in terms of mortality or were there other ways in which this could be measured? For some conditions measurements of sub-lethal events was straight-forwards, ie. the number of patients suffering arrhythmia requiring cardioversion post myocardial infarction. In other conditions

it was not so clear cut. These measures are discussed in more detail in the methodology section.

It is important at this stage to briefly discuss the author's position in relationship to the patients. All the information on the patients was gathered between October 1984 and April 1986. During this period the author was working first as a Senior House Officer in Neurosurgery, and then as a Medical Registrar. Thus to many of the patients the author was their primary ward physician, responsible for ordering investigations, management decisions, and speaking to their relatives. It was the uniqueness of this position, when compared to that of previous studies, that allowed repeated regular interviews from such an early stage in the patients admission, as well as complete access to the full range of investigations necessary to assess adequately each patients prognostic indicators.

In the review of the literature, those findings reflecting upon the aims of study have been specifically noted, such as the measurement of any acute psychiatric morbidity, along with its time course and its relationship to mortality. As regards the groups of patients chosen for the study, some work has previously been carried out on patients post myocardial infarction, but little in patients with either sub-arachnoid

haemorrhage, pulmonary embolism or gastro-intestinal haemorrhage.

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CHAPTER 1: DIAGNOSIS AND DEFINITION IN MEDICAL PATIENTS:

INTRODUCTION:

Depression is the name given to a clinical syndrome in which one symptom, dysphoria, is prominent in the clinical picture. Dysphoria is a common experience of mankind, occurring commonly in stressful and unsettling situations. Dysphoria can become more severe leading to a clinical state of depression, in which it may be accompanied by disordered sleep, appetite, libido, as well as lethargy, poor concentration, feelings of guilt and worthlessness. Some patients develop suicidal ideas, delusions and hallucinations.

The difference between dysphoria alone and clinical depressive illness is by no means clear, and problems with definition have long bedevilled psychiatric research. Differentiation becomes even more difficult in patients with medical illness, as the patients may have poor sleep, poor appetite, weight loss, poor concentration and lethargy because of an underlying illness. Thus medical illness can cause symptoms mimicking depressive illness and lead to an erroneous diagnosis. If dysphoria is recognized this may be referred to, or be diagnosed as, a "stress reaction"; an "adjustment disorder with depressed mood"; appropriate psychological distress; "major depressive

disorder" either primary or secondary; "reactive depression" or finally an "organic affective syndrome". Which diagnosis is given depends to some extent on the severity of the mood disturbance and the time course of the dysphoria, as well as the diagnostic classification used. It is perhaps not surprising therefore that there has been some confusion in the literature when studying these patients. It is also important to realise that the difference between mild anxiety and mild depression is not clear cut, as shown by Eaton and Ritter (1988) in a community survey. Since most patients with medical illness who are depressed have mild psychiatric morbidity the same findings may be true, and thus "anxiety disorder" or "affective disorder" might be more suitable terms for this condition.

In the study to be presented the patients were repeatedly examined from their first day of admission until discharge or 21 days, whichever was the sooner. Thus there was no single time at which they were measured. Because of this, it is not easy to fit the patients into any presently used definition of depression. As some patients were more dysphoric than others, with the duration of this dysphoria varying considerably, and in view of the problems with nomenclature outlined above, patients will be referred to either as "depressed" or "not

depressed". In the conclusions further consideration will be given to other, perhaps more appropriate, diagnoses.

REVIEW OF PREVIOUS PUBLICATIONS:

An editorial in the Lancet (1979) stated that between 25% and 83% of medical patients had a psychiatric diagnosis. The commonest was affective disorder. Such widely differing results clearly indicate varying approaches to methodology, patient selection and diagnostic criteria. As previously discussed, the somatic complaints characterizing depressive illness are likely to influence results unless positive steps are taken to avoid this possibility.

There have been over five hundred publications looking at psychiatric morbidity in both inpatients and outpatients, and in the acute phase and/or in the recovery period. These patients presented with a wide range of medical and surgical conditions, including renal failure, cancer and endocrine disorders. The literature reviewed here are those relevant to the study, ie. those studies involving medical patients, particularly inpatients, with either a general medical condition or a cardiological or neurological disorder, seen at least once during the acute phase of their illness. There are no papers reviewed in detail here regarding subarachnoid

haemorrhage. This is because all of the published work, such as that by Storey (1967: 1970), Logue et al (1968), Ropper and Zervas (1984) and Oyebode et al (1986) refers to long-term follow up rather than the acute psychiatric sequelae.

Querido (1959) carried out a prospective study of 2,200 consecutive patients admitted to a general medical hospital who fulfilled his entry criteria (age between 15 and 65, not in great pain or terminally ill, not a very short admission). However, when admissions were frequent, every other admission was selected. The patients had a semi-structured interview, the results of which were reported back to the research team who then categorised the type and amount of stress/distress the patient was under. On some occasions more information was felt to be needed and was duly collected. The patient was then described as having either somatic, psychic or social distress or combinations of these. His team managed to perform a follow-up interview, on average seven months later, on 1,630 patients. Of the original cohort they found that 46.6% had some degree of stress, half having 'somatic/psychic' stress. Querido suggested that the results obtained showed that the presence of distress led to a decreased chance of recovery.

The methodological approach, using a non-validated interview to which questions may or may not be added, is not ideal. This

also applies to his definition of stress, or "distress" as he terms it, which is subdivided into:- psychic; psychosomatic; somatic/psychic; somatic/social; and somatic/psychic/social. Despite these criticisms of this study the large number of patients seen initially and at follow-up, hint at the possibility of stress/distress in some way being linked to recovery, even if this is only a relationship between severity of illness and psychological distress.

Schwab et al. in two papers (1967a; 1967b) studied 153 admissions to a medical unit, representing 73% of admissions over a six week period. They administered the Beck Depression Inventory (BDI; Beck et al. 1961) and the 17 item Hamilton Rating Scale (HRS; Hamilton 1960) as well as noting any psychiatric diagnosis by the medical staff and later having the medical records reviewed by an independent psychiatrist. These four measures were combined to form a "Sum Rank". The authors "arbitrarily defined as depressed the highest 20% of the patients as rated on the Sum Rank". There was little correlation between the measures used to construct the Sum Rank, for instance the HRS identified only 15 of the 34 patients felt by the medical staff to be depressed. In addition 16% of all admissions were diagnosed as psychiatric and 70% of all patients scored on the somatic parts of the rating scales used. Because of these problems doubts must be expressed about the diagnosis of depression used. In the first publication the

authors conclude that depression can occur in many physical conditions and that physicians should become more sensitive to this. The conclusions drawn from the second study tend to overestimate the accuracy of the HRS in diagnosing depression in the medical ill.

Kimball (1969) studied the psychological response of patients undergoing open-heart surgery, and related this to mortality. The patients were interviewed in a non-standard manner, and the interview was subsequently reanalysed to assess the presence of anxiety, the patients "life-style", and their view of the future, including surgery. Post-operative follow-up was performed daily in a non-structured way, often involving "unobtrusive observation" and interviews with relatives designed to gain a perspective of the patients reaction. Prior to discharge the patient was again interviewed at length and the interviews were repeated at one to three month intervals after discharge until 15 months. The 54 patients were assigned to one of four groups; adjusted (13 patients); symbiotic (15 patients); anxious (12 patients); and depressed (14 patients). Both mortality and morbidity were much greater in the anxious and depressed groups. These interesting findings indicate a trend towards psychological factors being involved in outcome. However, in view of the non-standardized way in which the

information was gathered and the groups determined it cannot be considered unequivical supportive evidence for this.

Brughn et al. (1969) used the Minnesota Multiphasic Personality Inventory (MMPI; Dahlstrom and Welsh 1960) to study 47 patients who had previous myocardial infarctions. These patients were involved in a large prospective trial over a seven year period. They compared this group with 30 matched controls. In addition to the full MMPI, subscales for depression and anxiety were repeated every two months for the first eighteen months, and the general physician was asked to note the presence or absence of anxiety or depression at each visit. A range of blood investigations were also regularly performed. The controls had significantly higher I.Q. scores than those with heart disease. Those who subsequently died had significantly higher scores on the depression subscale of the MMPI. On entry to the study the survivors were more depressed and anxious at follow up than controls and (unsurprisingly) had higher serum cholesterols and triglycerides. The scores on the depression and anxiety subscales performed for the first eighteen months showed little correlation with the physicians estimate of patients mood. In this study there was little demographic detail given about patients or controls, apart from the fact that they were all white males. There is no information as to how the patients were selected, although a tantalizing glimpse is given by the fact that during the study patients got free medical care. The authors implied that the reason the survivors were more

depressed than controls at termination of the study is that this free care was to cease. Apart from the MMPI subscale, designed to measure personality traits rather than depression, there is no other indication that the patients were depressed. Indeed the physicians rating did not correlate with the score on the subscale. Thus one must treat with some caution the conclusion that patients who died were more depressed than those who survived.

Lipowski and Kiriakos (1972) describe a personal series of 200 patients referred to them over a six year period in a neurological hospital. This was a randomly selected group from a total population of 426 patients. A further group of 400 patients seen by Lipowski over the previous 10 year period were also mentioned. Of the 200 patients 30% were depressed. That this sample was probably atypical is likely from the fact that 15% of the patients had a hysterical conversion disorder and 13% had a functional psychosis. Only 10% had no psychiatric disorder. Thus although this is a very interesting article of the personal experience of an experienced liaison psychiatrist, the data presented are not comparable with other published work, especially as no details are given as to how each diagnosis was arrived at.

Maguire et al (1974) used a two stage screening procedure to examine successive acute medical admissions over a two month period. They gave the General Health Questionnaire (GHQ) (Goldberg 1972) to 74% of the 230 patients available. Patients who had attempted suicide were excluded from these figures, although it is likely that approximately 10% of admissions would have been due to this. Also excluded were those judged to be too physically ill by the medical staff. These patients who scored 12 or above on the GHQ then had a standardized psychiatric interview (Goldberg 1970). The case notes were then scrutinized independently. 45% of the sample scored above 11 on the GHQ and 26% were judged to have psychiatric morbidity following interview. Affective disorders accounted for 80% of the diagnoses. They note that a further 8 patients had been diagnosed as psychiatrically ill by other psychiatrists, 6 of whom scored less than 11 on the GHQ. They make the point that those referred for psychiatric evaluation were those whose behaviour gave rise to difficulties, rather than those with the most serious psychiatric morbidity. Their conclusion that 23% of admissions suffer psychiatric morbidity is likely to be an underestimate, which the authors note, especially as it did not consider the most seriously ill or those who had taken overdoses. In addition the screening measure failed to identify six of the eight patients whom other psychiatrists identified as ill (although it is unclear if in fact these were patients with affective disorder).

Hawton, who had taken part in the previous study, conducted a follow-up of these patients (Hawton 1981) by retrospective analysis of their case notes (medical and psychiatric where relevant) and by contacting their GP's for information. Of the original cohort of 230, 80 had died prior to follow-up eighteen months later. Of those known to be alive, information was available from 87% of their GP's. Hawton showed that the presence of psychiatric disorder during the initial admission was associated with a higher risk of subsequent death. The patients who died were also older than those who survived (mean age 64.9 vs 53.2). The study also demonstrated that the patients who had psychiatric morbidity in hospital were more likely to have this once they returned home. Hawton's findings about psychiatric disorder and subsequent mortality are interesting but must be qualified by the fact that the original study excluded some of the most seriously ill patients. A further potential problem was that no note was made of the severity of the medical condition, and the findings might simply reflect the fact that more seriously ill patients have more psychiatric morbidity.

Moffic and Paykel (1975) screened 150 patients on general medical wards, within seven days of admission, using the Beck Depression Inventory (BDI). They compared this group with 220 depressed psychiatric patients who were a mix of in-patients, out-patients and day patients. Those patients scoring above 14

on the BDI had a semi-structured clinical interview, the Clinical Interview for Depression (CID: Paykel 1970). 24% of the patients scored above 14 on the BDI and were categorized as depressed, most were in the range 14 to 22 indicating mild severity. In comparing the depressed with the non-depressed group there were no significant differences in age or sex, social class or marital status. However, 61% of those seriously ill were depressed as opposed to only 21% of those who were mildly ill. Depression was also more common in those in pain or confined to bed. Moffic and Paykel felt that in 65% of the depressed patients, the depression was a consequence of the physical illness. The depression tended not to be recognized by general physicians. Those in whom mood was noted to improve often had a recovery from a life threatening illness, and the authors felt that the physical recovery lead to mood improvement. When comparing the different groups the medically ill patients were more likely to suffer from pessimistic thoughts, helplessness, anxiety, agitation, retardation, self-pity, or to recognise a distinct quality to their depression. Considering the medical depressives are categorized as mildly depressed this is a surprising finding. The authors state that the depressed patients were more likely to die, but do not reproduce these figures.

Kilpatrick et al (1975) studied 87 patients undergoing open-heart surgery. The mean age of these patients was 35 years. 48

patients were excluded from the study since either their I.Q. was below 80, or they were illiterate (possibly indicating an unrepresentative population). The main measure of mood was the Minnesota Multiphasic Personality Inventory (MMPI: Dahlstrom and Welsh 1960). In addition, a battery of psychological testing was carried out. The patients were assessed the day prior to operation and then divided into a survivor group or fatality group depending upon survival at 30 months post-operatively. It is not clear why this time cut-off was chosen. The results showed no clear differences between the survivors and non-survivors for any of the components of the MMPI. However the battery of psychological tests were predictive of outcome, perhaps because this was a measure of severity of illness, ie. those patients with cognitive or performance deficits had the most widespread atherosclerosis.

Lloyd and Cawley (1978) studied psychiatric morbidity in men one week after their first myocardial infarction. These patients had a semi-structured interview (Goldberg et al 1970) on the seventh day post-admission. They were a consecutive series of 105 patients, all of whom were on diazepam 2-10mg twice daily. Note was also made of the severity of the illness. Five patients died prior to interview and of the remaining 100, 35 had psychiatric morbidity, in 28 of whom this was an affective disorder. Of the 35 patients, the authors felt that 18 had developed an affective disorder consequent to their

myocardial infarction. The groups did not differ in terms of severity of illness. This study used a standardized interview validated in the general population, but not in a hospital population, and missed out one of the eleven symptoms (fatigue) normally recorded. The scores for reported symptoms are higher in the 'psychiatric' group for somatic complaints, sleep disturbance, hypnotic abuse, impaired concentration and anxiety. The scores for observed abnormalities were higher in the psychiatric group for slowness, intellectual impairment and bodily concern. Many of these items could possibly be related to the underlying physical illness, a point mentioned in the article. Nonetheless, the study tends to strengthen the impression of psychiatric morbidity, particularly affective disorders, being precipitated by illness.

Lloyd and Cawley (1983) followed up 82% of their original cohort for 12 months. They found that in the group of patients in which the psychiatric morbidity preceded the myocardial infarction (Group 1) it continued throughout the follow-up period (9 out of 12 patients). However, in those patients whose morbidity was secondary to their illness (Group 2) only 4 out of 16 patients had any psychiatric morbidity at 12 months. They also found that 11 patients in the group which had no psychiatric problems at one week (Group 3) had developed diagnosable psychiatric illness at four months. During their follow-up a further eleven patients died, 5 from groups 1 and 2

(35 patients), and 6 from group 3 (originally 65 patients). Although they do not mention it, these differences in mortality during the follow-up period are not statistically significant.

Folstein and his colleagues published three papers on medical patients and depressive illness (DePaulo and Folstein 1978; DePaulo et al 1980; Knights and Folstein 1977) in which they also examined cognitive performance. This they did by using the Mini-Mental State Examination (MMS; Folstein et al 1975) in addition to the General Health Questionnaire (GHQ; Goldberg et al. 1976). The first article in 1977 studied 57 consecutive admissions to three medical wards and excluded 7 comatose patients. The staff were also interviewed about the cognitive and psychiatric status of patients under their care. 21 patients scored below the cut-off point on the MMS and were thus felt to have cognitive impairment and 46% of the patients scored above the cut-off point on the GHQ and were felt to be emotionally distressed. The staff were then taken to task for failing to recognise the problems 'identified'. No discussion is given about the difficulties of measuring emotional problems in this group or about the very high level of cognitive abnormality detected, 29 out of 62 patients. Although the patients were seen, no note was made of the observed depression. There is also no detail as to at which stage of their admission these patients were seen. Patients with low MMS

scores had GHQ tests despite this, the results of which must remain questionable.

The next two papers deal with neurological patients and again use the MMS and the GHQ. The 1978 study looks at 126 consecutive neurological admissions and the 1980 study is these patients plus a further 71 neurological admissions. In the initial study there were 140 admissions in 126 of whom it was possible to perform the MMS within three days of admission. If there was a low score on the MMS the GHQ was not performed. Again the medical staff were asked to rate their patients. The MMS appeared to differentiate well between patients with cognitive deficit and those without, half those with intracranial lesions had low scores, but none of those with peripheral lesions did. Approximately 50% of the patients who completed the GHQ had 'high' scores, when using the standard cut-off point of 5. 70% of the patients with abnormal scores on either measure were recognized by the medical staff. 11 of the neurological patients were referred for psychiatric examination, of which nine had completed the MMS and GHQ. They state that all nine had abnormalities in at least one test and four had abnormalities in both. They do not state how many of the psychiatric referrals had abnormal GHQ scores. The final study (1980) compared the MMS with the results from the Weschler Adult Intelligence Scale (WAIS) and found the correlation co-efficient, r, to be 0.56 for performance scales

and 0.40 for the verbal scales. The correlation co-efficient for the MMS when compared to lesions on the CT scan was 0.30. They also looked at specific neurological illnesses and found cognitive deficits in 61% of Parkinsonian patients and 38% in those who had either a stroke or a transient ischaemic attack (TIA), but that only 14% of multiple sclerosis sufferers had cognitive deficits. The GHQ was abnormal in 50% of the Parkinsonian and stroke patients, whilst 68% of the multiple sclerosis sufferers had a high GHQ score. In this later paper they question the high rate of GHQ 'cases' and discuss two other papers where the GHQ findings were checked by subsequent psychiatric interview. In one (Maguire et al 1974) a false positive rate of 42% was found. The other study is by Lobo and Folstein and is unpublished, but gives a false positive rate of 10%. They that suggest elevation of the cut-off point may help this problem.

Neilsen and Williams (1980) studied a population of general medical outpatients using the Beck Depression Inventory (BDI). The 526 patients were gathered from three different outpatient facilities. They give good demographic data which show a wide range of patients, however being skewed towards the higher social classes, with 25% coming from social class I. Of those patients who scored above the cut-off point on the BDI, 41 were randomly allocated to have an interview with one of four psychiatrists. The interview did not appear to have been

structured and the four raters did not standardized their technique. After the interview patients were rated using Feighner criteria for depression (Feighner et al 1972), and also with the Hamilton Rating Scale (HRS). The interviewers also reviewed the medical notes for evidence of depression. The authors used a cut-off point of 10 on the BDI and found that 88 (12.2%) of respondents were depressed, but with a cut-off point of 17 this fell to 5.5%. The results of the psychiatric interview are not well reported, but of a sample of 24 patients who scored above 10 on the BDI, 13 were depressed using Feighner Criteria. They state "virtually identical" results using the HRS but do not reproduce them. This paper does illustrate that a significant proportion of medical outpatients score highly on the BDI. That this in fact represents depressive illness is by no means clear, as only half of the sample scoring 10 or more on the BDI were diagnosed depressed by Feighner Criteria, and also the cut-off point for depression used on the BDI considerably influences the results.

Mayou and his colleagues assessed 100 patients and their spouses after myocardial infarction,and followed them up for one year (Mayou, Foster and Williamson 1978; Mayou, Foster and Williamson 1979; Mayou, Williamson and Foster 1978; Mayou 1979). These were 100 consecutive patients who had a semi-structured interview with ratings made from tape recordings according to the methods described by Brown (1969). One week

after admission a brief mental state examination was made and at two months a more structured mental state examination was repeated, with this being done again at one year. The patients psychological status was recorded on a simple four point scale, 'lack of concern', 'mild distress', 'moderate distress' and 'severe distress'. At the initial assessment 67% of the patients suffered from 'mild distress' and 11% suffered from 'moderate distress', with no differences being noted between the groups in terms of severity of illness. At two months 23% had mild and 30% had moderate or severe symptoms, whilst on mental state examination, 60% were depressed with 17% being moderately or severely depressed. This compares with 30% psychiatric morbidity in the sample which Lloyd and Cawley (1983) reinterviewed at four months. Mayou et al found that anxiety and depression were usually accompanied by fatigue, irritability, poor concentration and impaired memory, but there was little to suggest these somatic features were due to underlying medical illness. The patients were reviewed again at one year when 64% had psychological distress, of which mild anxiety and depression were most common. Unfortunately, so far as the present study is concerned, there was no attempt to link psychological distress to mortality figures.

Brody (1980) looked at a sample of 235 outpatients attending a medical clinic. The patients completed the GHQ (Goldberg et al 1976) immediately after seeing their physician and were then

interviewed. The author used a cut-off score of 4 and found that 63% "had scores..suggesting a psychiatric disturbance". A cut-off of 10 would have given 33.6% and a cut-off of 15 would have given 11.5% of patients having psychiatric morbidity. Interestingly, the physicians 'recognized' that two thirds of the original 63% had some psychiatric disturbance. What the physicians failed to recognize however, was the poor compliance with medication by 36% of the population. There is little discussion in the paper that a score or more than 4 on the GHQ might be anything other than genuine psychiatric diagnoses.

Kathol and Petty (1981), in a review, state that a depressive syndrome exists when there has been a low mood for at least one week accompanied by at least four other symptoms. They feel that individuals failing to meet this criteria have a minor depression, a category which includes adjustment reactions, bereavement, reactive depression and affective personality type. They note that most studies of depression in the medically ill do not consider severity of the illness or duration of depression.

Bridges and Goldberg (1984) assessed 121 acute neurology admissions, of whom 100 completed the GHQ (Goldberg et al 1979) on admission and 70 also were assessed with the Clinical Interview Schedule (CIS: Goldberg et al 1970) within three days

of admission. Of the 100 patients, 76 were interviewed prior to discharge. Using a threshold score for the GHQ of 11-12, 43% of the patients scored above this. Using the CIS 39% of patients had psychiatric morbidity, most of whom had a diagnosis of mild affective disorder. These two values do appear quite high at first, especially as the most seriously ill patients were excluded, but this may reflect chronic disabilities due to neurological illness. It might also have been helpful to show the percentage of patients above or below various cut-off points, especially since the authors do not reveal whether all the patients diagnosed as having psychiatric illness using the CIS were those who scored above the cut-off on the GHQ. A further potential problem in the paper is that it does not address any cognitive deficits these neurological patients may have had, or discuss and how this might have affected the results. That this may involve a significant proportion of patients was demonstrated by DePaulo et al. (1980).However, the authors do make an important point as to the frequent failure of physicians to recognise underlying psychological distress.

Lepine and his colleagues (1985) compared the Hospital Anxiety and Depression rating scale (HAD; Zigmond and Snaith 1983) with a questionnaire derived from the Composite International Diagnostic Interview (CID: Wing et al 1982). The modified CID was used to give diagnosis of major depressive episode according to DSM III (American Psychiatric Association 1980)

with which the HAD results were compared. This was done on 133 medical admissions and the results show that the sensitivity and specificity of the HAD vary according to its cut-off point. No mention was made of the number of these patients felt to have affective disorders, and there was no discussion about the fact that the CIS was not designed for use in medical patients (unlike the HAD) and may therefore not be a suitable 'gold standard'.

Channer et al (1985) looked at 87 patients undergoing exercise testing for suspected coronary heart disease, asking them to complete the HAD prior to this test. 56% of the patients were anxious, over half of these had scores indicating "significant anxiety". Those who were most anxious were least likely to have abnormal treadmill tests. It would also have been informative to have known these patients anxiety levels after testing, especially if it had been normal. Nine percent of the patients scored above 8 and five percent scored above 10, a score which indicated significant depression. As a group these patients were also less likely to have a positive exercise test. The article however fails to clarify whether the anxious or depressed patients have normal tests or submaximal tests, (when the target heart rate is not achieved prior to exercise ceasing), indeed depressed patients walked for a shorter time (5.8 min) compared with non-depressed patients (8.8 min). Thus these patients may have had coronary artery disease that was

not picked up by exercise testing. Atypical chest pain was a better guide to a negative test than anything else, although this occurred more often with the more anxious patients. Thus this paper demonstrates that anxiety occurs prior to exercise testing. It also suggests a level of depression of 5% in the same patients. As 13 of the patients had also had previous coronary bypass surgery this level of depression found is low by comparison with previous studies. Their conclusion that "the HAD scale provides a simple and quick way of identifying abnormalities of mood" should perhaps be balanced by Lepine et al's (1985) statement that "used to evaluate the prevalence of depression in medical settings (outpatient or inpatient), this (HAD) assessment scale can only provide an estimate of depressive symptoms; it cannot be used to study depressive disease".

Rodin and Voshart (1986), in a review, point out the lack of clarity regarding the definition of a 'case' as well as the lack of standardization for psychiatric rating scales subsequently used with general medical patients. In addition they comment on the selection bias of the populations studied, the heterogenicity of the subjects and the lack of suitable control groups in most published works.

Mayou and Hawton (1986), also in a review, point to a lack of research into psychiatric morbidity in hospital patients, and especially its relationship to other factors such as long-term social problems, past history of psychiatric illness and increasing age of medical populations. They contrast this with the "extensive research" in primary care. They also discuss the differences between individual hospitals and the changing pattern of medical care and state that "it is particularly difficult to distinguish between 'appropriate distress' and affective disorder, especially in the presence of medical symptoms".

Mai, McKenzie and Kostuk (1986) looked at a cohort of 91 patients referred for cardiac transplantation over a four year period. Of these patients 66 had a modified version of the Present State Examination (PSE: Wing, Cooper and Satorius 1974) and the GHQ (Goldberg 1972). The PSE was modified in such a way as to eliminate those items concerned with psychotic illness and additional items were added, such as history of alcohol abuse and attitude towards dying. Interestingly it was not modified to take account of the way physical problems might interfere with the ratings in this group of very ill patients. From this group 33 men had transplantation, 22 of whom survived. From the group of 66 patients, 26 were diagnosed as anxious and 8 as depressed, thus approximately half were diagnosed as having an affective disorder. The results for

patients who had operations showed that those who did not survive had significantly higher scores on the somatic components of the GHQ. The authors noted that in most subjects pre-operative anxiety and depression improved as the medical condition did so. Few, if any, conclusions can be drawn from this study that would be applicable to other groups. The suggestion that higher GHQ scores may indicate a greater risk of mortality might instead be due to a worsening of the patients clinical state.

Maeland and Havik studied anxiety and depression in 249 patients post myocardial infarction (Maeland and Havik 1987: Havik and Maeland 1988). They first studied the patients at a mean of 9 days post infarction, again at 1 day prior to discharge and then at 2 weeks 6 weeks and 6 months after discharge. Their measure of anxiety and depression was a "semantic-differential type questionnaire" of which no further details are given. A combined score from this was then graded into four points; low, somewhat low, somewhat high and high. They found that at 9 days 35% scored either in the somewhat high or high range and at 14 days this figure was 32%. Two weeks after discharge this had increased to 49.5%. The authors also studied longer term social outcome by measuring return to work at six months. They found that this correlated well with "emotional reaction" measured at nine days, such that patients with a somewhat high or high level of anxiety or depression

were significantly less likely to return to work ($p<0.001$). They mention that this finding could not be explained by age, educational level or severity of the heart attack. One major problem with this study is that it used an unvalidated scale to assess depression and anxiety, the contents of which is also uncertain. Having said this, the second paper does refer to previous validation (Havik and Maeland 1980), however this paper is not available in English. Furthermore the validity of combining the scores for both the depressive and anxiety components is uncertain. Thus the finding of a level of affective disorder of 35% at 9 days must be regarded as unproven despite the large number of patients involved in the study. The finding that initial emotional state is linked to psychosocial outcome at 6 months is an interesting finding, and might be taken to suggest that a patients emotional reaction to a life threatening event has long term consequences.

Lloyd (1987) discusses the long history of the relationship between "heart and mind", and suggests that myocardial infarction patients have a higher than expected level of psychiatric morbidity. Most patients developing morbidity following infarction will have a minor affective illness which will frequently resolve spontaneously without treatment. Indeed, Lloyd feels that rehabilitation programmes designed to help such patients are not successful unless carefully targeted. He also described that these patients might be more

accurately thought of as having an adjustment reaction rather than a depressive illness.

Trelawny-Ross and Russell (1987) studied 32 patients who were admitted with suspected myocardial infarction and subsequently interviewed using the Clinical Interview Schedule (CIS: Goldberg et al 1970). The authors do not state at what time post admission this first interview occured, but they were interviwed again at 10 days, 2 months and 6 months post discharge. The authors only give the ratings for depression and anxiety after discharge, thus at 10 days post discharge 20% were depressed and 39% were anxious, whilst at 2 months these results were 26% and 52% respectively. At 6 months the percentage working was 55%, as opposed to 71% prior to admission. Outcome was measured in terms of leisure, exercise, and sexual activity at six months. Social and psychological factors were more closely linked to outcome than myocardial damage. However, this paper does not specify what method of calculation, or cut-off point for depression, was used with the CIS. It is also not clear whether the patients were consecutive admissions, or if any exclusion criteria were used. Thus it does not allow confirmation of previous findings about affective disorder occurring in patients post myocardial infarction.

Kennedy et al (1987) studied the affective state of 83 patients undergoing programmed stimulation of cardiac arrhythmias for diagnosis and treatment, mainly ventricular tachycardia or fibrillation (75% of the patients). These patients were not consecutive admissions and were selected where "symptoms represented varying degrees of risk for arrhythmia recurrence (and sudden death)". Prior to treatment the patients had an unstructured interview and were then scored and assigned to one of four 'profiles' according to Kimball's method (Kimball 1969). These were adjusted, dependent, anxious, and depressed. Prior to treatment 9% were depressed and 25% anxious, and after treatment these were 5% and 20% respectively. Note was made in this study of the patients cognitive state, with 14 patients having cognitive impairment. During the follow-up period, mean length 18 months, 15 patients had died (2 from non-cardiac causes). Both cognitive function and the presence of depression were significantly correlated with mortality. The authors point out that poor cognitive function may be common in those surviving severe arrhythmia or in those undergoing cardiac surgery. They do not, however, discuss how cognitive impairment may interfere with reported affect, or if it is suitable to perform assessments in these circumstances. A problem with the paper is the use of an unvalidated method for diagnosing the presence of affective disorder. This potentially throws into doubt the otherwise very interesting finding that depression may predict mortality in this group of patients.

Cormier et al (1988) assessed a group of 98 patients with a history of chest pain at the time of cardiac investigation. Of these patients 50% had chest pain but normal cardiological investigations. Psychiatric assessment was carried out by means of a modified Diagnostic Interview Schedule (DIS: Robins et al 1981), although the authors do not state in which way the DIS was modified. In addition the patients completed the Symptom Check List-90, (Derogatis 1977), again modified in an unspecified way. Of those patients who had no cardiological problem 80% received a psychiatric diagnosis, as opposed to 26% of those with cardiological disease. The commonest diagnoses were panic disorder and multiple phobias which together accounted for 57% of the psychiatric diagnoses in the investigation negative group. Depression was found in 23 patients, 19 of whom were in the investigation negative group (24% of psychiatric diagnoses in this group were depression). For the self rating scales there were no significant differences between the groups using the symptom checklist between those with and without cardiac diagnosis. The authors fail to discuss why there is such a marked difference between the DIS findings and those of the symptom checklist. Thus, the prevalence of affective disorder in this group of patients cannot clearly be compared with previous studies.

Rosenberg et al (1988) studied 130 consecutive admissions to general medical units. Patients were excluded if they had an

organic brain symptom, or scored less than 7 on the vocabulary subtest of the Weschler Adult Intelligence Test, and only 71 patients were entered into the study. The assessment of premorbid depression was elucidated by the Profile of mood states (McNair et al 1971). That occurring whilst an inpatient, at a mean of three days post admission, was measured by the Beck Depression Inventory (BDI: Beck 1967). An assessment was also made of the severity of the patients illness, as well as of factors that may contribute to the precipitation of depression such as perceived loss of social support. Their results showed that 38% of patients were depressed, most of whom were mildly depressed. In subsequent analysis they linked the presence of depression to pre-hospitalization depression, social functioning, patients' perception of physician supportiveness and patients' perception of illness, but not to severity of illness. The subsequent discussion doesn't discuss the potential problems of using rating scales unvalidated in this patient group to diagnose depression accurately.

DISCUSSION:

The preceding review of 30 relevant articles leads to several potential conclusions, with the proviso that few authors discussed the multiple factors involved in measuring affective disorders in the physically ill. The results of studies

frequently differ widely, especially in the numbers of patients felt to have psychiatric morbidity. A large part of these differences is due to the differing methods of measuring this morbidity and this problem is discussed in the next chapter. Despite the methodological problems previously discussed many of the articles point firstly to a large amount of psychiatric morbidity in the physically ill. Secondly, this is generally unrecognized by the general physicians in charge of the patients care (Maguire et al 1974; Lloyd and Cawley 1978; DePaulo et al 1980; Neilsen and Williams 1980). Thirdly, most of the morbidity recognized is mild rather than severe. Nonetheless, as shown by follow-up studies (Lloyd and Cawley 1983; Mayou et al 1979) it may still interfere with the patients life. Fourthly, several studies demonstrate that psychiatric morbidity can be precipitated by physical illness (Moffic and Paykel 1975; Lloyd and Cawley 1978), and that it may improve as the underlying medical condition improves (Moffic and Paykel 1975).

It is difficult to determine from these studies as whether or not psychiatric morbidity has an effect on prognosis. Several studies suggest this (Querido 1959; Brughn et al 1969; Hawton 1984; Moffic and Paykel 1975; Mai et al 1986) but none of these studies makes a clear-cut case; for instance, the patients who died in Hawton's study were significantly older, and Moffic and Paykel showed that more seriously ill patients had more

psychiatric illness. The question of severity of physical illness is one that has often not been addressed, but is of importance in any discussion of prevalence and significance of psychiatric morbidity. The problem of the cognitive function of these patients is also not always studied.

An overall conclusion from a review of the previous literature might be that between 15-25% of medical inpatients would be expected to show some evidence of moderate to severe psychiatric morbidity, mainly affective disorders. A larger, and more variable proportion have mild affective disorders. The more seriously ill a group of patients, the greater the proportion expected to have psychological morbidity. Thus in patients with a life- threatening illness, approximately 40-60% might have some degree of psychiatric morbidity.

CHAPTER 2: RATING SCALES:

The study presented looks at depression in life-threatening medical conditions, the measurement of depression clearly being of great importance. Thus it is necessary to review which rating scale is likely to be most suitable for the aims previously discussed. There are three ways of standardizing diagnosis - by using self-administered questionnaires, by rating scales such as the Hamilton Rating Scale or by a semi-structured interview with precisely defined diagnostic criteria, such as the Present State Examination. However, as Williams, Tarnopolsky and Hand (1980) point out psychiatric "caseness" is a difficult concept, and although operational criteria such as that of Feighner et al (1972) and Spitzer et al (1976) are a great help, they are standardized on psychiatric patients. These patients themselves are probably atypical of the population having psychiatric morbidity: using these criteria in other situations may well invalidate them. They also point out that deciding which symptoms to measure can be difficult, for instance patients may not differentiate between anxiety and depression and questions designed to elicit such differences may therefore fail in their objectives. The authors describe three further problems in measuring symptoms; firstly whether the number of symptoms or their severity are deemed important; secondly the time period over which the symptoms are measured. The third problem is that of response

bias, particularly acquiescence set and social desirability set. Acquiescence set is the tendency to agree with items irrespective of their content, and social desirability set is the tendency to agree with items which are considered more socially acceptable. In addition they discuss Salkind's observation (1976) that there are three time courses for response to stress; a rapid rise and fall in anxiety; a sub-threshold level of anxiety which, following stress, leads toa more prolonged period of anxiety; and those with chronic anxiety. As most case finding instruments are administered on one occasion only, these patients will all be considered 'cases'. All of these potential problems should be considered in the design of a study and in analysis of its results.

SELF-REPORT QUESTIONNAIRES:

Self-report questionnaires may be unreliable for several reasons, as pointed out by Rodin and Voshart (1986). The cut-off point chosen may lead to a high percentage of false positives, the symptoms may reflect medical illness or the transient nature of depressive symptoms, and the false negative diagnoses may occur when depression is somatized. The most widely used self-report questionnaire is that designed by Goldberg et al (1972; 1976; 1979), which can be 60 items, 30 items or 28 items. Of the papers previously discussed, eight

used the GHQ as their sole, or intial screening instrument. Four used the 30 item scale as the sole measure of psychiatric morbidity (Knights and Folstein 1977; DePaulo and Folstein 1978; DePaulo, Folstein and Gordon 1980; Brody 1980); three using as a screening test the 60 item GHQ (Maguire et al 1974; Hawton 1981; Mai et al 1986) and one used the 28 item GHQ for screening (Bridges and Goldberg 1984).

More recently the GHQ 30 has been used to delineate the occurance of psychological problems in women attending a G.P. for antenatal care (Sharp 1988), where 35% of women scored above a cut-off point of 5/6. The GHQ 28 has also recently been compared with the Hospital Anxiety and Depression scale (HAD) in a variety of medical outpatients (Aylard et al 1987). In this study the authors were rightly concerned about previous use of inappropriate rating scales to measure affective disorder. They however used a modified Montgomery-Asberg Rating Scale to validate both the GHQ and the HAD, ignoring the fact that this scale has also not been validated in this situation! Indeed, the modification they made, removing the item for feelings of inner tension, resulted in the MARS being even more dependent on physical symptoms, Their results showed that of a sample of 133 patients 41 (31%) were mildly depressed, using a MARS cut-off point of 7, and 31 (23%) were more seriously depressed. None of the problems previously outlined were discussed by the authors. Their findings would suggest a very

high level of psychiatric morbidity in these outpatients, even if only considering those patient felt to have serious depression.

Part of the problem with the GHQ is its reliance on somatic complaints likely to score heavily in medical patients. Mayou and Hawton (1986) conclude that when using the GHQ "it is apparent that in medical populations both sensitivity and specificity are low, especially in the most severely physically ill groups".

The Hospital Anxiety and Depression Scale (HAD: Zigmond and Snaith 1983) is the first scale designed for use with medical patients. It has seven questions each designed to measure the psychic components of depression and anxiety respectively. The depressive symptoms are heavily weighted towards anhedonia (five out of seven questions), because the authors felt this best represented the psychic component of depression. They then used the HAD with one hundred medical outpatients, followed by a clinical interview in which ratings of depression and anxiety were made. The clinical ratings were then compared to the scores on the HAD and a cut-off point derived. The cut-off point given for anxiety was 10 which efficiently separated cases from non-cases or doubtful cases. However, this was not the same situation with the depression scale where only 8 out

off 12 cases were correctly categorized, 3 cases scoring in the range of 8-10. They also found that depression scores on the HAD correlated with interview ratings of severity of depression (r=+0.74). The authors felt that the scores were not influenced by the patients physical condition. This was after they had matched patients scoring 0 or 1 with rating scores from a normal population (hospital staff) and calculated that there was no difference. However, a possible concern is that there appears to have been no correlation between the severity of the patients illness and the scores on the HAD, which previous studies have suggested is likely. The authors recognize that the cut-off point may lead to false positive results or false negative results and suggest the cut-off might be raised or lowered. They also make the point that it has to be validated before being used on hospital patients. The two studies reviewed in which the HAD was used (Channer et al 1985; Lepine et al 1985) suggested it was good at identifying anxiety, but probably not as useful in depression. Aylard et al (1987) however concluded that "the HAD scale is a valid instrument in .... the detection and assessment of the mood disorders of anxiety and depression in hospital outpatient clinics." However, it has not been clearly validated amoungst hospital inpatients.

SCREENING TESTS FOR DEPRESSION:

The Beck Depression Inventory (BDI: Beck 1961) has been a widely used screening tests (Moffic and Paykel 1975; Neilson and Williams 1980) but has not been validated in the physically ill. In the initial study Beck validated the scale using a mixed population of 598 psychiatric inpatients and outpatients. The scale includes 7 out of 21 items that could reasonably be expected to be affected by physical illness. Beck and Beck (1972) recognized these problems and developed a shorter 13 item inventory which was then validated (Beck et al 1974) against 93 attenders at a general practice clinic, as well as 241 hospitalised patients who had attempted suicide, 58 depressed patients and 39 hospitalised schizophrenics. In this short BDI only three items are likely to be affected by physical illness. Nonetheless both the Moffic and Paykel study (1975) and the Neilson and Williams (1980) study used the 21-item Beck Inventory.

Clark et al (1983) looked at the non-somatic components of the BDI in both medical inpatients (335) and psychiatric inpatients with a diagnosis of depression (101) and a similar number of controls,the 'psychiatric-normal' group. The psychiatric-normal group received the BDI and a standardized interview, the Schedule for Affective Disorders and Schizophrenia (Endicott

and Spitzer 1978) whereas the medical inpatients received only the BDI. Using a cut-off point of 10 36% of the medical inpatients were depressed as opposed to 39% of the psychiatric-normal patients, with a cut-off of 20 then these figures were 16% and 27% respectively. The authors feel their results show that "the BDI items measure a single underlying dimension of depressive severity". The authors generate 6 of the 21 items of the BDI which they feel "may represent criteria for depressive severity that are not confounded by the presence of physical illness". These items are suicidal ideas, sense of failure, sense of punishment, loss of social interest, indecision and dissatisfaction. This might suggest that 15 of the BDI items might not discriminate effectively. It is also interesting to note that of these 6 items only one concerns anhedonia, compared with 5 out of 7 for the Hospital and Anxiety Depression Scale. This research did not therefore, fully validate the unmodified BDI in the physically ill.

The Hamilton Rating Scale (HRS; Hamilton 1960) has been widely used in psychiatric research and is widely validated in these circumstances,but has been less widely used in medical patients. Schwab et al (1967b) used the Hamilton Rating Scale with 153 medical patients and noted that somatic anxiety and commonly encountered symptoms such as difficulty in sleeping and weight loss did not discriminate well between depressed and non-depressed subjects. As previously discussed, this study has

severe methodological problems and the authors conclusion that "the Hamilton Rating Scale is a useful tool for evaluating depression in medical inpatients" does not seem to be justified. Moffic and Paykel (1975) used the HRS in their study of 150 medical patients, and of the symptoms rated 8 out of 26 might have been affected by medical illness. They also compared the medical patients scores with a similar number of psychiatric patients matched for severity of depression. Interestingly, the medical patients scored significantly more on retardation, agitation, self-pity, pessimism and hopelessness as well as psychic anxiety. There were no significant differences in work impairment or fatigue, somatic anxiety, constipation, anorexia, initial, middle or delayed insomnia. These are the very symptoms one would expect to be increased in the medically ill, especially more seriously ill patients, and such a finding is therefore surprising. The authors found that 61% of the severely medically ill were depressed, as opposed to 21% of those moderately or mildly ill.

Robins et al (1984) looked at patients with duodenal ulceration prior to treatment in a placebo controlled trial of ranitidine, an H2-receptor antagonist. The HRS and the Montgomery Asberg Rating Scale for depression (MARS: Montgomery and Asberg 1979) were administered at baseline then at 2 and 4 weeks. The mean score on the HRS fell from 25 to 9 over the four week trial period, there being no difference between patients on

ranitidine or placebo. The MARS fell from a mean score of 10 to 1.75 over the trial period. The fall in scores of both the HRS and MARS accompanied a decrease in reported symptoms.

The Montgomery Asberg Rating Scale (MARS) was originally validated in a series of psychiatric patients. In this paper the authors incorporated clear instructions as to the way scores were to be allotted. They eventually selected ten items for inclusion, depression assessed by the interviewer; depression reported by the patient; feelings of inner tension; disturbance of sleep; disturbance of appetite; difficulties concentrating; feelings of lasitude; interest in surroundings; pessimistic thoughts and suicidal thoughts. Each of these were to be scored on a scale of 0-6, with clear instructions about what constituted each additional 2 points. There remained four items which might be affected by physical illness; sleep, appetite, concentration and lassitude.

Davidson et al (1986) tested the reliability and validity of the MARS in 44 depressed psychiatric inpatients. They found the MARS useful and reliable with an average patient score of 32.2. They also found the MARS differentiated endogenous from non-endogenous depression. The authors found that for three items, sleep, appetite and suicidal thoughts, the scale did not correlate well with severity. This appears to have been because

most patients consistently scored highly on sleep disturbance and low on appetite loss and suicidal ideas. Snaith and his colleagues (Snaith et al 1986) used the MARS and Clinical Anxiety Scale (CAS; Snaith et al 1982) in depressed psychiatric patients to establish ranges of scores making diagnosis more or less probable. With 80 patients they delineated four ranges, absent or recovered 0-6, mild depression 7-19, moderate 20-34 and severe 35-60. Kearns et al (1982) compared three rating scales, the BDI, HRS and MARS and concluded that the MARS "would be more suitable if the investigation was conducted on patients who suffer from concurrent physical illness".

More recently Goldberg et al (1988) have suggested a series of questions suitable for use in the physically ill to determine the presence of depression. As many of these questions are about physical symptoms, they would not be suitable for use in the severely physically ill.

SEMI-STRUCTURED INTERVIEWS:

Two semi-structured interviews have been used, usually after initial screening with the GHQ, namely the Present State Examination (PSE; Wing, Cooper and Sartorius 1974) and the Clinical Interview Schedule (CIS; Goldberg 1970). Large parts of the PSE concern psychosis, not normally present in medical

patients, and it can be difficult to use with the physically ill. In addition, symptoms are only rated positive if they are definitely present and thus it is only likely to identify the more clinically severe cases. A further problem is that "appropriate distress" is excluded from any ratings. For these reasons and the fact that it takes a long time to perform, it is unsuitable for use with medical patients.

The Clinical Interview Schedule was designed to study general populations as part of community surveys. As discussed by Mayou and Hawton (1986) it "is sensitive to psychiatric symptoms seen in general hospitals and is acceptable to patients. Unfortunately there is no single accepted procedure for case definition, which can be based on arbitrary total score, or a psychiatric judgement, or on a combination of both methods". Lloyd and Cawley (1978; 1983) used the CIS in their study of psychiatric morbidity following myocardial infarction. Here the patients were given the CIS alone. Eleven of twelve symptoms were scored and twelve abnormalities observed; the observed abnormality score was then doubled and added to the symptom score to give an overall clinical rating from 0-4. 35% were felt to have moderate or more severe psychiatric morbidity. Bridges and Goldberg (1984) using the same technique (apart from scoring all twelve symptoms) found that 39% of neurology patients had psychiatric morbidity. Maguire et al (1974) concluded, (after initial GHQ screening) that 20% of the

patients on general medical wards had psychiatric morbidity. Since the patients were in general more seriously ill it might be expected that there would be a higher level of psychiatric morbidity than in neurological patients. Trelawney-Ross and Russell (1987) did not specify the method by which they arrived at their cut-off score for depression. With such widely differing results reported, it may be that the CIS may not be suitable for use with hospital patients, having been designed initially for use in general practice. This problem might be because twice the score is given to observed abnormalities which include suspicions, histrionic behavior, elated mood, delusions, hallucinations and intellectual impairment, as to reported symptoms. The observed abnormalities listed comprise half the total and are not typical of hospitalised medical patients.

COGNITIVE SCREENING:

Screening for depression is clearly the major part of the work previously reviewed. However, few authors seem to have taken note of cognitive performance of those patients subjected to the various screening instruments. Clearly it is an obvious problem if a patient is unable to understand the questions or remember how they slept the previous night. They would thus be unable to complete the rating scales in a worthwhile manner.

Most authors have referred to the patients as being "too ill" to have an assessment or complete a questionnaire, this judgement usually having been made by the general physician. The exceptions to this have been mentioned, but only in the studies by Folstein and his colleagues (Knights and Folstein 1977; DePaulo and Folstein 1978; DePaulo, Folstein and Gordon 1980) was a validated measure of cognitive state used, ie. the Mini Mental State examination (Folstein, Folstein, McHugh 1975), to examine the cognitive status of their patients. Is the MMS a suitable screening instrument for use with medical patients? The alternatives are firstly a brief non-standardized clinical assessment of cognitive function, another brief rating scale or a lengthy standardized interview such as the Geriatric Mental State (Copeland et al 1976). Clearly for a screening procedure a rating scale seems the best compromise. The MMS is brief and easy to use, with good patient acceptance and validity (Mayou and Hawton 1986) when compared with the Weschler Adult Intelligence Scale (WAIS; Weschler 1955). However, in a review of its uses Antony et al (1982) found it less useful amongst poorly educated patients and it does not adequately distinguish between educational level and delirium or dementia. The other brief cognitive rating scale is the Cognitive Assessment Schedule (CAS; Pattie and Gilleard 1979; McPherson et al 1985) but it does not yet appear to have been adequately tested in general medical patients.

DISCUSSION:

This study was designed to study medical inpatients with a range of life-threatening illnesses, to study them continuously over a 21 day period following admission, and to relate mood and outcome. It is clear from preceding reviews that there is no one ideal rating scale or measurement that is both suitable and well validated in this population. Because the patients to be seen were frequently very ill, it was also felt necessary to have some measure of cognitive performance, especially as the group of patients with sub-arachnoid haemorrhage were particularly likely to have fluctuating levels of consciousness.

From the previous review several important points emerge. The first is that symptoms in which medical patients might be expected to score highly, such as poor sleep, poor appetite, weight loss, lethargy, fear of the future (possibly realistic), and poor concentration, are included in nearly all the rating scales or questionnaires, although it is possible that medical patients might not score more highly on these symptoms (Moffic and Paykel 1975; Davidson et al 1986). A second point is that it is not clear which non-somatic features accurately delineate depression, as illustrated by the different emphasis put on anhedonia. Thirdly, as previously discussed, severity of

illness, cognitive performance, and pain suffered have only rarely been studied or correlated with the scores from the rating scales or interviews.

In view of these problems it was felt that an interview was necessary for both cognitive assessment and to assess the patients mood. A rating scale would also be the best way of validating the patients mood over time, rather than a self-assessment questionnaire or a larger semi-structured interview. A combination of approaches was considered but felt to be too demanding of the patients time, especially when they were likely to be seriously ill. The assessment procedure selected was the Montgomery Asberg Rating Scale for several reasons. Firstly it was designed to be sensitive to change, secondly, it was not unduly reliant on somatic features, thirdly, it was reasonably brief and lastly, because it gave clear instructions for scoring. It was anticipated that there might be some false positives using this technique alone. It was felt that this problem could be dealt with in one of two ways, either to raise the cut-off point or retrospectively exclude the answers to somatic questions if these appeared to be causing false positive results. As regards the cognitive assessment, it was decided to use the MMS as it had been used previously with similar patients by Knights and Folstein (1977). The same cut-

off point of 22 was decided upon; patients scoring below 22 were not rated on the MARS.

The relationship between pain and mood has been little studied. In one of the few relevant investigations Ahles at al (1984) examined the relationship between pain, as measured by a visual analogue scale, and depression. Depression was measured in 29 outpatients by the BDI, the Symptom Checklist-90 (Derogatis 1977) and in 11 inpatients by a simple visual analogue scale. The authors showed that in this group of patients there was a significant relationship between pain and depression. Despite critisism of the study in terms of its unreliable measure of depression it suggests the need to measure the amount of pain experienced by patients. In a study of patients with chronic pain (greater than 6 months duration) Kremer and Atkinson (1984) using the McGill Pain Questionnaire (Melzack 1975) showed that the pain score was related to the affective components of the McGill Questionnaire.

In a study of pain in chronic back sufferers France et al (1986) studied 80 patients with chronic back pain assessing described pain on the basis of a semi-structured interview. Depression was measured by using the Montgomery-Asberg Rating Scale and the Beck Depression Inventory. In addition the patients were assigned Research Diagnostic Criteria diagnoses

(RDC: Spitzer, Endicott and Robins 1975) on the basis of the interview. The mean duration of pain was 56 months and the mean number of operations was 1.7. Using RDC criteria 80% of patients were depressed (21% with Major depressive Disorder; 54% with Intermittent Depressive Disorder; 5% with minor depressive disorder). The authors found no difference in the number of operations or other measures of pain between the depressed and non-depressed groups, although the authors seem not to have determined the degree of pain experienced at the time of the interview. The authors felt that the Montgomery-Asberg Rating Scale differentiated well between the groups identified using RDC diagnostic criteria.

In terms of measurement of pain Jensen et al (1987) discuss previous pain measuring instruments and also the relationship of attitudes to pain and its experience. They demonstrate that pain coping strategies are important in contolling chronic pain. However, none of the pain rating scales they mention would be suitable for the current study as they were either too long, or the questions asked were designed primarily for chronic pain, or pain in cancer sufferers. It was also felt that a visual analogue scale, or questionnaire was less suitable than a brief question designed to elicit the degree of pain experienced at the time of interview.

CHAPTER 3: METHODS:

This study tests one hypothesis on four groups of patients. The means of testing the hypothesis are similar, any differences being given in each section. Outlined here are the exclusion and inclusion criteria, the Montgomery Asberg Rating Scale for depression (MARS; Montgomery and Asberg 1979), the Mini Mental State Examination (MMS; Folstein et al 1975), the Pain Rating Scale and the measures of morbidity and mortality.

SUBJECTS

Consecutive patients suspected of having one of the required conditions were entered into the study, provided they were above 18 years old. Patients were excluded if they were below 18 years of age, scored less than 22 on the Mini-Mental State Examination, were admitted when the author was on leave or had their first interview more than 48 hours after admission. The patients were also excluded if the onset of their illness occurred more than one week before the date of admission. With patients entered into the study who subsequently were proven not to have serious illness, rating scales were continued until discharge where possible.

RATING SCALES:

The Montgomery Asberg Rating Scale (MARS) was first performed between 2 and 48 hours following admission (within 24 hours if possible) provided that the patient scored more than 22 on the Mini-Mental State Examination. The rating was carried out during an interview with the patient which lasted approximately 10-15 minutes, conducted at the patient's bedside. The MARS has clear instructions as to how each component should be scored, and these instructions were followed. Prior to using this scale the author discussed at length, with a consultant psychiatrist, the meaning of each individual rating and how the instructions could be best applied to medical patients. The MARS was performed on alternate days until discharge or 21 days post-admission, whichever was the sooner. The MARS was not performed within 2 hours of administration of any drug that might affect mood or cognitive performance, such as opiates. It was also not performed within 4 hours of any technical procedure, such as insertion of a pacing wire, which did not involve general anaesthesia, and not within 24 hours of a procedure, such as angiography, which did involve general anaesthesia.

The Mini-Mental State Examination (MMS) is a 30 item test of cognitive function with patients scoring between 30 and zero. The patients were tested immediately before the MARS and any

patient scoring 22 or less was considered unable to perform the MARS adequately, which was therefore not done. The MMS was first administered between 2 and 48 hours after admission (preferably within 24 hours) then on alternate days until 21 days or discharge. As with the MARS it was not performed within 2 hours of medication likely to affect cognitive performance, within 4 hours of any procedure, or within 24 hours of general anaesthesia.

Because of the potential problem that depressed patients might suffer more pain than non-depressed patients, a Pain Rating Scale was devised. This ranged from a score of zero to three. Zero represented no pain; one represented slight pain; two represented moderate pain; and three represented pain as severe, or more severe, than that on admission. Each patient was asked following each interview if they had suffered any pain that day. If they answered in the affirmative they were then asked how severe the pain was. Each group of patients was asked about pain specific to their illness, for instance, those with myocardial infarction were asked about chest pain and those with sub-arachnoid haemorrhage were asked about headache.

OUTCOME:

Measurement of mortality was straightforward, any patient who had been entered into the study and died within 28 days of admission was counted as fatal outcome. Those patients who died after this time were not entered into the fatal outcome group even if they had remained in hospital until they died. The reason it was felt necessary to extend the length of time during which fatal outcome was still counted (28 days) as opposed to the length of time the patients still had rating scales performed (21 days) was because it was envisaged that some patients may suffer an event, such as a cerebrovascular accident (CVA), which might lead to their death in the few days after the rating scale had ended. Since the aim of the study was to test the strength of any link between depression and mortality, it was felt it would be reasonable to extend the 21 day limit by 7 days. 21 days was chosen as the time limit for testing because the numbers of patients being tested made it impractical to continue formal testing beyond this time, as well as the fact that the large majority of discharges and deaths occurred within this time period. The measurements of morbidity were also carried out over the same time period of 28 days. Morbidity was measured by the number of serious but non-fatal events that happened to the patient. Those included were; cardiac arrest with successful resuscitation; a Cerebro-Vascular Accident; or a pulmonary embolus. Thus patients fell

into one of three groups, those with a good outcome, those who suffered a serious non-fatal event, and those who died. These end points were chosen as measures of outcome as they were both easily verifiable and also were of clear importance to management. It is possible to divide the patients into two groups, good outcome and poor outcome and in the results sections, both these methods are statistically examined.

DATA ANALYSIS:

The statistical methods of analysis used throughout the study are either chi-squared, always using Yates correction, or alternatively Students 't' tests, except where stated in the text.

DATA INTERPRETATION:

Once the data for the MARS had been gathered it was analysed in several ways. Firstly three increasing cut-off points to define depression were analysed separately; 7,14 and 21. Secondly, the scores for the somatic components of the MARS were excluded, and a cut-off point of 7 was then applied to the remaining items. There are several reasons for this approach. Firstly, the cut-off points for depression validated in the

psychiatrically ill by Snaith et al (1986: 7 for mild depression, 20 for moderate depression, 35 for severe depression) may not be applicable to the physically ill, the lower cut-off point in particular might need to be raised in this group. Thus is is necessary to look at several cut-off points. An additional cut-off point between thosefor mild and moderate depression might be able to illuminate this point. Secondly, if several cut-off points are examined it is potentially easier to see the advantages and disadvantages of each, rather than using retrospective analysis to determine which score gives the best fit between results obtained. Thirdly the increasing cut-off points are intended to show any variations within the depressed population when the cut-off point is raised as well as the differing percentage of population in each. Therefore it can be seen if any findings are simply dependent on one cut-off point or occur with all of them. This technique can answer questions such as is there a difference between a cut-off point of 7 and 21 in the number of females who are depressed, or does a higher cut-off point illustrate those most at risk of a poor outcome?

Looking at the results with the somatic components excluded from the score allows examination of mood without the potential bias of physical illness influencing the results. It also allows an understanding of what percentage of each individuals

total score is possibly due to the underlying illness. This percentage can then be compared with other cut-off points.

SECTION 2:

CHAPTER 4: MYOCARDIAL INFARCTION: INTRODUCTION:

CHAPTER 5: MYOCARDIAL INFARCTION: RESULTS:

CHAPTER 6: SUB-ARACHNOID HAEMORRHAGE: INTRODUCTION

CHAPTER 7: SUB-ARACHNOID HAEMORRHAGE: RESULTS

CHAPTER 8: PULMONARY EMBOLISM: INTRODUCTION:

CHAPTER 9: PULMONARY EMBOLISM: RESULTS:

CHAPTER 10: GASTRO-INTESTINAL BLEEDING: INTRODUCTION:

CHAPTER 11: GASTRO-INTESTINAL BLEEDING: RESULTS:

CHAPTER 12: COMBINED RESULTS

CHAPTER 4: MYOCARDIAL INFARCTION

INTRODUCTION:

Myocardial infarction is the end-point of coronary artery disease. As progressive myocardial ischaemia occurs the heart may either fail, develop ischaemic pain (angina), suffer disordered conduction or abnormal rhythm. When the ischaemia becomes so severe that the blood supply is unable to sustain the heart muscle it supplies, infarction results. This is often heralded by a ventricular arrhythmia, usually ventricular tachycardia or asystole. Although myocardial infarction is usually preceded by a symptomatic period, in 25% of deaths the first announcement of coronary heart disease is the fatal infarction (Oakley 1983). Half the patients who have a myocardial infarction will die from it, with two thirds of this group dying before they reach hospital. Of the remainder, half will die in the acute stage in hospital and half will die in the following year (Oakley 1983). The number of patients dying in hospital will be studied but this number varies considerably; for instance, in a study by Rasmussen et al (1986) 14% died in the first four weeks post-infarction but Reznik et al (1987) report ranges from 19-22% depending on the hospital. This wide range reflects differences in management (Hutchinson and Cobbe 1987). Mortality has clearly decreased

over the last 15 years, although the role of medical management in this change is uncertain (Beaglehole 1986). In a large study by O'Doherty et al (1983) 23% of patients admitted died in hospital but it became apparent that the earlier patients were admitted, the higher the risk of dying, ie. with a rapid ambulance service, more people who would have died at home, died in hospital. A recent Lancet editorial (1985) discussed rehabilitation after myocardial infarction and noted common psychological reactions amongst patients, but tended to minimise these, "anxious doctors have anxious patients."

There are several prognostic indicators predicting the likelihood of death in those patients who arrive in hospital. As a review by Rosenthal et al (1985) discusses, these predictors fall into three main groups; disturbances of cardiac rhythm and conduction, abnormalities of left ventricular function and lastly, the residual myocardium at risk from ischaemia. It used to be felt that abnormalities of the ventricular rate or the number of ectopic beats seen on cardiac monitoring in the 48 hours post-infarction could predict those patients who were going to have subsequent ventricular arrhythmias. This has now been shown not to be the case. There is some evidence that prolonged monitoring, until 48 hours prior to discharge, predicts death rates in the subsequent

year. This finding is not, however, relevant to the current study.

The only electrocardiography (ECG) feature noted to predict early mortality was the presence of Bundle Branch Block (BBB), as this is a general indicator of the size of the infarction. Left ventricular dysfunction or failure (LVF) is also usually a measure of the size of the infarction. The presence of LVF can be detected by clinical examination or on a chest x-ray. In some units (such as routinely done in the USA) this is carried out by insertion of a Swan-Ganz catheter into the right side of the heart and thence to the pulmonary artery. Left ventricular function is then measured by calculation of the various ejection fractions from which a quantifiable measure of LVF can be derived. In Britain it is much less common to insert a catheter unless clinically indicated, where clinical examination and chest x-ray are relied upon to detect LVF, as in the present study.

Rosenthal also discusses other techniques which correlate well with infarct size determined at post-mortem, these are thallium and technetium scanning and measurement of cardiac enzymes, specifically creatinine phosphokinase (CPK). As neither of the scanning techniques are routinely available, the size of the infarction is determined by measurement of the serum levels of

the so-called 'cardiac' enzymes. There are three enzymes routinely measured, each appearing at a different time post-infarction. The first is CPK, more specifically the cardiac iso-enzyme of CPK, which is most closely correlated with infarct size. The next is aspartate transaminase (AST) and lastly lactate dehydrogenase (LDH). Unfortunately however, CPK serum measurement was not routinely available at the hospital where the study took place until near the end of the study period. For this reason the size of the infarction has been estimated by using a combination of AST and LDH values, the value being used being the highest obtained during in-patient stay. Peak serum AST and LDH levels are related to infarct size, but not as closely as CPK. Furthermore the serum levels of all the cardiac enzymes may be significantly raised by other events such as cardioversion (D.C. shock).

Residual myocardial ischaemia may become clinically apparent by post-infarction angina associated with reversible changes in the ECG. It may also be elicited during exercise testing with ECG monitoring, when ST-segment elevation occurs. Jennings et al (1983) demonstrated that 'reciprocal' ST-segment changes occurring in the first 48 hours post-infarction may be reflecting addition ischaemia, which would be detected later by exercise testing. Thus its presence denotes increased risk of early death.

The findings previously outlined lead to the adoption of several prognostic indicators by which each patient may be assessed. These are the presence of LVF clinically or radiographically, BBB or ST-segment changes on the ECG, and the peak serum levels of AST and LDH.

PATIENTS AND METHODS:

All patients admitted to a district general hospital (East Surrey Hospital) under one Consultants care with suspected myocardial infarction were entered into the study, provided they fulfilled the entry criteria previously outlined. Once admitted the patients were transferred to the intensive care unit where they had continuous cardiac monitoring for between 48-72 hours. If the patients remained free of complications at this point they were transferred to a medical ward where a graded rehabilitation programme would proceed for the next 7-8 days, thence leading to discharge 10 days post admission. The author was on duty one night in three and thus the study population represent approximately one third of the total admissions to the hospital for suspected myocardial infarction during the study period.

On each of the three days following admission the patients had an ECG and serum cardiac enzyme analysis. They also had a chest

x-ray on admission, repeated as necessary. Further investigations or procedures were performed as dictated by the patients clinical condition. For the first seven days of admission the patients had daily ratings with the Mini-Mental State examination followed by the Montgomery-Asberg Rating Scale and Pain Rating Scale as outlined in chapter 3. These rating scales were continued on alternate days to a maximum of 21 days post-admission. Those patients in whom investigation subsequently showed that they had not sustained a myocardial infarction were usually discharged on day 3 or 4 if otherwise well

CHAPTER 5; MYOCARDIAL INFARCTION

RESULTS:

Over the one year study period 145 patients were potentially eligible for entry into the study, but 27 were excluded for the following reasons; in 13 patients brought to the accident and emergency department for resuscitation after cardiac arrest resuscitation was unsuccessful. A further 2 patients died within two hours of admission and 11 patients scored less than 22 on their initial Mini-Mental State examination (MMS). One patient was excluded as his myocardial infarction had occurred more than one week prior to his presentation. Of the 118 patients entered into the study 18 (15%) were subsequently shown not to have sustained a myocardial infarction. Of the 100 patients remaining 8 died during the course of the study, on days 2,3,6,8,13,14,16,and 19. A further 17 patients suffered either cardiac arrest with successful resusitation, pulmonary embolus or cerebro-vascular accident. Of the 100 patients 74 were men and 26 women (sex ratio 2.8:1). The mean age of the patients was 64.6 years (range 39-86). For men the mean age was 63 (S.D. 6.3) years and for women 69.2 (S.D. 6.6). this difference is not statistically significant ($t=1.8$; $p>0.05$).

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 7

When using a cut-off point of 7 in the Montgomery-Asberg Rating Scale to determine the presence of depression then 59 patients were depressed. The mean age of the depressed group was 60.3 years (S.D. 8.9) and of the non-depressed group 70.7 years (S.D. 10.3). This difference is not statistically significant ($t=1.1$; $p>0.1$). Of the depressed group 45 were men and 14 women (sex ratio 3.2:1) as opposed to 29 men and 12 women in the non-depressed group (sex ratio 2.5:1).

Table 1 demonstrates the outcome of the depressed and non-depressed groups.

The mean Montgomery-Asberg Rating Scale scores post-admission are given in Figure 1. As those patients who did well were almost all discharged before 10 days post-infarction only the measurements for the first 7 days are shown.

The results for the pain rating scale showed no significant differences between the depressed and non-depressed groups. However, the mean scores show that there was a trend for the scores to be higher in the depressed group.The results are shown in Table 5.

Prognostic indicators of outcome following myocardial infarction, namely serum levels of cardiac enzymes, the presence of bundle branch block or reciprocal ST-segment elevation on the electrocardiogram, and the presence of left ventricular failure were measured in all patients. The results are given in Table 6. The serum cardiac enzyme level given is the highest recorded during repeated analysis. However although the levels reflect the degree of cardiac damage, the can also be greatly increased by cardioversion. Thus two sets of results are given, the first set being the highest serum level recorded and the second set (in brackets) being the highest prior to cardioversion.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 14

When using a cut-off point of 14 in the Montgomery-Asberg Rating Scale to determine the presence of depression then 41 patients were depressed. The mean age of the depressed group was 61.5 years (S.D. 9.3) and of the non-depressed group 68.4 years (S.D. 10.2). This difference is not statistically significant. Of the depressed group 29 were men and 12 women (sex ratio 2.4:1) as opposed to 45 men and 14 women in the non-depressed group (sex ratio 3.2:1).

Table 2 demonstrates the outcome of the depressed and non-depressed groups.

The mean Montgomery-Asberg Rating Scale scores over time are given in Figure 1.

The results for the pain rating scale showed no significant differences between the depressed and non-depressed groups. However, the mean scores show that there was a trend for the scores to be higher in the depressed group.The results are shown in Table 5. Prognostic indicators of outcome following myocardial infarction are given in Table 7.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 21

When increasing the cut-off point to 21 on the Montgomery-Asberg Rating Scale to determine the presence of depression then 19 patients are depressed. The mean age of the depressed group was 59.2 years (S.D. 8.0) and of the non-depressed group 67 years (S.D. 9.4). This difference is not statistically significant. Of the depressed group 15 were men and 4 were women (sex ratio 3.75:1) as opposed to 59 men and 22 women in the non-depressed group (sex ratio 2.7:1).

Table 3 demonstrates the outcome of the depressed and non-depressed groups.

The mean Montgomery-Asberg Rating Scale scores over time are given in Figure 1.

The results for the pain rating scale showed no significant differences between the depressed and non-depressed groups. However, the mean scores show that there was a trend for the scores to be higher in the depressed group.The results are shown in Table 5.

Prognostic indicators of outcome following myocardial infarction are shown in Table 8.

MONTGOMERY-ASBERG RATING SCALE:

CUT-OFF 7 WHEN SOMATIC COMPONENTS EXCLUDED (7-SCE)

The scores on the Montgomery-Asberg Rating Scale were re-examined, with the scores for four of the items then being excluded. These items were disturbance of sleep; disturbance of appetite; concentration difficulties; and lassitude. When a cut-off point of 7 was then applied to the remaining score to

determine the presence of depression 37 patients were depressed. The mean age of the depressed group was 61.1 years (S.D. 9.2) and of the non-depressed group 67.5 years (S.D. 9.6). This difference is not statistically significant. Of the depressed group 27 were men and 10 women (sex ratio 2.7:1) as opposed to 47 men and 16 women in the non-depressed group (sex ratio 2.7:1).

Table 4 demonstrates the outcome of the depressed and non-depressed groups. The results for the pain rating scale showed no significant differences between the depressed and non-depressed groups, although there is a trend for the depressed patients to score more highly. The results are shown in Table 5.

Prognostic indicators of outcome following myocardial infarction showed no statistically significant differences, as shown in Table 9.

NON-MYOCARDIAL INFARCTION GROUP:

In addition to the 100 patients who had a myocardial infarction there were 18 patients admitted who were thought to have sustained an infarction but in whom this was subsequently shown

not to be the case. Of these 18 patients, mean age 63.7 years, 14 were men and 4 were women (sex ratio 3.5:1). As regards their scores on the Montgomery-Asberg Rating Scale, 8 scored more than 7 (44%), 5 more than 14 (28%), 2 more than 21 (11%) and 4 more than 7-SCE (22%). This compares with the percentages from the study group of 59%, 41%, 19%, and 37% respectively. Of the 8 depressed patients, 6 subsequently developed serious medical problems, with 2 patients sustaining a subendocardial myocardial infarction, 3 developing left ventricular failure and one having severe anaemia. Of the 10 non-depressed patients one developed left ventricular failure. Of the four patients in the 7-SCE all developed a serious medical problem. As only those who developed complications were likely to remain in hospital for more than three days the rating scale scores over time are not illustrated.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups using any of the different cut-off points. When comparing the non-infarction patients with the study population, the infarction patients had significantly more pain in the first three days than the non-infarction patients. Most of the latter were discharged at this stage.

SUMMARY

To briefly summarise the results from the myocardial infarction study, 100 consecutive patients with myocardial infarction were repeatedly interviewed using the Montgomery-Asberg Rating Scale. When using the cut-off point of 7 then 59% of the patients were depressed This group was no more seriously ill than the non-depressed group. They were also no significant differences in age, sex, or in the amount of pain suffered. However, the depressed patients did significantly worse in terms of morbidity. These findings also applied to the depressed groups when using the cut-off points 14 and 7-SCE, but was most significant for the 7-SCE group. Here, 50% of the depressed group had a poor outcome as opposed to 12% of the non-depressed group, and 20% of the depressed patients died compared to less than 2% of the non-depressed patients.

The percentage of patients who were depressed varied across cut-off points from 59% to 19%. With the depressed patients there was a tendency for their MARS scores to decrease over time. There was also a trend for the depressed patients to experience more pain.

TABLE 1

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	36	39	75
POOR OUTCOME	*** 23	*** 2	25
(DIED)	(7)	(1)	(8)
TOTAL	59	41	100

*** This difference is highly significant (Chi-Squared 13.24; $p<0.001$)

TABLE 2

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 14

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	24	51	75
POOR OUTCOME	** 17	** 8	25
(DIED)	(5)	(3)	(8)
TOTAL	41	59	100

** This difference is significant (Chi-Squared 8.6: $p<0.01$)

TABLE 3

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 21

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	11	64	75
POOR OUTCOME	8	17	25
(DIED)	(2)	(6)	(8)
TOTAL	19	81	100

TABLE 4

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7-SCE

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	19	56	75
POOR OUTCOME	*** 18	*** 7	24
(DIED)	** (7)	** (1)	(8)
TOTAL	37	63	100

*** This difference is statistically significant (Chi-Squared 15.6; $p<0.001$)

** This difference is statistically significant (Chi-Squared 7.3; $p<0.01$)

Table 5: Mean Pain Rating Scale Scores
In Myocardial Infarction Patients

	Cut-Off Point 7		Cut-Off Point 14		Cut-Off Point 21		Cut-Off Point 7-SCE	
	D.	N.D	D.	N.D	D.	N.D	D.	N.D
Day 3	0.98	0.22	1.12	0.36	1.36	0.4	1.19	0.38
Day 5	0.83	0.17	0.68	0.22	0.74	0.33	0.70	0.29
Day 7	0.37	0.15	0.44	0.17	0.53	0.22	0.68	0.21
Day 9	0.24	0.01	0.34	0.07	0.47	0.11	0.47	0.09
Day 11	0.15	0.01	0.34	0.01	0.10	0.07	0.21	0.02

There are no statistically significant differences between the Depressed (D.) and Non-Depressed (N.D.) groups at any of the differing cut-off points.

Table 6. Prognostic Indicator Scores in Myocardial Infarction:

Cut-Off Point 7

	Depressed Group	Non-Depressed Group
Mean Scores and (S.D.)		
Serum AST	226 (202)	199 (213)
Pre D.C. AST	185 (193)	199 (213)
Serum LDH	623 (523)	461 (240)
Pre D.C. LDH	501 (528)	461 (240)
Bundle Branch Block	17 (29%)	10 (24%)
ST-Segment elevation	30 (52%)	20 (49%)
Left Vent. Failure	22 (37%)	11 (26%)

There are no significant differences between the two groups.

The Serum value is the maximum serum value obtained.
The Pre D.C. value is the maximum value obtained prior to cardioversion when this occured, otherwise it is the maximum serum value.

Table 7. Prognostic Indicator Scores in Myocardial Infarction:

Cut-Off Point 14

	Depressed Group	Non-Depressed Group
Mean Scores and (S.D.)		
Serum AST	239 (287)	195 (121)
Pre D.C. AST	195 (277)	195 (121)
Serum LDH	* 682 (522)	* 471 (327)
Pre D.C. LDH	508 (341)	471 (327)
Bundle Branch Block	13 (31%)	14 (23%)
ST-Segment elevation	21 (52%)	29 (49%)
Left Vent. Failure	16 (39%)	17 (29%)

*This difference is statistically significant ($t=2.15$; $p<0.05$). There are no other significant differences between the two groups.

The Serum value is the maximum serum value obtained.
The Pre D.C. value is the maximum value obtained prior to cardioversion when this occured, otherwise it is the maximum serum value.

Table 8. Prognostic Indicator Scores in Myocardial Infarction:

Cut-Off Point 21

	Depressed Group	Non-Depressed Group
Mean Scores and (S.D.)		
Serum AST	302 (213)	194 (112)
Pre D.C. AST	169 (91)	194 (112)
Serum LDH	* 806 (557)	* 498 (354)
Pre D.C. LDH	432 (309)	498 (354)
Bundle Branch Block	6 (32%)	21 (26%)
ST-Segment elevation	13 (68%)	37 (46%)
Left Vent. Failure	9 (47%)	24 (30%)

*This is a statistically significant difference between the two groups ($t=2.28$; $p<0.05$). There are no other significant differences between the two groups.

The Serum value is the maximum serum value obtained.
The Pre D.C. value is the maximum value obtained prior to cardioversion when this occured, otherwise it is the maximum serum value.

Table 9. Prognostic Indicator Scores in Myocardial Infarction:

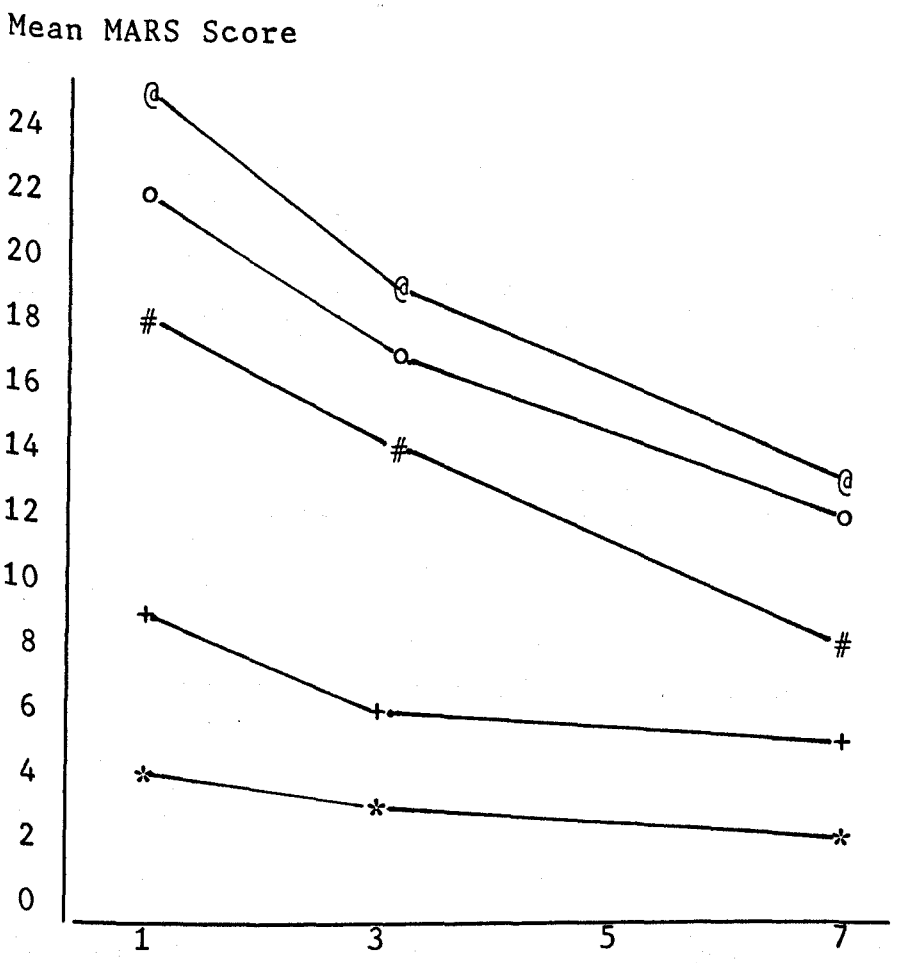
Cut-Off Point 7-SCE

	Depressed Group	Non-Depressed Group
Mean Scores and (S.D.)		
Serum AST	263 (207)	187 (181)
Pre D.C. AST	187 (171)	187 (181)
Serum LDH	557 (691)	491 (281)
Pre D.C. LDH	326 (584)	491 (281)
Bundle Branch Block	11 (30%)	16 (26%)
ST-Segment elevation	17 (46%)	33 (52%)
Left Vent. Failure	15 (40%)	18 (29%)

There are no significant differences between the two groups.

The Serum value is the maximum serum value obtained.
The Pre D.C. value is the maximum value obtained prior to cardioversion when this occured, otherwise it is the maximum serum value.

Figure 1: Montgomery-Asberg Rating Scale over Time Myocardial Infarction



* = MARS Score 0-7

\+ = MARS Score 7-14

\# = MARS Score 14-21

@ = MARS Score >21

o = MARS Score >7-SCE

CHAPTER 6: SUB-ARACHNOID HAEMORRHAGE

INTRODUCTION:

Sub-arachnoid haemorrhage describes a condition in which blood gets into the sub-arachnoid space (SAS).Patients with sub-arachnoid haemorrhage (SAH) usually present clinically with an acute onset of a severe headache This can occur spontaneously in one of four ways (Lockley et. al. 1966); an effusion from within the subdural space rupturing into the SAS; a haemorrhage breaking through the pia mater into the SAS; a deep-seated cerebral haemorrhage rupturing into one of the ventricles, and thence into the SAS; the haemorrhage occurs from one of the vessels located within the SAS, usually due to spontaneous rupture of an aneurysm. It is this last group that this study will consider. Some patients have a proven SAH, but subsequent investigation demonstrates no aneurysm. Locksley and his colleagues (1966) have shown that these patients have a much better prognosis than those in whom a ruptured aneurysm is the cause of the SAH (confirmed by Shephard 1984). Locksley also demonstrated the high mortality of an aneurysmal bleed. In his group there was a 30% mortality within 48 hours of onset, with 48% dying within the first week. Of those patients who survived a further 28% will die from a re-bleed within six weeks (a total mortality rate of 78%). Thus the therapeutic aim

is to try and surgically repair any aneurysm as soon as possible whenever practicable.

These patients were studied for several reasons. Firstly, they have an acute onset of a potentially life-threatening illness, the cause usually being clearly apparent. Secondly, they may have both organic and psychological reasons for any affective disorder noted, and this might prove to be related to the position of any aneurysm or bleeding. Thirdly, this group of patients has a high rate of early mortality and thus may help demonstrate any differences between groups. Lastly, these patients may be particularly prone to depression since their treatment involves being confined to bed in a prone position for long periods of time.

Previous work has demonstrated three prognostic indicators for the short-term outcome in patients with sub-arachnoid haemorrhage. Jane et. al (1977) followed up over 200 patients who were not treated surgically and found that initial hypertension predicted the incidence of rebleeding within six months. Arterial spasm, demonstrated by cerebral angiography, has also been clearly linked to outcome. This vasospasm occurs in two phases, a short initial episode followed by a longer, more severe phase (Brawley et. al. 1983). It is the second phase which causes clinical effects. The cause of this

vasospasm is not clear at present, although several mediators have been suggested following experimental work, including haemoglobin (Wellum et al 1982); neuropeptide Y (Allen et al 1984); serotonin (Allen et al 1974); noradrenalin (Alksne and Greenhoot 1974); and prostaglandins (Yamamoto et al 1972).

A further prognostic indicator is the Computed Tomographic (C.T.) findings (Turnbull 1980) . Turnbull showed that a poor prognosis was associated with two findings , firstly focal areas of low attenuation and secondly the presence of a haematoma greater than 2.5 cm in diameter. The areas of low attenuation correlated well with the site of cerebral spasm. The site of the haematoma did not affect prognosis.

The work of Turnbull was confirmed in a further study by Bell et al (1980) in which quantification of blood in the basal cisterns noted on CT scan correlated significantky with the outcome of surgery, as did the presence of pre-operative hypertension and the presence of cerebrovascular spasm. Patients who did not undergo surgery were not included in this study and thus it is uncertain if this finding is true in all patients with a subarachnoid haemorrhge due to ruptured aneurysm.

Hunt and Hess (1967) designed a prognostic classification which predicted the prognosis depending upon the time of surgical intervention in different groups of patients.

For the present study the prognostic indicators used were initial systolic and diastolic blood pressure measurements, the size of any haematoma and any areas of focal attenuation seen on C.T. scanning, and the presence of vasospasm when angiography was performed. It was decided not to use the classification of Hunt and Hess since it did not include C.T. findings, and not all of the patients would undergo surgery.

A further group of patients studied were those patients on the same ward undergoing laminectomy. The only previous relevant work is that by France et al (1986), in which the authors have studied the incidence of depression in 80 patients with chronic low back pain using the BDI, MARS and Research Diagnostic Criteria (RDC: Spitzer et al 1975). The mean duration of pain was 58 months and the mean number of operations 1.7. Using RDC criteria 21% of patients had a major depressive illness and 54% had intermittent depressive disorder. The mean MARS scores for the depressed group was 25.3 and for the intermittently depressed group 16.3 as opposed to 7.4 for the non-depressed patients.

PATIENTS AND METHODS:

Patients consecutively admitted to the South East Thames Regional Neurosurgical Unit with first proven subarachnoid haemorrhage, within 5 days of the bleed, formed the study population. Those patients who met the entry criteria previously outlined in the chapter on methodology were included.

There was also another population studied which consisted of consecutive admissions to the same ward for lower spinal laminectomy. These patients were all undergoing there first operation for back pain. The management of these patients involved prolonged periods post-operatively being confined to lying flat in bed. These laminectomy patients were often in some not inconsiderable pain during this period, despite analgesia. Because of these factors this group was felt to represent a good comparison group for the conditions in which patients with subarachnoid haemorrhage have to lie flat for prolonged periods, often in pain. The reason such patients are sometimes not given what might be considered adequate analgesia is because of the problems associated with cerebral depression in subarachnoid haemorrhage patients secondary to drug use.

All patients had psychological testing as previously outlined in chapter 3, ie. Montgomery-Asberg Rating Scale, Mini-Mental State and pain rating scale. Investigations performed on all patients were a C.T. scan and blood pressure measurement on admission, and cerebral angiography unless contra-indicated by clinical condition. In those patients where an aneurysm was seen its position was noted.

CHAPTER 7: SUB-ARACHNOID HAEMORRHAGE

RESULTS:

Fifty-six patients were potentially eligible for entry into the study, but fifteen had to be excluded for the following reasons; three patients scored below 22 on the MMS; two patients had re-bleeds; four patients had arterio-venous malformations responsible for their sub-arachnoid haemorrhage rather than aneurysms; in six patients no evidence of sub-arachnoid haemorrhage was found after full investigation. Thus forty-one patients fulfilled the entry criteria and were entered into the study. Of these, twenty-five were seen within two days of the initial haemorrhage, the rest within five days.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 7

When the Montgomery-Asberg Rating Scale cut-off was 7 then 28 patients were classed as depressed, and 13 as not depressed. The mean age of the depressed patients was 46.3 years with 11 men and 17 women (sex-ratio 1:1.5), and of the non-depressed patients 47.3 years with 7 men and 6 women (sex-ratio 1:0.9). The outcome for these patients is shown in Table 10.

The prognostic indicators also showed no statistically significant differences, as shown in Table 14.

The Pain Rating Scale scores showed no significant differences between the depressed patients and non-depressed patients over the study period. The results are shown in Table 18.

The location of the aneurysms showed an increased distribution in two areas in the depressed patients, namely the Vertebral-Basilar system and the Internal Carotid arteries, on both the right and left sides. This is shown more fully in Table 19. It should be noted that the number of aneurysms exceeds the number of patients. This is due to five patients having multiple aneurysms (three patients had two aneurysms and two patients had three aneurysms ie. a total of 42).

The mean scores for the Montgomery-Asberg Rating Scale over 21 days are shown in Figure 2. It is important to note that over this time period there were several discharges and deaths and thus the number of patients decreases over time.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 14

When the cut-off on the Montgomery-Asberg Rating Scale was increased to 14 then 15 patients were classed as depressed, and 26 as not depressed. The mean age of the depressed patients was 46.5 years with 2 men and 13 women (sex-ratio 1:6.5), and of the non-depressed patients 46.7 years with 16 men and 10 women (sex-ratio 1:0.6). The outcome of the patients are shown in Table 11.

The prognostic indicators again showed no statistically significant differences, as shown in Table 15.

The Pain Rating Scale scores showed no significant differences between the depressed patients and non-depressed patients over the study period. The results are shown in Table 18.

In the location of the aneurysms then the Vertebral-Basilar system and the Internal Carotid arteries seem the sites that occur most regularly, as shown in Table 19.

The mean scores for the Montgomery-Asberg Rating Scale over 21 days are shown in Figure 2.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 21

When the cut-off on the Montgomery-Asberg Rating Scale was increased to 21 then there were 3 patients classified as depressed, and 38 not depressed. The mean age of the depressed patients was 36 years with 0 men and 3 women. Of the non-depressed patients the mean age was 47.5 years with 18 men and 20 women (sex-ratio 1:1.1). The outcome of the patients is shown in Table 12.

The prognostic indicators also showed no statistically significant differences, as shown in Table 16.

The Pain Rating Scale scores showed no significant differences between the depressed patients and non-depressed patients over the study period. The results are shown in Table 18.

Of the three depressed patients two had aneurysms on the Right Internal Carotid Artery and one on the Anterior Communicating Artery. This is shown in Table 19.

The mean scores for the Montgomery-Asberg Rating Scale over 21 days are shown in Figure 2.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF 7 WHEN SOMATIC COMPONENTS EXCLUDED (7-SCE)

When the cut-off point on the Montgomery-Asberg Rating Scale was 7-SCE then 10 patients were depressed, and 31 not depressed. The mean age of the depressed patients was 47.4 years with 2 men and 8 women (sex-ratio 1:4), and of the non-depressed patients 46.4 years with 16 men and 15 women (sex-ratio 1:0.95). The patients outcome is given in Table 13.

The prognostic indicators are shown in Table 17, but showed no statistically significant differences between the two groups.

The Pain Rating Scale scores showed no significant differences between the depressed patients and non-depressed patients over the study period. The results are shown in Table 18.

The location of the aneurysms in the depressed patients is particularly interesting. As shown in Table 19 there are three aneurysms in the right internal carotid artery in depressed patients and a similar number in the non-depressed patients. However, of the two patients categorised as non-depressed who have aneurysms in this area one of the patients has two

aneurysms in the Right Internal Carotid Artery . This patient is also interesting in that she was the only patient to develop depression within the first week after scoring 6 on admission (her total Montgomery-Asberg Rating Scale scores rose from 6 to 14 and then to 28 within 7 days, and stayed around this level for the rest of the study period). Thus were she to be included in the group of depressed patients there would a significant correlation between depression and aneurysm of the right internal carotid artery (chi-squared 13.05; $p<0.05$). This finding may be considered all the more striking since the other non-depressed patient who had an aneurysm at this site had multiple aneurysms with the right internal carotid artery aneurysm being the smallest of three.

The usual frequency of carotid artery aneurysms is 15% of all aneurysms, equally divided between right and left. Thus the expected frequency of right internal carotid artery aneurysm is one in the group of depressed patients. This finding will be returned to in the discussion section of this thesis.

The mean scores for the Montgomery-Asberg Rating Scale over 21 days are shown in Figure 2.

PATIENTS EXCLUDED FROM THE TRIAL:

Of those patients excluded from the study, for the reasons outlined at the beginning of the chapter, it was possible to perform limited assessment on 10. Of these 1 patient had a rebleed, 5 had no sub-arachnoid haemorrhage demonstrated, and 4 had arterio-venous malformations. The length of in-patient stay was between 2 and 4 days for those with no haemorrhage and between 10 and 21 days for the rest. It was possible to study the Montgomery-Asberg Rating Scale scores for the first three days in 10 patients, 6 patients scored more than 7 (60%), 2 scored more than 14 (20%), and 1 scored more than 21 (10%), this patient was also the only one in the the 7-SCE group (10%).

In terms of pain rating scale scores the mean for the group who scored less than 7 on day 3 was 1, as compared with 0.92 for the patients with aneurysms. For those scoring 7 to 14 the mean pain rating scale score was 0.3 compared with 1.5. For those scoring 14 to 21 the mean score was 1 compared with 1.7. In the patient who scored over 21 the pain rating scale score was 0 compared with the three patients with aneurysm who had the same score whose mean score was 1.3. In those 10 patients who were depressed when the somatic components were removed the mean score was 1.9. Those without aneurysms experienced less pain

PATIENTS UNDERGOING LAMINECTOMY:

Eight consecutive patients admitted for laminectomy were also interviewed. All but one were assessed pre-operatively and all of these patients scored less than 7 on the Montgomery-Asberg Rating Scale (MARS) at this stage.

Post-operatively the patients were followed up for between 3 and 10 days (mean 6.4). Of the patients, 6 scored less than 7 on the MARS, 1 scored between 7 and 14, and 1 scored between 14 and 21. By day 6 both of these patients MARS scores were less than 7, and at no point did either of them score more than 7 if the somatic components were removed.

The pain rating scale scores were considerably affected by the operation and also by the tendency on the part of the patients to only discuss the post-operative pain if it was more severe than they had expected. Thus the mean score for the group was 2.1 on day 3, 0.8 on day 5 and 0.5 on day 7. This compares with a mean score for those with sub-arachnoid haemorrhage of 1.3 on day 3, 1.2 on day 5 and 1.05 on day 7.

SUMMARY

A brief summary of the results for the subarachnoid patients show that of the 41 patients 14 patients had a poor outcome, 6 of whom died. Depressed patients were not more severely ill, or in significantly more pain, but were significantly likely to have a poor outcome. This occued in three of the four different cut-off points; 7,14 and 7-SCE. In the latter group 70% had a poor outcome as opposed to less than 25% of the non-depressed group. The percentage of patients who were depressed varied between 7% and 68%, depending upon the cut-off point used. There is also a suggestion that depression occured more frequently with aneurysms of the right internal carotid artery.

TABLE 10

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	15	12	27
POOR OUTCOME	* 13	* 1	14
(DIED)	(6)	(1)	7
TOTAL	28	13	41

* This difference is statistically significant (chi-squared 4.32: $p<0.05$)

TABLE 11

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 14

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	6	21	27
POOR OUTCOME	9	5	14
DIED	(4)	(2)	6
TOTAL	15	26	41

TABLE 12

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 21

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	2	25	27
POOR OUTCOME	1	13	14
DIED	(1)	(5)	6
TOTAL	3	38	41

TABLE 13

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7-SCE

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	3	24	27
POOR OUTCOME	* 7	* 7	14
(DIED)	(2)	(4)	6
TOTAL	10	31	41

* This difference is statistically significant (Chi-Squared 5.59; $p<0.02$)

Table 14. Prognostic Indicator Scores in Subarachnoid Haemorrhage:

Cut-Off Point 7

	Depressed Group	Non-Depressed Group
Initial B.P.	137/83	131/77
>2.5 cm Blood on C.T. Scan	7 (25%)	0 (0%)
Low Atten. on C.T. Scan	7 (25%)	1 (8%)
Cerebrovascular Spasm on Angio	10 (35%)	3 (24%)

There are no significant differences between the two groups.

Table 15. Prognostic Indicator Scores in Subarachnoid Haemorrhage:

Cut-Off Point 14

	Depressed Group	Non-Depressed Group
Initial B.P.	138/84	129/79
>2.5 cm Blood on C.T. Scan	3 (20%)	4 (15%)
Low Atten. on C.T. Scan	3 (20%)	5 (19%)
Cerebrovascular Spasm on Angio	7 (47%)	6 (23%)

There are no significant differences between the two groups.

Table 16. Prognostic Indicator Scores in Subarachnoid Haemorrhage:

Cut-Off Point 21

	Depressed Group	Non-Depressed Group
Initial B.P.	125/70	133/82
>2.5 cm Blood on C.T. Scan	1 (33%)	6 (16%)
Low Atten. on C.T. Scan	0 (0%)	8 (21%)
Cerebrovascular Spasm on Angio	1 (33%)	12 (30%)

There are no significant differences between the two groups.

Table 17. Prognostic Indicator Scores in Subarachnoid Haemorrhage:

Cut-Off Point 7-SCE

	Depressed Group	Non-Depressed Group
Initial B.P.	141/84	129/79
>2.5 cm Blood on C.T. Scan	2 (20%)	5 (16%)
Low Atten. on C.T. Scan	2 (20%)	6 (19%)
Cerebrovascular Spasm on Angio	5 (50%)	8 (26%)

There are no significant differences between the two groups.

Table 18: Mean Pain Rating Scale Scores In Subarachnoid Haemorrhage Patients

	Cut-Off Point 7		Cut-Off Point 14		Cut-Off Point 21		Cut-Off Point 7-SCE	
	D.	N.D	D.	N.D	D.	N.D	D.	N.D
Day 3	1.46	0.92	1.66	1.01	1.66	1.26	1.90	1.01
Day 5	1.28	1.00	1.65	1.01	1.66	1.21	1.39	1.18
Day 7	1.27	0.69	1.43	0.84	1.00	1.05	1.30	0.89
Day 9	0.89	0.61	1.02	0.56	0.86	0.68	0.85	0.54
Day 11	0.72	0.59	0.80	0.49	0.80	0.57	0.76	0.55

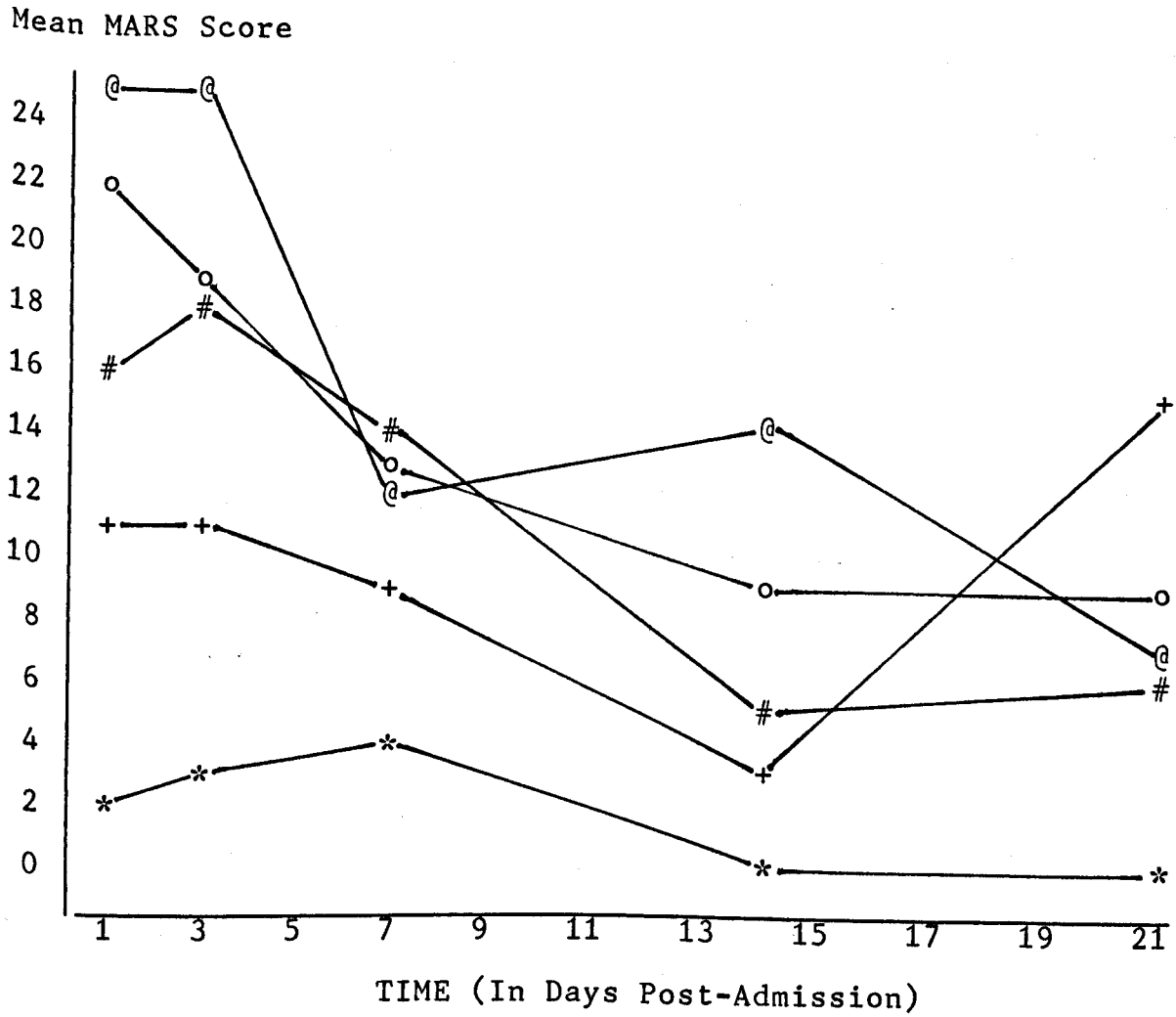
There are no statistically significant differences between the Depressed (D.) and Non-Depressed (N.D.) groups for any of the different cut-off points.

Table 19: Site of Aneurysms related to Presence of Depression

	Score on Montgomery Asberg Rating Scale				
	0-7	7-14	14-21	>21	7-SCE
Ant.Comm.	2	3	3	1	3
Int.Car. Right Left	1		4 3	2	3
Mid.Cer. Right Left	1		1		
Post.Com. Right Left	3				
Bas./Ver. P.I.C.	1	1	5		3
None	3		1		1

The intracranial arteries are abbreviated as follows; Anterior Communicating (Ant.Comm.); Internal Carotid (Int.Car.); Middle Cerebral (Mid.Cer.); Posterior Communicating (Post.Com.); Basilar or Vertebral (Bas./Ver.); Posterior Inferior Cerebellar (P.I.C.); No Aneurysm Identified (None).

Figure 2: Montgomery-Asberg Rating Scale over Time In Sub-arachnoid Haemorrhage Patients



* = MARS Score 0-7

\+ = MARS Score 7-14

\# = MARS Score 14-21

@ = MARS Score >21

o = MARS Score >7-SCE

CHAPTER 8: PULMONARY EMBOLISM:

INTRODUCTION:

Pulmonary embolism is obstruction of the arterial blood supply to the lungs, usually due to emboli arising from the veins of the lower leg. This condition in turn is commoner where there has been a period of venous stasis, such as post-operatively or during other periods of bed rest. Thus pulmonary embolism often arises in the course of other illnesses. When pulmonary embolism occurs it is often missed clinically. One estimate (Dalen and Alpert 1975) is that in only 30% of cases is a clinical diagnosis made. These authors also show that pulmonary embolism is the sole, or major contributing cause, of 15% of deaths in adults dying in acute general hospitals. When pulmonary embolism occurs the greatest percentage of deaths, 66%, occur within the first hour (these patients are commonly diagnosed at post-mortem). In the authors series of 144 patients 14% died, but of those 6% died from other causes and of those diagnosed the mortality was 8%.

In a recent review of course and prognosis in pulmonary embolism (Ansari 1987) the author indicated a mortality of 10% for all types of embolism, with a mortality of 66% for those with massive pulmonary embolism, 75% of deaths occurring within

the first hour. Thus those patients who survive this period are in the good prognosis group. Furthermore, the author points out that the most important factor affecting mortality is acute massive pulmonary embolus leading to right ventricular failure and subsequent shock. Pre-existing cardiac failure or shock also increases the mortality.

Diagnosis of pulmonary embolism can be problematic and should ideally be done with pulmonary angiography, the so-called "gold standard" (Hockberger and Rothstein 1983). However, it is common for other investigations to be used in the diagnosis such as arterial blood oxygen analysis, chest x-ray, lower limb venography and lung ventilation/perfusion radionucleotide scans. The relevance of this is that without pulmonary arteriography it is difficult to be entirely confident that the patient hadn't had a massive pulmonary embolism, for which the prognosis is worse (Widimsky 1979). Apart from differentiation into massive or sub-massive pulmonary embolism there are no other clear prognostic indicators for patients, unless these relate to any underlying illnesses or the presence of shock.

PATIENTS AND METHODS:

All patients admitted, or already inpatients, with a suspected or proven diagnosis of pulmonary embolism were eligible for

entry into the study. This group of patients were studied as they presented with life-threatening disease due to arterial blockage and subsequent confinement in bed for several days, thus having many similarities to the other patient groups.

Once admitted the patient had multiple investigative procedures to ascertain the diagnosis, as outlined above. The presence of shock was also determined clinically and by using appropriate investigations. The patients had psychological ratings as previously outlined.

CHAPTER 9: PULMONARY EMBOLISM

RESULTS:

Patients with a history suggestive of pulmonary embolism admitted to, or already inpatients in , the East Surrey hospital were eligible for entry into the trial. Forty-three patients were potentially eligible for entry into the trial, but 3 were excluded as they proved not to have had a pulmonary embolism.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 7:

When the cut-off for depression was 7 then 29 patients were depressed and 11 were not depressed. The mean age of the depressed group was 56.7 and the non-depressed group 56.9. Of the depressed group 19 were men and 10 women (sex ratio 1:0.5) and for the non-depressed group 7 men and 4 women (sex ratio 1:0.5). The outcome is given in Table 20.

The mean Montgomery-Asberg Rating Scale scores for the depressed and non-depressed groups are shown in Figure 3.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 24.

No patients entered into the study had massive pulmonary embolism. The other prognostic indicator, ie.the presence of shock in three patients showed no significant differences between the two groups.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 14:

When the cut-off for depression was 14 then 17 patients were categorized as depressed. The mean age of the depressed group was 55.3 and of the non-depressed group 57.8. Of the depressed group 11 were male and 6 female (sex ratio 1:0.5) and in the non-depressed group there were 15 men and 8 women (sex ratio 1:0.5). The outcome is given in Table 21. The scores for the Montgomery-Asberg Rating Scale over time are shown in Figure 3.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 24.

No patients entered into the study had massive pulmonary embolism. The other prognostic indicator, the presence of shock, showed no significant differences between the two groups.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 21:

When the cut off for depression was 21 then 7 patients were depressed. Of the depressed group the mean age was 51 and in the non-depressed group it was 58. This difference is not statistically significant. In the depressed group there were 4 men and 3 women (sex ratio 1:0.8), in the non-depressed group there were 22 men and 11 women (sex ratio 1:0.5). The outcome is given in Table 22. The results for the Montgomery-Asberg Rating scale over time are shown in Figure 3.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 24.

No patients entered into the study had massive pulmonary embolism. The other prognostic indicator, ie.the presence of shock showed no significant differences between the two groups.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 7 WHEN SOMATIC COMPONENTS EXCLUDED (7-SCE):

When the cut-off for depression was 7 with the somatic components excluded, then 13 patients were depressed. The mean age of the depressed group was 52 and of the non-depressed group 59. This difference is not statistically significant. In the depressed group there were 9 men and 4 women (sex ratio 1:0.4) and in the non-depressed group 18 men and 9 women (sex ratio 1:0.5). The outcome is given in Table 23. The results for the Montgomery-Asberg Rating scale over time are shown in Figure 3.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 24.

No patients entered into the study had massive pulmonary embolism. The other prognostic indicator, ie. the presence of shock showed no significant differences between the two groups.

NO EMBOLISM GROUP:

Three patients were seen who subsequently were shown not to have had a pulmonary embolism. One of these patients scored less than 7 and the other two scored between 7 and 14 on admission. Both of the latter two patients scored more than 7 when the somatic components were removed from the Montgomery-Asberg Rating Scale. Since there were only three patients in this group these findings are of questionable significance.

SUMMARY

A brief summary of the results of the pulmonary embolism group shows that of the 40 patients who had pulmonary embolism 6 had a poor outcome, 4 of whom died. Most of these patients were depressed, although this difference did not always reach statistical significance it was a clear overall trend. The most significant results were with the 7-SCE group in whom 45% had a poor outcome compared with none of the non-depressed patients. There were no differences in the limited prognostic indicators between the depressed and non-depressed groups. The patients scores on the MARS decreased over time.

TABLE 20

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	23	11	34
POOR OUTCOME	6	0	6
(DIED)	(4)	(0)	(4)
TOTAL	29	11	40

These differences are not statistically significant.

TABLE 21

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 14

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	11	23	34
POOR OUTCOME	** 6	** 0	6
(DIED)	(4)	(0)	(4)
TOTAL	17	23	40

** This difference is statistically significant (chi-squared=6.98; $p<0.01$)

TABLE 22

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 21

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	4	30	34
POOR OUTCOME	3	3	6
(DIED)	* (3)	* (1)	(4)
TOTAL	7	33	40

* This is a statistically significant difference (chi-squared=4.15; $p<0.05$)

TABLE 23

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7-SCE

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	7	27	34
POOR OUTCOME	*** 6	*** 0	6
(DIED)	** (4)	** (0)	(4)
TOTAL	13	27	40

*** This is a highly statistically significant difference (chi-squared=11.26; $p<0.001$)

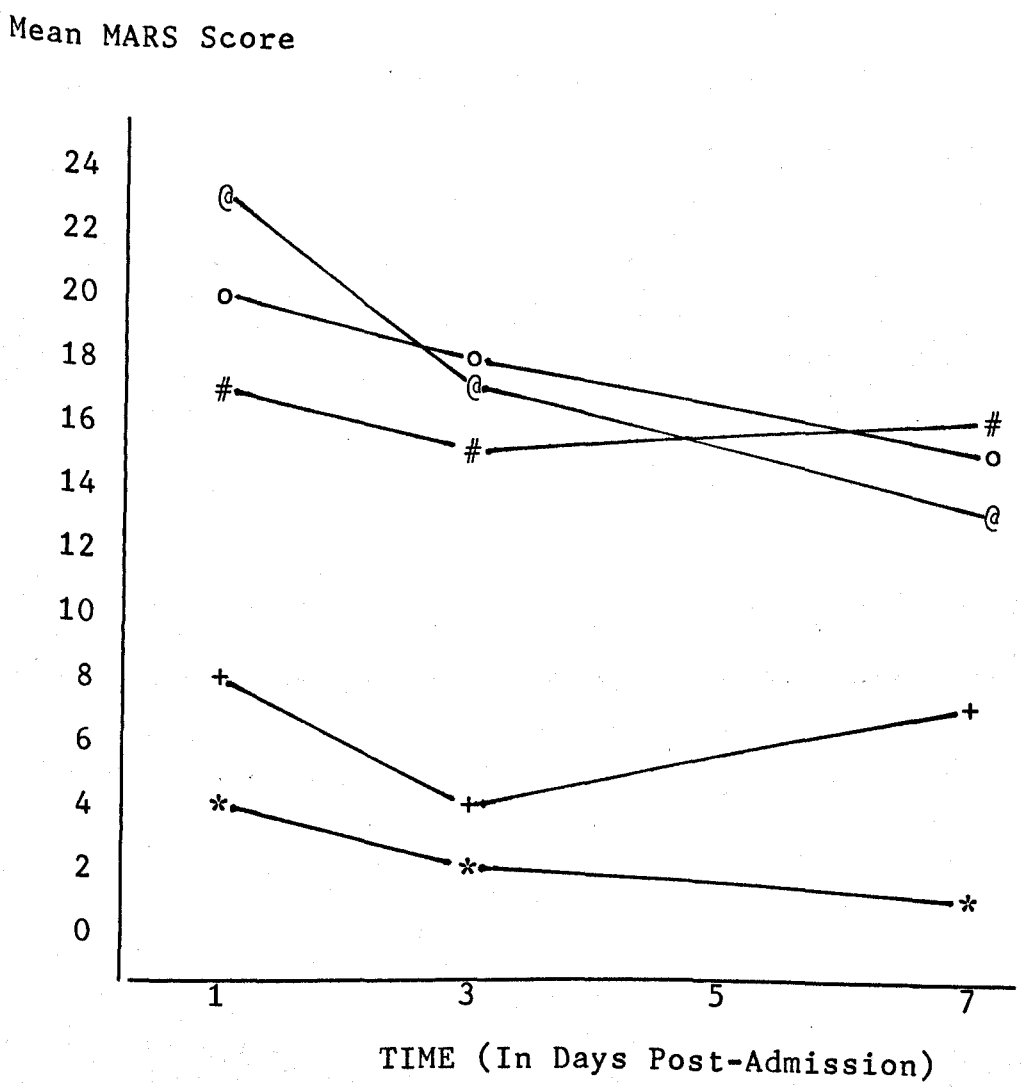
** This is a statistically significant difference (chi-squared=6.12; $p<0.02$)

Table 24: Mean Pain Rating Scale Scores
In Pulmonary Embolism

	Cut-Off Point 7		Cut-Off Point 14		Cut-Off Point 21		Cut-Off Point 7-SCE	
	D.	N.D	D.	N.D	D.	N.D	D.	N.D
Day 3	1.32	0.55	1.61	0.78	1.00	1.10	1.61	0.78
Day 5	0.92	0.18	1.15	0.44	0.42	0.76	1.15	0.44
Day 7	0.64	0.20	0.69	0.28	0.00	0.52	0.69	0.28
Day 9	0.32	0.20	0.46	0.12	0.00	0.35	0.46	0.12
Day 11	0.31	0.10	0.30	0.15	0.14	0.28	0.30	0.15

There are no statistically significant differences between the Depressed (D.) and Non-Depressed (N.D.) groups for any of the different cut-off points.

Figure 3: Montgomery-Asberg Rating Scale over Time In Pulmonary Embolism Patients



* = MARS Score 0-7

\+ = MARS Score 7-14

\# = MARS Score 14-21

@ = MARS Score >21

o = MARS Score 7-SCE

CHAPTER 10: GASTRO-INTESTINAL BLEEDING:

INTRODUCTION:

Upper gastro-intestinal bleeding refers to haemorrhage occurring in the oesophagus, the stomach, and the upper third of the duodenum. This condition has many underlying causes such as carcinoma, drugs, hepatic cirrhosis, and trauma. Haemorrhage can thus occur in many different ways, via ulceration, carcinoma, oesophageal varices, Mallory-Weiss tears, and small erosions. Because of these multi-factorial causes patients presenting with acute upper gastro-intestinal bleeding tend to be a less homogenous group than the other patients studied. This problem is not unique to this study, and has lead in the past to greatly differing estimates of the mortality in this condition of between 10 and 30% (Pimpl et al 1987). Other authors have reported even higher mortality figures in differing populations such as Fogelman et al (1966), who in a review of 88 cases report a mortality rate of 58%.

The reason this population was studied is that in this life-threatening illness it has been previously suggested, especially by Alexander, that psychological pressures can cause peptic ulceration, the commonest cause of upper gastro-intestinal bleeding. Thus it seems interesting to see if

psychological processes have any effect on the prognosis. There is furthermore the practical arguments that it is a fairly common condition and like the other three conditions studied involves the arterial system.

Because of the difficulty with differing patient populations it has, until recently, been difficult to accurately determine the prognosis for an individual patient. Serada et al (1977) presented the results on 513 patients, in whom the cause of gastro-intestinal bleeding was duodenal ulceration in 28%, acute peptic ulceration or erosions in 20%, gastric ulceration in 9%, Mallory-Weiss syndrome in 8%, no lesion in 10%, oesophageal varices in 8% and miscellaneous causes including carcinoma accounting for the rest. The overall mortality rate was 8.8%. In this series increasing age, shock on admission and gastro-intestinal bleeding due to varices were the most significant factors in the prognosis.In a further report from the same unit (Korman 1982) a poor prognosis was felt to be related to age over 60, the presence of complicating disease such as heart disease, the nature of the lesion (with oesophageal varices having an especially poor prognosis), and the severity of the bleed especially if associated with a recurrent haemorrhage.

Recent advances in diagnostic techniques, especially endoscopy, have lead to attempts to improve on prognostic indicators. Foster et al (1978) studied the predictive value of specific endoscopic findings in 233 patients. The findings indicate whether a lesion has bleed recently or not. These signs, which they labelled the 'stigmata of recent haemorrhage (SRH)' include fresh bleeding, adherent clot, or a protruding vessel seen during endoscopy performed within 24 hours of the initial gastro-intestinal bleed. They felt that the presence of any of these findings proved superior to any other single factor in predicting rebleeding or the need for surgery. Despite the increase in diagnostic ability there has been great debate as to whether or not endoscopy has improved mortality. Tobias (1985) in reviewing upper gastro-intestinal bleeding concluded "despite the introduction of this concept of SRH , the mortality of patients with upper gastro-intestinal haemorrhage has been little affected....because of the poor effect on mortality of using SRH as a management strategy, efforts today are directed towards nonsurgical means to stop rebleeding. However, a multi-centre trial (Dombal et al 1986) involving 44 centres and 4010 patients suggested that identifying the bleeding source via endoscopy aided short-term prognosis since the source and activity of the haemorrhage could be identified. Other prognostic indicators identified were patient age, and type and number of associated illnesses. The overall mortality

rate was 8.3% , but for varices this rose to 30% and for cancer 14.2%.

More recently Pimpl et al (1987) have proposed a scoring system to estimate the risk of mortality. The 7 factors they consider and then allocate a score to, are the age of the patient, the source, site, activity and intensity of the haemorrhage and the number and severity of associated illnesses. Each factor was scored between 0 and 6, with the total score relating to risk of mortality, with a score of less than 20 the mortality was 0%, but with a score of >35 the mortality was 83.3%.

PATIENTS AND METHODS:

All patients admitted to the East Surrey Hospital with a history of upper gastro-intestinal bleeding were considered eligible for entry in to the trial. In this hospital the policy was that patients over 65 were admitted under the surgeons, with younger patients being admitted under the physicians. All patients had endoscopy within 24 hours of admission (with note being taken of the prognostic features previously outlined) , as well as recording the patients age and the presence and severity of other illnesses.

Psychological testing involved the Montgomery-Asberg Rating Scale, the Mini-Mental State examination and the Pain Rating Scale as previously outlined.

CHAPTER 11: GASTRO-INTESTINAL BLEEDING

RESULTS:

During the study period 64 patients were admitted, under both the surgeons and the physicians, to the hospital with upper gastro-intestinal haemorrhage. Of these 34 were excluded; 18 patients scored less than 22 on the Mini-Mental State examination, 12 patients were transferred to a tertiary referral centre for laser coagulation via endoscopy shortly after admission, and a further 4 patients refused to be interviewed. Thus 30 patients entered the study, 2 of whom died. Of the 30 patients 15 were women, mean age 61 years (S.D. 21.5), and 15 men, mean age 46 years (S.D. 19). This age difference is not statistically significant.

Those patients excluded because of a low score on the MMS were more elderly than the study population (mean age 71). In addition, those transferred for further treatment were often those at high risk due to continued bleeding. Thus many of the group most at risk were not included in the study. These findings may in part account for the low mortality of the group (6.8%). There is no Non Gastro-Intestinal Bleed group in this part of the study.

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 7:

When the cut-off for depression was 7 then 18 patients were depressed and 12 were not depressed. The mean age of the depressed group was 48.4 and the non-depressed group 47.2. Of the depressed group 8 were men and 10 women (sex ratio 1:1.25) and for the non-depressed group 7 men and 5 women (sex ratio 1:0.7). The outcome is given in Table 25.

The mean Montgomery-Asberg Rating Scale scores over time are shown in Figure 4.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 29.

The scores for the prognostic indicators demonstrated no significant differences between the two groups. The mean score for the depressed group was 15.6 (range 3-30) and for the non-depressed group 13.0 (range 3-26).

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 14:

When the cut-off for depression was 14 then 9 patients were depressed and 21 were not depressed. The mean age of the depressed group was 71.7 (S.D 19.4) and the non-depressed group 49.3 (S.D. 17.4), this age difference being statistically significant; $t=3.2$, $p<0.01$. Of the depressed group 12 were men and 9 women (sex ratio 1:0.75) and for the non-depressed group 3 men and 6 women (sex ratio 1:2). The outcome is given in Table 26.

The mean Montgomery-Asberg Rating Scale scores over time are shown in Figure 4.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 29.

The scores for the prognostic indicators demonstrated no significant differences. The mean score for the depressed group was 19.5 (range 11-30) whilst for the non-depressed group it was 13.9 (range 3-37).

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 21:

When the cut-off for depression was 21 then 3 patients were depressed and 27 were not depressed. The mean age of the depressed group was 59 and the non-depressed group 55.7. Of the depressed group 1 was male and 2 female (sex ratio 1:2) and for the non-depressed group 14 men and 13 women (sex ratio 1:1). The outcome is given in Table 27.

The mean Montgomery-Asberg Rating Scale scores over time are shown in Figure 4.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 29.

The scores for the prognostic indicators demonstrated no significant differences. The mean score for the depressed group was 19.3 (range 11-26) and in the non-depressed group 15.2 (range 3-30).

MONTGOMERY-ASBERG RATING SCALE: CUT-OFF POINT 7 WHEN SOMATIC COMPONENTS EXCLUDED (7-SCE)

When the cut-off for depression was 7 when the somatic components were excluded then 10 patients were depressed and 20 were not depressed. The mean age of the depressed group was 65.2 (S.D 22.7) and the non-depressed group 51.7 (S.D. 19.4). This difference is not statistically significant. Of the depressed group 4 were men and 6 women (sex ratio 1:1.5) and for the non-depressed group 11 men and 9 women (sex ratio 1:0.8). The outcome is shown in Table 28.

The mean Montgomery-Asberg Rating Scale scores over time are shown in Figure 4.

The pain rating scale scores showed no significant differences between the depressed and non-depressed groups. The results are shown in Table 29.

The scores for the prognostic indicators demonstrated no significant differences. The mean score for the depressed group was 18.4 (range 3-30) and for the non-depressed group 14.2 (range 3-27).

SUMMARY

A brief summary of the results shows that there were no statistically significant differences in age, sex, pain experienced, or prognostic indicators between those patients with depression, and those without. However, the trend was for the depressed patients to be more likely to die, although this did not reach statistical significance. This finding might be explained by the relatively large number of exclusions, especially amoungst those most seriously ill.

TABLE 25

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	16	12	28
POOR OUTCOME	2	0	2
(DIED)	(2)	(0)	(2)
TOTAL	18	12	30

TABLE 26

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 14

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	7	21	28
POOR OUTCOME	2	0	2
(DIED)	(2)	(0)	(2)
TOTAL	9	21	30

TABLE 27

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 21

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	3	25	28
POOR OUTCOME	0	2	2
(DIED)	(0)	(2)	(2)
TOTAL	3	27	30

TABLE 28

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7-SCE

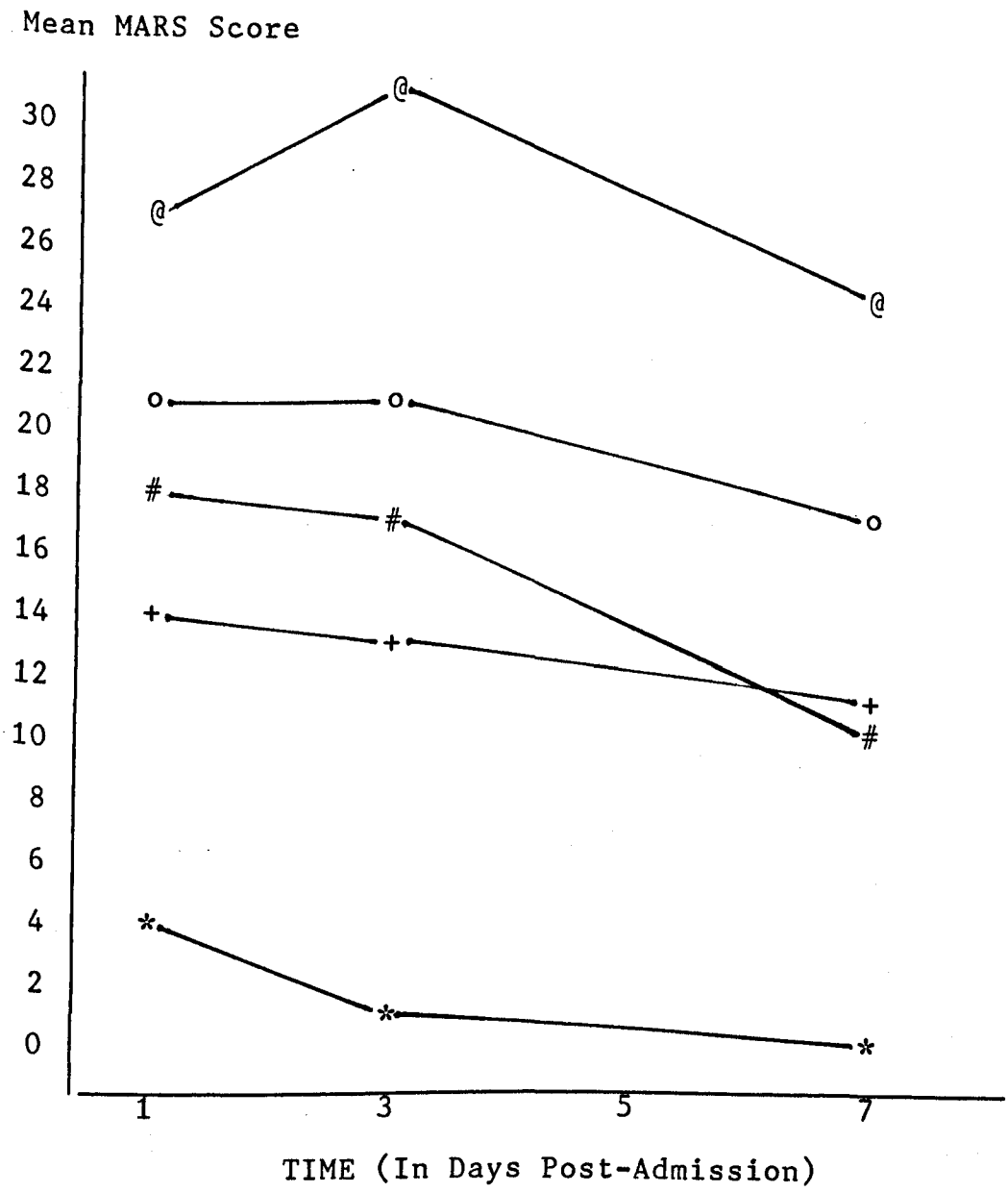
	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	8	20	28
POOR OUTCOME	2	0	2
(DIED)	(2)	(0)	(2)
TOTAL	10	20	30

Table 5: Mean Pain Rating Scale Scores
In Gastro-Intestinal Bleed Patients

	Cut-Off Point 7		Cut-Off Point 14		Cut-Off Point 21		Cut-Off Point 7-SCE	
	D.	N.D	D.	N.D	D.	N.D	D.	N.D
Day 3	0.72	0.25	1.11	0.29	1.66	0.41	0.90	0.35
Day 5	0.39	0.16	0.44	0.24	1.00	0.22	0.40	0.25
Day 7	0.27	0.08	0.11	0.24	0.00	0.22	0.20	0.20
Day 9	0.11	0.00	0.00	0.10	0.00	0.07	0.00	0.10
Day 11	0.05	0.00	0.00	0.05	0.00	0.04	0.00	0.05

There are no statistically significant differences between the Depressed (D.) and Non-Depressed (N.D.) groups for any of the different cut-off points.

Figure 4: Montgomery-Asberg Rating Scale over Time In Patients Post Gastro-Intestinal Bleeding



* = MARS Score 0-7

\+ = MARS Score 7-14

\# = MARS Score 14-21

@ = MARS Score >21

o = MARS Score 7-SCE

CHAPTER 12;

RESULTS OF ALL FOUR GROUPS COMBINED:

The results for all of the four groups of patients can be combined to give a total patient population of 211. The rational behind this is that if the entry criteria and methodology are the same for all of the groups, which they are, then in combining the patient populations it is possible to study the effect of mood upon outcome with a greater degree of statistical accuracy. The results for the differing cut-off points when this is done are shown in Tables 30-33.

It can be seen from these tables that with the increased numbers of patients the statistical significance of the findings increases, such that for all the groups (except mortality alone when using a cut-off of 21) the presence of depression was a significant determinant of outcome and mortality. For the 7-SCE group, in which the most significant findings occured, 47% of the depressed group did poorly as opposed to 10% of the non-depressed group, and 21% of the depressed group died compared to less than 4% of the non-depressed group.

MONTGOMERY-ASBERG RATING SCALE ITEMS OVER TIME

Previously published work has often not fully considered the influence of somatic complaints, due to the underlying illness, upon the scores obtained using conventional psychiatric rating scales or interview techniques. If the various items from the MARS are studied over 7 days, as shown in Tables 34-36, then it can be seen that for those patients with a total score of less than 14 on admission over 75% of this score was due to somatic components, and that this percentage remained constant over 7 days. This suggests that for many patients somatic items are not measuring depression, but are a consequence of the underlying illness. Even for the group scoring more than 7 with the somatic components excluded (>7-SCE) the percentage score from somatic items was around 50%. It is therefore clear that unmodified rating scales have a large potential bias since they often contain many somatic items.

Following the patients up for 14 days, as shown in Table 37, the percentage of the total score due to somatic items increased to at least 79% for those scoring less than 14, and 58% for the 7-SCE group. This 14 day group of patients is atypical however, since it tends to represent those patients with medical complications. It does nonetheless illustrate the influence of somatic items upon the total score obtained.

Tables 34-37 also illustrate that with the varyious cut-off points only 5 of the 6 non-somaticitems seem to differentiate well between the depressed and non-depressed groups. The item that does poorly is suicidal ideas which seems to have little relevance to this population. It is also clear from these tables that the group scoring 7-14 is much more similar to the group scoring 0-7, ie. non-depressed patients, than to the groups scoring >14. This might suggest that raising the cut-off point to 14 would be appropriate for the definition of depression.

It can be seen from Tables 34-37 that the mean score of the 7-SCE group would place them in the 'moderate' depression range as defined by Snaith et al. (1986). It is also interesting to note that only 75% of the patients who scores were in the range 14-21 also scored in the 7-SCE range. This implies that simply raising the cut-off point for depression will not overcome the problem of those patients who have severe somatic complaints due to their underlying illness being categorized as depessed.

There are ten items in the Montgomery-Asberg Rating Scale (MARS) which are scored between 0-6. They are abreviated in Tables 34-37 in the following way; Sleep Disturbance (SLEEP); Appetite Disturbance (APPT.); Poor Concentration (CONC.);

Feelings of Lethargy (LETHARGY); Assessed Depresssion (ASS.DEPR.); Reported Depression (REP. DEPR.); Inner Tension (I.TENSION); Lack of Interest in Surroundings (INTEREST); Poor View of the Future (PESSIMISM); and Thoughts of Suicide (SUICIDE). The total mean score is given (TOTAL), as is the percentage of that score due to the somatic items (% TOT). It should be noted that since not all of the patients were seen on each day the numbers of patients in the tables fall slighty below the number of patients in the study, ie. on day 1 post-admission only 190 patients from a total sample of 211 were seen, the rest being seen on day 2.

Previously published work has generally not involved assessing patients until at least 7 days post admission. If the non-somatic items, using the 7-SCE cut-off, are studied over this period, as shown in Figure 5, it can be seen that patients' mood changed considerably. Thus it is important to note at what time post-admission patients are interviewed, since even postponing interview by a few days will alter the number of patients who appear to be depressed at any given cut-off point.

TABLE 30

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	90	74	164
POOR OUTCOME	*** 44	*** 3	47
(DIED)	** (19)	** (1)	(20)
TOTAL	134 (66%)	77 (33%)	211

*** This is a highly statistically significant difference (chi-squared=22; $p<0.001$)

** This is a statistically significant difference (chi-squared=8.1; $p<0.01$)

TABLE 31

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 14

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	48	116	164
POOR OUTCOME	*** 34	*** 13	47
(DIED)	** (15)	** (5)	(20)
TOTAL	82 (39%)	129 (61%)	211

*** This is a highly statistically significant difference (chi-squared=26.7; $p<0.001$)

** This is a statistically significant difference (chi-squared=10.5; $p<0.01$)

TABLE 32

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 21

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	20	144	164
POOR OUTCOME	* 12	* 35	47
(DIED)	(6)	(14)	(20)
TOTAL	32 (15%)	179 (85%)	211

* This is a statistically significant difference (chi-squared=4.1; $p<0.05$)

TABLE 33

NUMBER OF DEPRESSED PATIENTS AND OUTCOME: CUT-OFF 7-SCE

	DEPRESSED	NOT DEPRESSED	TOTAL
GOOD OUTCOME	37	127	164
POOR OUTCOME	***' 33	***' 14	47
(DIED)	*** (15)	*** (5)	(20)
TOTAL	70 (33%)	141 (66%)	211

***' This is a highly statistically significant difference (chi-squared=35.2; $p<0.001$)

*** This is a highly statistically significant difference (chi-squared=15.4; $p<0.001$)

Table 34: Mean Scores For Each Component of the Montgomery-Asberg Rating Scale for Depression (MARS)

DAY 1;

M.A.R.S. ITEMS	INITIAL SCORE ON MONTGOMERY-ASBERG RATING SCALE				
	0-7	7-14	14-21	>21	>7-SCE
SOMATIC					
SLEEP	0.8	1.9	2.1	2.5	2.4
APPT.	1.3	2.3	3.2	3.4	3.0
CONC.	0.3	1.2	1.5	2.6	2.0
LETHARGY	0.6	2.1	2.2	3.0	2.4
NON-SOMATIC					
ASS.DEPR.	0.1	0.4	1.5	2.3	2.1
REP.DEPR.	0.1	0.4	1.3	3.0	2.5
I.TENSION	0.5	1.0	2.0	3.7	3.1
INTEREST	0.0	0.4	1.3	1.9	1.6
PESSIMISM	0.1	0.3	1.5	2.5	2.1
SUICIDE	0.0	0.0	0.1	0.0	0.1
TOTAL	3.8	10.0	16.7	24.9	21.3
% TOT	80%	75%	54%	46%	46%

There were 190 patients; 71 scored 0-7, 45 scored 7-14, 43 scored 14-21, 31 scored >21, and 64 scored >7-SCE

Table 35: Mean Scores For Each Component of the Montgomery-Asberg Rating Scale for Depression (MARS)

DAY 3:

M.A.R.S. ITEMS	INITIAL SCORE ON MONTGOMERY-ASBERG RATING SCALE 0-7	7-14	14-21	>21	>7-SCE
SOMATIC					
SLEEP	0.8	2.0	2.0	2.6	2.2
APPT.	1.1	2.6	2.8	3.1	2.8
CONC.	0.3	1.0	1.6	2.0	1.8
LETHARGY	0.4	1.4	2.3	2.4	2.2
NON-SOMATIC					
ASS.DEPR.	0.1	0.3	1.1	2.0	1.7
REP.DEPR.	0.0	0.4	0.9	1.8	1.5
I.TENSION	0.1	0.4	2.0	2.9	2.7
INTEREST	0.1	0.5	1.3	1.6	1.3
PESSIMISM	0.1	0.3	1.3	1.8	1.3
SUICIDE	0.0	0.0	0.0	0.0	0.0
TOTAL	3.0	8.9	15.3	20.2	17.5
% TOT	87%	79%	57%	50%	51%

There were 182 patients; 72 scored 0-7, 40 scored 7-14, 43 scored 14-21, 27 scored >21, and 58 scored >7-SCE

Table 36: Mean Scores For Each Component of the Montgomery-Asberg Rating Scale for Depression (MARS)

DAY 7:

	INITIAL SCORE ON MONTGOMERY-ASBERG RATING SCALE				
M.A.R.S. ITEMS	0-7	7-14	14-21	>21	>7-SCE
SOMATIC					
SLEEP	0.7	1.3	1.8	1.9	2.1
APPT.	0.9	1.9	2.0	2.2	2.0
CONC.	0.1	0.9	1.3	1.0	1.2
LETHARGY	0.2	1.1	1.5	1.5	1.4
NON-SOMATIC					
ASS.DEPR.	0.1	0.2	0.8	1.4	1.1
REP.DEPR.	0.1	0.3	0.8	1.3	1.0
I.TENSION	0.1	0.6	1.4	2.1	1.9
INTEREST	0.1	0.5	1.4	1.2	1.3
PESSIMISM	0.0	0.1	0.8	1.4	1.2
SUICIDE	0.0	0.0	0.0	0.0	0.0
TOTAL	2.3	6.9	11.8	14.0	13.2
% TOT	82%	75%	56%	47%	51%

There were 163 patients; 67 scored 0-7, 39 scored 7-14, 32 scored 14-21, 25 scored >21, and 49 scored >7-SCE

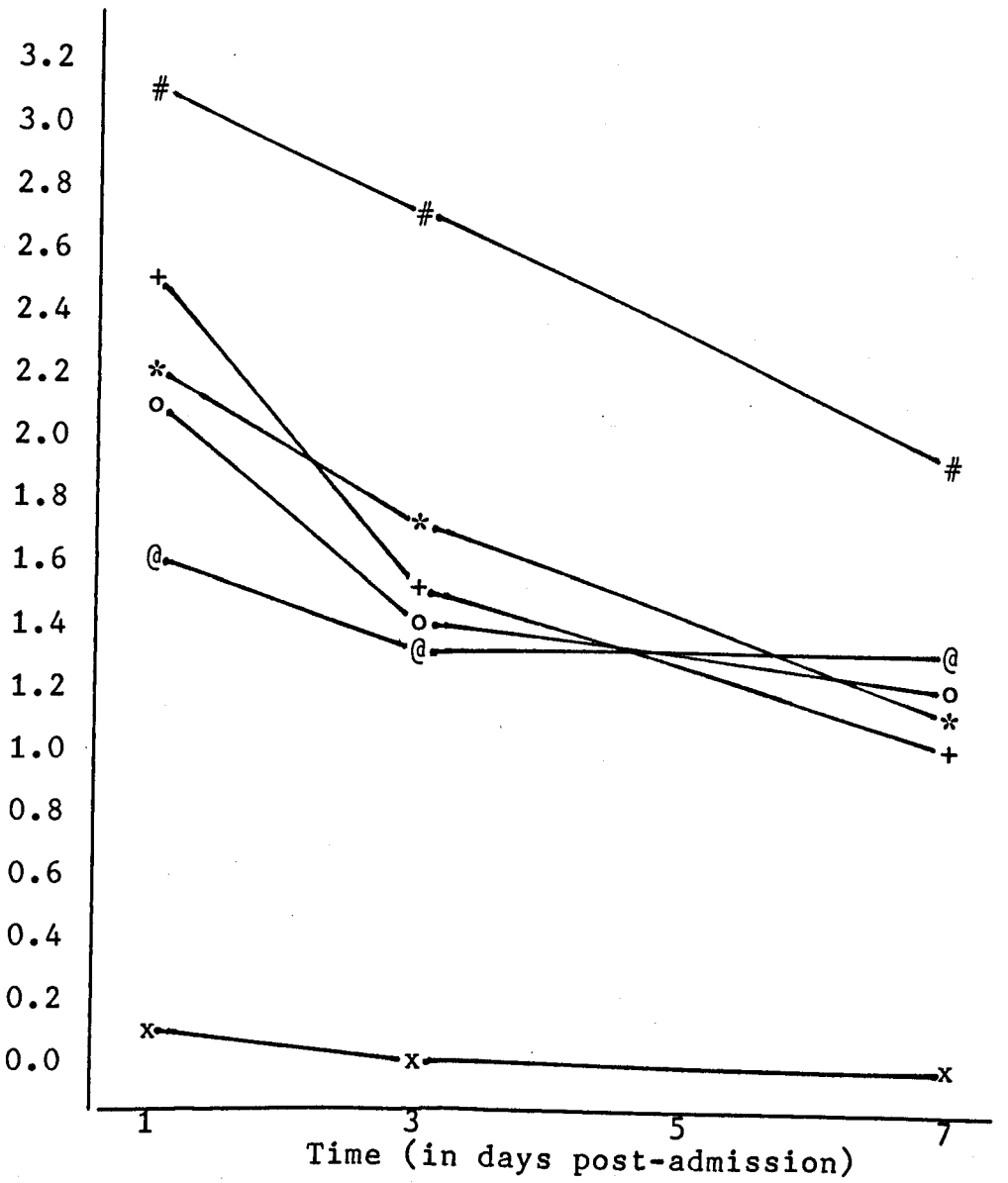
Table 37: Mean Scores For Each Component of the Montgomery-Asberg Rating Scale for Depression (MARS)

DAY 14:

	INITIAL SCORE ON MONTGOMERY-ASBERG RATING SCALE				
M.A.R.S. ITEMS	0-7	7-14	14-21	>21	>7-SCE
SOMATIC					
SLEEP	0.5	0.5	2.0	1.3	2.0
APPT.	0.5	1.3	2.6	2.0	2.8
CONC.	0.1	0.2	1.6	1.0	1.5
LETHARGY	0.3	0.5	1.8	2.0	2.2
NON-SOMATIC					
ASS.DEPR.	0.0	0.0	1.0	1.0	1.2
REP.DEPR.	0.0	0.0	1.0	1.0	1.2
I.TENSION	0.1	0.2	1.0	1.7	1.7
INTEREST	0.0	0.2	1.0	1.3	1.0
PESSIMISM	0.1	0.2	1.0	1.0	1.0
SUICIDE	0.0	0.0	0.0	0.0	0.0
TOTAL	1.6	3.1	13.0	12.3	14.6
% TOTAL	88%	79%	62%	51%	58%

There were 43 patients; 16 scored 0-7, 11 scored 7-14, 10 scored 14-21, 6 scored >21, and 13 scored >7-SCE

Figure 5. Mean MARS scores over 7 days for the Non-Somatic items when the cut-off point for depression was 7-SCE



* = Assessed depression

\+ = Reported depression

\# = Inner Tension

@ = Interest in surroundings

o = Pessimism

x = Suicide

SECTION 3:

CHAPTER 13: DISCUSSION AND CONCLUSIONS

REFERENCES:

ACKNOWLEDGEMENTS:

CHAPTER 13: DISCUSSION

The central aim of this research was to answer the question: does affective state influence outcome in serious, life-threatening disease? To this end changes in morbidity and mortality were studied in four clinical conditions, myocardial infarction, sub-arachnoid haemorrhage, pulmonary embolism and gastro-intestinal bleeding. Each of the four condtions will be considered seperately in turn. Following this the implications of the results as a whole will be discussed. Before going on to discuss these findings it is necessary to consider some methodological issues.

METHODOLOGICAL ISSUES

Depression

Rating depression in the medically ill is made difficult by several factors which can potentially lead to bias in the results: symptoms from a physical illness can imply the presence of psychiatric illness; cognitive dysfunction may alter the presence and measurement of depression; the amount of pain suffered might increase the incidence of depression; the time course of any changes in affective response to illness is

not clear, and the time of measurement might be important; patients with more severe illnesses may be more likely to suffer from depression. Previous publications have discussed these problems, Kathol and Petty (1981) noted that most prior studies of depression and medical illness had not considered duration of depression or severity of illness. Rodin and Voshart (1986) discussed five methodological problems of diagnosing depression in this group of patients: poor defintion of depression, lack of validated psychiatric measuring instuments, selection bias in populations studied, the inclusion of non-homogeneous populations, and the absence of appropriate control groups. Mayou and Hawton (1986) state that "research in the general hospital has largely been of poor quality, failing to describe adequately the medical populations surveyed or to use an adequate nomenclature or standard measures."

In view of these potential problems it is important to consider the possibility of limitations in the measuring instrument used in this study to measure depression. It has been demonstrated that the Montgomery-Asberg Rating Scale is a good indicator of the presence and degree of depression in psychiatric patients (Davidson et al 1986; Snaith et al 1986). This does not mean however, that a particular score on the Montgomery-Asberg Rating Scale indicates the presence of clinical depression, ie. it is not a diagnostic measure. Nonetheless, this is how it has

been used in this study, where a given score has been taken to indicate the presence and severity of depression. In this context the cut-off point taken for the definition of depression assumes considerable importance. Snaith et. al. (1986) recommended a lower cut-off point of 7, above which the patient should be considered depressed, with another cut-off point of 20 which they equated with being 'moderately' depressed. In the present study three cut-off points were examined to test the effect of increasing the cut-off point, namely 7, 14 and 21, this latter score corresponding to Snaiths 'moderately' depressed group. In addition, an attempt was made to modify the scale such that the four items relating to physical symptoms of depression were excluded. The excluded items were poor sleep, poor appetite, poor concentration and lethargy. This abreviated form of the scale (the Somatic Components Excluded scale) has not been validated. Nonetheless, the items which were retained included depressed appearance, reported depression, a feeling of inner tension, an interest in surroundings and people, the patients view of the future, and any suicidal feelings. These questions and observations certainly have face validity in terms of a depressive episode. Furthermore, the modified version was likely to afford a more accurate measure of affective state in the seriously physically ill than the use of the unmodified scale with the standard cut-off point. A cut-off point of 7 on the modified scale (7-SCE) was taken to indicate depression.

Previous studies have assessed inpatients using several different methods. Some have used unmodified questionairres with cut-off points standardized for psychiatric patients. Such studies reported a large percentage of patients with psychiatric morbidity, for example Knights and Folstein (1977) found that 46% of medical inpatients had psychiatric morbidity. Other groups have used standardized questionairres with a raised cut-off point, either alone, or as a screening instrument to be followed by subsequent interview. In the first group a smaller percentage of inpatients were diagnosed as depressed, for example Moffic and Paykel found that 24% of medical inpatients were depressed although in the most seriously ill group of patients 61% were depressed as opposed to only 21% of those mildly or moderately ill. Maguire et al (1974) and Bridges and Goldberg (1984) both used the General Health Questionairre (GHQ) followed by interview with the Clinical Interview Schedule (CIS). These studies found that between 26-39% had psychiatric morbidity. Other studies have used the CIS as the sole measure of morbidity in patients post myocardial infarction, such as the study by Lloyd and Cawley (1978) in which 35% of patients had psychiatric morbidity one week after infarction, and the study by Trelawney-Ross and Russell (1987) who showed that 10 days after discharge 20% of patients were depressed. Mayou et al (1978) using a semi-structured interview one week after myocardial infarction found that 67% of patients had mild distress, and 11% moderate

distress. It can be seen that the methods used to determine the presence of depression do affect the percentage of patients diagnosed as depressed, as does the cut-off point chosen. To compare these results with the findings from this study it is best to analyse the results for all the groups combined, to test the effects of time, of raising the cut-off point, and of modifying the rating scale to exclude somatic items.

When the scores for all of the groups were combined there were considerable changes over time. For example, when using a cut-off point of 7 to define depression, 62% of patients were depressed on admission, 46% at one week, and 37% at two weeks (using the mean scores, not those for each patient). With the 7-SCE cut-off point 34% of patients were depressed on admission, falling to 16% at one week and 14% at two weeks.

Previous authors have raised the cut-off point for the diagnosis of depression when using a psychiatric measuring instrument, to attempt to overcome the bias inherent when including somatic symptoms in determining the presence of depression. The effect of raising the cut-off point to 14 in the present study can be assessed. In those patients who scored less than 14, approximately 4/5 of this total was accounted for by somatic components. It is thus likely that a score on the Montgomery-Asberg Rating Scale of 14 or less is very dependent

upon somatic components, and might not represent depression. Above this score, approximately 50% of the total score was accounted for by somatic components, with this percentage increasing over time. In the results from the combined group it can be seen that 22% of those patients who scored in the range 14-21 did not score in the >7-SCE range. This strongly suggests that a significant proportion of patients who scored above 14 did so because of high somatic scores, and that simply increasing the cut-off point is not the most appropriate way of overcoming this bias. Use of the SCE Group overcame this problem, but by comparison with previous studies the 7-SCE cut-off point gave a lower prevalence of depression at one week after admission

With the marked change in the scores over time, and the considerable changes that both increasing the cut-off point and using the SCE rating scale have upon the percentage of patients categorised as depressed, it is not surprising that in previous work using different rating methods at different times widely different results were obtained. It also probably accounts for the findings in some of the studies previously reviewed, such as Rosenberg et al (1988), that much of the depression they diagnosed was related to pre-admission mental state. As the results show, depression in life-threatening illness often comes and goes fairly rapidly and thus the time of measurement

will determine how much of this acute psychiatric morbidity is diagnosed.

Pain

That a relationship exists between chronic pain and depression has been shown in a pain clinic population by Kramlinger et al (1983), by Ahles et al (1984) in patients with cancer, and by Maruta et al (1976) in chronic back pain sufferers. However, the relationship between acute pain and depression has not previously been studied. The pain rating scale used in this study is a measure which is designed to compare the pain experienced by different patients in an attempt to see whether the degree of pain related to the depression score. It has thus far not been validated. It is best used to compare patients within each of the diagnostic groups, rather than to compare one group with another.

THE CONCEPT OF DEPRESSION:

Depression is the name given both to an emotion common to all mankind occuring following loss, and to a syndrome in which dysphoria is a prominent symptom. In this syndrome dysphoria may be accompanied by other symptoms, such as feelings of low

self-esteem or worthlessness, anhedonia, lethargy and sleep disturbance. Throughout the present study 'depression' has been the term used to refer to the affective disorder revealed. Is this appropriate? The answer to this question depends to a large degree upon the definition of depression used. In two recently developed diagnostic systems for use in psychiatry (Diagnostic and Statistical Manual Third Edition, Revised 1986; DSM-IIIR; International Classification of Disease Tenth Edition, Field Trial Version, 1987; ICD-10) there are three possible diagnostic categories into which the patients classified as depressed in the present studies could be placed. These are Organic Mood State, Depressive Disorder, and Adjustment Disorder with Depression.

Organic mood syndrome is defined in DSM-IIIR as a depression equivalent to major depressive disorder occurring in the context of an organic illness, where the organic factors are aetiologically related to the mood state. As examples of such aetiology, toxic or metabolic factors are mentioned. ICD-10 has an organic depressive state, but here direct causation by cerebral or other disorder is assumed. It is clear from these criteria that this category would not apply to the patients in the present study who were depressed.

Depression is subsumed under the heading Major Depressive Disorder in DSM-IIIR. To meet the diagnostic criteria for this condition five out of nine items have to be present. Of these nine items four are the physical symptoms excluded from the 7-SCE version of the Montgomery-Asberg Rating Scale. Such symptoms must have been present for at least two weeks. ICD-10 has categories for mild and severe depression, with most of the study group being similar to the description of mild depression. However there is also an exclusion insisting that the symptoms have been present for at least two weeks. Thus the study patients do not fit properly either of the diagnostic criteria for depressive illness.

Adjustment Disorder with depressive reaction is defined in DSM-IIIR as a psychological reaction to identifiable psychosocial stress, which may be physical illness, accompanied by maladaption, defined here either as impairment of function or an excessive response. ICD-10 has the category of Brief Depressive Reaction subsumed under Adjustment Disorder. This is defined as a transient mild depressive state of a duration not exceeding one month in the presence of a clearly established stressful event. Both of these definitions fit the patients in the present study who were depressed. Thus the standardized diagnosis for the patients would be Depression in the context of an Adjustment Reaction.

In looking at this question of definition it is worth comparing the present study with previously published work. Moffic and Paykel (1975) studied patients within seven days of admission to medical wards. They classified patients as depressed (24%) or not and compared these with depressed psychiatric patients. According to the above definitions such comparison is invalid as the medically ill patients only had a 7-day history and could not therefore be included in the definition. Lloyd and Cawley (1978) also saw patients within 7-days of admission, although here the patients were post-myocardial infarction. Of those patients felt to have psychiatric morbidity (35%) some were given the diagnosis Depressive Neurosis (18%) and some Anxiety Neurosis (10%). However they would not be so classified using more recent diagnostic criteria. If the diagnostic criteria for Depressive Disorder was that the symptoms had to be present for only 7 days duration then the patients included in the studies discussed would meet the diagnostic criteria.

It would probably be accurate to say that the findings in the present study, particularly those relating to the 7-SCE version of the Montgomery-Asberg Rating Scale, reflect the degree of depressive reaction to a stressful life-threatening illness, and thus a form of adjustment disorder. Is it important that a more accurate term is Adjustment Disorder with Depressive Reaction, rather than Depressive Disorder? The results

throughout the study have shown that the way an individual patient responds psychologically to a life-threatening illness affects the prognosis for that patient. Whether this is termed Depression or Adjustment Disorder does not alter the significance of this finding. It would however be relevant to any discussion of the mechanisms proposed to explain how this occurs, particularly were it believed that Depression and Adjustment Disorder with Depressive Reaction were two separate clinical entities. As the evidence for this rests on arbitrary time cut-off points used for the definition of Depressive Disorder the author believes such a distinction has not been clearly demonstrated. The central findings remain that that those patients with serious life-threatening physical illness who become depressed had a worse prognosis than those who were not depressed, and this relationship was independent of the severity of their physical illness.

RESULTS FOR INDIVIDUAL CONDITIONS:

MYOCARDIAL INFARCTION:

For all of the patients admitted with myocardial infarction the author was involved in their clinical care. Although this has some advantages it also introduces a potential bias, such as the interviewer being aware of the prognosis which might lead

to more persistent questioning about depression, or to a different style of interviewing. This potential bias was minimized by not analysing the data on prognostic indicators until after the study was over. Furthermore, this only applied to the myocardial infarction patients.

Among patients who had a myocardial infarction the results obtained clearly showed that those who were depressed had a significantly worse outcome than those who were not. This finding did not reflect other variables such as age, sex, pain experienced, or severity of illness. Although the cut-off point for depression on the Montgomery-Asberg Rating Scale at which depression was diagnosed altered the closeness of this relationship between depression and outcome, there were statistically significant differences between the depressed and non-depressed groups in terms of morbidity when the cut-off point was either 7, 14, or 7-SCE. When the criteria for depression was 7-SCE, a significant difference in terms of mortality emerged between the depressed and non-depressed patients. Furthermore, the use of different cut-off points led to different percentages of patients being diagnosed depressed, varying from 19-59%, with 37% of the 7-SCE group being classified as depressed shortly after admission. If the patients were studied on day 7 then 29% were depressed with a cut-off point of 7 and 18% using the 7-SCE cut-off point.

The pain rating scale score results did not show any statistically significant differences between the depressed and non-depressed groups with any of the cut-off points. Nonetheless, there was a tendency for depressed patients to experience more pain. As has already been noted the depressed group did not appear to be more seriously ill on admission. It may be that both groups of patients experienced the same amount of pain, but those who were depressed were more ready to complain of it, or that depression lowers the threshold for experiencing pain. Finally pain may be an epiphenomenon of depression, such that whilst depressed the patient felt that the future was poor or hopeless. Thus their bodily sensations were perceived as pain, indicating the awfulness of their prognosis. All three explanations must remain speculative at present as there is no evidence to support or refute any one of them.

When the cut-off point was either 14 or 21 the depressed group had significantly higher serum LDH levels, when including post-cardioversion levels. This might indicate that the depressed patients were more severely ill. The prognostic factors normally taken into account in predicting the outcome of myocardial infarction do not support this. Pre-cardioversion serum LDH and AST serum levels were the same in the two groups, as were ECG abnormalities and the presence of left ventricular failure. This finding of raised serum LDH levels in the

depressed patients did not occur when using a cut-off point of either 7 or 7-SCE. As the most statistically significant findings in terms of the relationship between poor outcome and depression were when using these cut-off points, it seems unlikely that there were any differences between the depressed and non-depressed groups, for any cut-off point, in terms of severity of illness.

There have been four previous studies of the short-term psychological response amoungst patients following myocardial infarction. Lloyd and Cawley (1978) studied 100 men one week after infarction. Using a semi-structured interview they found that 35 patients had psychiatric morbidity, in 28 of whom this was an affective disorder. Mayou et al (1978c) followed up 100 patients and their spouses over two months, as part of a year long follow-up (Mayou et al 1978b). On initial mental state examination, performed one week after admission, 67% of patients had mild distress, and 11% had moderate distress. It is unclear if the presence of distress implies the presence of an affective disorder. Maeland and Havik (1987) used a questionairre to assess 249 patients at 9 days post-infarction. At 9 days 35% of patients scored in the high range, and were felt to have a significant emotional reaction. These results compare with the findings in the present study at one week of 29% with a cut-off of 7, and 18% with a cut-off of 7-SCE.

The non-infarction patients were similar to the myocardial infarction patients in terms of age and sex, and were admitted under very similar conditions to the same wards. The findings in the non-infarction group, raise some interesting questions. On admission the patients did not know whether or not they had an infarction, but proportionaly fewer were depressed who did not have an infarction than were those who did. This difference in the incidence of depression occured with all cut-off points, the difference being between 30-70%. The increased incidence of depression in patients who had an infarction might imply that it was something about the infarction itself which predisposed to depression. However, those patients who did not have an infarction were likely to have suffered less initial pain, although not in all cases. Furthermore, in the majority of patients admitted post-myocardial infarction there were changes on the electrocardiogram (ECG); this was not the case with the non-infarction group. Most of those without ECG changes would have been told they were being admitted to exclude infarction, and their relatives probably would have been given a less gloomy prognosis. The nursing and medical staff would have been aware of these ECG differences. There are thus several ways in which this information might have affected both the patients attitudes and feelings about admission, and the development of depression, even at such an early stage in their admission.

SUBARACHNOID HAEMORRHAGE

In the 41 patients who had a sub-arachnoid haemorrhage none of the prognostic indicators showed any significant differences between the depressed and non-depressed groups. Thus it is unlikely that the depressed patients were more seriously ill. Nonetheless the depressed group did significantly worse in terms of outcome when the cut-off points for depression were 7, 14 and 7-SCE. However, when considering mortality alone there were no significant differences. Comparing the cut-off points also shows considerable variation for the percentage of patients diagnosed as depressed, ranging from 7% to 68%.

The patients admitted with sub-arachnoid haemorrhage formed a relatively homogenous group in that they had all been treated locally before transfer to a regional neurosurgical centre. However, the patients were seen after the diagnosis had been made. Furthermore, because of the time taken to make the diagnosis and effect transfer the patients were seen at a later stage in their illness than the other groups, with some not being seen until 3 or 4 days after the initial event.

In considering whether simply raising the cut-off point allows an accurate definition of depression in this group of patients, it is of note that 5 of the patients who were categorized as

depressed using a cut-off point of 14, were not depressed using the 7-SCE criteria. This suggests that in patients with sub-arachnoid haemorrhage many suffer particularly from somatic problems such as poor sleep, poor appetite and poor concentration. Because of this problem it is likely that the 7-SCE modification of the Montgomery-Asberg Rating Scale may be the most appropriate method way of studying depression occuring in patients with sub-arachnoid haemorrhage.

The right internal carotid artery divides into the middle cerebral artery, the anterior communicating artery and the posterior communicating artery. The anterior communicating arteries lead onto the anterior cerebral artery, whilst the posterior communicating artery helps form the posterior cerebral artery. Thus any disturbed flow in the right internal carotid artery would be expected to affect the right hemisphere as a whole, and not simply one small area. Bleeding, subsequent to rupture of an internal carotid artery aneurysm, is most likely to be seen on C.T. scan at the base of the brain. The finding in this study of a correlation between aneurysm of the right internal carotid artery and the presence of depression, using the 7-SCE cut-off, is in keeping with previous studies which have linked right hemisphere disturbance to depression. Previous studies of psychiatric sequelae following sub-arachnoid haemorrhage have shown an increase in middle cerebral artery aneurysms in patients who were depressed (Oyebode et al

1986), but the information to allow differences between hemispheres to be studied was not included. Lishman (1968) studied patients after head injury and found an association between right hemisphere damage and the development of depression. Folstein et al (1977) studied patients after a stroke and linked the presence of depression to lesions in the right hemisphere. More recent work in patients following a stroke, using C.T. scan assessment of the site of the lesion, has linked the left hemisphere to the development of depression, particularly cerebral infarction in the left frontal cortex (Robinson at al 1984; Starkstein et al 1987). Eastwood et al (1989) in a study of post-stroke patients using C.T. findings show that depression occured in 30% of patients with a left hemisphere lesion, and in 60% of those with a right hemisphere lesion. Those patients who had small lesions in the left frontal cortex were significantly more likely to be depressed than patients who had a larger lesion more posteriorly in the left hemisphere. There are several problems in using C.T. scan findings to determine the site of any lesion, not least that nearly half of clinically diagnosed strokes do not produce changes on the C.T. scan, especially small lesions. This problem may be resolved by magnetic resonance imaging (MRI) which is more sensitive than C.T. in detecting infarctions at an earlier stage (Kertesz et al 1987). It is clear that at present neither hemisphere alone has been conclusively linked to the development of depression following

cerebral damage or infarction. Future research involving both MRI and positron emission tomography might help elucidate further the nature of this link.

Sub-arachnoid patients might be expected to have a high incidence of depression since they often have to lie flat on their backs in pain for long periods whilst awaiting surgery. Previous studies of the psychiatric problems following sub-arachnoid haemorrhage have concentrated on the longer term follow-up. Storey (1967 and 1970) demonstrated that 55% of patients had disability, mainly due to organic deficits. Logue et al (1968) followed up patients after anterior cerebral artery rupture and found that 12.6% had depression. Oyebode et al (1986) reported on 20 patients post sub-arachnoid haemorrhage who were referred for psychiatric assessment, 70% of these patients had a depressive illness, often accompanied by organic brain damage. In the present study the incidence of depression is not raised in comparison with other patient populations, most convincingly in the 7-Somatic Components Excluded (7-SCE) group. This may possibly reflect late attendance. Against this however, is the lack of any difference in the incidence of depression in the early and late attenders, and also the fact that the level of depression stays relatively constant in this group during the first few days. The patients with laminectomy form a suitable control group for examining the theory that lying flat in bed in pain is the cause of

depression in the sub-arachnoid patients. Of the 8 patients undergoing laminectomy, 7 were seen pre-operatively, and at this point none of the patients were depressed. Post-operatively 2 patients became depressed, one scoring between 7 and 14 and the other between 14 and 21. Neither of these patients scored more than 7 using the 7-SCE cut-off point. This finding demonstrates that being on a particular ward forced to lie on ones back in pain is not, in itself, enough to cause depression.

The results suggest that the laminectomy patients might possibly have suffered from more subjective pain for the first three days than the sub-arachnoid haemorrhage patients. However, the increased incidence of pain in the laminectomy patients demonstrates the problems that may occur when using the pain rating scale to compare different groups of patients with each other. With the pain rating scale the maximum score is 3, representing pain as severe as the pain on admission. In sub-arachnoid haemorrhage the initial experience is often described in such terms as "I thought my head was going to burst" and it is not surprising that very few patients again experienced this degree of pain, despite quite considerable levels of discomfort. Post-laminectomy, however, patients sometimes continued to experience a similar level of post-operative pain for some days and thus scored more highly than the sub-arachnoid haemorrhage patients on the pain rating

scale. The other important difference was the planned nature of the operation, with the possibility that the laminectomy patients were looking forward to the operation to relieve their chronic back pain. The different expectations combined with the nature of the pain rating scale might explain the higher pain ratings of the laminectomy patients.

PULMONARY EMBOLISM:

Among the patients with a pulmonary embolism there were none who had had a massive pulmonary embolism, and only three were shocked. There were no significant differences in prognostic indicators between the depressed and non-depressed groups. Neither were there differences in terms of pain experienced. However there were statistically significant differences in outcome, varying with the cut-off point used on the Montgomery-Asberg Rating Scale. Outcome was poorer at or above the cut-off points of 14 and 7-SCE, and mortality was greater with cut-off points of 21 and 7-SCE. The most statistically significant findings were for the 7-SCE group.

Those patients who had had a pulmonary embolism were a mixed group since many were in hospital already for other reasons, such as surgery, whilst others developed the condition de novo. In addition, the patients were under several different

consultants and the advice and treatment regime often differed. There were very few non-embolism patients for comparison.

There has been no previous studies of the psychological response of patients following pulmonary embolism, although work in general medical inpatients, for example Maguire et al (1974) and Moffic and Paykel (1975), has shown that about 1/4 of such patients had psychiatric morbidity. The results in the present study for the percentage of patients who were depressed varied with the cut-off points between 18-72%, with 33% of patients depressed on the 7-SCE cut-off point. Of the 29 patients (72.5%) who scored more than 7 on the Montgomery-Asberg Rating Scale only 13 (32.5%) were in the 7-SCE group, and only 6 out of 10 patients scoring in the range 14-21 were in the 7-SCE group. This is similar to the results for the sub-arachnoid haemorrhage patients and suggests that both groups are similar in the amount of physical problems suffered, and that the 7-SCE cut-off point may be the most accurate measure of depression in both groups of patients.

GASTRO-INTESTINAL BLEEDING:

The patients with gastro-intestinal bleeding who were included in the present study may well not be typical of those with the condition due to the large number of patients who were

excluded. Many of those excluded were those at greatest risk, and this probably explains the relatively low mortality (6.7%) seen among those who were included. There was also considerable difference in age between the men (mean age 46) and women (mean age 61). It may be that elderly men more frequently became confused and were thereby excluded in greater numbers, and/or older men admitted for surgical care were more likely to have been referred to a tertiary centre. Of the thirty patients with upper gastro-intestinal bleeding who were entered into the present study, outcome was measured only in terms of mortality since all the survivors had a good outcome. As there were only two deaths during the study period none of the differences reached statistical significance. The trend however, is similar to that seen with the other patient groups in that both the patients who died were depressed, scoring between 7 and 14 and also being in the 7-SCE group.

There has been no comparable previous work upon the acute psychological response of patients to the development of upper gastro-intestinal bleeding. However, since the work of Alexander (1952) interest has focused upon the presence of peptic ulcers reflecting underlying psychological stress or illness. This work has been directed firstly towards the role of personality in the development of ulceration, and secondly the role of stress, both acute and chronic.

RESULTS FOR ALL OF THE FOUR GROUPS COMBINED:

When the findings from all of the illness groups were combined a definite link between depression and mortality emerged, as well as a link with morbidity. The results also indicated that the cut-off point on the Montgomery-Asberg Rating Scale chosen to define depression made a considerable difference to the results. With a cut-off point of 7 to define depression, as suggested by Snaith et al (1986), 62% of patients were depressed on admission. Of the total score approximately 4/5 was accounted for by somatic items, and this was also the case for patients scoring up to 14. It is thus likely that a score on the Montgomery-Asberg Rating Scale of 14 or less was highly dependent upon somatic components, and therefore did not accurately represent depression.

Increasing the cut-off point for depression to 14 gave a figure of 39% of patients who were depressed on admission, and increasing the cut-off point further to 21 yielded a figure of 16%. The patients who were categorised as depressed by using the 7-SCE cut-off point comprised 33% of the total patient population on admission, and across all four study populations the percentage in the 7-SCE group was similar; 37% in myocardial infarction; 25% in subarachnoid haemorrhage; 32.5% in pulmonary embolism; and 33% in gastro-intestinal bleeding.

What varied much more between the different study populations were the percentages of patients categorised as depressed in each group when using alternative cut-off points. The 7-SCE group had a mean total score of 21.3 on admission, 13.2 at one week, and 14.6 at two weeks. Of this score 46% was due to somatic components on admission, 51% at one week and 58% at two weeks. Thus it is likely that for all groups somatic factors became relatively more important with time. Using the 7-SCE criteria demonstrated most significantly the relationship between depressed mood and outcome, with the results being highly statistically significant for both mortality and poor outcome. Thus for all study populations increasing the cut-off point was a less accurate method of measuring depression than modifying the rating scale to exclude somatic items.

There were marked change in the depression scores over time in all diagnostic groups. The implications of this finding are that the time in the course of the illness at which measurement of mood is undertaken can markedly affect the results. Even by the third day there was a decrease of approximately 25% in the depression scores in three of the groups, with the subarachnoid haemorrhage patients having generally being seen later in the course of their illness. This reduction was even more marked by days 7 and 14. Thus leaving the assessment of depression until after the third day post-admission will miss

considerable numbers of patients who were clearly depressed on admission.

The previous findings show clearly that depressive symptoms wax and wane during the course of a serious life-threatening illness. For a comprehensive picture of such changes it is necessary to assess depressive symptoms at frequent intervals, using a scale in which the influence of somatic symptoms is minimised.

RELEVANT PSYCHIATRIC ASPECTS

The findings outlined previously link depressive symptoms in the physically ill to poor outcome. Before consideration of any possible mechanisms by which this link may occur, it is neccessary to examine the psychiatric aspects of the relationship between depression and physical illness. The possible physical causes leading to a patient becoming depressed, such as pain, disturbed cognitive function and the severity of the patients illness have all previously been discussed. The psychiatric aspects of why an individual might become depressed following acute medical illness will be reviewed with relevance to the patients' individual predisposition and vunerability, factors felt to be important in those patients who develop adjustment reaction with

depression (ICD-10). Three interlinked factors help determine predisposition and vunerability, these are personality, evironmental stress and life events, and coping styles.

Personality

The role of personality in the development of coronary heart disease (CHD) has been intensively studied over the past two decades. In particular a link has been described between 'Type A' behavior patterns and CHD. Rosenman et al (1964) defined Type A patients as those who were competitive, achievement-orientated, time-urgent (concerned with time over the next few seconds), multiphasic (often doing more than one thing at a time), easily aroused, and hostile or angry. Patients with a relative absence of these characteristics were classified as Type B. The relationship between Type A behavior and CHD has been demonstrated using self-assessment rating scales (Kenigsberg et al 1974; Keegan et al 1979; Kormitzer et al 1981). The link between Type A behavior and CHD was further strengthened firstly when it was shown that patients with Type A behavior had more extensive cardiac disease at the time of cardiac catheterization (Blumenthal et al 1978; Frank et al 1978), and secondly by the findings of a longitudinal study, the Western Collaborative Group Study (Rosenman et al 1975; Rosenman et al 1976), which showed that patients with Type A

behavior had twice the risk of developing CHD. This lead to the conclusion by the National Institute of Health (1981) that "the available body of scientific evidence demonstrates that Type A behavior...is associated with an increased risk of clinically apparent CHD in employed middle-aged U.S. Citizens." Taken with the evidence that other known risk factors, such as raised serum cholesterol and smoking, account for only 50% of the variance in the development of CHD (Jenkins 1976) the case for Type A behavior having a significant role in CHD development seemed very strong.

More recent research has, however, cast doubt upon these findings. Recent studies have not found that Type A patients have more severe coronary atherosclerosis (Dimsdale et al 1979; Scherwitz et al 1983; Young et al 1984). Several longitudinal studies, such as the Framingham Heart Study (Haynes et al 1980), the Honolulu Heart Study (Cohen and Reed 1985), the Multiple Risk Factor Intervention Trials (Shekelle et al 1985a), the Asprin Myocardial Function Study (Shekelle et al 1985b), and the Beta-Blocker Heart Attack Trial (Ruberman et al 1984), have all failed to confirm the findings of the Western Collaborative Group Study (WCGS) that the incidence of CHD was increased in the presence of Type A behavior. Indeed, a recent follow-up of WCGS patients over 22 years showed that Type B patients were at greater risk of developing CHD than Type A patients (Ragland and Brand 1988), although these findings have

been disputed (Friedman 1988). A recent cross-sectional study also found no link between Type A behavior and coronary atherosclerosis (Langeluddecke et al 1988). Other recent studies have tended to show that if personality is important in the development of CHD it is likely to reflect either hostility alone (Hecker et al 1988; Koskenvuo et al 1988; Wielgosz et al 1988) and/or time-urgency (Wright 1988).

Three recent reviews have differed in their conclusions about the relevance of Type A behavior to the development of CHD. One (Dimsdale 1988) felt that it was no longer clear that Type A behavior was a risk factor in the development of CHD, another (Byrne 1987) felt that Type A behavior was important, whilst a third (Wright 1988) felt that it was likely that only some of the components of the Type A behavior pattern were important determinants. Part of this confusion might be due to the somewhat poor correlation between the instruments used to measure Type A behavior (Byrne et al 1985), and/or that the Type A behavior pattern measures both significant and non-significant factors in the development of CHD (Hecker et al 1988) with differing measurement techniques inadvertantly emphasising different factors.

The relationship between personality and the development of peptic ulceration has also been previously studied, with a

'typical' peptic ulcer patient being felt to have a striving ambitious and competitive personality (Weiner et al 1957; Alp et al 1970; Paulus 1979; Feldman 1980). Personality factors such as extroversion and neuroticism have not been shown to be increased in peptic ulcer disease or functional dyspepsia (Stockton et al 1985). Studies of the relationship between Type A behavior and the development of peptic ulcer disease have yielded conflicting results, with some studies demonstrating a relationship (Keltikangas-Jarvinen 1987) whilst others show no such relationship (Langeluddecke et al 1987). The reasons for these conflicting results are not clear, but may be similar to those in coronary heart disease patients.

In conclusion therefore, the relationship between personality factors and both coronary heart disease and peptic ulceration is unclear, as is the importance of personality measurement in determining the prognosis for an individual patient.

Environmental Stress and Life Events

Holmes and Rahe (1967) demonstrated a relationship between major life events and illness, and many studies have replicated these findings in different illnesses, both physical and psychiatric illness (Wolff 1962; Rahe et al 1970), neurotic disorders (Cooper and Sylph 1973), depression (Paykel et al

1969), and schizophrenia (Brown and Birley 1968). The difference between enviromental stress and life events is by no means clear. They can be envisaged as chronic and acute components of the same factor, and the relative importance of a chronic 'mild' enviromental stress compared to an acute 'severe' life event is uncertain. In view of this it is more suitable to consider the research findings about these two factors together. Despite previous findings regarding the importance of these factors in the development of illness, both Paykel (1980) and Tausig (1982) point out that life-events account for only a small percentage of the variance in depressive illness scores. That this might also be the case in physical illness is suggested by the finding of Creed (1981) that life events were important aetiologically in patients who had a normal appendix histologically, but not in patients whose appendix was inflammed.

Support for the role of enviromental stress and life events in the development of coronary heart disease (CHD) originally came from follow-up studies of patients who had suffered traumatic events such as being prisoners of war (Freed et al 1968), concentration camp victims (Eitinger and Strom 1981), survivors of natural disasters (Trichopoulos et al 1983), or survivors after their spouse had died (Parkes et al 1969). This was further supported by work using more standardized measuring instruments (Theorell and Rahe 1981; Rahe et al 1974), although

other studies have found no relationship between life events and CHD (DeFaire 1975; Orth-Gormer 1979). Recent work has demonstrated that mental stress can cause transient, and often silent, myocardial ischaemia in patients (Rebecca et al 1986; Freeman et al 1987; Rozanski et al 1988), which is relevant to previous research with animals in which enviromental stress led to the appearance of arrythmias (Lown et al 1980).

Other recent research has concentrated on the link between Type A behavior and life events. This is because there are suggestions that the behavior pattern of Type A individuals may itself create both occupational and social stresses which increase the incidence of life-events (Byrne 1981; Matteson and Ivancevich 1982). This suggestion has been demonstrated both in healthy populations (Jarvikoski and Harkapaa 1988) and patients with CHD (Dimsdale et al 1978; Byrne and Rosenman 1986), especiallly with regard to occupational stress.

The link between chronic stress and the development of peptic ulceration has been previously demonstrated in animals (Weiss 1968). That patients with peptic ulceration were more likely to have experienced stressful events has been previously suggested (Alp et al 1970), although a number of studies found that the incidence of discrete life events was not increased (Piper et al 1978; Thomas et al 1980; Stockton et al 1985). More recent

work has suggested that it is the presence of chronic stress that increases the incidence of peptic ulceration, and other gastro-intestinal disorders, rather than acute events (Craig and Brown 1984; Chaney et al 1985; Gilligan et al 1987).

In conclusion, acute or chronic stress, possibly related to the presence of Type A personality, increases the prevelance of coronary artery disease and peptic ulceration. Whether this finding can be generalised to other physical illnesses is unclear at present.

Coping Styles

Coping styles describe the way in which an individual responds to a particular event. Edwards and Cooper (1988) discuss the relationship between stress, coping and health. They point out that there is often great confusion in what is meant by the terms 'stress' and 'coping', and that different coping styles can either reduce or increase stress.

In patients who have suffered from an illness, their coping style might affect their recovery. Previous work with psychiatric patients has demonstrated that patients who are depressed have different coping styles to non-depressed

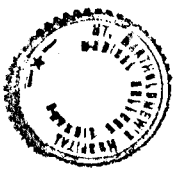
patients (Billings and Moos 1981; Billings et al 1983). This difference also occurs between depressed and non-depressed medical inpatients, with the depressed patients more often using avoidance strategies, rather than active coping techniques (Cavanaugh et al 1983; Rosenberg et al 1987). Recent evidence suggests that patients with a more serious illness use different coping mechanisms to those with less serious illnesses (Fiefel et al 1987). Although there is some evidence that Type A personality groups have different coping styles to Type B groups (Hart 1988) the role of personality seems less important than the nature of the stress itself in determining an individual's response (Fiefel et al 1987).

Of the many studies of coping styles in patients following coronary heart disease (CHD) most have concentrated upon the coping mechanism of 'denial' (Gentry et al 1972; Stern et al 1976; Shaw et al 1985; Shaw et al 1986; Levine et al 1987; Havik and Maeland 1988). The role of denial in affecting outcome has also been investigated with some studies suggesting that denial of illness lead to an increased likelyhood of a favourable outcome (Hacket et al 1968; Gentry et al 1972; Stern et al 1976; Levenson et al 1984) whereas other studies have shown that denial leads to late attendance at hospital and a worse outcome (Greene et al 1974; Gentry and Haney 1975). Some longitudinal studies have found that denial has a beneficial outcome in the short term, but that it is detrimental in the

longer term (Levine et al 1987), whilst others have found certain types of denial to lead to a better outcome (Havik and Maeland 1988). These differences might be explained by the suggestion that denial has several different components, such as denial of illness, denial of impact, and suppression, and that each component might have different effects (Havik and Maeland 1986).

It is clear from the preceding review that no one single conclusion can be drawn regarding the complex interaction between personality, acute and chronic stress, and coping styles. In addition, none of the three possible psychiatric mechanisms discussed previously seems able, by itself, to explain why certain individuals become depressed following severe life-threatening illness, but not others. There is no clear evidence that patients who do become depressed either have a particular type of personality or a particular method of coping. What seems somewhat more likely is that following severe stress the response of patients is more dependent upon the nature of the stress than the patients personality. This would suggest that it does not matter which particular life-threatening illness the patient had, since a similar proportion of patients would become depressed. This was the finding in the present study.

POSSIBLE MECHANISMS:



If the occurence of a life-threatening illness is accepted as a stress, or major life event, is there a mechanism by which psychological factors may be linked to outcome? Is it possible that the poor outcome associated with depression is mediated by the effects of the sympathetic system on blood vessels? This theory is not new; it has been suggested on many occasions in the last four decades. A brief review of some of the recent relevant literature might help elucidate this question.

Adrenaline release occurs in response to mentally stressful situations with males releasing more catecholamines than females in these situations (Steptoe 1987). It is also clear that circulating catecholamines affect vasoconstriction, and may be invoved directly in the genesis of some types of illness, shown most notably in cardiac arrhythmia and peptic ulceration. Dimsdale (1977) and Lown et al (1980) both postulated that higher nervous activity affected the electrophysiological properties of the heart via the autonomic nervous system, and could cause sudden cardiac death. Lown et al also demonstrated that the incidence of venticular premature beats increased during stress. Katz et al (1985) showed that patients who had arrythmia but not myocardial infarction were more anxious and depressed than a group of patients who had

arrythmia and infarction. Reich et al (1981) interviewed 117 patients about psychological events in the 24 hours preceding ventricular arrythmia. 25 of these patients had experienced psychological events which were considered important to them, with 15 experiencing the event in the hour preceding the onset of arrythmia. Lane and Schwartz (1987) suggested that individuals who show greater frontal lobe lateralization in response to emotional stress, also generate greater lateralized sympathetic input to the heart. This hypothesis seeks to explain why some some patients are at greater risk of developing cardiac arrythmia in response to stress. Krantz et al (1987) demonstrated that patients with type A personality respond differently to Beta-adrenergic blockage. Stress mediated through the sympathetic nervous system is also involved in the generation of gastric ulceration in the rat (Salim 1987).

On balance it appears that the weight of evidence is in keeping with the view that the effects of depression upon outcome may be mediated via sympathetic outflow, either to the arterial system generally, or selectively to the organ involved.

POSSIBLE TREATMENT:

Having identified that depression occurs in one third of patients immediately following life-threatening illness, and that this depression is linked to increased morbidity and mortality the question then arises: Is it possible to treat these patients? The aims of treatment would be to relieve distress and to decrease the risk of a poor outcome. Since much of the depressive reaction has a short time course it is clear there is no role for conventional anti-depressant drugs which take at least a week to begin to act. Antianxiety drugs, such as benzodiazepines, are unlikely to be helpful as there is little evidence that appropriate anxiety leads to increased risk. In the Lloyd and Cawley study (1975) all of the patients were treated with diazepam in the coronary care unit, and yet the level of psychiatric morbidity was still significant. Previously attempted treatment has been empirical. Stern et al (1983) and Stern and Cleary (1981) claim that 'exercise therapy' improves patients psychological functioning post myocardial infarction. Stern (1987) describes many practical steps physicians might undertake in the coronary care unit to try and reduce patients anxiety and depression. Although the validity of these suggestions is unproven, there has been some work which supports the idea that supportive psychotherapy helps patients immediately post myocardial infarction (Gruen

1975). However, until more is known about the aetiology of depressive reactions, treatment must remain uncertain.

CONCLUDING REMARKS:

Using a rating scale modified to minimise the influence of physical symptoms upon depression rating scale scores in patients with serious life-threatening disease there was a clear link between the occurance of depression in the short-term and outcome. The patients with myocardial infarction, subarachnoid haemorrhage, pulmonary embolism, and gastro-intestinal haemorrhage who were depressed did worse in terms of morbidity and mortality than those patients who were not depressed. This was not due to any differences in physical state. This link may be mediated via the sympathetic nervous system.

FUTURE RESEARCH:

This study has demonstrated the need for future research to develop a reliable and well validated means of measuring depression in the presence of physical illness. This measuring instrument should be validated both in psychiatric patients with clinically diagnosed depression, and in medically ill

patients by using a standardized clinical interview such as the Present State Examination (World Health Organization 1974, 9th Edition).

ACKNOWLEDGEMENTS:

I would like to thank all of the Physicians and Surgeons who allowed me to interview their patients repeatedly. Particular thanks are due to Dr. Eileen Phillips and Dr. Paget Davies, Consultant Physicians at the East Surrey Hospital, for their continued support and encouragement. I would also like to express my thanks to Professor E. Paykel for his help in the preparation of this thesis.

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