On some aspects of

Post-traumatic Psychopathology and Recovery after Musculoskeletal Injury

A thesis presented for the degree of Doctor of Medicine (MD) at the University of Aberdeen

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To my father Colin for always encouraging independent thought,

and to my wife Alison and son James for making everything worthwhile.

ABSTRACT

Introduction: Psychological disturbance after combat and major civil accident has long been recognised, but it has become clear that more "everyday" trauma such as road traffic accidents can lead to similar problems. Post-traumatic Stress Disorder (PTSD) is the extreme of a spectrum of Post-traumatic Psychopathology (PTP), is known to influence the Metabolic Response to Trauma (MRT), and may affect physical recovery after injury. This thesis details the results of a large study of accident victims, following their physical, physiological and psychological recovery.

Methods: Cohort study of 200 patients aged 16-60 y with musculoskeletal injuries. The patients completed questionnaires that examined their psychological health (GHQ), and their physical and psychosocial health (SIP, SF-36, MFA), and trauma scores were calculated. Assessments were made on admission (*vice* health before the accident), and were repeated at two and six months. A subgroup of 82 patients also gave blood samples at each of the follow up points, and these were analysed for pro-inflammatory markers of the MRT (CRP, IL-6, soluble IL-6 receptor, and TNF-α).

Results: Follow up was 79% and 75% at two and six months for the main group, and 82% and 59% respectively for the Metabolic Markers subgroup. PTP was found in 11% of patients at initial assessment, 46% at two months and 22% at six months. It was strongly related to impaired physical and psychosocial functioning. There were also associations between PTP and sIL-6r and TNF-α at six months. Injury Severity Score was predictive of PTP at two and six months.

Discussion: There are strong associations between psychological and physical health after musculoskeletal trauma. Injury Severity Score is predictive of this psychological disturbance, which is also associated with disturbance of pro-inflammatory markers. Truly holistic care of patients who have suffered musculoskeletal trauma must include management of the psychological injury as well as the more obvious physical injuries.

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DECLARATION

On some aspects of
Post-traumatic Psychopathology and Recovery after Injury

I hereby declare that I wrote this thesis, and that it has not been submitted or accepted in any previous application for a degree. C-Reactive Protein assays were carried out in the department of Chemical Pathology of the University of Aberdeen, and Staff Nurse Linda Bowes recruited some of the patients to the study. I carried out all the rest of the work represented here. All quotations are distinguished by the use of quotation marks and the sources of information acknowledged.

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1.INTRODUCTION

1.1 BACKGROUND

Stress is an inevitable part of everyday existence. The effects on the individual depend upon the nature of the stress and on the character and social background of the person. The link between intense combat and profound psychological disturbance has been investigated in detail. While a similar link with civil disasters has also been established, there is little published work on the psychological consequences of more "everyday" trauma, such as road traffic accidents. Outside times of war, such everyday trauma affects many more people than combat or major civil disaster, and its psychological effects may impinge upon the recovery of a large volume of patients. This introduction will trace the development of our multidisciplinary collaborative research on the psychological effects of musculoskeletal trauma, and then place the development of our understanding of posttraumatic psychopathology in its historical context, before examining its relationship with everyday trauma, and its importance in modern orthopaedic trauma care.

1.1.1 "It's not really orthopaedic surgery, is it….?"

For some time, it had been clear to us that not all orthopaedic trauma patients recover in the same way, even allowing for differences in injury patterns and injury severity. Some patients seemed to face up well to their injuries, with strong motivation and application to rehabilitation regimes, while others remained more introspective and passive. These differences were often reflected in different rates of recovery, but it was not possible to say whether there was any "cause and effect" at work.

The foundation for studying this effect was based upon the serendipity of office placements that put a Professor of Orthopaedics (with an interest in trauma - JDH) across the hall from a Professor of Mental Health (with an international reputation in the field of post-traumatic stress studies - DAA). Discussion between these two led to collaborative work investigating the relationship between physical injury and post-traumatic psychological disturbance. What became clear from this work was that many orthopaedic trauma patients suffered with post-traumatic psychopathology. This allowed the development of ideas that might explain this relationship and its effects upon physical recovery, as well as providing an insight into the best way of identifying and treating such patients.

The development of this work has attracted a degree of scepticism from other surgeons, who have suggested that the psychiatrists should deal with the mind, and the surgeons with the body. We believe, however, that the two are linked, and have attempted to develop an approach to the trauma patient that includes more than just treating the fracture, and that provides holistic care.

1.1.2 The Military Setting

Various labels have been applied to the combat-related psychological disturbance in soldiers. What was often called "nostalgia" in the American Civil War (Dean 1997) became "shell shock" (affecting up to 10% of British officers (Gersons & Carlier 1992)) or "neurasthenia" (a syndrome of somatic symptoms caused by "non-adaption

of the individual to a continuous emotive cause" (Mott 1918)) on the Western Front in the Great War. "Combat fatigue" was the most commonly applied label in the Second World War (Dean 1997).

There is a large body of literature that provide harrowing descriptions of modern mechanised warfare and its effects upon the writers and their comrades. Books such as "All Quiet on the Western Front" (Remarque 1994) have become modern classics, describing the despair and destruction of soldiers' spirits. The poet Robert Graves fought on the Western Front in the Great War with the Royal Welch Fusiliers. He suggested that neurasthenia was virtually universal among officers who survived the trenches for long enough (Graves 1960). The expectancy of trench service for an officer, before being killed or wounded, was half of that of an ordinary soldier.

> *For the first three weeks, an officer was of little use in the front line; he did not know his way about, had not learned the rules of health and safety, or grown accustomed to recognizing degrees of danger. Between three and four weeks he was at his best, unless he happened to have any particular bad shock or sequence of shocks. Then his usefulness gradually declined as neurasthenia developed. At six months he was still more or less all right; but by nine or ten months, unless he had been given a few weeks' rest on a technical course, or in hospital, he usually became a drag on the other company officers. After a year or fifteen months he was often worse than useless.*
>
> *Robert Graves*
>
> *Goodbye to all that (Graves 1960)*

Siegfried Sasson, also a war poet, served with Graves, and was awarded the Military Cross (Sassoon 1965). Although not affected by shell shock, he was sent to

Craiglockhart Hospital in Edinburgh after he wrote a declaration that was fiercely critical of the way in which the war was being waged – he was declared a victim of shell shock to avoid the further publicity of a Court Martial. At Craiglockhart, Sassoon was treated by Dr WHR Rivers, a pioneer in the treatment of shell shock, and was exposed to the distress of his disturbed fellow officers (Sassoon 1974).

I was not just the Great War that produced such literature or such suffering. Spike Milligan described how "*the conflict caught up with me*" in the fourth volume of his war memoirs (Milligan 1980). The bewilderment that he felt at his situation – uninjured, but unable to function - is palpable.

The Major thinks I'm a coward, perhaps I am? If so why didn't I run from the line the first day in action in North Africa…I manage to stop crying, but I am stammering very badly, so I can't be of any use passing wireless messages or Fire Orders…

To add to the misery I am 'Court Martialed' by the major…..I am now completely demoralised. All the laughing had stopped.

Spike Milligan

Mussolini: His part in my downfall (Milligan 1980)

Neither are such problems new. The Greek historian Herodotus described the story of a soldier called Epizelus at the battle of Marathon (490 BC). The soldier standing next to him was killed by a man of great stature who had appeared before Epizelus in the melee of battle. "*Epizelus….was fighting bravely when he suddenly lost the sight*

of both eyes, though nothing had touched him anywhere – neither sword, spear, nor missile". Prior to the battle of Thermopylae (480 BC) a group of soldiers were dismissed from the field when they were recognised as psychologically spent and unable to take part in the action: "*..they had no heart for the fight and were unwilling to take their share of the danger*" (Herodotus 1996).

What links all of these examples, apart from the military setting, is that the reported psychological distress occurs in the absence of physical injury. There was virtually no literature that dealt with the psychological effect of physical injury until relatively recently. This may be because those injured in war or accidents were "allowed" to be upset or even disturbed, because they had physical injuries to explain their state.

The military establishment has historically been reluctant to acknowledge the psychological effects of combat on soldiers (witness Spike Milligan's Court Martial after he broke down under heavy mortar fire, *vide supra*). The commanders held that combat caused long term psychological problems only in those who lacked "moral fibre" or who had failed to negotiate the trauma of early development (Alexander 1996). This approach was reflected in the diagnosis of *Gross Stress Reaction* (GSR), which appeared in the first edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-1) in 1952 (American Psychiatric Association 1952). GSR was considered to be a transient disorder unless there were pre-existent personality defects, an assumption that is in keeping with the Freudian psychoanalytical principles that were applied in its formulation.

It was the war that the USA waged in Vietnam in the late 1960's and early 1970's, and its aftermath, which crystallised modern thinking on combat stress. It was not that the Vietnam was particularly stressful on US soldiers – the American Civil War had been just as bloody and painful. Neither was it that a large number of soldiers fought – only one in seven of the three million US troops who served in Vietnam saw any combat, and for the majority time in Vietnam was limited to one tour of one year only. The evidence that the returning troops were universally spurned and rejected is also lacking, and it is clear that the US population was generally supportive of Veterans, who received a generous GI Bill. What made the difference was that the generation that produced Vietnam veterans was more actively vocal in their demands and more successful in lobbying for recognition of combat stress than veterans of previous conflicts. It is this more than anything else about Vietnam that led to the modern formulation of Post Traumatic Stress Disorder (Dean 1997), and the readily identifiable image of the troubled "Nam Vet".

"I haven't really slept for twenty years. I lie down, but I don't sleep. I'm always watching the door, the window then back to the door. I get up at least five times to walk my perimeter, sometimes it's ten or fifteen times. There's always something within reach, maybe a baseball bat or a knife, at every door. I used to sleep with a gun under my pillow, another under my mattress, and another in the drawer next to the bed. You made me get rid of them when I came into the program here. They're over at my mother's, so I know I can get them any time, but I don't. Sometimes I think about them – I want to have a gun in my hands so bad at night it makes my arms ache……

I think I don't have long to live because I have these dreams of guys in my unit standing at the end of the sofa. I wake up screaming and the sofa covered with sweat. It seems like if the blood reaches me I'm going to die when it does. Other nights I dream of the guys calling to me from the graveyard. They're calling to me 'Come on, come on. Time to rest. You paid your dues. Time to rest.' "

Jonathon Shay

Achilles in Vietnam (Shay 1994)

1.1.3 The Civilian Setting

Reactions to stress have not been confined to battle. Samuel Pepys gives eloquent descriptions of the after-effects of the Great Fire of London: "*But much terrified in the nights nowadays, with dreams of fire and falling down of houses*". News of a chimney fire some months later caused him "*much upset*" (Daly 1983; Pepys 1993).

The Lancet in 1875, contained a paper describing the depression and attempted suicide of a previously well woman involved in a train accident (Hood 1875). Train accidents produced much psychomorbidity, but the development of the diagnoses of "Railway Spine" and "Compensation Neurosis" reflect the view of the time that these

conditions were hysterical or factitious (Trimble 1981; Harrington 1996; Turnbull 1998).

Charles Dickens described how his involvement in a railway accident later resulted in unsteadiness and depression (Forster 1872; Trimble 1981). There is, however, much less attention to such conditions in published literature, medical or general, in comparison with combat-related stress conditions, prior to the development of Post Traumatic Stress Disorder as a diagnostic entity.

1.1.4 The Development of Modern Diagnoses in Post Traumatic Psychopathology

It was only in 1980 that the psychological disturbance, by then clearly associated with Vietnam combat veterans, was formally recognised and classified in DSM-III (American Psychiatric Association 1980) as Post Traumatic Stress Disorder (PTSD). This diagnosis was innovative because it attributed the primary responsibility to the stressor and not to some deficiency in the patient (Alexander 1996). To this was added the diagnosis of Acute Stress Disorder (ASD) in DSM-IV (American Psychiatric Association 1994).

As well as work with combat veterans and holocaust survivors, the psychological effects of major civil disasters such as the Piper Alpha oil rig disaster (Alexander 1991; Alexander 1993) and the King's Cross fire disaster (Turner, Thompson &

Rosser 1995) have been discussed in some detail. Similarly, survivors of the Nazi Holocaust have provided a fertile ground for PTSD research (Rosen *et al*. 1991; Kuch & Cox 1992; Yehuda *et al*. 1996a; Yehuda *et al*. 1998). It has, however, been increasingly recognised that PTSD can also be suffered by victims of assault and of road traffic accidents (Mayou, Bryant & Duthie 1993; Feinstein 1993).

It is simplistic to consider that individuals will either cope with a significantly stressful situation and remain "normal" or will develop frank PTSD, as if the reaction were an "on-off" phenomenon. PTSD is, rather, the extreme end of a spectrum of post-traumatic psychological reactions. This spectrum extends from a non-pathological "normal" reaction to an abnormal situation, through post-traumatic conditions including anxiety and depression, to PTSD. Some patients may exhibit some of the features of frank PTSD, coupled with other symptoms, but fail to meet the strict criteria for the full diagnosis to be made (Malt 1988). A great number of victims of traumatic events are commonly reported to have ASD or clinical levels of anxiety or depression that are more difficult to define as post-traumatic (Barclay 1996). It is more practical, therefore, to consider psychological reactions to severe stressors under the umbrella title of Post-Traumatic Psychopathology (PTP).

The psychopathology associated with stressful events is widespread. It seems logical to suggest that it may influence the patient's physical recovery, but this has not been extensively studied. In order to study possible effects, it is necessary to define the psychopathology and its possible metabolic correlates, and to define ways of

assessing outcome after trauma that may be complicated by such psychopathology.

1.2 DIAGNOSIS

Contrary to the former view that psychological reactions are specific to the stressful event, the American Psychiatric Association has recognised that response patterns are remarkably similar whatever the cause (Alexander 1996). The formulation of diagnostic criteria for PTSD, which first appeared in DSM III, reflects this recognition. These criteria are outlined below:

1. *The experience of a markedly distressing event, outside the range of normal experience*.

This would include a serious threat of loss of life or of serious injury, or seeing another person killed or maimed as a result of an accident or assault.

2. *Re-experiencing the traumatic event.*

This would include recurrent or intrusive recollections of the event, recurrent dreams, sudden acting or feeling that the event was recurring, severe distress in response to events which symbolise or resemble the event (*e.g.* anniversary, certain sounds or smells).

3. *Numbing of responsiveness or persistent avoidance of stimuli associated with the*

event.

This may manifest in attempts to avoid thoughts and feelings associated with the event, inability to recall feelings associated with the event, markedly diminished interest in significant activities, feelings of detachment or estrangement from others, restricted mood variation and sense of foreshortened future.

4. Persistent symptoms of increased arousal

These may include sleep disturbance, irritability and anger, memory and concentration impairment, increased vigilance and intensification of symptoms by exposure to events resembling the traumatic event.

5. Duration of symptoms of at least one month

Symptoms need not arise immediately after the index event, but may become manifest later. This allows subdivision of the condition into acute PTSD (with onset within six months of the event and generally resolving within six months) and chronic PTSD (with symptoms arising after six months and a generally poorer prognosis). Symptoms arising soon after the event, but lasting for less than one month are considered part of a normal post-stress reaction.

There is significant overlap between these symptoms and other syndromes that may coexist, such as alcohol and drug dependence, antisocial personality disorder, depression and organic mental state syndromes. Moreover, a period spent in hospital may compound the anxieties related to the accident itself, and its long-term impact

(Barclay 1996). The diagnosis of PTSD may be difficult in the presence of comorbidities, such as anxiety, depression and substance abuse, which may have common symptoms. The diagnosis of other post-traumatic conditions, making up the spectrum of PTP, is less specific. Detailed discussion of these conditions is beyond the scope of this thesis. PTSD diagnosis, aetiology and pathogenesis has much in common with the spectrum of PTP, and it is helpful to discuss the particulars of PTSD as a way to understand other, related conditions.

1.3 AETIOLOGY AND PATHOGENESIS

Much of the published literature on the spectrum of PTP focuses upon work on combat veterans. Although PTSD is more common in combat veterans than in the general population (Helzer, Robins & McEvoy 1987), it is clear that civilian incidents can also be significantly stressful. Lifetime prevalence of PTSD in the USA has been put at 1% in a general population survey of psychiatric disorders (Helzer, Robins & McEvoy 1987), and 9% in a group of inner city young people (aged 21-30) (Breslau *et al*. 1991). The differences between these figures may reflect the different samples studied.

1.3.1 The Role of "Everyday" Trauma in development of PTP

Physical trauma in the UK currently leads to more than 500 000 hospital admissions per year, requiring a hospital bed occupancy rate of 13 000 beds daily. This reflects

the whole spectrum of admissions, from sports, industrial, domestic, assaults and RTA injuries. In the North East of Scotland there are 1500 road traffic accidents per year, resulting in 45 deaths, 350 serious casualties and 1600 minor injuries (Chief Constable's report, Grampian Police, 1995). This represents a serious burden upon the health service, in addition to the loss of the patients' economic productivity, quite apart from the physical and social disruption to the patients and their families.

Road traffic accidents are very much more common than major civil accidents and combat stressors in our society. They are outwith people's general experience, and can carry all the hallmarks of significant stressors - chance of death or seriously disabling injury to self and/or others. It has been estimated that approximately 10% of victims of RTAs suffer PTSD (Brom, Kleber & Hofman 1993), and many more may suffer other post traumatic psychological morbidity (Parker 1977), (Mayou, Bryant & Duthie 1993). This constitutes a large number of unrecognised problems that may delay the return to productive work.

1.3.2 PTP and the Individual's Background

The development of PTP after a traumatic experience is not simply dependent upon the nature and severity of the experience. The person's pre-existing personality and social environment also play a large part. Patients with a previous history of childhood abuse or depression or with a higher level of neuroticism or introversion are more likely to suffer PTSD (Bremner *et al*. 1993). Socially extreme behaviours such as alcohol and drug abuse are also correlated with abnormal response patterns

(Breslau *et al*. 1991; Breslau, Davis & Andreski 1995). Antecedent factors such as poor-quality parenting, parental death or child abuse (Bremner *et al*. 1993; Yehuda & McFarlane 1996) were found more commonly in Vietnam veterans with PTSD than in those without PTSD. This is supported further by studies from Australia (which had a significant involvement in Vietnam), highlighting family histories dominated by alcohol abuse among veterans with PTSD (Watson *et al*. 1993).

Support from the patient's immediate family and social group is important. The veterans of the Vietnam conflict were exposed to a vocal (but, as mentioned above, by no means majority) public disapproval of the war. The generally supportive attitude of the Israeli public to the several Arab-Israeli conflicts may be one reason for the lower rates of PTSD, alcohol and drug abuse and antisocial personality features found among Israeli veterans(Yehuda, Teicher & Giller 1995).

1.3.3 The Importance of the "Meaning" of the Trauma

The setting in which a traumatic event or injury is sustained affects the victim's response to it. This correlates with the "psychological meaning" of the injury to the victim (DA Alexander, personal communication), and has been shown to affect the incidence of PTSD (Holbrook *et al*. 2001).

Similar injuries sustained by civilians and by soldiers in combat have quite different effects. It has been noted that, despite serious injuries, soldiers often do not complain of pain and required little by way of analgesia. For the soldier, a non-life threatening

wound provides an escape from the battlefield to relative safety. In contrast, a similar wound for a civilian has a different meaning, and will result in quite different requirements for analgesia (Beecher 1946). Further experimental work showed that the pain threshold was remarkably similar in a group of healthy volunteers, but that the tolerance level varied widely with factors such as age, sex, cultural background and personality type. Pain threshold is physiologically determined, while tolerance is a learned response (Weisenberg 1977). These factors may to some extent allow some prediction of pain behaviour, and may be linked to psychological responses to physical trauma.

Predisposition to PTP is integrally related to the individual's specific interpretation of the traumatic event. The effects of stressors will affect people in different ways, according to the perceived impact of the event upon them (Alexander *et al*. 1995).

1.4 BIOLOGICAL EFFECTS

1.4.1 The Metabolic Response to Trauma

The characteristic physiological response of the body to stress is the "fight, flight and fear" response, which is mediated by the sympathetic nervous system and the hypothalamic/pituitary/adrenal axis (HPA). It is this response that readies the body in a state of hypervigilance, and releases energy stores to provide the body with the fuel to take appropriate action. The HPA axis also forms the backbone of the physiological response to physical injury, the Metabolic Response to Trauma (MRT)

(Fig 1.1, Table 1.1). This maintains the body in a catabolic state, liberating energy stores. It is only once the "turning point" of the MRT is reached that the body turns towards anabolic activity, promoting active healing rather than just preservation of life.

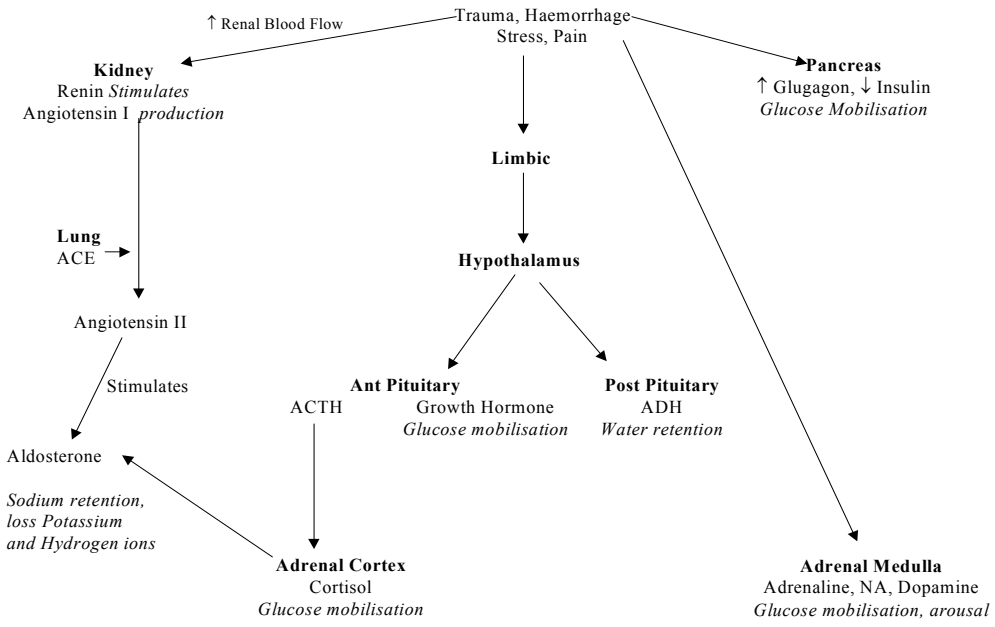

Fig 1.1 The Main Components of the Metabolic Response to Trauma (MRT) (ACE=Angiotensin Converting Enzyme, ACTH=Adreno-Cortico-Trophic Hormone, ADH=Antidiuretic Hormone, NA=Noradrenaline).

Stages		***Time***	***Nitrogen Balance***	***Potassium Balance***	***Sodium Balance***	***Water Balance***	***Cortisol levels***	***Weight***
Injury	*Ebb* ↓ CO ↓ BMR ↑adrenaline *Flow* ↑ CO ↑ BMR	5-7 days	Negative (catabolic + damage)	Negative (aldoster-one)	Positive (aldoster-one)	Positive (ADH)	High	Falling rapidly
Turning Point		7-10 days	Negative to Positive	Negative to Positive	Positive to Negative	Positive to Negative	Falling	Falling (diuresis)
Protein Anabolism		Once Turned	Positive	Positive	Normal	Positive	Normal	Increasing
Fat Anabolism		6+ weeks	Positive	Positive	Normal	Positive	Normal	Increasing Rapidly

Table 1.1 Stages of the Metabolic Response to Trauma (MRT)
(NB: CO=Cardiac Output, BMR=Basal Metabolic Rate, ADH=Antidiuretic Hormone)

1.4.2 The Effects of Post-Traumatic Psychopathology on the Metabolic Response to Trauma

In PTSD the state of hypervigilance, and abnormal response to certain stimuli, is known to maintain a prolonged and abnormal MRT (Yehuda *et al*. 1991; Yehuda & McFarlane 1996). This maintains the catabolic state and restricts the body's anabolic capacity (Van der Kolk & Saporta 1993). The cortisol response to trauma reflects the HPA dysfunction, with previous trauma and severity of trauma correlating with the lower cortisol excretion (Resnick *et al*. 1996; Yehuda *et al*. 1996a; Yehuda *et al*.

1996b). These effects have been noted also in Holocaust survivors with PTSD (Yehuda *et al*. 1996a). The normal stress responses may be involved in an amplified way in the symptoms of PTP, and may represent an exaggeration of a normal response to an abnormal event (Editorial 1995).

Recent work has focused upon pro-inflammatory cytokines, such as Interleukin-6 and its soluble receptor (IL-6 and sIL-6r), Tumour Necrosis Factor (TNFα) and others as indicators of the inflammatory response to physical stress and HPA disruption (Hirano *et al*. 1990; Biffl *et al*. 1996; Hisano *et al*. 1997; Sutherland & Deehan 2000). These may offer a further way of defining the physiological effects of psychological disturbance after physical trauma. Physical and psychological stressors elevate IL-6 levels, and IL-6 is involved in control of HPA function (Zhou *et al*. 1993).

There is now some emerging evidence for elevation of these cytokines in patients with established PTSD, although this work is retrospective (Spivak *et al*. 1997; Maes *et al*. 1999). A pilot study in Aberdeen looked further at C-Reactive Protein (CRP), an acute phase protein produced by the liver, and at least partly controlled by IL-6. Some correlation was found with symptoms in patients with established PTSD (Miller *et al*. 2001). The assay for CRP is readily available in hospital laboratories, and may offer an easy way of assessing the physiological state of the recovering trauma patient and of monitoring recovery.

1.4.3 Post-Traumatic Psychopathology and Sleep Disturbance

Sleep is vital. It allows rest, healing, and consolidation of memory and information in the form of dreams (Adam & Oswald 1984). Cell division and protein synthesis are highest during sleep, due to inhibition of the secretion of catabolic hormones, such as cortisol and catecholamines. Deep sleep is also the principal stimulus to release of growth hormone (Adam & Oswald 1984). There are two distinct states - Rapid Eye Movement (REM) or paradoxical sleep, and non-REM or orthodox sleep. Growth hormone is released and catabolic hormones inhibited during non-REM sleep. REM sleep is the time of synthesis and organisation of mental events. Sleep begins with four stages of non-REM sleep before REM sleep can begin. The normal sleep cycle initially lasts 90 minutes, but as the sleeping period progresses, the periods of REM sleep become longer, and those of non-REM shorter. If the cycle is interrupted, it generally must begin again at the beginning.

PTSD may affect sleep in a variety of ways. The hyperaroused state makes any form of sleep difficult. Hypnagogic hallucinations (experienced as the patient falls asleep) related to the traumatic event make sufferers unwilling to sleep. Recurrent waking from sleep repetitively disrupts the normal sleep cycle. The deleterious effects on sleep may be exacerbated by the use of alcohol and other drugs. These effects combine again to maintain the hypercatabolic response, inhibiting the body's ability to heal damaged tissues. It has been suggested that disturbance of normal sleep is pathognomic of PTSD, with dysfunctional REM sleep being at the heart of the condition (Schlosberg & Benjamin 1978; Ross *et al*. 1989).

The combination of a deranged MRT and disturbed sleep patterns may act synergistically to disrupt physical healing.

1.5 TREATMENT OF POST TRAUMATIC STRESS DISORDER

A detailed discussion of the treatment is beyond the scope of this work; but it is important to stress that there are effective treatments available. These include medication, cognitive and behavioural psychotherapy, and novel treatments such as eye movement desensitisation and reprocessing. So it is worth giving attention to PTP and PTSD in orthopaedic trauma patients as part of holistic care, as these distressing symptoms can be treated.

1.5.1 Preventative Treatment for PTP

While prophylactic treatment for psychological morbidity after trauma may seem appropriate, there is some evidence to suggest that it is not always helpful. Treating all such patients may be at best expensive and ineffective (Raphael & Meldrum 1995) and at worst detrimental to those least likely to suffer PTSD (Mayou, Bryant & Duthie 1993). Putting patients unnecessarily in the sick role may lead to maladaptive behaviour. Further, treatment of PTP nearly always involves re-exposure to the traumatic event, and this "re-traumatisation" may be counter-productive. Work in Aberdeen and elsewhere has, therefore, focused upon identifying those patients most

at risk of PTP, identifying those with abnormal dissociative symptoms in the early phase (Koopman, Classen & Spiegel 1994), and treating them accordingly (Perry *et al*. 1992).

1.6 TRAUMA SCORING AND OUTCOME MEASURES

To study any effect that PTP may have on recovery after trauma, it is necessary to find a reproducible measurement of physical function in surviving patients, and to compare this with a reproducible measurement of the initial injury. Many different trauma scores and outcome measures have been used in orthopaedic musculoskeletal research; this decreases the value of such research, as the different studies cannot be compared with one another.

1.6.1 Trauma Scores

The development of trauma scoring systems has been an attempt to provide objective comparisons between patients, based on certain aspects of their injuries, and thus predict their survival or the extent of disability and functional recovery. The earliest universally accepted trauma scoring system was the Abbreviated Injury Scale (AIS) (Joint Committee on Injury Scaling 1980). This anatomical system allows scoring from 1-6 (minor to unsurviveable) for the various body regions. It is not possible to add these to give a total score for a patient with multiple injuries. The Injury Severity Score (ISS) (Baker *et al*. 1974) is a refinement of the AIS, taking the squares of the

highest three AIS scores together to give a single, non-linear score. If any AIS regional score is 6, this is unsurviveable, and the ISS score is a nominal 75 (the maximum possible score), regardless of the other two scores. The ISS which was lethal for 50% of patients (LD50) differs in according to age: LD50 for ages 15-44 years is 40, for ages 45-64 years it is 29, and for those above 65 years it is 20. There is, however, some doubt about the robustness with which these systems are applied in different centres with different caseloads (Champion, Sacco & Copes 1995). Other systems, such as Revised Trauma Score (RTS) (Champion *et al*. 1989) and Acute Physiology And Chronic Health Evaluation (APACHE) (Knaus *et al*. 1981; Knaus, Draper & Zimmerman 1985) are physiological. The weakness of such systems is that the outcome studied is death rate; they offer little prediction of how well the survivors function.

1.6.2. Orthopaedic Outcome Measures and Fracture Healing

Fracture healing is often used as a way of assessing outcome after injuries. For every fracture there is a classification system. Each such system aims to give prognostic information on time to union and on functional outcome of the fracture. Coupled with the scoring of soft tissue injuries in closed fractures (Tscherne scoring system (Tscherne & Oestern 1982)) and open fractures (Gustillo grading (Gustillo & Anderson 1976; Gustillo, Gruninger & Davis 1987)), a good deal of useful prognostic information is available. But it is only possible to compare like with like, and it is difficult to make meaningful comparisons between patients with different injury patterns.

There have been many attempts to provide a method of defining the time to union of fractures, all with flaws; fracture stiffness (associated with enormous inter-observer variation (Webb *et al*. 1996)), X-ray appearances (for which there may be up to 50% inaccuracy (Hammer, Hammerby & Lindholm 1985)), X-ray scoring (which is still to be validated (Panjabi *et al*. 1985; Lane & Sandhu 1987; Oni *et al*. 1991)), X-ray densitometry (which is expensive, uses large radiation dosages, and has not been validated (Tiedeman *et al*. 1990)), radionuclide scanning (which is invasive, expensive, and useful only for long-bone fractures (Smith *et al*. 1987) (Oni *et al*. 1989)), and serum osteocalcin (Taylor *et al*. 1988), tritiated thymidine uptake (Lau *et al*. 1995) and histology (Urist 1954)(all of which are invasive). Other mechanical investigations including load sharing tests, sound transmission through bone, transfer functions and vibration analysis, are all still to be validated (Andrew & Kay 1994), (Nokes 1999).

In addition to their individual limitations, each of the above measures of fracture healing suffers because the patient cannot be examined every day during the healing process. In the routine assessment of healing, fractures are "united" on the day that they are seen at the clinic, the fracture is pain free and non-mobile, and the X-ray shows progression of healing. As patients are often seen at four, six or even twelve week intervals during later healing, this renders statements such as "*time to union was an average of 13.5 weeks*" of limited value. The aim of treatment of all injuries is to achieve rapid return to normal or maximal function with the minimum of inconvenience to the patient. The major cost to society of trauma is the loss of

economically active young people from the workforce. Time to return to work may, therefore, be one of the most important outcome measures, although it can be partly dependent upon the type of work (MacKenzie *et al*. 1998). It will be affected by the severity of the initial injury, the efficiency of treatment, and the development and treatment of complications such as infection, non-union - and posttraumatic psychopathology.

Functional scoring systems are often used in a haphazard way to describe outcomes. The various scores take account of symptoms and functional restriction, but the weight placed on each is assigned by the orthopaedic surgeon and not by the patient. Many systems use process factors in assessment (non-union, range of motion, infection, and so on), while patient factors (such as pain or ability to carry out activities of daily living) are often given lower priority (Swiontkowski 1995).

1.6.3 Patient Derived Outcomes Measures

There are validated and reproducible outcomes measures available. The Short Form-36 health survey questionnaire (SF-36) concentrates on physical and social functioning, limitations due to physical and emotional problems, well-being and general health perceptions. It produces an overall picture of the patient's physical, functional and emotional recovery. It has been widely validated for a variety of settings (Brazier *et al*. 1992; Garratt *et al*. 1993; Swiontkowski 1995; McCarthy *et al*. 1995).

The Sickness Impact Profile uses a validated 136-item questionnaire, focusing upon physical health, psychosocial health, and independent categories such as sleep, work and recreation. It has been extensively tested for reliability and internal consistency, and has been used in assessment after trauma (Jurkovich *et al*. 1996).

The Musculoskeletal Function Assessment (MFA) is a tool produced specifically for research in orthopaedics and traumatology (Martin *et al*. 1996) (Engelberg *et al*. 1996; Martin *et al*. 1997a). This instrument examines the patient's function in activities of daily living, work and recreation, but also includes assessment of sleep and rest, relationships, cognition and emotional adjustment. It has been tested for validity in the USA, but still has to be validated in the UK.

A review (Gross 1988)of three years of publications in the American edition of the Journal of Bone and Joint Surgery and the Journal of Orthopaedic Trauma revealed 228 papers relating to hip arthroplasty. No two of these used the same outcome measures (Gross 1988), and similar problems bedevil the literature relating to musculoskeletal trauma (Swiontkowski 1995). A great deal of published research utilises outcome measure that do not reflect the overall functioning of the patient, resulting in difficulty in validating results (Gartland 1988). In order to study the effects of PTP on outcome after trauma, it is necessary to identify suitable validated outcome measures. It may be that patient centred outcome measures, such as the SF-36 and the MFA, offer the best available tools for such research.

1.7 ASSESSMENT OF TRAUMA OUTCOME AND THE EFFECT OF PTP

Although it is postulated that PTP affects healing after trauma, through its effects on the hypothalamic-pituitary axis and the metabolic response to trauma, there is no easy way of measuring this objectively. In order to study the effects of PTP on physical recovery after trauma, it is necessary to turn to objective health questionnaires such as the SF-36, MFA and the SIP. Markers of the inflammatory response to physical trauma, such as IL-6, TNF and CRP may offer a way of monitoring the physiological disturbance.

This thesis will address the following hypotheses:

1) That PTP is an important problem in the treatment of patients with common musculoskeletal injuries.

2) That the presence of PTP is associated with impaired physical recovery, as assessed by validated outcome instruments.

3) That biochemical markers, such as IL-6, sIL-6r, TNF and CRP, can be used to monitor the physiological disturbance in the victims of physical trauma with PTP.

2. MATERIALS AND METHODS

2.1 PATIENTS & RECRUITMENT

The patients who took part in this study were recruited from the Orthopaedic Trauma Unit (OTU) of Aberdeen Royal Infirmary between 1st April 1999 and 23rd February 2000. All had sustained musculoskeletal injuries. Patients were eligible for recruitment if they were aged between 16 and 70 years, had had no significant head injury (unconscious for more than 15 minutes) and had no impending legal action associated with the accident (e.g. Drink-Driving prosecution). Patients with low energy falls leading to hip fractures were also excluded.

Patients were identified from those admitted each day to the OTU, excepting weekends and Public Holidays. During the author's leave periods, a research nurse attached to the Unit (Staff Nurse Linda Bowes) undertook recruitment of 16 patients (8%). Suitable patients were approached on the ward once they were well enough to co-operate, generally within 48 hours of admission, but up to 72 hours in the case of those with multiple injuries. A brief explanation of the study detailed the desire to study factors that affected the way that people cope with and recover from injuries, with no direct mention of PTSD or other specific syndromes. Once patients had agreed to take part, they were given an Information Sheet (see Appendix 1), and offered the opportunity to ask any questions. They were then asked to sign a consent form approved by the Joint Ethical Committee (see 2.4.2 below and Appendix 1). Demographic data, and information on the accident and injuries sustained, were collected, and blood samples taken if appropriate (see 2.1.2 below).

Once the project had been introduced, and consent obtained, patients were then given the Patient Assessment forms. These were designed to be self-administered, and consisted of questions requiring the marking of boxes or circling of answers, to ensure that those with upper limb injuries could still complete the forms. A brief explanation of what was required was confined to demonstrating the manner in which the questions should be answered. No specific advice was given on which answer to give. Patients were allowed to complete the questionnaires with the physical assistance of family or friends, but not with the assistance of medical or nursing staff.

2.1.1 GRAMPIAN TRAUMA OUTCOMES STUDY

Patients recruited to the main part of the study (Grampian Trauma Outcomes Study – GTOS) were asked to complete the series of questionnaires soon after their admission (Initial Assessment Documents, see Appendix). They were reviewed again at two and six months (2-Month Assessment Documents and 6-Month Assessment Documents, see Appendix 3) (see 2.4.1 Study Timetable below)

The Initial Assessment Documents contained the General Health Questionnaire (GHQ) and the three patient-derived outcomes measures: the Sickness Impact Factor (SIP), the Musculoskeletal Function Assessment (MFA) and the Short Form-36 (SF-36). The measures were altered slightly to ask how the patient had been before their injury, in order to obtain baseline data. For example, the introduction to SF-36 in the

initial documents was as below:

SHORT FORM 36

We are interested in finding out about your health, feelings and general activities over the four weeks before your injury. For each question, please mark the most appropriate answer.

In the subsequent documents the introduction was restated as follows:

SHORT FORM 36

We are interested in finding out about your health, feelings and general activities over the past four weeks. For each question, please mark the most appropriate answer.

The two and six month documents were identical apart from their front cover, and contained the GHQ, SIP, MFA and SF-36. Each set of documents was accompanied by a short covering letter reminding the patients of their earlier kind help with the study, and requesting them to complete and return the follow-up documents. If patients had a clinic follow-up appointment at two and six months after their injury, I saw them briefly at that appointment and gave the follow-up documents to them, with a stamped envelope for returning the completed forms. The majority of two month documents (153 patients) and a minority of the six-month documents (24 patients) was given to patients in this way, with the remainder being sent by post. If forms were not returned within 2-3 weeks, a further set of the documents was sent along

with a short hand written note politely urging the patient to return the documents.

2.1.2 GRAMPIAN TRAUMA OUTCOMES (METABOLIC MARKERS) STUDY

Patients recruited to the Metabolic Markers arm of the study (GTOS-MM) completed the same documentation as those in the main part of GTOS, i.e. at initial assessment and then again at two and six months after their injury. At each of these assessments, two 10ml blood samples were also taken for plasma and serum. Samples were taken at clinic reviews where possible, and at visits to the patient's home where necessary. In the clinic, samples were stored at 4°C shortly after being drawn, prior to being transferred to the laboratory. When I had taken the samples at the patient's home, the samples were transferred to the laboratory in a cool bag. There the samples were centrifuged at 2500 rpm for 15 minutes before being stored as 750-1000µl aliquots (five each of serum and plasma) in Eppendorf vials at -70°C.

The separated samples remained in cold storage until they were required for analysis (for between one and sixteen months), when they were removed and thawed at room temperature.

2.2 MEASURES

2.2.1 Trauma Scores

2.2.1.1 Injury Severity Score

The Abbreviated Injury Score was first introduced in 1971 as a comprehensive system for rating tissue damage after RTA, and was later updated (Joint Committee on Injury Scaling 1980). The body was divided into seven regions: 1) External; 2) Head and Face; 3) Neck; 4) Thorax; 5) Abdomen/pelvic contents; 6) Spine; 7) Extremities and bony pelvis. For each of these regions a severity code describes individual injury severity: 1) minor; 2) moderate; 3) serious, non-life threatening; 4) severe, life threatening; 5) critical; 6) maximum injury (virtually unsurviveable); 9) unknown. This provided useful information on the severity of individual injuries, but does not describe the patient as a whole. The Injury Severity Score (ISS) was developed in 1974, using the AIS as its basis (Baker *et al*. 1974). The ISS score is produced by adding together the squares of the AIS scores of the three most severely injured areas. A single maximum (unsurviveable – AIS score 6) injury attracts an automatic score of 75 (fatal injury). Scoring charts allow ready classification of injuries and production of the ISS (Greenspan, McLellan & Greig 1985).

2.2.1.2 Revised Trauma Score

The original version of the Trauma Score (TS) was published in 1981 (Champion *et*

al. 1981). This aimed to overcome the purely retrospective scoring nature of the AIS and ISS by providing a score that included physiological data in order to predict survival more accurately. This score was revised in 1989 to overcome the problem that the TS underestimated the severity of head injured patients (Champion *et al*. 1989). The Revised Trauma Score (RTS) takes the Glasgow Coma Score, the systolic blood pressure and the respiratory rate of the injured patient. Coded values give weighted scores, producing a total RTS up to a maximum of 7.841 (Tables 2.1 and 2.2).

GCS	**Sys BP**	**Resp Rate**	**Coded Value**
13-15	>89	10-29	4
9-12	76-89	>29	3
6-8	50-75	6-9	2
4-5	1-49	1-5	1
3	0	0	0

Table 2.1 Revised Trauma Score Coded Values

	Value	**Weighting**	**Value x Weighting**
GCS		0.9368	
Sys BP		0.7326	
Resp Rate		0.2908	_____
		Total	

Table 2.2 Revised Trauma Score Weighted Values and Total Calculation

In order to reduce the potential for errors arising in calculating scores, RTS values were calculated using a trauma score calculator produced by the internet site trauma.org (http://www.trauma.org/scores/trisscalc.html last checked 9 October, 2003).

2.2.1.3 TRISS Methodology

This method of evaluating trauma care outcome arose from a combination of the **TR**auma score and the **I**njury **S**everity **S**core, hence the acronym **TRISS**. By combining both scores, the physiological and anatomical assessment of the severity of injury are brought together, along with a correction for age and type of injury (blunt or penetrating), to produce a probability of survival. This probability is expressed as a percentage, and has been shown to be reliable in predicting trauma survival, and in assessing effectiveness of trauma care provision, particularly in the United States (Boyd, Tolson & Copes 1987). In the UK it is principally a research tool.

As for the RTS, TRISS scoring was undertaken using the trauma.org scoring calculator (http://www.trauma.org/scores/trisscalc.html, last checked 9 October, 2003).

2.2.2 GENERAL HEALTH QUESTIONNAIRE

The scaled version of the General Health Questionnaire (GHQ-28, referred to as GHQ in this thesis) was introduced as a self-administered screening measure to detect

psychiatric disorders in community and non-psychiatric clinical settings (Goldberg & Hillier 1979). It has been widely validated and accepted as a robust measure of such disorders (Goldberg & Williams 1988).

The scaled GHQ is a 28-item questionnaire, with each item having four possible answers, which are scored on a 0-0-1-1 basis *e.g.*

Have you recently					
Al — been feeling perfectly well and in good health?		*Better than usual*	*Same as usual*	*Worse than usual*	*Much worse than usual*
	SCORE	*0*	*0*	*1*	*1*

This scoring system allows the production of a total score and four sub-scales: 1) somatic symptoms; 2) anxiety and insomnia; 3) social dysfunction, and 4) severe depression. The total score further allows a threshold to be applied that defines "caseness" – the situation where an individual is defined as being a "case" with defined psychiatric disturbance. The threshold for this caseness definition is generally taken at the 4/5 level (out of 28), where a score of 5 and above represents caseness. Studies on medical in-patients have shown that a higher threshold may be more appropriate, as they may have higher levels of somatic illness and social dysfunction as a result of their illness (Goldberg & Williams 1988). For this reason, in this study of injured individuals, threshold scores have been taken both at the standard 4/5 level and at a higher 6/7 level.

2.2.3 SHORT FORM-36

The Short Form-36 (SF-36) is a valid, sensitive and reliable measure of change in health status, and was first introduced in 1992 (Ware & Sherbourne 1992; McHorney, Ware & Raczek 1993). It has been validated for use in the North East of Scotland (Garratt *et al*. 1993), and the latest version (SF-36 II) has been further validated in a general UK population (Jenkinson *et al*. 1999). This version was used in the present study, and will be referred to generically as SF-36.

The SF-36 measures health status in a way that is not disease specific, and consists of 36 questions with multiple choice answers *e.g.*

Overall Health

1) In general, would you say that your health is:
Excellent □ Very Good □ Good □ Fair □ Poor □

The questions are grouped to produce eight health scales, in three main categories.

SF-36 scales	**No. of Items**
I Functional Status	
a) Physical functioning	10
b) Social functioning	2
c) Role limitations due to physical problems	4
d) Role limitations due to emotional problems	3
II Wellbeing	
a) Mental health	5
b) Energy and fatigue	4
c) Pain	2
III Overall evaluation of health	
a) General health perception	5
Total	35

Table 2.3 Subscales of the Short Form-36 (The 36th question [asking patients to compare present health with one year ago] does not form part of the eight scales).

Scoring the SF-36 was undertaken using a standard syntax developed for the purpose with the Statistical Package for Social Sciences (SPSS version 9.0, SPSS Inc, Chicago, USA, 1999) by the department of Public Health, University of Aberdeen.

2.2.4 SICKNESS IMPACT PROFILE

The Sickness Impact Profile (SIP) is a behaviour-based health status measure developed in the 1970s and widely used since (Bergner *et al*. 1976; Bergner *et al*. 1981). It consists of 136 statements covering dysfunction in activities associated with daily living. The patient is asked to mark those statements that apply to him/her and are related to their health, *e.g.*

Section A
Please mark only those statements that you are *sure* describe you and are related to your state of health.

1) I spend much of the day lying down in order to rest □

Each item has a weighted score, and these are used to produce 12 category scores, two dimension scores and a total score, all out of a maximum of 100 (maximal dysfunction) (Table 2.4).

Dimension	**Category**
Physical	Ambulation Mobility Body care and movement
Psychosocial	Communication Alertness behaviour Emotional behaviour Social interaction
Independent Categories	Sleep and rest Eating Work Home management Recreation and pastimes

Table 2.4. Categories and Dimensions of the Sickness Impact Profile outcome measure.

Scoring of the SIP and subscales was undertaken using syntax prepared for SPSS by the author.

2.2.5 MUSCUSKELETAL FUNCTION ASSESSMENT

The Musculoskeletal Function Assessment (MFA) was developed with the aim of combining the benefits of disease-specific outcomes measures in musculoskeletal conditions with the robustness of more general patient-derived outcomes measures such as SF-36 and SIP (Martin *et al*. 1996; Engelberg *et al*. 1996). The measure contains 100 items, answered as Yes/No tick boxes, *e.g.*

ACTIVITIES USING YOUR ARMS or LEGS

This first set of questions is about changes or problems you may have using your arms or legs to do such things as reaching, walking, and carrying.

This week, because of your injury	**YES**	**NO**
1. Are you unable to walk?	☐	☐

Each item has a weighted score, with the 100 items producing ten category scores and a total MFA score (Table 2.5).

Category
Mobility
Hand/fine motor
Housework
Self care
Sleep/rest
Leisure/recreation
Family relationships
Cognition/thinking
Emotional adjustment/coping/adaptation
Employment/work

Table 2.5. Musculoskeletal Function Assessment outcome measure categories.

Each category also has a patient-rating question, although this is not incorporated into the final scores, *e.g.*

How much are you bothered by problems you are now having using your arms or legs? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

Scoring of the MFA was undertaken using a standard SPSS syntax provided by the MFA Project team at the University of Washington, Seattle, USA.

All instruments are included in Appendix 3.

2.2.6 DOCUMENT PROCESSING

The information collected for each patient represents approximately 400 data fields, with 320 of these being derived from the self-completed assessment documents. For this reason, grant funding was secured to purchase an optical document scanner and software to process the documents (Canon DR 3020 scanner and Eyes and Hands for Forms version 4.1, Readsoft AB, Sweden).

2.3 METABOLIC MARKERS

2.3.1 C-REACTIVE PROTEIN

The acute phase reactant C-Reactive Protein (CRP) is so called because of its ability to bind the C protein of pneumococci (*Streptococcus pneumoniae*). It is produced by the liver, under stimulation predominantly by Interleukin-1 and Interleukin-6, and acts as an opsonin. Opsonins are special molecules that can be used to increase the phagocytic rate of macrophages. They make the pathogen "tastier" for the macrophage, by coating the microorganism with complement that the macrophage recognizes. The opsonin binds easily to the macrophage, thus enhancing phagocytosis.

CRP levels in serum give a general, non-specific indication of deranged immune homeostasis (Gabay & Kushner 1999). The serum assay is readily available from hospital laboratories, and is used routinely in the management of patients, particularly as a marker of an active inflammatory process. A pilot study, undertaken in Aberdeen, had shown that CRP levels correlated with intrusion and depression scores in patients with established PTSD (Miller *et al*. 2001).

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2.3.2 INTERLEUKIN-6 (IL-6) AND SOLUBLE INTERLEUKIN-6 RECEPTOR (sIL-6r)

The release of IL-6 by a variety of cells has multiple biological effects, in particular

on immune and inflammatory responses. It plays a significant role in the inflammatory response to surgery and trauma, and can be used as a marker of the severity of the insult (Hirano *et al*. 1990). The IL-6 receptor found on cells has two parts: a binding chain protein (80kDa) and a surface-borne signal transducing chain protein (130 kDa), known as gp130. Production of the soluble receptor (sIL-6r) is achieved either by shedding (a process of limited proteolysis of the binding chain protein to produce the 55kDa sIL-6r), or by direct cellular production (Mullberg *et al*. 1999).

The majority of soluble receptors to cytokines act as antagonists, but sIL-6r can bind circulating IL-6 and present it directly to the cell-borne gp130, and thereby act as an agonist (Hibi *et al*. 1990; Schobitz *et al*. 1995). This receptor-IL-6 complex has been shown to be of particular importance in the activation of the inflammatory response in vascular endothelial cells, where the sIL-6r is the limiting signal, rather than the IL-6 (Modur *et al*. 1997). Serum and urine levels of IL-6 and its receptor give an indirect measure of the general inflammatory response to physical trauma and surgical stress (Pearl, Sladen & Rosenthal 1987; Hisano *et al*. 1997; Sutherland & Deehan 2000). They may also reflect the inflammatory response to deranged HPA function in PTP.

IL-6 and sIL-6r assays used a commercially available **E**nzyme-**L**inked **I**mmuno**S**orbant **A**ssay (ELISA) kit (Quantikine, R&D Systems Inc, Minneapolis, MN, USA, distributed in the UK by R&D Systems Europe, Abingdon, Oxon.). ELISA kit processing is standardised, and the kit instructions are included as Appendix 10.

The author, under the guidance of an experienced laboratory technician, performed assays.

2.3.3 TUMOUR NECROSIS FACTOR - α

TNF-α is a 157-amino acid peptide, formed from a 233 amino acid pro-hormone by macrophages. Although initial work on the peptide focused upon its effects upon tumour cells (McCall & Parry 1990), a more accurate descriptive name might be "Tissue Necrosis Factor". It is produced in response to a variety of stimuli, including physical trauma, and is *"perhaps the most prominent mediator of metabolic changes at all levels of organisation – cell, tissue and organism"* (Manogue, van Deventer & Cerami 1991). It initiates the energy substrate mobilisation required to meet the heightened fuel demands associated with immunological, inflammatory and wound-healing activities (McCall & Parry 1990). In addition, it has direct effects upon vascular endothelium and leukocytes, and indirectly triggers a cascade of additional inflammatory mediators. While generally evolved to provide protection to the organism, excessive release may follow certain stimuli and can trigger shock and death.

TNF-α levels have been shown to reflect severity of physical trauma and offer some prediction of multiple organ failure and death (Roumen *et al*. 1993; Nast-Kolb *et al*. 1997; Martin *et al*. 1997b). There is no work on its prediction of function in survivors.

Like those for IL-6 and its receptor, TNF-α assays used a commercially available **E**nzyme-**L**inked **I**mmuno**S**orbant **A**ssay (ELISA) kit (Quantikine, R&D Systems Inc, Minneapolis, MN, USA, distributed in the UK by R&D Systems Europe, Abingdon, Oxon.).

2.4 PROCEDURE

2.4.1 STUDY TIMETABLE

The timetable of study over the period 1st January 1999 to 31st December 2000 was as below:

Timing	**Instruments**	**Method**	**Notes**
Baseline	MFA, SF-36, SIP, GHQ ATSS +/- biochemical markers	Interview + Self completion +/- blood sample	24-72 hours
2 months	MFA, SF-36, SIP, GHQ +/- biochemical markers	Self completion +/- blood sample	
6 months	MFA, SF-36, SIP, GHQ +/- biochemical markers	Self Completion +/- blood sample	
Months	0-3 set up 4-14 recruitment 6-20 follow-up + data analysis 21-24 data analysis and write up		

2.4.2 ETHICAL APPROVAL

Ethical approval was sought from the Joint Ethical Committee of the University of

Aberdeen and Grampian Health Board (now known as the Grampian Regional Ethics Committee). The project (Project No 99/0062) was given provisional approval on 31st March 1999, and full approval was confirmed on 29th April 1999 after minor revisions and clarifications (see Appendix 2).

Patients received one of two Patient Information sheets, and signed one of two consent forms, depending upon whether they were entered to the main study or to the Metabolic Markers sub-study (see Appendix 1). These were developed from standard forms and were approved by the Joint Ethical Committee.

2.5 STATISTICAL ANALYSIS

Analysis of data was under taken using the Statistical Package for Social Sciences (SPSS v9.1, SPSS Inc, Chicago, USA) on a personal computer.

The preliminary exploration of the data revealed that they were mostly non-normally distributed. Non-parametric statistical tests have therefore been used in most cases. Exceptions to this are dealt with as they arise.

Demographic descriptive statistics included assessment of mean, mode, range and standard deviation. Differences between the main group and the metabolic marker subgroup in terms of categorical data (sex, marital status, socioeconomic class *etc*) were studied using the Pearson chi-square test. Differences in the age composition of the two groups were assessed by grouping ages by decade (*ie* <20, 21-30 *etc*) (recode

function SPSS), and then applying the Pearson chi-square test.

Differences between initial GHQ scores and two- and six-month GHQ scores were assessed the Wilcoxon signed ranks test. Differences between initial GHQ caseness and caseness at two and six months were assessed by applying the paired Wilcoxon signed ranks test. Differences between the subscores and total scores at each follow up for each group for SIP, SF-36 and MFA were assessed by the Wilcoxon signed ranks test. Differences between mean values of the metabolic markers at each follow-up point were assessed by the Wilcoxon signed ranks test.

In order to assess their use as predictors of PTP, differences between demographic data for cases and non-cases were assessed using Fisher's exact test. Similarly, the relationship between trauma scores and caseness was examined using the Mann Whitney U test and the relationship between caseness and mechanism of injury using the Pearson Chi square test. Differences in the three outcomes measures (including subscores and total scores) by GHQ caseness were assessed using the Mann Whitney U test. Differences in the mean values of the four metabolic markers by GHQ caseness were assessed using the Mann Whitney U test.

Correlations between the four metabolic markers and the three outcomes measures, and between the metabolic markers and the three trauma scores, were assessed using scatterplots and the Pearson product moment correlation coefficient. This analysis was repeated with the partial correlation analysis, controlling for GHQ caseness.

The significance level was taken as $p<0.05$ for all comparisons.

3. RESULTS

3.1 PATIENTS

3.1.1 GTOS Main Group

Two hundred and twenty seven patients were formally approached to take part in the study, between 12th April 1999 and 21st February 2000. Six patients declined to take part. Twelve patients agreed to take part, but failed to complete the initial questionnaires, and were excluded from the study. A further nine did not fully understand what was being asked of them and their recruitment was not pursued. These difficulties occurred early in the study. Thereafter patients were approached by the investigator and recruited after a discussion to establish their ability to understand what was asked of them. Two hundred patients were recruited to the study, and completed the initial documentation.

The mean age of the patients was 37 years (range 16-68 years), and 136 (68%) were male. Fifty one per cent were married or cohabiting, while 45% were single and 4% separated, divorced or widowed. Table 3.1 summarises the socioeconomic composition of the group. Smokers represented 38% of the group. Alcohol consumption was greater than 20 units per week for 32 subjects (16%), while 4 (2%) admitted use of controlled substances. Seventeen (8.5%) abstained completely from alcohol use.

Socioeconomic Class	No. of Patients (%)
I	24 (12)
II	16 (8)
IIInm	56 (28)
IIIm	24 (12)
IV	50 (25)
V	30 (15)

Table 3.1. Socioeconomic Class of GTOS Main group.

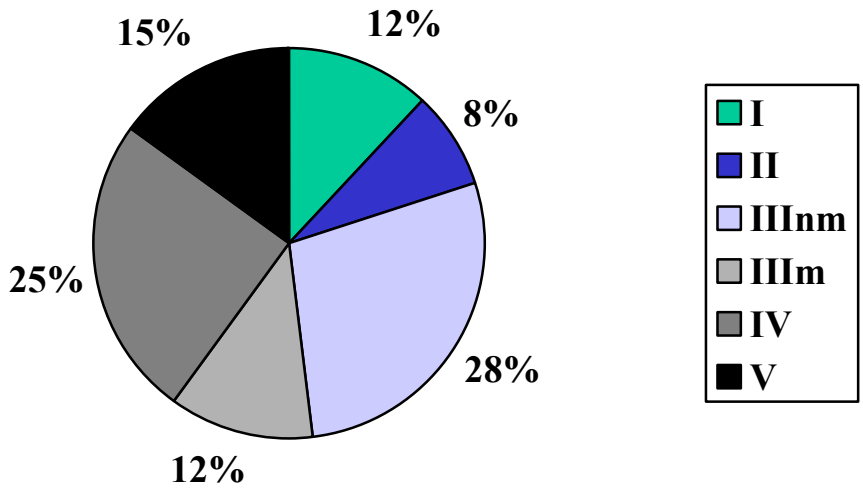


Fig 3.1 Socioeconomic Class of GTOS Main group.

A history of psychiatric problems, including consultation with their GP, was recorded for 12 patients (6%). Medical problems that may adversely affect physical recovery, such as diabetes or chronic steroid use, were recorded for 39 patients (20%).

The patients had sustained injuries by a variety of mechanisms, summarised in Table 3.2.

Mechanism		**No. Patients (%)**
Fall	Total	79 (39)
	low energy	49 (25)
	from Height	30 (15)
Work incl machinery		21 (11)
RTA	Total	67(33)
	Driver	23 (12)
	Passenger	12 (6)
	Motorcycle	17 (9)
	Cyclist	7 (4)
	pedestrian	8 (4)
Sport		26 (13)
Assault		6 (3)
Other		1(1)

Table 3.2 Mechanism of injury for GTOS Main group (RTA=Road Traffic Accident).

Patients had sustained a variety of musculoskeletal injuries, predominantly fractures. Multiple injuries were sustained by 46 (23%), with 11% having three or more injuries. Table 3.3 summarises the regions injured, and indicates that lower limb injuries predominated. Table 3.4 summarises the type of injuries sustained.

Region		**No. of Injuries**
Upper Limb		
	Hand	8
	Wrist	13
	Forearm	16
	Elbow	7
	Upper arm	7
	Shoulder	10
Lower Limb		
	Foot	25
	Ankle	46
	Lower leg	50
	Knee	15
	Thigh	24
	Hip	11
Pelvis		16
Abdomen		5
Chest		10
Neck/Spine		5
Head/Face		24

Table 3.3. Region injured in GTOS Main group (Note that the total exceeds 200, as 23% of cases had two or more injuries).

Type of injury			**No. of Injuries**
Fractures			238
	Closed		210
	Open		
		Grade I	15
		Grade II	7
		Grade IIIa	3
		Grade IIIb	3
Amputation			1
Dislocation			6
Cut/laceration			14
Contusion/haematoma			14
Cut+tendon damage			2
Tendon tear/rupture			9

Table 3.4. Injuries classified by type for GTOS Main group (Note that total exceeds 200, as 23% of cases had two or more injuries).

The mode ISS was 9 (range 4-44), and the distribution of scores (Fig 3.2) show that the majority of injuries were of moderate severity. The mode RTS was 7.84 (range 6.38-7.84), and Fig 3.3 shows that few cases had significant alteration of consciousness or indications of shock. The mode TRISS survival probability was 99.4% (range 92.1-99.8%), indicating that the patients were not severely injured. Fig 3.4 shows that the majority had a survival probability of greater than 99%. Operative treatment was used in 79% of patients.

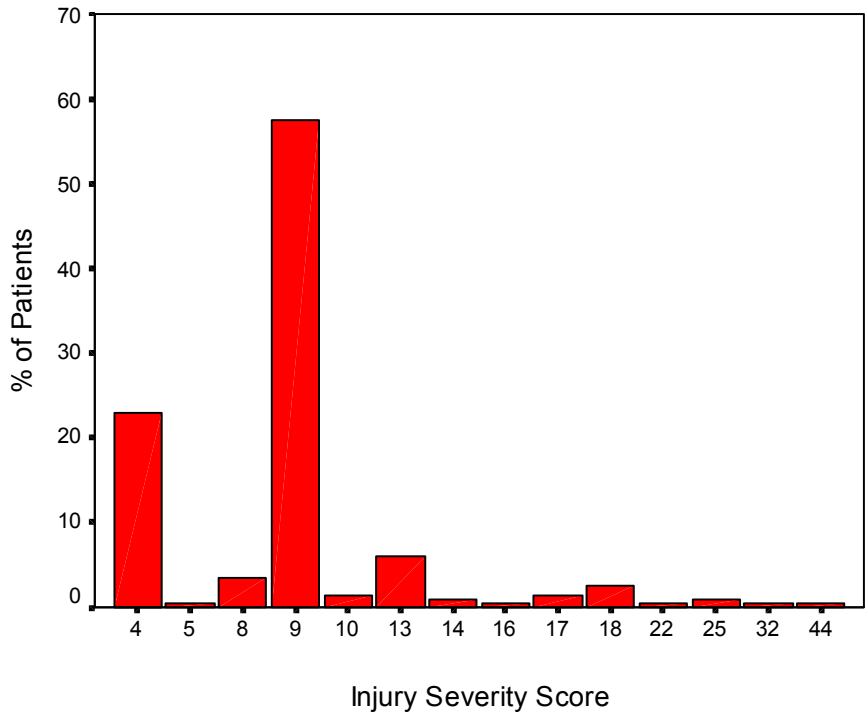


Fig 3.2. Distribution of ISS scores in GTOS Main group.

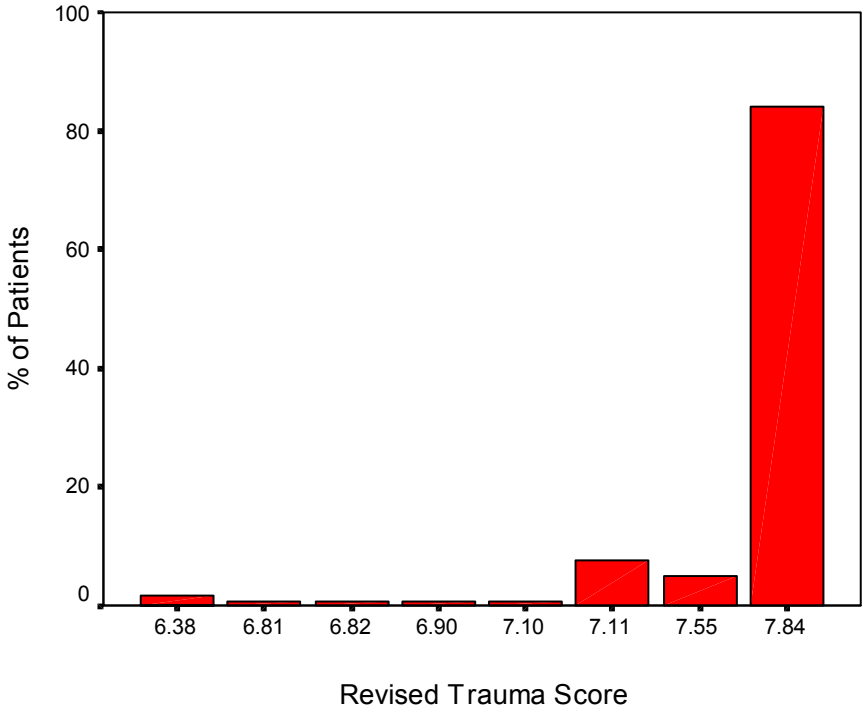


Fig 3.3. Distribution of RTS scores in GTOS Main group.

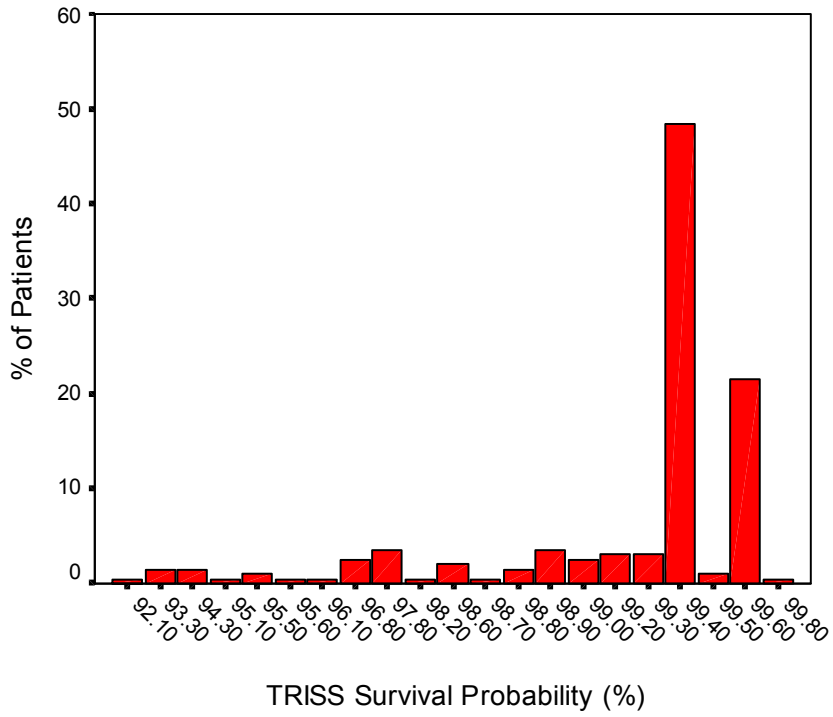


Fig 3.4. Distribution of TRISS Survival Probability scores in GTOS Main group.

3.1.2 GTOS-METABOLIC MARKERS SUBGROUP

Of the 200 patients who entered the GTOS Main group, a subgroup of patients were asked to join the GTOS Metabolic Markers (GTOS-MM) subgroup. All of these patients were part of the GTOS Main group, but also agreed to give blood samples at each follow-up. Patients who lived more than an hour's drive from Aberdeen where not asked to join this subgroup, in order to simplify follow-up for the study. No attempt was made to select patients according to perceptions about their likely progress and recovery. Fifteen patients who were not willing to give blood samples agreed to be entered into the main GTOS group. In all, 84 patients were recruited to the GTOS-MM subgroup and all completed the initial documentation, between 21st June 1999 and 23rd February 2000.

The mean age of the patients was 36 years (range 16-68 years), and 75% were male. Fifty per cent were married or cohabiting, while 45% were single and 5% separated, divorced or widowed. Table 3.5 summarises the socioeconomic composition of the group. Smokers comprised 35% of the group. Alcohol consumption was more than 20 units per week in 14 (17%), while one patient (1.2%) admitted use of controlled substances. Six (7%) abstained completely from alcohol use.

Socioeconomic Class	No. Patients (%)
I	13 (16)
II	9 (11)
IIInm	27 (33)
IIIm	8 (6)
IV	16 (19)
V	11 (13)

Table 3.5 Socioeconomic Class of GTOS Metabolic Markers subgroup. (nm=Non Manual, m=Manual)

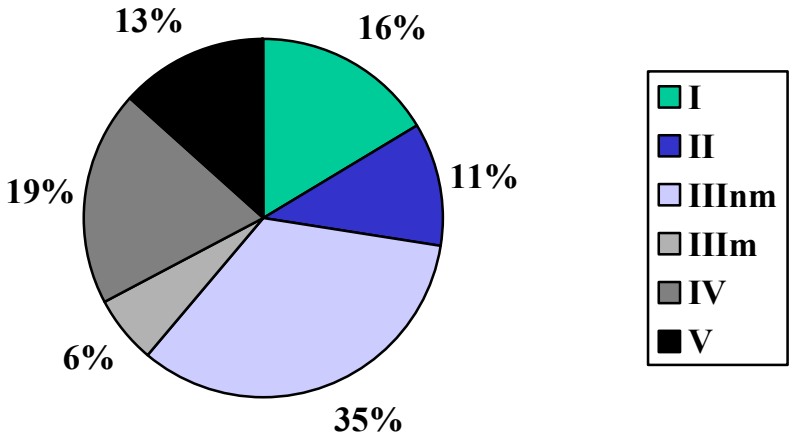


Fig 3.5. Socioeconomic Class of GTOS Metabolic Markers subgroup.

A history of psychiatric problems, including consultation with their general practitioner, was recorded in 8 patients (10%). Medical problems that may adversely affect physical recovery, such as diabetes or chronic steroid use, were recorded in 15 patients (18%).

The patients had sustained injuries by a variety of mechanisms, summarised in Table 3.6.

Mechanism		**No. Patients (%)**
Fall	Total	29 (36)
	low energy	18 (22)
	from Height	11 (14)
Work incl. machinery		8 (10)
RTA	Total	35 (41)
	Driver	12 (14)
	Passenger	7 (8)
	Motorcycle	11 (13)
	Cyclist	2 (2)
	Pedestrian	3 (4)
Sport		11 (14)
Assault		1 (1)

Table 3.6 Mechanism of injury for GTOS Metabolic Markers subgroup (RTA=Road Traffic Accident).

Patients had sustained a variety of musculoskeletal injuries, predominantly fractures. Multiple injuries were sustained by 28 (35.3%), with 16.7% having three or more injuries. Table 3.7 summarises the region injured, and indicates that lower limb injuries predominated. Table 3.8 summarises the type of injuries sustained.

Region		**No. of Injuries**
Upper Limb		
	Hand	3
	Wrist	7
	Forearm	7
	Elbow	3
	Upper arm	7
	Shoulder	5
Lower Limb		
	Foot	13
	Ankle	14
	Lower leg	27
	Knee	10
	Thigh	12
	Hip	6
Pelvis		5
Abdomen		1
Chest		3
Neck/Spine		3
Head/Face		1

Table 3.7 Region injured in GTOS Metabolic Markers subgroup.

Type of injury			**No. of Injuries**
Fractures			108
	Closed		94
	Open		14
		Grade I	6
		Grade II	4
		Grade IIIa	3
		Grade IIIb	1
Amputation			0
Dislocation			4
Cut/laceration			10
Contusion/haematoma			3
Cut+tendon damage			0
Tendon tear/rupture			7

Table 3.8 Injuries classified by type for GTOS Metabolic Markers subgroup.

The modal ISS was 9 (range 4-25), and the distribution of scores (Fig 3.6) shows that the majority of injuries were of moderate severity. The mode RTS was 7.84 (range 6.38-7.84), and Fig 3.7 shows that few cases had experienced significant alteration of consciousness or had displayed indications of shock. The modal TRISS survival probability was 99.40% (range 93.30-99.80%). Fig 3.8 shows that the majority had a survival probability of greater than 99%. Operative management was undertaken in 89% of cases.

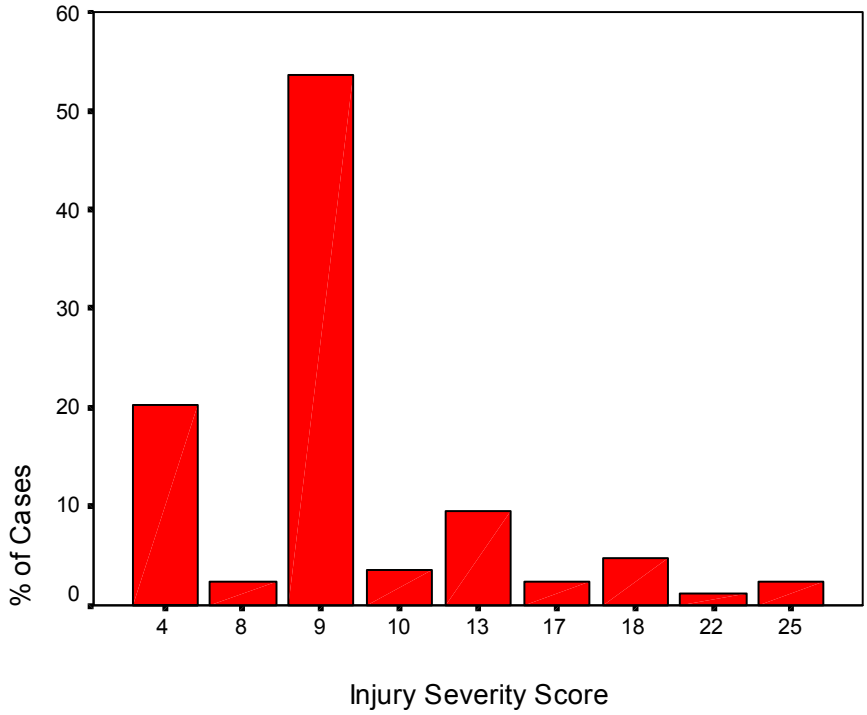


Fig 3.6. Distribution of ISS scores in GTOS-MM subgroup.

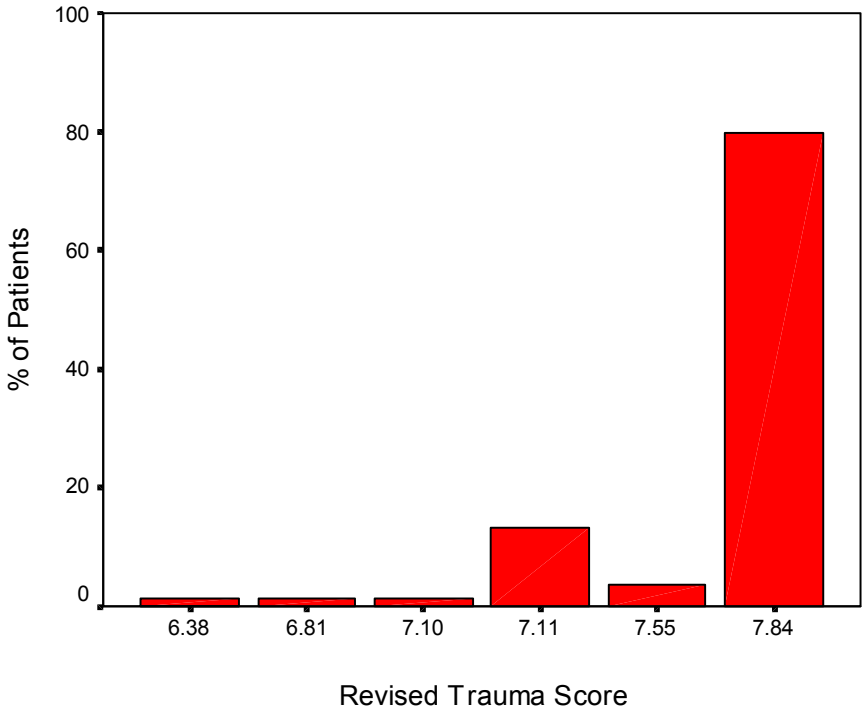


Fig 3.7 Distribution of RTS scores in GTOS-MM subgroup.

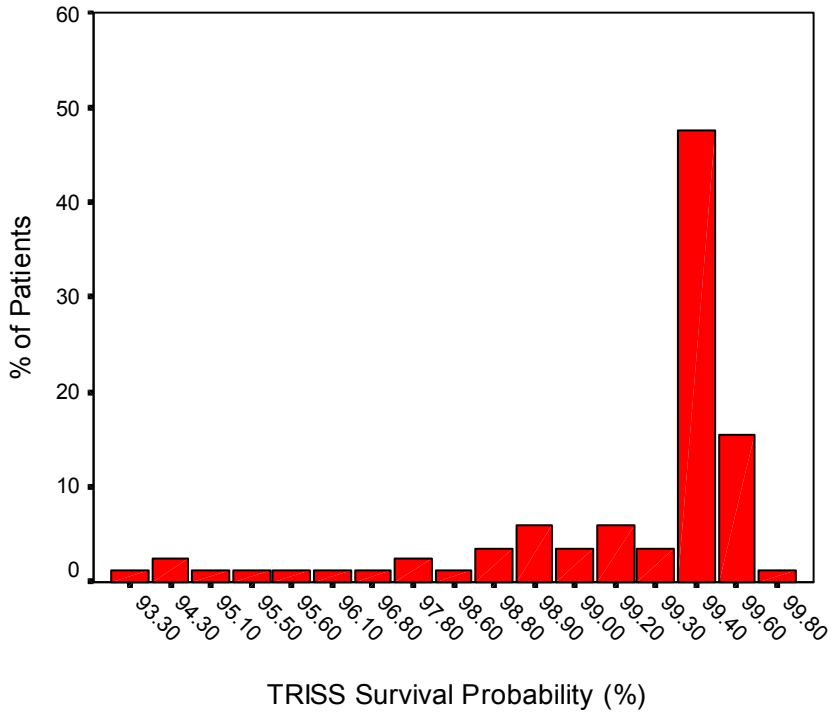


Fig 3.8 Distribution of TRISS Survival Probability scores in GTOS-MM subgroup.

3.1.3 DIFFERENCES BETWEEN METABOLIC MARKERS SUBGROUP AND THE REMAINING GTOS GROUP

In order to ensure that there was no bias in recruiting patients to the GTOS-MM subgroup, statistical analysis of differences between the GTOS-MM patients and the rest of the GTOS Main group was undertaken.

There were no statistically significant differences between the two groups in terms of age (p=0.655), marital status (p=0.966), socioeconomic group (p=0.234), alcohol consumption (p=0.651), cigarette use (p=0.571), narcotic use (p=0.470), medical history (p=0.618), and mechanism of injury (p=0.294) (Pearson chi-square test). The metabolic markers group was more likely to be treated operatively (89% vs. 72%, p=0.007).

The differences between the two groups in terms of sex (more males in GTOS-MM, p=0.071), psychiatric history (more psychiatric history in GTOS-MM, p=0.074), while not statistically significant, showed a trend towards significance.

3.1.4. FOLLOW UP RATES

Two hundred patients were successfully entered into the GTOS main group. Of these, 159 (79%) completed the two month follow up forms, and 149 (75%) completed the six month follow up forms. Seventeen patients (9%) completed 6-month forms after

failing to complete follow up at two months, and 132 patients (66%) completed all three sets of forms.

Of the main group of 200 patients, 83 were entered to the GTOS-MM subgroup. Follow up overall for this subgroup was 68 at two months and 62 at six months (82% and 75% respectively). Eight patients (10%) completed the 6 month follow up after failing to complete follow up at two months, and 41 patients (49%) completed all three sets of forms. For some of this subgroup, however, it was not possible to arrange a meeting to obtain the final blood sample at six months, although patients were willing and able to complete the follow-up forms by post. This involved 13 patients, and means that follow-up with blood samples for the GTOS-MM subgroup was 68 at two months and 49 at six months (82% and 59% respectively)

3.2 MEASURES

3.2.1 General Health Questionnaire

Initial analysis of the results of GHQ scores revealed that the data did not have a normal distribution, thereby requiring the use of non-parametric statistical analysis. Results are presented for the main GTOS group. The results for the GTOS-MM subgroup were broadly similar, and are presented separately as Appendix 4. Analysis includes the GHQ subscores, total scores, and caseness.

Table 3.9 displays the GHQ total scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 28. Statistically significant

differences are noted between GHQ scores at initial and two months, and between scores at initial and six-month assessments. The GHQ subscores at each assessment point are shown in table 3.10. Significant differences are noted between GHQ subscores at initial and two months and between scores at initial and six-month assessments.

	Number	***Mean***	***Median***	***SD***	***Range***
Initial	200	1.34	0.00	2.47	0-14
2 months	158	5.54***	4.00	5.52	0-26
6 months	149	3.18***	0.00	5.38	0-24

Table 3.9 Analysis of GHQ total scores (possible total=28) for GTOS main group (Differences between baseline and follow-up: ***p<0.001; Wilcoxon signed ranks test).

	Initial (n=200)			***2 Mo (n=158)***			***6 Mo (n=149)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
GHQ A ***Somatic***	0.34 (0.97)	0	0-7	1.14*** (1.57)	0	0-6	0.86*** (1.69)	0	0-7
GHQ B ***Anxiety***	0.46 (1.05)	0	0-6	1.07*** (1.76)	0	0-7	0.88** (1.87)	0	0-7
GHQ C ***Social***	0.40 (1.12)	0	0-6	2.90*** (2.22)	3	0-7	1.29*** (1.99)	0	0-7
GHQ D ***Depression***	0.13 (0.59)	0	0-4	2.30*** (1.28)	0	0-7	0.28* (1.04)	0	0-7

Table 3.10. Analysis of GHQ subscores (each possible total =7) for GTOS main group (Differences between baseline and follow-up: *** $p<0.001$, **$p<0.01$, *$p<0.02$; Wilcoxon signed ranks test).

Results for GHQ caseness, at each of the three assessment points, are shown in Table 3.11. Significant differences are noted in caseness between initial and two-month and between initial and six-month follow-up. These are seen in Fig 3.9, which also clearly shows the increase in caseness at two months, followed by a decrease between two and six months, albeit not back to the initial levels.

	No of GHQ cases (%)
Initial	22 (11)
2 months	73 (46)***
6 months	33 (22)***

Table 3.11. Analysis of GHQ Caseness for GTOS main group (Differences between baseline and follow-up: *** p<0.001; Wilcoxon signed ranks test).

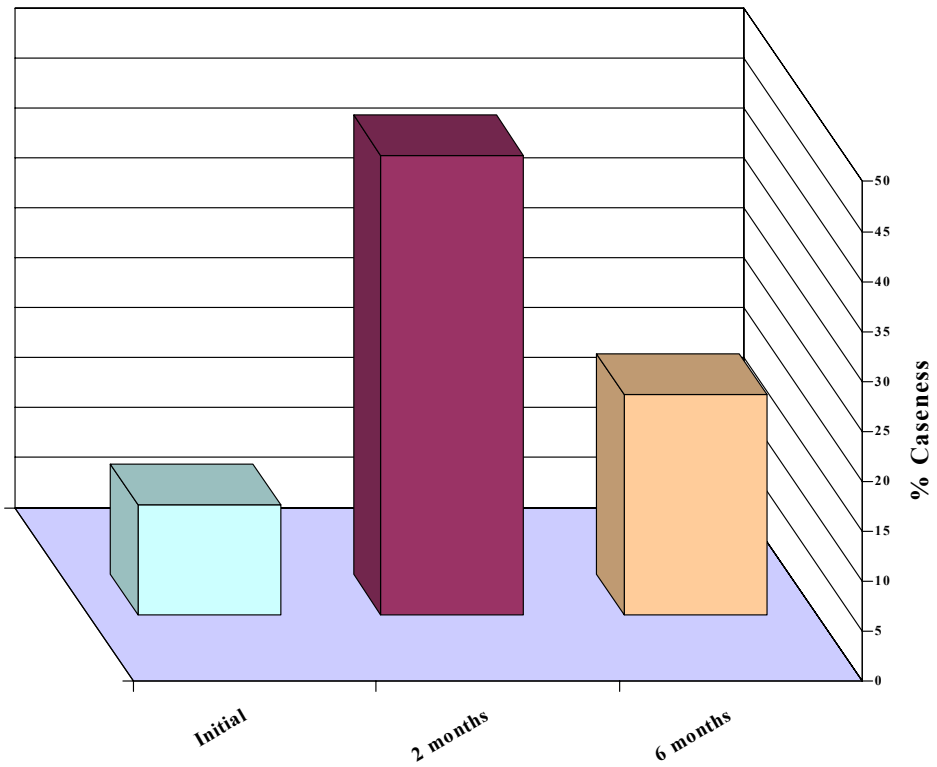


Fig 3.9 GHQ Caseness for GTOS main group

3.2.2 Short Form-36

Initial analysis of the results of the SF-36 scale and total scores revealed that the data were not normally distributed, and therefore statistical analysis was by means of non-parametric tests. Results are presented for the main GTOS group. The results for the GTOS-MM subgroup were broadly similar, and are presented separately as Appendix 5. Analysis includes the SF-36 scale and total scores.

Table 3.12 displays the SF-36 scale scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 100 (maximum function). Statistically significant differences are noted between SF-36 scale and total scores at initial and two months, and between scores at initial and six-month assessments. Fig 3.10 graphically shows the fall in SF-36 scores at two months and their partial recovery by six months.

SF-36 Scale/total scores	***Initial (n=200)***			***2 Mo (n=158)***			***6 Mo (n=149)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Physical Function	95.14 (7.96)	100	85-100	56.36 (30.21)	65.00 ***	0-100	72.86 (25.53)	80.00 ***	0-100
Social Function	94.04 (13.86)	100	37-100	66.80 (28.40)	75.00 ***	0-100	83.59 (22.08)	100 ***	12-100
Limitation – Physical probs.	76.50 (9.75)	80.00	20-80	37.09 (24.80)	35.00 ***	0-80	60.00 (24.10)	70.00 ***	0-80
Limitation-emotional probs	76.65 (9.72)	80.00	13-80	61.49 (25.62)	80.00 ***	0-80	70.88 (17.69)	80.00 ***	13-80
Mental Health	75.71 (9.89)	80.00	25-90	69.92 (13.91)	75.00 ***	25-90	72.35 (12.74)	75.00 ***	35-93
Energy & Fatigue	68.62 (11.95)	70.00	30-90	55.13 (16.78)	55.00 ***	10-85	58.88 (15.68)	60.00 ***	15-90
Pain	92.87 (14.77)	100	22-100	55.17 (24.94)	52.00 ***	0-100	66.73 (24.58)	72.00 ***	12-100
General Health Perception	81.90 (16.66)	87.00	15-100	61.64 (14.55)	62.00 ***	15-97	63.78 (16.94)	62.25 ***	17-100
Change in Health	55.96 (16.35)	50.00	25-100	39.12 (19.99)	50.00 ***	0-100	42.93 (19.92)	50.00 ***	0-100

Table 3.12 Analysis of SF-36 scale and total scores for GTOS Main Group. (Differences between baseline and follow-up: ***p<0.001; Wilcoxon signed ranks test).

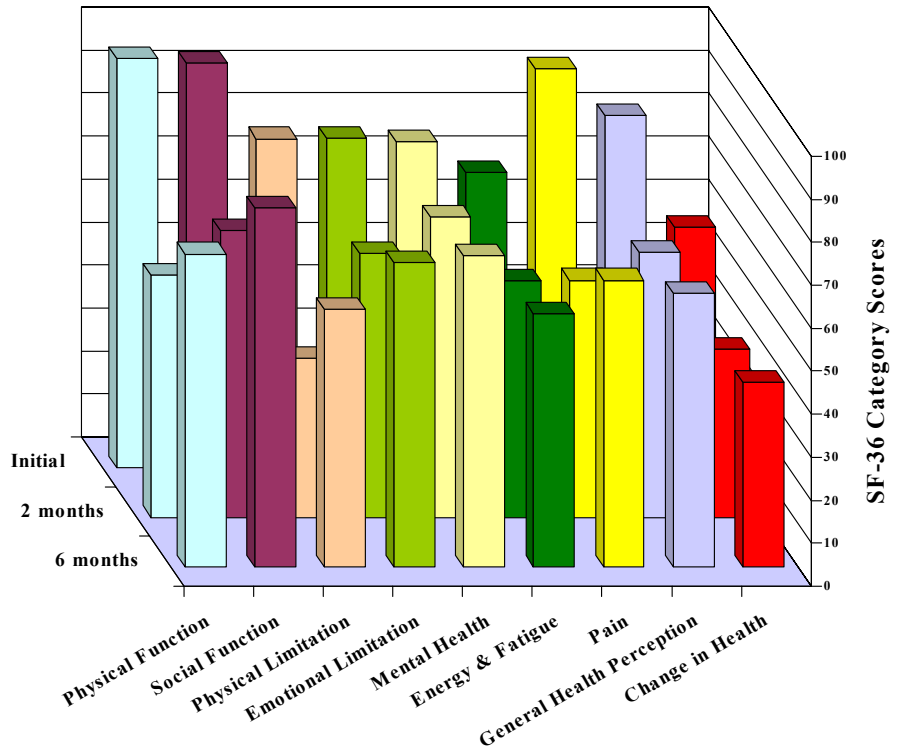


Fig 3.10 SF-36 Scale Scores for GTOS Main Group.

3.2.3 Sickness Impact Profile

Initial analysis of the results of the SIP category, dimension and total scores revealed that the data were not normally distributed, and therefore statistical analysis used non-parametric tests. Results are presented for the GTOS Main group. The results for the GTOS-MM subgroup were broadly similar, and are presented separately as Appendix 6. Analysis includes the SIP category, dimension and total scores.

Table 3.12 displays the SIP category scores, and descriptive statistics, at each of the

three assessment points, from a maximum possible score of 100 (maximum dysfunction). Statistically significant differences are noted between SIP category scores at initial and two months, and between scores at initial and six-month assessments. The SIP dimension and total scores at each assessment point are shown in table 3.13. Significant differences are noted between GHQ subscores at initial and two months and between scores at initial and six-month assessments. Figs 3.11 and 3.12 show the increase in dysfunction at two months and partial recovery by six months.

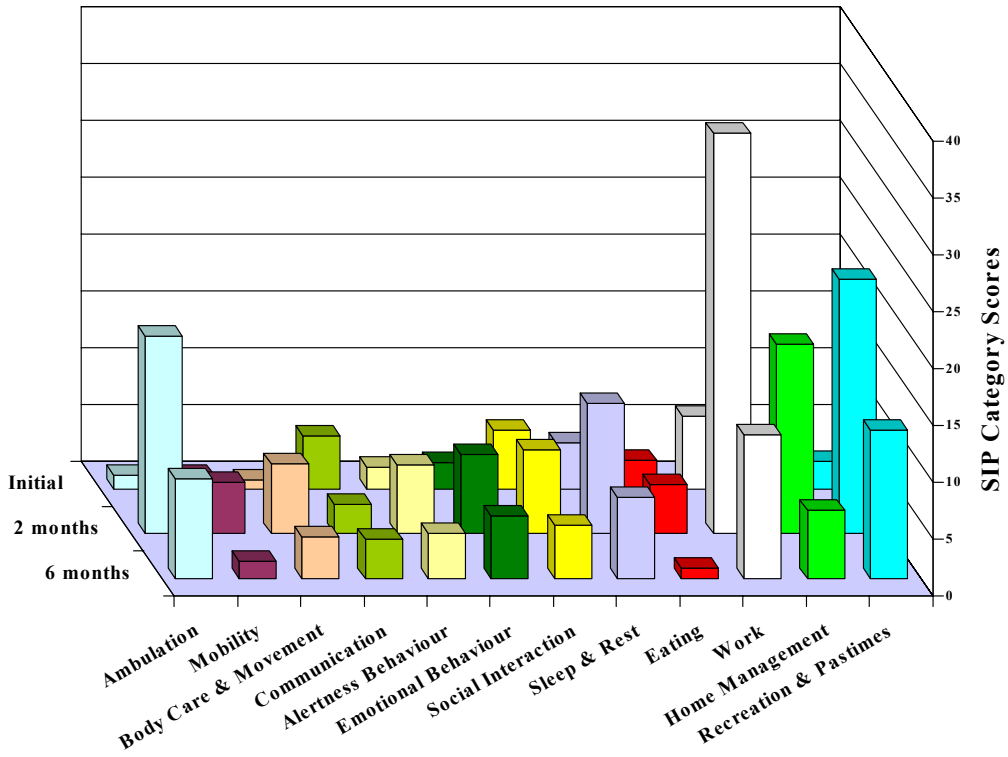


Fig 3.11 SIP Category scores for GTOS Main group.

SIP Category	*Initial (n=200)*			*2 Mo (n=158)*			*6 Mo (n=149)*		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Ambulation	1.14 (5.54)	0	0-47	17.36 (15.81)	16.44 ***	0-68	8.77 (12.61)	0 ***	0-50
Mobility	1.19 (0.92)	0	0-9	4.58 (8.13)	0 ***	0-42	1.55 (5.26)	0 *	0-38
Body Care & Movement	0.73 (2.98)	0	0-32	6.15 (7.56)	3.60 ***	0-35	3.70 (7.95)	0 ***	0-43
Communication	4.68 (9.41)	0	0-66	2.58 (5.99)	0 *	0-30	3.55 (9.19)	0	0-63
Alertness Behaviour	1.85 (7.24)	0	0-52	6.03 (13.73)	0 ***	0-86	3.99 (9.69)	0 **	0-53
Emotional Behaviour	2.28 (7.40)	0	0-59	6.98 (10.19)	0 ***	0-47	5.53 (10.56)	0 ***	0-69
Social Interaction	5.14 (9.42)	0	0-82	7.35 (9.47)	5.52 ***	0-47	4.70 (8.18)	0	0-57
Sleep & Rest	4.05 (7.73)	0	0-38	11.50 (12.76)	9.80 ***	0-57	7.21 (9.21)	0	0-51
Eating	2.53 (8.51)	0	0-98	4.33 (9.67)	0 *	0-77	0.93 (3.85)	0 *	0-28
Work	6.42 (16.02)	0	0-80	35.21 (33.70)	22.23 ***	0-120	12.72 (23.67)	0 **	0-69
Home Management	0.83 (3.62)	0	0-25	16.66 (18.04)	11.92 ***	0-80	6.10 (14.56)	0 ***	0-82
Recreation & Pastimes	2.45 (8.51)	0	0-55	22.39 (19.15	19.32 ***	0-81	13.06 (15.99)	9.00 ***	0-67

Table 3.13 Analysis of SIP category scores for GTOS Main Group.
(Differences between baseline and follow-up: ***p≤0.001, **p<0.01, *p<0.05; Wilcoxon signed ranks test).

SIP Dimension/ Total	***Initial (n=200)***			***2 Mo (n=158)***			***6 Mo (n=149)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Physical	0.70 (2.65)	0	0-29	8.41 (8.44)	5.89 ***	0-36	4.42 (7.53)	1.09 ***	0-38
Psychosocial	3.73 (6.35)	1.80	0-60	5.95 (6.88)	4.09 ***	0-40	4.40 (6.38)	2.21	0-37
Total	2.51 (3.96)	1.50	0-35	9.99 (7.33)	8.91 ***	0-32	5.24 (6.57)	2.87 ***	0-34

Table 3.14 Analysis of SIP Dimension and Total scores for GTOS Main Group. (Differences between baseline and follow-up: ***p<0.001; Wilcoxon signed ranks test).

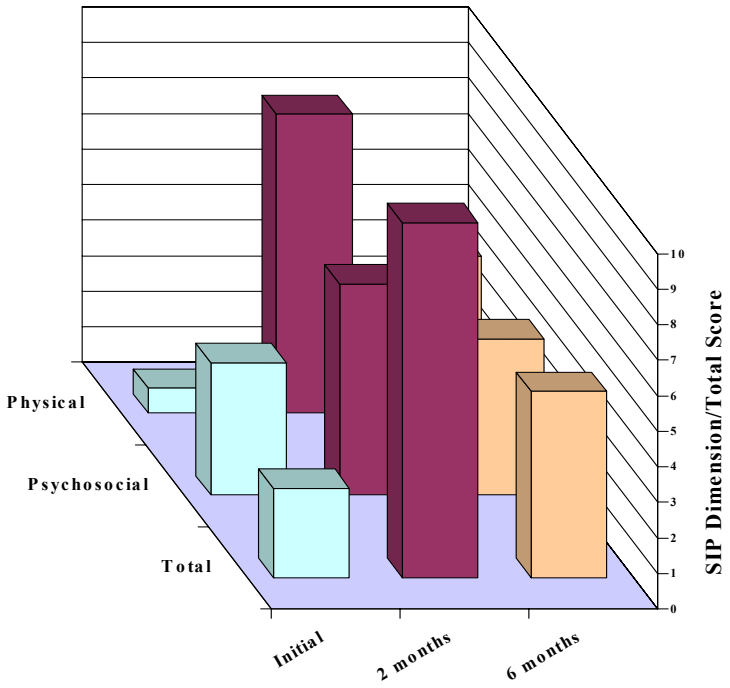


Fig 3.12 SIP dimension and total scores for GTOS Main group

3.2.4 Musculoskeletal Function Assessment

Initial analysis of the results of MFA scores revealed that the data did not have normal distribution, requiring the use of non-parametric statistical analysis. Results are presented for the main GTOS group. The results for the GTOS-MM subgroup were broadly similar, and are presented separately as Appendix 7. Analysis includes the MFA subscores and total scores.

Table 3.15 displays the MFA total scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 100. Statistically significant differences are noted between MFA total scores at initial and two months, and between scores at initial and six-month assessments. The MFA category scores at each assessment point are shown in Table 3.16. Significant differences are noted between MFA category scores at initial and two months and between scores at initial and six-month assessments. These differences are shown graphically in Fig 3.13.

	Number	***Mean***	***Median***	***SD***	***Range***
Initial	200	6.59	3.00	8.33	0-57
2 months	158	30.61	31.00***	15.25	0-60
6 months	149	18.99	15.00***	15.91	0-72

Table 3.15 Analysis of MFA total scores (maximum score=100) for GTOS Main Group. (Differences between baseline and follow-up: ***p<0.001, Wilcoxon signed ranks test).

MFA Category	***Initial (n=200)***			***2 Mo (n=159)***			***6 Mo (n=150)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Mobility	13.68 (20.61)	0	0-65	37.52 (25.11)	40.00 ***	0-95	26.13 (24.18)	20.00 ***	0-85
Hand/Fine Motor	2.56 (11.76)	0	0-100	12.58 (26.28)	0 ***	0-100	5.90 (17.53)	0	0-86
Housework	7.19 (12.52)	0	0-78	18.22 (29.23)	55.55 ***	0-100	20.59 (25.73)	11.11 ***	0-100
Self Care	3.01 (11.33)	0	0-100	14.54 (15.93)	11.11 ***	0-78	5.48 (11.64)	0 **	0-61
Sleep/Rest	17.74 (25.00)	0	0-100	32.08 (30.55)	33.33 ***	0-100	23.22 (30.09)	8.33 *	0-100
Leisure/ Recreation	8.08 (21.21)	0	0-100	71.38 (30.92)	75.00 ***	0-100	45.83 (39.01)	50.00 ***	0-100
Family Relations	7.96 (16.89)	0	0-100	16.98 (22.21)	10.00 ***	0-100	11.20 (18.09)	0 ***	0-80
Cognition/ Thinking	6.97 (18.90)	0	0-100	9.28 (22.07)	0	0-100	9.17 (24.48)	0	0-100
Emotional Adjustment	0 (0)	0	0	33.79 (19.50)	33.33 ***	0-89	25.22 (21.12)	22.22 ***	0-83
Employment /Work	0.50 (7.05)	0	0-100	58.49 (46.37)	100.00 ***	0-100	31.33 (41.18)	0	0-100

Table 3.16 Analysis of MFA category scores (maximum score=100) for GTOS Main Group (Differences between baseline and follow-up: ***p≤0.001, **p<0.01, *p<0.05; Wilcoxon signed ranks test).

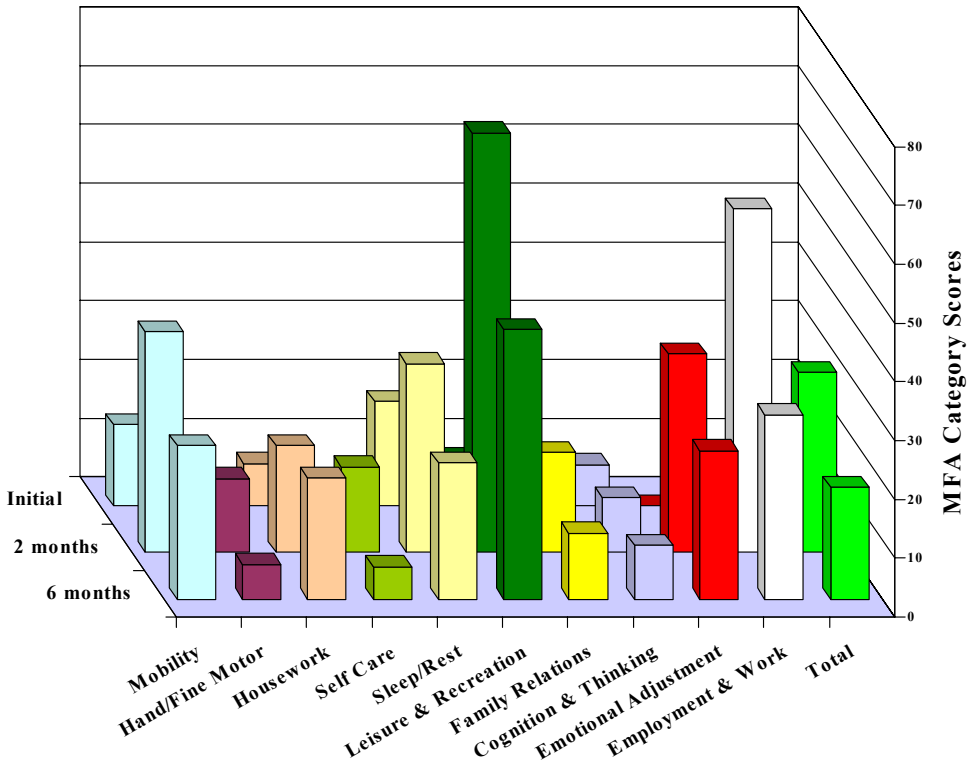


Fig 3.13 MFA category and total scores for GTOS Main group.

3.3 METABOLIC MARKERS

Analysis of the assay results for the four metabolic markers studied is summarised in Table 3.17. Significant differences are noted between the initial mean values and the two-month mean values for each marker. Values for CRP and IL-6 were not normally distributed, and therefore the values were compared using the Wilcoxon signed ranks test, while the normally distributed sIL-6r and TNF-α values were compared using the paired t-test.

Metabolic Markers	***Initial (n=83)***			***2 Mo (n=66)***			***6 Mo (n=62)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
CRP ($mg.l^{-1}$)	44 (49.81)	27.10	0-251.20	0.59 (3.49)	0 $^{+++}$	0-24.90	2.41 (16.86)	0 $^{+++}$	0-118
IL-6 ($pg.ml^{-1}$)	83.75 (386.22)	25.19	0-3393.08	201.08 (544.82)	2.37 $^{+++}$	10-2496	10.24 (39.74)	0	0-266.68
sIL-6r ($pg.ml^{-1}$)	36361 (8418)	37420	14587-66958	41710** (11524)	40622	14146 73176	35045 (9649)	34586	21337-83084
TNF -α ($pg.ml^{-1}$)	27.37 (95.28)	0	0-754.01	284.04*** (375.50)	55.37	0-1562.9	22.32 (124.91)	2.64	0-868.95

Table 3.17 Analysis of Metabolic Markers for GTOS-MM Subgroup
(Differences between baseline and follow-up: ***p<0.001, **p<0.01; paired t-test. $^{+++}$p<0.001; Wilcoxon signed ranks test).

The mean values (+1 standard deviation) for each separate marker are shown in Figures 3.14-3.17. At the initial assessment, all patients had detectable CRP levels. At the subsequent assessments, most patients had non-detectable levels, taken as zero for analysis. Mean values of the other markers all rose by the two-month follow-up, before falling towards initial levels by the time of the six-month follow-up. There was wide variation in the values of each metabolic marker at each assessment, as demonstrated by the wide SD bars on figs 3.14-3.17.

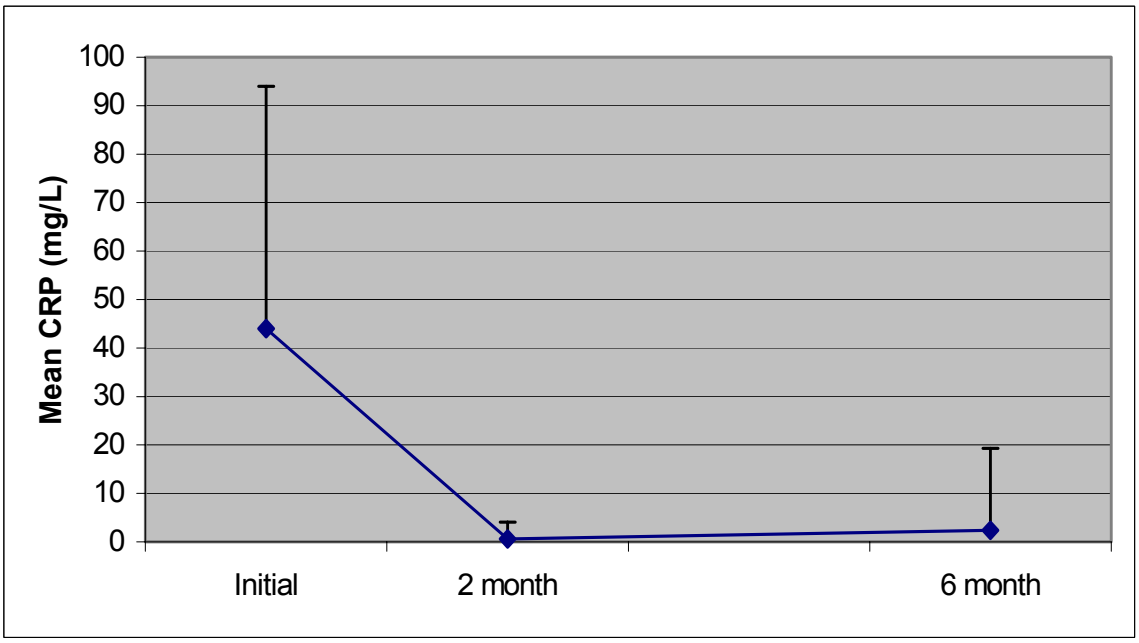


Fig 3.14 Mean CRP values (+ 1 SD) for GTOS-MM subgroup.

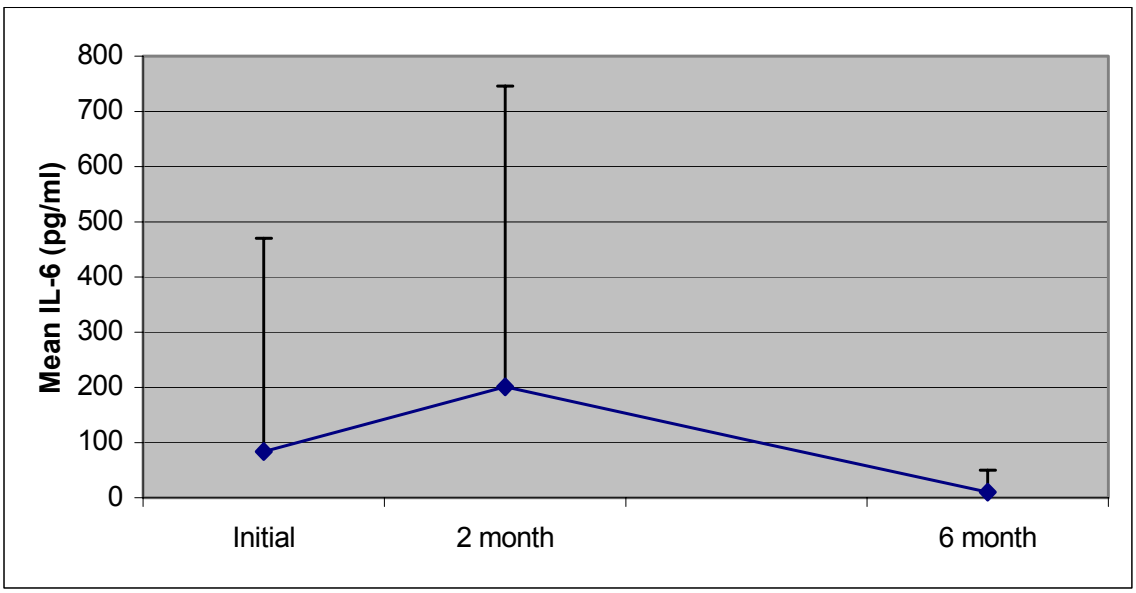


Fig 3.13 Mean IL-6 values (+ 1 SD) for GTOS-MM Subgroup.

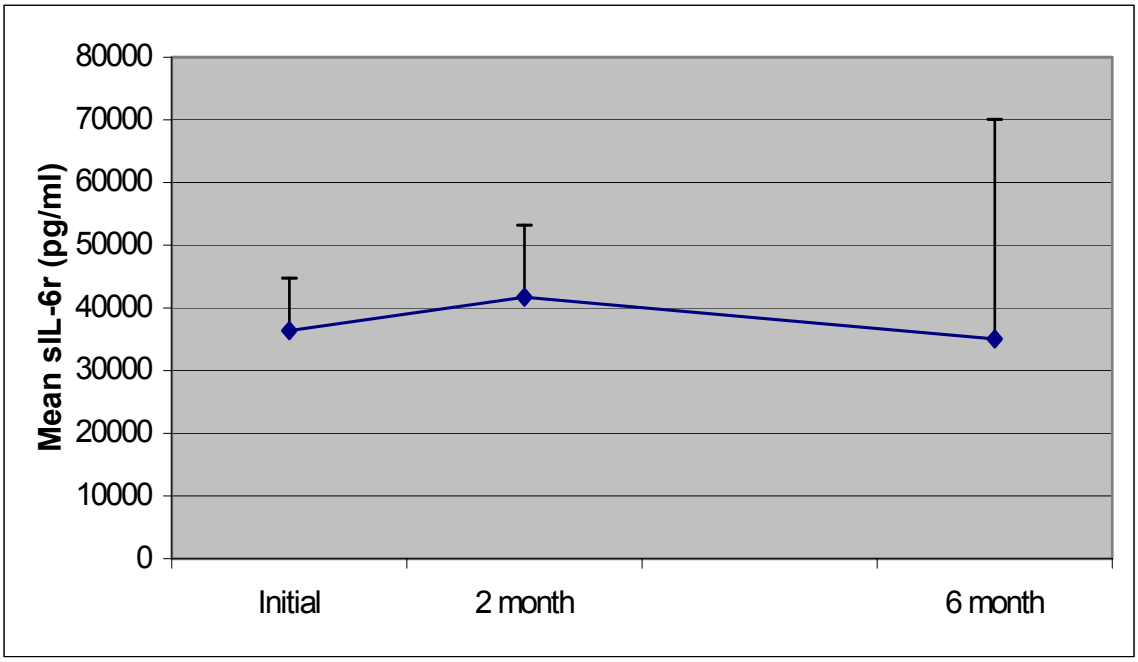


Fig 3.14 Mean sIL-6r levels for GTOS-MM Subgroup.

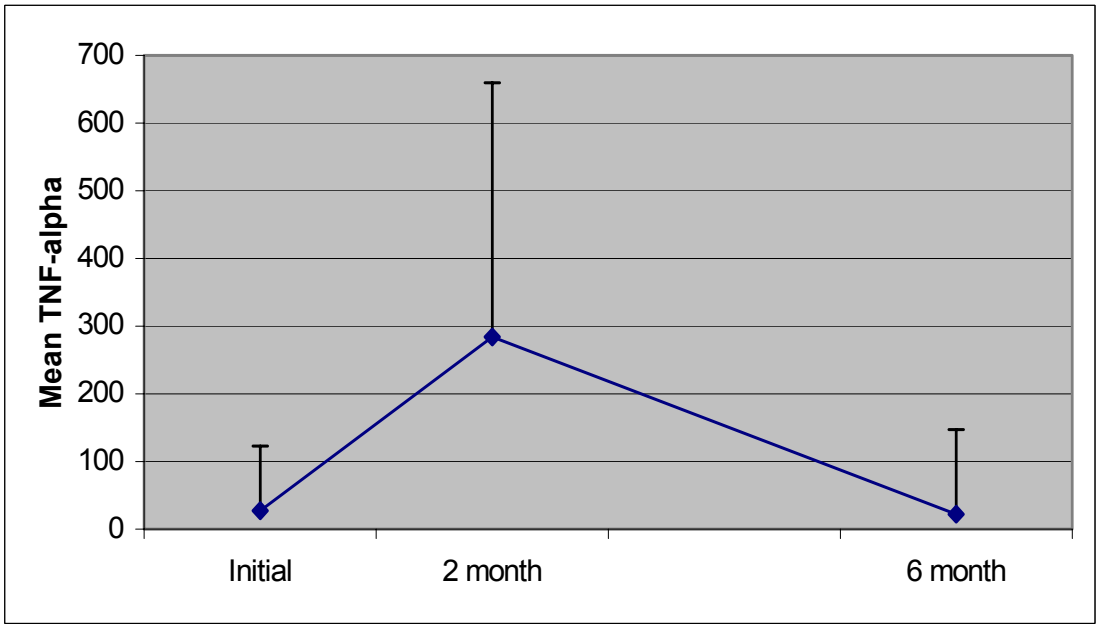


Fig 3.15 Mean TNF-α levels for GTOS-MM Subgroup.

3.4 ASSOCIATIONS

This section examines the statistical relationship between GHQ caseness and the demographic data, trauma scores, outcomes measures and metabolic markers. The differences between cases and non-cases for each are analysed and presented in turn.

3.4.1 GHQ Caseness *vs* Demographics

The results for analysis of the differences in demographic data for cases and non-cases are presented here for the main group. This analysis allows assessment of whether demographic data in any way predict psychological outcome after injury. The results for the GTOS-MM subgroup were broadly similar, and are presented as Appendix 8.

At the initial assessment, 22 patients (11%) had GHQ scores above the 4/5 threshold ("cases"). At the two-month assessment, 73 patients (46%) were cases, and at the six-month assessment, 33 patients (22%) were cases. There were no differences between cases and non-cases for the principal demographic information: age, sex, socioeconomic group, marital status, past medical history, past psychiatric history, smoking or alcohol use at each follow-up point. At the initial assessment, there was a significant association between caseness and previous or present use of narcotics ($p=0.042$) (Fisher's exact test). This involved two patients, and so must be interpreted with care.

3.4.2 GHQ Caseness *vs* Type of Injury and Trauma Scores

The differences in injury type and severity data for cases and non-cases are presented here for the main group. This analysis allows assessment of whether type of injury, or injury severity, in any way predicts psychological outcome. The results for the GTOS-MM subgroup were broadly similar, and are presented as Appendix 9.

Table 3.18 demonstrates the trauma scores for cases and non-cases at each of the three assessments, for the main GTOS group.

		ISS			**RTS**			**TRISS**		
		Mean (SD)	Median	Range	Mean (SD)	Median	Range	Mean (SD)	Median	Range
GHQ Initial	Non-case	9.09 (4.95)	9.00	4-44	7.73 (0.29)	7.84	6.38-7.84	98.95 (1.30)	99.40	92.10-99.80
	Case	8.23 (2.62)	9.00	4-13	7.72 (0.26)	7.84	7.11-7.84	98.97 (1.35)	99.40	94.30-99.60
GHQ 2 month	Non-case	8.82 (5.33)	9.00	4-44	7.76 (0.26)	7.84	6.38-7.84	98.94 (1.29)	99.40	94.30-99.60
	Case	10.01 (4.40)	9.00 **	4-32	7.73 (0.27)	7.84	6.38-7.84	98.93 (1.31)	99.40	92.10-99.60
GHQ 6 month	Non-case	8.87 (4.66)	9.00	4-44	7.74 (0.29)	7.84	6.38-7.84	98.92 (1.36)	99.40	93.30-99.60
	Case	10.79 (5.22)	9.00 *	4-32	7.62 (0.33)	7.84 **	6.82-7.84	98.63 (1.50)	99.40 *	92.10-99.60

Table 3.18 Trauma score analysis for cases and non-cases for GTOS Main Group. (Differences between baseline and follow-up: ** $p<0.01$, * $p<0.05$; Mann Whitney U Test).

Mechanism of injury, ISS, RTS and TRISS were not significantly different between

cases and non-cases at initial assessment. Mechanism of injury, RTS and TRISS TRISS were not significantly different between cases and non-cases at two months. ISS score was higher for cases (p=0.003) (Mann-Whitney U test).

At six months cases had a higher ISS (p=0.01) and a lower (*ie* worse) TRISS survival score, (p=0.016). Cases also had a lower, less favourable, RTS score (p=0.002) (Mann-Whitney U test). The victims of RTAs and falls from height were more likely, and victims of sports accidents less likely than expected to be cases (p=0.009) (Pearson's chi square test).

3.4.3 GHQ Caseness vs Outcomes Measures

The differences in outcomes measures between cases and non-cases are presented here for the main group. This analysis allows assessment of there is a relationship between psychological outcome, as measured by GHQ, and physical and psychosocial outcome. The results for the GTOS-MM subgroup were broadly similar, and are presented as Appendix 10.

Tables 3.19-3.21 and Figs 3.19-3.27 summarise the analysis of subscores and total scores of each of the three outcomes measures compared with for the main GTOS group. At two and six month follow-ups, there are strong associations between psychological and physical dysfunction.

SF-36 Scale/total scores	***Initial (n=200)*** **GHQ**		***2 months (n=158)*** **GHQ**		***6 months (n=149)*** **GHQ**	
	Non-case Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)
Physical Function	94.95 (15.78)	96.59 (6.62)	69.25 (27.73)	41.54*** (25.98)	79.09 (21.42)	53.42*** (26.79)
Social Function	95.01 (12.84)	86.93 ** (19.09)	78.12 (23.27)	53.76*** (28.40)	90.49 (16.64)	61.74*** (22.08)
Limitation – Physical probs.	77.35 (8.08)	69.54*** (17.11)	46.012 (24.90)	26.83*** (20.45)	66.50 (19.81)	39.24*** (24.56)
Limitation-emotional probs	77.28 (8.84)	71.52*** (14.43)	66.44 (26.49)	55.79** (27.87)	75.01 (12.26)	57.86*** (24.49)
Mental Health	76.56 (9.66)	69.54*** (9.87)	74.20 (11.93)	65.07*** (14.47)	75.56 (9.99)	62.32*** (14.78)
Energy & Fatigue	69.94 (11.29)	58.64*** (12.83)	61.57 (15.68)	47.80*** (14.95)	63.16 (12.86)	44.84*** (16.22)
Pain	93.59 (14.29)	87.77 (17.59)	63.36 (22.61)	44.60*** (23.39)	71.71 (22.75)	51.33*** (22.79)
General Health Perception	83.19 (16.18)	71.09*** (17.43)	64.96 (13.25)	57.83*** (15.11)	66.57 (16.57)	54.73*** (15.02)
Change in Health	55.63 (15.74)	59.09 (21.19)	47.56 (13.95)	29.51*** (21.53)	48.20 (16.06)	26.51*** (21.59)

Table 3.19 Analysis of initial SF-36 scores against GHQ Caseness for GTOS Main Group (Differences between cases and non-cases: *** $p<0.001$, ** $p<0.01$; Mann Whitney U Test).

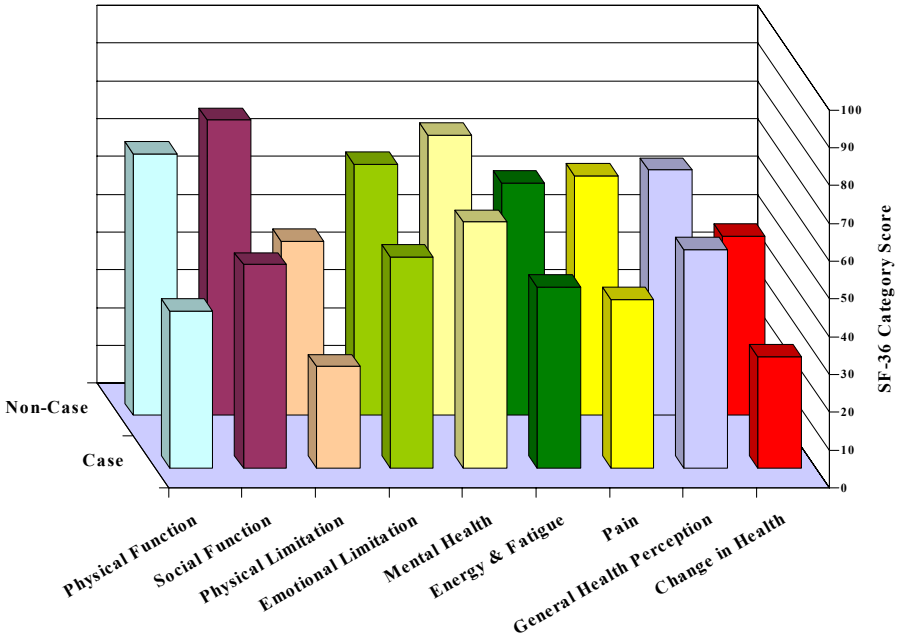


Fig 3.19 Analysis of initial SF-36 scores against GHQ Caseness for GTOS Main Group.

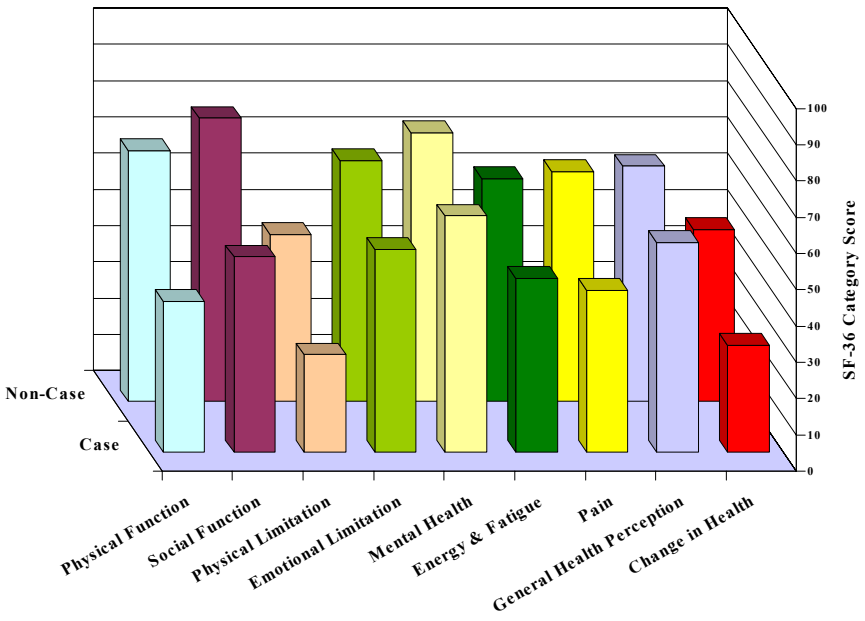


Fig 3.20 Analysis of 2 month SF-36 scores against GHQ Caseness for GTOS Main Group.

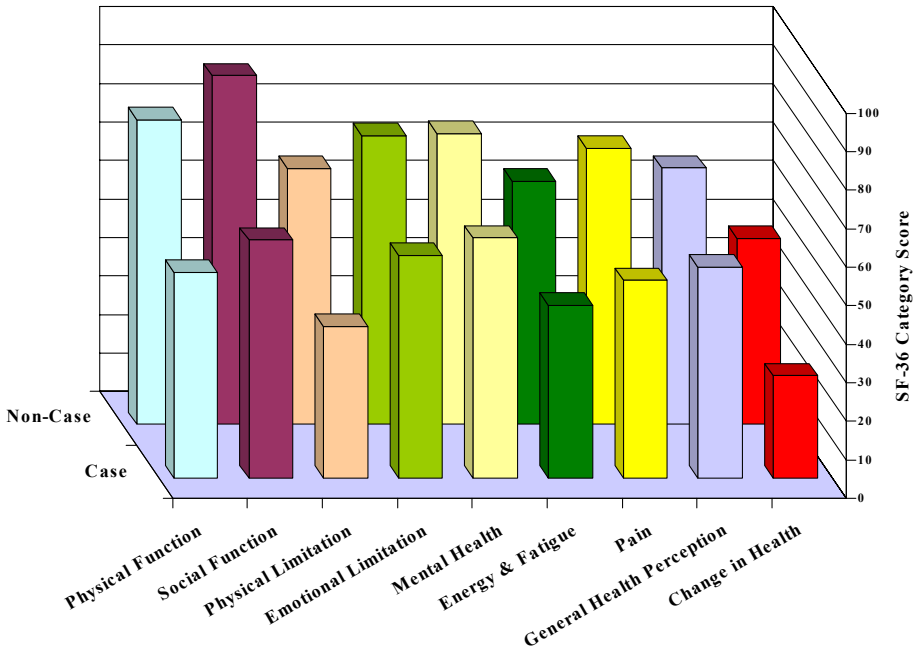


Fig 3.21 Analysis of 6-month SF-36 scores against GHQ Caseness for GTOS Main Group.

SIP Category	*Initial (n=200)* GHQ		*2 months (n=158)* GHQ		*6 months (n=149)* GHQ	
	Non-case Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)
Ambulation	1.28 (5.89)	0.19 (0.89)	12.46 (14.98)	23.05 * (14.90)	6.27 (10.75)	16.46 *** (14.08)
Mobility	0.05 (0.69)	0.42 (1.97)	3.09 (7.39)	6.33 * (8.63)	0.83 (4.76)	3.58 *** (5.77)
Body Care & Movement	0.59 (2.86)	1.97 ** (3.77)	3.31 (5.87)	9.45 * (8.04)	1.84 (4.58)	9.23 *** (11.92)
Communication	4.85 (9.78)	3.83 (6.30)	2.13 (5.65)	3.09 (6.35)	2.48 (6.58)	7.42 ** (14.76)
Alertness Behaviour	1.49 (6.57)	4.91 * (11.22)	4.43 (11.01)	7.89 (16.23)	1.39 (5.95)	12.91 *** (14.23)
Emotional Behaviour	1.84 (7.04)	5.07 ** (8.91)	3.02 (6.18)	11.59 * (11.91)	2.87 (6.66)	12.99 *** (12.31)
Social Interaction	4.50 (9.22)	9.83** (9.75)	3.64 (5.63)	11.66 * (11.11)	2.71 (4.81)	10.08 *** (9.89)
Sleep & Rest	3.80 (7.13)	8.02 ** (8.65)	7.25 (10.92)	17.86 * (13.41)	5.53 (7.63)	13.19 *** (11.56)
Eating	2.39 (8.74)	3.89 (6.78)	4.40 (10.84)	4.25 (8.17)	0.35 (2.52)	2.99 *** (6.38)
Work	5.77 (15.18)	11.52 (21.81)	25.89 (32.64)	46.06 * (31.81)	8.68 (20.50)	27.32 *** (28.53)
Home Management	0.68 (3.29)	2.11* (5.70)	11.00 (17.52)	23.25 * (16.42)	3.68 (11.83)	12.81 *** (17.50)
Recreation & Pastimes	2.33 (7.92)	3.02 (6.81)	16.58 (16.91)	29.16 * (19.50)	9.93 (14.65)	22.72 *** (15.04)
Physical Dimension	0.64 (2.71)	1.23 (2.27)	5.38 (7.46)	11.94 * (8.18)	2.66 (5.09)	9.73 *** (10.15)
Psychosocial Dimension	3.36 (6.26)	6.57** (6.49)	3.33 (4.23)	9.01 * (8.05)	2.37 (3.21)	10.53 *** (8.06)
Total SIP	2.27 (3.85)	4.41 ** (4.50)	6.60 (6.10)	13.94 * (6.67)	3.24 (4.27)	11.45 *** (7.46)

Table 3.20 Analysis of initial SIP Caseness against GHQ Scores for GTOS Main Group (Differences between cases and non-cases: *** p≤0.001, ** p<0.01; Mann Whitney U Test).

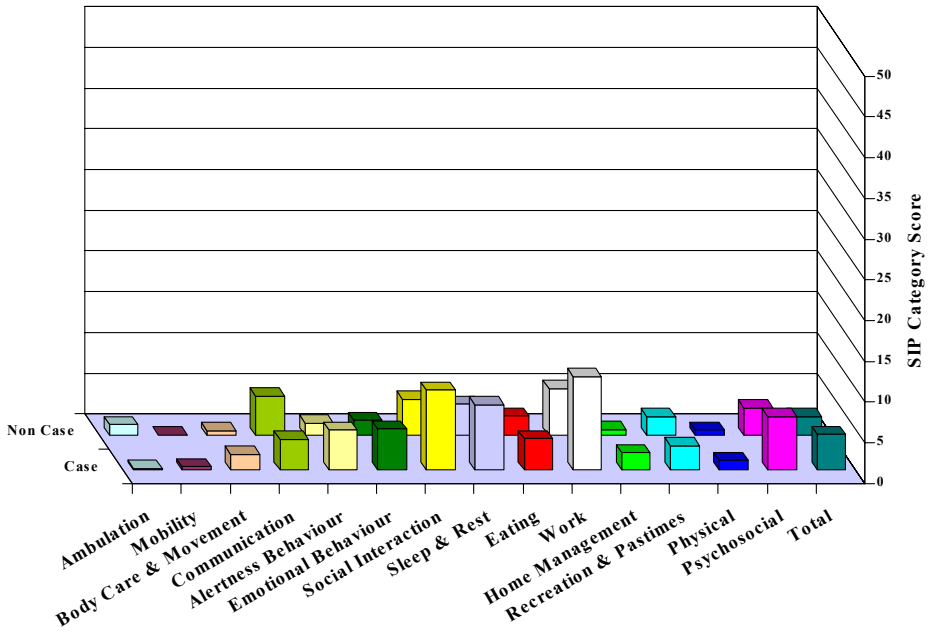


Fig 3.22 Analysis of initial SIP scores against GHQ Caseness for GTOS Main Group.

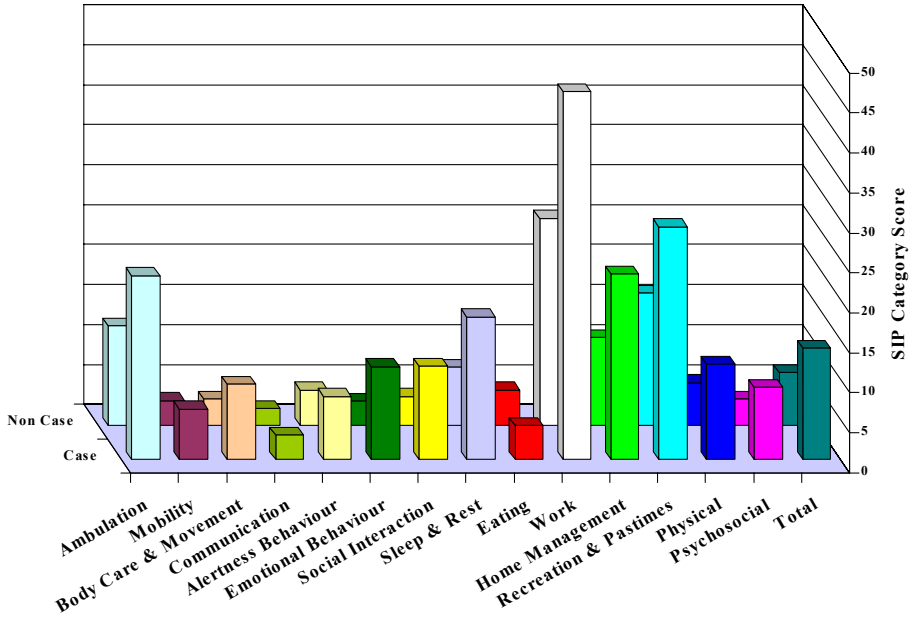


Fig 3.23 Analysis of 2-month SIP scores against GHQ Caseness for GTOS Main Group.

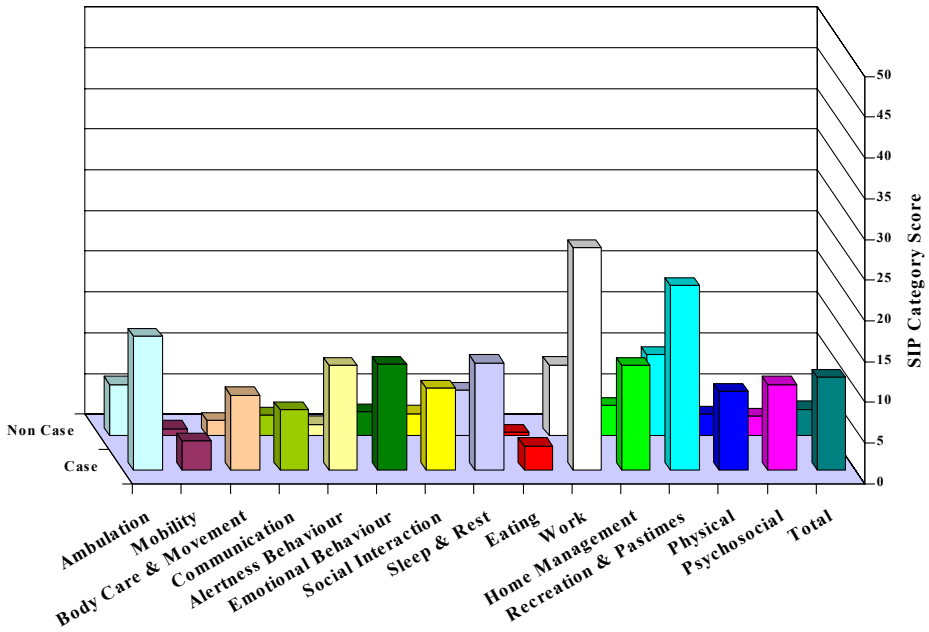


Fig 3.24 Analysis of 6-month SIP scores against GHQ Caseness for GTOS Main Group.

MFA Category	*Initial (n=200)* GHQ		*2 months (n=158)* GHQ		*6 months (n=149)* GHQ	
	Non-case	**Case**	**Non-case**	**Case**	**Non-case**	**Case**
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Mobility	12.24	23.18 *	27.35	49.73 ***	21.08	42.12 ***
	(19.92)	(23.38)	(23.55)	(21.29)	(22.73)	(20.00)
Hand/Fine	2.26	5.19	10.59	14.87	5.17	8.66
Motor	(11.06)	(16.81)	(24.06)	(28.81)	(16.68)	(20.50)
Housework	6.78	10.61	35.56	62.71 ***	15.90	35.02 ***
	(12.08)	(15.89)	(30.52)	(19.54)	(23.09)	(26.95)
Self Care	3.08	2.78	10.13	19.71 ***	3.40	11.61 ***
	(11.87)	(6.36)	(14.98)	(15.66)	(9.20)	(14.98)
Sleep/Rest	15.91	31.82 **	16.27	50.68 ***	17.24	42.43 ***
	(24.35)	(27.17)	(23.98)	(26.99)	(24.47)	(37.98)
Leisure/	7.63	10.23	60.00	84.93 ***	37.93	71.97 ***
Recreation	(21.11)	(21.35)	(32.09)	(23.47)	(37.66)	(31.10)
Family	6.72	18.63 **	9.29	26.16 ***	6.72	24.85 ***
Relations	(15.43)	(24.16)	(18.24)	(23.13)	(11.33)	(25.51)
Cognition/	4.94	22.73 **	4.71	14.38 ***	3.23	29.55 ***
Thinking	(14.61)	(36.11)	(19.09)	(24.26)	(16.33)	(35.61)
Emotional	0	0	24.44	44.82 ***	20.02	42.26 ***
Adjustment	(0)	(0)	(17.49)	(15.78)	(18.63)	(21.38)
Employment/	0.56	0	48.23	71.23 **	20.26	68.18 ***
Work	(7.52)	(0)	(48.30)	(40.75)	(35.34)	(37.64)
Total	5.93	11.54 ***	22.06	40.73 ***	14.39	33.70 ***
MFA	98.22)	(7.90)	(13.14)	(10.84)	(12.26)	(16.35)

Table 3.21 Analysis of initial MFA scores against GHQ Caseness for GTOS Main Group (Differences between cases and non-cases: *** $p \leq 0.001$, ** $p < 0.01$, *$p < 0.05$; Mann Whitney U Test).

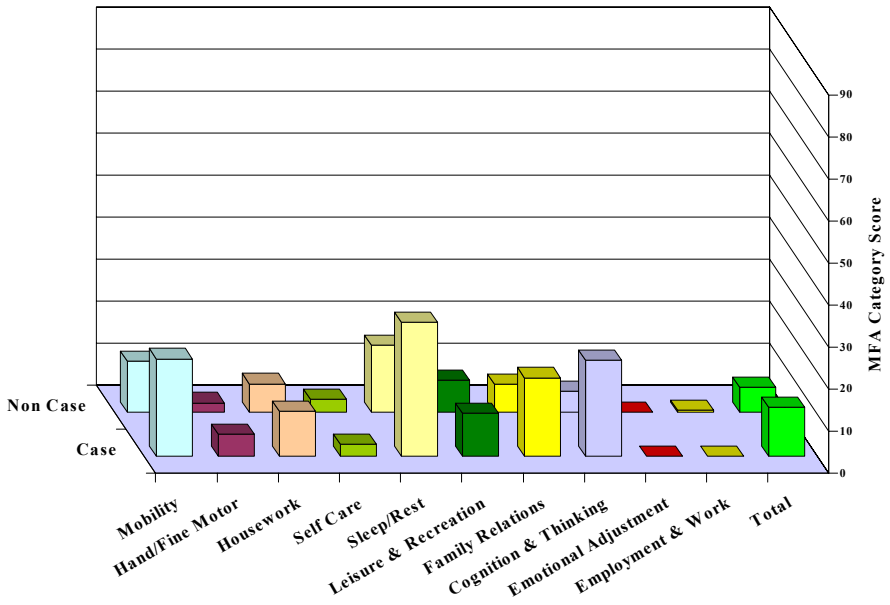


Fig 3.25 Analysis of initial MFA scores against GHQ Caseness for GTOS Main Group.

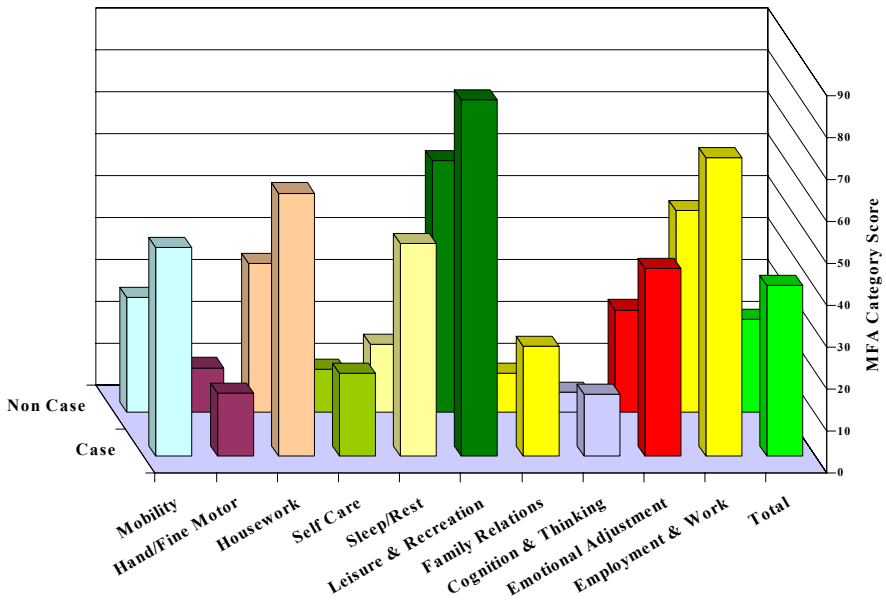


Fig 3.26 Analysis of 2-month MFA scores against GHQ Caseness for GTOS Main Group.

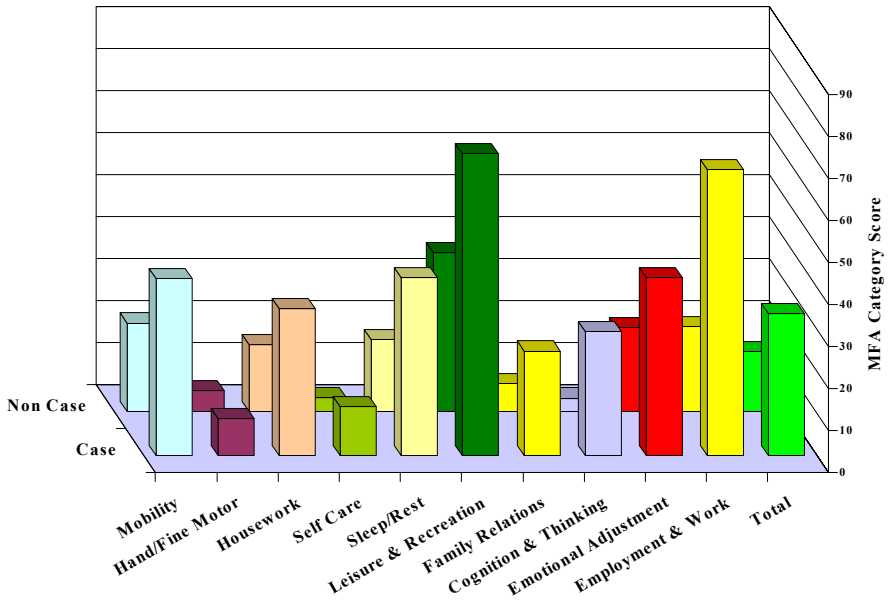


Fig 3.27 Analysis of 6-month MFA scores against GHQ Caseness for GTOS Main Group.

3.4.4 GHQ Caseness *vs* Metabolic Markers

Table 3.22 summarises the analysis of the differences between the mean values of the four metabolic markers for cases and non-cases. The non-normally-distributed CRP and IL-6 means were assessed using the Mann-Whitney U test, while the normally distributed sIL-6r and TNF-α were assessed using the independent samples t-test.

At two months, IL-6 levels were higher for cases ($p=0.042$). At six months, sIL-6r levels ($p=0.034$) and TNF-α levels ($p=0.047$) were higher for cases.

Metabolic Markers	***2 months (n=66)***		***6 months (n=62)***	
	GHQ		**GHQ**	
	Non-case Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)
CRP	0	0.46	3.37	0
	(0)	(2.56)	(19.95)	(0)
IL-6	139.29	271.84*	11.76	5.22
	(441.62)	(643.52)	(46.44)	(7.41)
sIL-6r	39784	39784	33505	41325*
	(43259)	(11488)	(6470)	(15810)
TNF-α	302.28	257.06	3.87	72.11*
	(385.30)	(373.00)	(4.48)	(239.52)

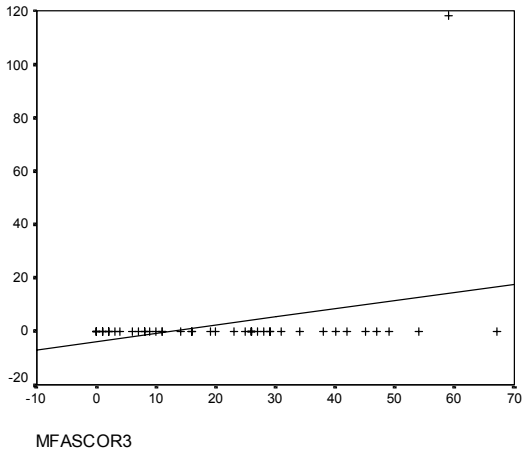
Table 3.22 Analysis of Biological Markers compared with GHQ Caseness at 2- and 6-month assessments for GTOS-MM Subgroup (Differences between cases and non-cases: * $p<0.05$; Mann-Whitney U Test).

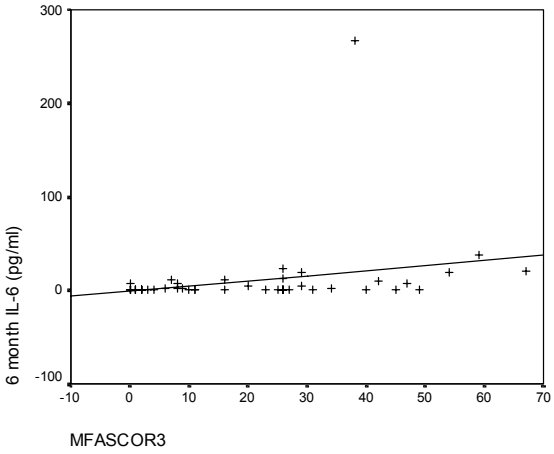
3.4.5 Metabolic Markers vs Outcomes Measures

Having analysed differences between GHQ caseness and metabolic markers and the outcomes measures, correlations between outcomes scores and the metabolic markers were analysed. This allowed an assessment of whether either was exerting an effect upon caseness indirectly. The intention was to attempt to rule out such an effect, rather than undertake a crude form of data trawling.

Apparently significant correlations existed between six-month MFA and CRP values, six-month MFA and IL-6 values and between six-month SIP total and CRP values. These were seen when the simple Pearson correlation was applied, and when partial

correlation, controlling for the effect of GHQ caseness, was applied. Fig 3.28, however, suggests that the presence of outlying values is distorting the scatter, weakening the association. Exclusion of the outlier leaves scatterplots that clearly show no correlation. Thus, it appears that there is little or no correlation between the metabolic markers and outcomes measures for this group.





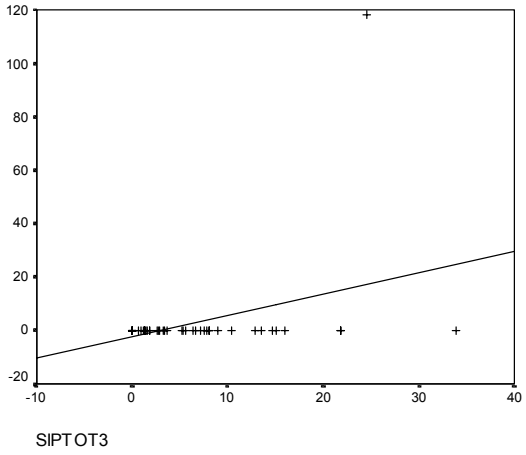


Fig 3.28 Scatterplots of apparantly significant correlations between metabolic markers and outcomes scores for GTOS-MM subgroup: 6 month MFA total score vs 6 month CRP and 6 month IL-6, and 6 month SIP total score vs 6 month CRP. Outlying values are noted.

3.4.6 Metabolic Markers vs Trauma Scores

Having analysed differences between GHQ caseness and metabolic markers, and between GHQ caseness and trauma scores, correlations between these were analysed. This allowed an assessment of whether either was exerting an effect upon caseness indirectly. The intention was to attempt to rule out such an effect, rather than undertake a crude form of data trawling.

Apparently significant correlations are suggested between ISS and initial CRP, IL-6 and TNF values, between RTS and six-month TNF values, and between TRISS and initial and six-month values. Once again, however, the scatterplots (Fig 3.29) indicate that while the plots for ISS vs initial CRP and TRISS vs initial CRP appear to support a correlation, all of the other plots are distorted by outliers. Thus, it appears that there is only a correlation between the initial CRP and trauma scores, and that otherwise there is little or no correlation between the metabolic markers and outcomes measures for this group.

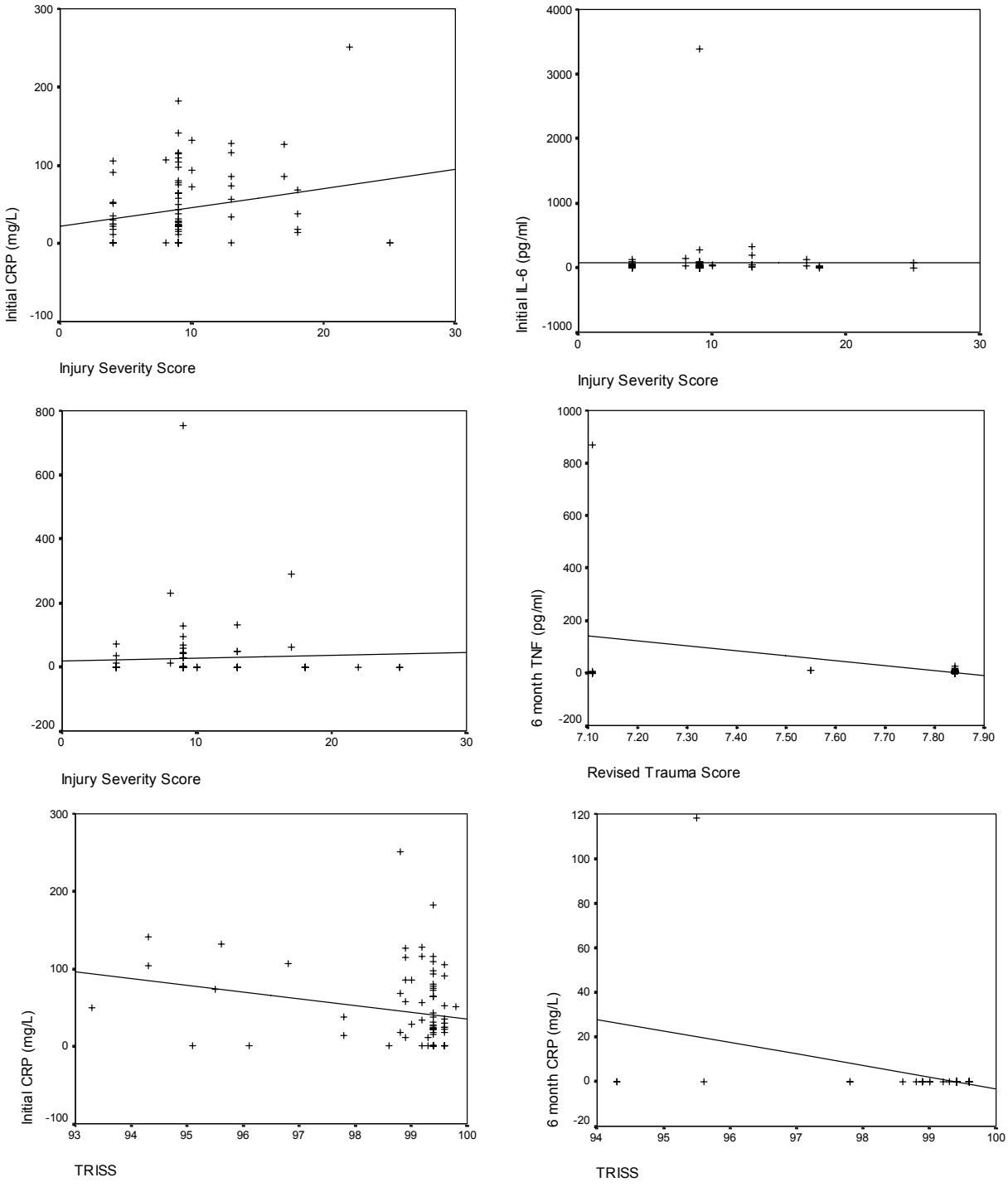


Fig 3.29 Scatterplots of apparently significant correlations between metabolic markers and trauma scores for GTOS-MM subgroup; ISS vs initial CRP, IL-6 and TNF; RTS vs 6 month TNF; TRISS vs initial and 6-month CRP.

4. DISCUSSION

4. DISCUSSION

There have been only two previous attempts to examine the relationship between physical and psychological recovery after injury, both published since the start of the present study. A study in Oregon, USA, (Michaels *et al*. 2000) used SF-36 and the SIP work scale, along with the Brief Symptom Inventory depression scale and the Mississippi Scale for PTSD. They found that work status, general health and overall satisfaction after injury were dependant upon mental health. There is no indication from the paper of the magnitude of the psychiatric problems of their patients. They make the point that "*Trauma centers that fail to recognize, assess, and treat these injury-related mental health outcomes are not fully assisting their patients to return to optimal function*". The second study, from San Diego, USA (Holbrook *et al*. 1999), used the Quality of Well Being scale to measure Quality of Life (QoL). This rates quality of life on a scale from zero (death) to one (maximal QoL). They found PTSD, by DSM-IV criteria, in 32% of their patients at six months, and found that this had a profound impact upon outcome at up to 18 months. The use of such a simple QoL as an outcome measure is very simplistic, and gives no indication of physical functioning.

There is a small number of other studies that have examined psychological and physical health after surgery (Stoll *et al*. 2000), cancer treatment (Meeske *et al*. 2001) and Intensive Therapy Unit treatment (Schelling *et al*. 1998). Others have examined physical wellbeing in patients with established PTSD (Schonfeld *et al*. 1997; Linares

et al. 1999; Malik *et al*. 1999; Weine *et al*. 2000; Butterfield *et al*. 2000). As with the present study, SF-36 has been used as the prime measure of physical health. The collective view of these studies is that those patients with PTSD, in the various settings studied, had worse physical health than those without.

The present study is unique in its detailed, prospective assessment of physical, psychosocial and physiological outcome after "everyday" trauma. This discussion will examine patient recruitment and assessment, and discuss the strengths and weaknesses of the measures used. This will allow the discussion of the results to be placed in their proper context, and will allow the significance and relevance of this study to be placed within the context of our developing understanding of PTP and its effect upon recovery after injury.

4.1 Patients, Injuries and Recruitment

A study of this type requires a high degree of understanding and motivation on the part of the patients taking part. The period after an injury is often extremely difficult, particularly if the patient has multiple injuries. The author attempted to recruit a random subgroup from all of the patients admitted to the OTU during the study period, but certain biases may have appeared.

It was difficult to recruit patients with multiple injuries. These patients were often unwell after their injury for a long time, and required a great deal of care from nurses,

physiotherapists, doctors and other staff. They also often had family and friends visiting throughout the day (the Unit has a relaxed visiting policy). For these reasons, there were relatively few patients with an Injury Severity Score (ISS) of 16 or above, and thus the group does not necessarily represent the full spectrum of injured patients seen. In spite of this, we have seen high levels of measurable psychological distress in our group.

It is impossible to assess other specific biases that may depend upon the interaction between investigator and patient in a study such as this. At all times the made every attempt to take patients as they came and ask for help from all equally. Very few patients refused to take part, and the follow-up rates (79% and 75% at two and six months respectively for the main group) reflect the high level of commitment of the patients to assisting with the study. This may be considered a definitive strength of the project.

The age and sex make up of both groups reflects that of the patients routinely admitted to the OTU, once injuries related to osteoporosis, such as hip fractures, are excluded. The male: female ratio was 2:1, and mean age 37 years. Patients were from the full social spectrum, with a preponderance of skilled manual and non-manual workers (IIIm and IIInm). Falls and RTAs made up two thirds of the injuries, and a variety of injuries, mostly fractures, were sustained. There were no deaths in the study, again reflecting the exclusion of more seriously injured patients. There was a

low incidence of excess alcohol use, although excluding patients who had been under the influence at the time of their injuries will almost certainly have skewed this somewhat. Few patients admitted to using narcotics, and there was a low incidence of prior psychiatric illness, which was particularly relevant as previous studies have highlighted the importance of these factors in the potential development of PTP (Breslau *et al*. 1991; Breslau, Davis & Andreski 1995; Shalev *et al*. 1998; Yehuda *et al*. 1998).

Detailed demographic data are not available for all patients admitted to the OTU, but the author believes that this group is largely representative of the total population of patients with musculoskeletal injuries.

4.2 Measures

4.2.1 Trauma Scores

The majority of the widely used trauma scores, including the three used in this study, originate in the USA. Much of the work using them has focused upon mortality after trauma, and there are shortcomings in their applicability to predicting physical dysfunction in trauma survivors. The TRISS methodology specifically gives a survival probability, which in the GTOS main group ranged from 92.1%-99.8%. In fact, there were no deaths, and the TRISS values tell us little else about the patients.

RTS similarly was developed to predict survival (Champion *et al*. 1989), and in the main GTOS group yielded a narrow range (6.38-7.84), with the vast majority scoring the maximum of 7.84.

The ISS has gained the most widespread use in the UK, and is simple to apply in general terms. It has, however, become clear to us, and to others (Michaels *et al*. 2001), that the ISS underestimates the severity of multiple orthopaedic injuries. The score is reached by adding the squares of the highest AIS scores in each of the three most severely injured areas. In this way, a patient with one isolated long bone fracture may have the same ISS as another patient with multiple skeletal injuries, when clearly the expected functional outcome will be different. Two centres seem to have arrived independently at the same solution to this problem (Osler, Baker & Long 1997; Brenneman *et al*. 1998). They have suggested that the New ISS (NISS) should be calculated from the squares of the three highest AIS scores, regardless of the body region in which they occur. This modification has been tested in the centres where it was formulated, but has to gain widespread acceptance and validation, and was not used in the current study.

There are many other systems that could have been used, each with shortcomings in their complexity or validity, or with a lack of applicability to the function of survivors. In the current study we have, therefore, had to make the best use possible of the trauma scoring systems that we felt would give us the most useful information without adding excessive complexity.

4.2.2 Measurement of Psychological Disturbance

The General Health Questionnaire is not a measure that is specific for PTSD or even for PTP. It measures general psychological distress across four main categories, and gives a total score that can be used to derive "caseness", as discussed earlier (see Section 2.2.2 above). It has been extensively used and tested in a variety of settings to assess levels of psychological distress that may arise from trauma, medical illness or other causes. It has also been used as a general population screening tool (Goldberg *et al*. 1997; Werneke *et al*. 2000; Failde, Ramos & Fernandez-Palacin 2000; Taubman-Ben-Ari *et al*. 2001; Alexander & Klein 2001).

The guide to the GHQ (Goldberg & Williams 1988) discusses the different thresholds that are available to define caseness. The majority of UK-based studies quoted have taken the standard threshold at the 4/5 level. Some studies have used higher thresholds in order to control for the effect of the physical illness upon somatic symptoms and social dysfunction. This is useful in single assessments, but of less importance in a prospective study of this type, where the GHQ can be used to compare changes over time. For this reason, the standard threshold was used, in spite of the potential effect of physical illness upon individual scores. In so doing, the data are also more readily compared to the large number of studies that have used the standard threshold.

Doubt has been cast upon the use of the shorter GHQ (GHQ-12) in Australia (Donath

2001), and there may be cultural problems with using any of the versions of the GHQ outside the UK, where they were developed. This does not cause particular concern with a study on a UK based population.

The intention in the present study was not to identify PTSD, the extreme end of the spectrum of PTP, but rather to identify those patients with any form of psychological distress. In this, GHQ has been effective, identifying a "background" caseness rate at initial assessment of 11% and rates of 46% and 22% at two and six months after the injury. The GHQ is easy to administer and to score, and gives useful non-specific psychiatric information on a population.

4.2.3 Outcomes Measures

Selection of validated instruments to measure outcome is vital (Swiontkowski 1999). Of the patient-derived, objective measurements available, SF-36 has the longest pedigree. It is widely used in both trauma and elective orthopaedic research. Several recent papers, investigating a variety of orthopaedic conditions, have used the SF-36 as an outcome measure (Egol, Dolan & Koval 2000; Hall *et al*. 2000; McKee & Yoo 2000; Hoogendoorn & van der 2001; Coester *et al*. 2001). It has been previously validated and shown to be robust in a population-based study in Aberdeen (Garratt *et al*. 1993). In this study, it has shown impaired functioning of patients at initial assessment (a background level), as well as deterioration at two months and partial recovery by six months after trauma.

The SIP also has a long pedigree of use in orthopaedic research, both in trauma and elective studies. It is often applied in conjunction with the SF-36, and gives good agreement with it (Jurkovich *et al*. 1996; Swiontkowski *et al*. 2000; Lipsett *et al*. 2000; Michaels *et al*. 2000). The personal view of the author was that it had an interpretation problem: patients are invited to mark a box only if the statement relates to them, and to mark a box at the end of each section. It was a concern that a page of blank boxes may indicate normal function for that section, but might just as easily mean that the page had been passed over. In fact, the SIP data mirrored those for the SF-36 questionnaire in the detection of impaired functioning, and correlated in similar ways to the GHQ caseness, but some doubt remains. It is, certainly, a long questionnaire, and may not be so suitable for routine use as SF-36.

The MFA is a much more recent instrument for measuring outcome, and was constructed in an attempt to provide more musculoskeletal-specific outcome information (Martin *et al*. 1996). It has previously been tested against the SIP and SF-36 (Martin *et al*. 1997a), and found to be at least as robust as both, and more responsive than SF-36. The use of Yes *vs* No questions removes the doubt as to the answer given (see SIP, *vide supra*), and anecdotally the few patients asked found the questions easier to follow than the SIP. It is a large questionnaire, and a short version has been produced since the start of this project, and this may prove useful in future (Swiontkowski *et al*. 1999).

4.2.4 Metabolic Markers

No one single marker can be used to monitor the inflammatory response to trauma. Each of the three cytokines (IL-6, sIL-6r and TNF-α) that we have tested have been used in various studies of the response to surgical and accidental trauma, as well as other conditions (Gebhard *et al*. 2000), (Hoch *et al*. 1993; Roumen *et al*. 1993; Martin *et al*. 1997b) (McCall & Parry 1990; Hoch *et al*. 1993; Tan *et al*. 1993; Strieter, Kunkel & Bone 1993; Jiang *et al*. 1997; Connolly & Vernon 2000; Lin, Calvano & Lowry 2000). CRP has also been characterised in similar settings (Kalabalikis *et al*. 1999; Kristiansson *et al*. 1999; Schulze *et al*. 2000; Leung *et al*. 2000; Craig *et al*. 2001). The advantage of CRP over the three cytokines is the ease with which it can be assayed. Our pilot study in patients with established PTSD (Miller *et al*. 2001; Meeske *et al*. 2001) gave hope that CRP might prove useful in the current study; however this proved not to be the case (see Section 4.3.3 below)

4.3 RESULTS

4.3.1 GHQ Caseness

The GHQ-28 detected a background rate of psychological dysfunction of 11%. It is not possible to compare these rates with other published studies, as the GTOS study group cannot be fully matched to any previously published population-based study. Further, it is not possible to control completely for the effect that the patient's injury

may have upon their interpretation of how their psychological health had been over the previous few weeks before the injury. What is more important, however, is that the instrument detected significant differences between the background scores and those at two- and six-month follow up. These differences were not confined to caseness levels, but were also seen in GHQ subscores and total scores. The GHQ detected measurable psychological dysfunction at two months in 46% of patients, falling to 22% by six months.

4.3.2 Outcomes Scores

As with the GHQ (*vide supra*), it is difficult to define a "population normal" for the three outcomes measures used. It is possible to compare scores with those of previously published series, but this raises the problem of "comparing apples with oranges". This is not a truly population based study, being based upon people suffering musculoskeletal injuries, and could only be accurately compared with an identical group. In order to avoid this difficulty, the patients were asked at initial assessment to approach the questionnaire with regard to how they had been before their injury. This approach has been recommended by the team that formulated the MFA (Prof Marc Swiontkowski, personal communication). Although this approach runs the risk that the initial scores may be influenced by the effect of the injury, it is still possible to compare the patients' scores at initial assessment with those at two- and six-month follow-up points. Reference values for the MFA have since been published, and may prove useful in future studies (Engelberg *et al*. 1999)

Using this approach, all three of the outcomes measures used have detected significant differences in function at the two follow-up points, as compared with the initial assessment.

For the SF-36 questionnaire, the dysfunction measured at each follow-up was significantly different to initial assessment for all of the scale scores and for the total score (General Health Perception).

The SIP similarly measured physical and emotional dysfunction at follow-up assessments. At two months, each of the category scores showed statistically significant differences to those at initial assessment. By six months, however, the category scores for Communication, Social Interaction, and Sleep and Rest had returned towards initial values, and differences were not significant. Other category scales had also returned towards normal, but differences were still significant, albeit less so (Mobility, Alertness Behaviour, Eating, Work). While the Physical dimension score and SIP total score remained significantly different at six months, the Psychosocial dimension score had returned towards normal and the difference with initial score was non-significant. This reflects the more rapid recovery of psychosocial function than physical function in the group.

In the same way, the MFA category and total scores at two months were all significantly different to initial scores, with the exception of Cognition/Thinking. By six months, Hand/Fine Motor function had returned towards normal, with differences

non-significant. Self Care and Sleep & Rest had also returned towards normal, but were still significantly different to initial scores.

The SIP and MFA have shown that some aspects of psychosocial and physical function in this group were returning towards normal by six months. It might be expected that as the individual recovers, self care and social interaction would return towards normal before full mobility and work. These findings support this. It would appear that each of the outcomes measures used measures psychosocial and physical function in slightly different ways – SIP shows Social Interaction being back to normal by six months, while MFA still detects significant problems with Family Relations.

The use of all three measures gives a full indication of the function of this group, but might prove excessive in long-term studies. The SF-36 has the advantage of being widely used and validated in all manner of settings, but the results in this study suggest that it may not be so responsive to change. The SIP has the similar advantage of widespread use, but the author's concern about the lack of "yes-no" or multiple option answers remains. The MFA lacks the long track record of the other two, but it appears to be more responsive to change than the SF-36, and less open to doubt of its reliability than the SIP. Its musculoskeletal-centred approach may make it more useful in orthopaedic research, and the short version may be more "user-friendly".

4.3.3 Metabolic Markers

The results of all of the metabolic markers showed a wide variation. This demands a cautious interpretation of the relevance of results, particularly in conjunction with GHQ caseness and outcomes scores, but some useful comments can be made.

CRP levels were highest at initial assessement, falling largely to normal ($<1 mg.l^{-1}$) at two- and six-month assessments. The acute phase response is therefore most marked initially, and was generally not raised in recovering patients. By contrast, the three cytokines were all increased at two months, showing falls back to initial levels at six months. The relationship between the metabolic markers and GHQ caseness and outcomes scores is discussed below (Section 4.4.4).

4.4 ASSOCIATIONS

4.4.1 GHQ vs Demographics

There was no relationship between GHQ and the majority of the demographic information collected. The GHQ users' guide (Goldberg & Williams 1988) gives data that broadly are in keeping with this. The guide does comment on increased scores in divorced or separated individuals, but this was not the case in this series. Patients who had taken narcotics were more likely to be cases at initial assessment, but the number of patients involved was small.

These findings support the view that the patient's background, as revealed by the limited demographic data collected, has little influence upon the development of PTP.

4.4.2 GHQ vs Injury Type and Trauma Scores

There were no correlations between nature of injury or trauma scores and initial GHQ caseness. This supports the view that the patients were completing the GHQ with regard to their previous psychological health.

ISS correlated with standard GHQ caseness at both two and six months. Caseness was also correlated with RTS and TRISS at six months, but not at two months. The ISS is a purely anatomical score, and yet has been more predictive of psychological disturbance than either of the physiological scores. This supports its continued use, although further work needs to be done to assess the increased value in orthopaedics of NISS (*vide supra*).

4.4.3 GHQ vs Outcomes

At the initial assessment, all three of the outcomes measures detected more dysfunction in those patients who exhibited psychiatric morbidity, and were defined as cases. With the SF-36, this was most marked in the scales with a psychosocial aspect as well as the SF-36 total score (General Perception of Health). Similar findings were noted for the SIP. Of note is the increased dysfunction in sleep and rest among cases; as noted above, sleep disturbance is central to PTSD. The sleep and rest disturbance was also seen in the subscale results for the MFA. Here again

differences between cases and non-cases were most marked in psychosocial areas (*eg* cognition/thinking, family relations), and were not seen in the more physical subscores (*eg* Hand/Fine Motor, Self Care, Housework *etc*).

The background of psychological disturbance in the study group before their injuries is reflected in a background of physical and psychosocial dysfunction. In particular, disturbance of function was most marked in the subscores that had a psychological component: Social Function, Limitation- Emotional Problems, Mental Health for SF-36; Emotional Behaviour, Sleep & Rest for SIP; Sleep & Rest, Family Relations and Cognition for MFA. There is considerable overlap in what is being measured by the GHQ and each of the three outcomes measures used.

At two months, all of the SF-36 subscores, as well as the total score, were significantly worse in cases than non-cases. These findings were repeated at six months, with significant differences ($p<0.001$) across the board. SIP scores were also worse at two months for cases, but this was not across the board: Communication and Eating were not significantly different for cases. By six months, however, there were significant differences between cases and non-cases for all category, dimension and total scores. These findings of impaired function were repeated for the MFA at both two- and six-month follow up. The only exception to this was the subscale Hand/Fine Motor at two months (but not at six months).

All three of the outcomes measures detected a background of physical and

psychosocial dysfunction, which correlated with psychological dysfunction. They have also demonstrated increased levels of physical and psychosocial dysfunction in GHQ cases at each of the follow up assessments. Although it is not possible to determine whether one caused the other, it is clear that there is interdependence between physical and psychological recovery after musculoskeletal injury.

4.4.4 GHQ vs Metabolic Markers

At the two-month assessment, there was a significant relationship between IL-6 levels and GHQ caseness, while at six months sIL-6r and TNF-α levels were higher in cases than non-cases. The IL-6 ELISA measures free IL-6, and any elevated levels at six months would be obscured by binding to the soluble receptor, which is clearly present at that stage.

We have demonstrated that there is a disturbance in pro-inflammatory cytokines in patients with PTP. This is in keeping with the findings of the only other published study of cytokines and PTSD, which looked at IL-6 levels in patients with PTSD after accidental trauma (Maes *et al*. 1999). The relationship between psychiatric illness and cytokine disturbance has been more widely studied, particularly with regard to schizophrenia (Lin *et al*. 1998; Erbagci *et al*. 2001; Capuron, Bluthe & Dantzer 2001; Theodoropoulou *et al*. 2001). An interesting recent article looked at the effect of an injection of *Salmonella abortus equi* endotoxin upon both cytokine levels (IL-6, TNF-α and TNF receptor) and anxiety, depression and impaired memory function. There

were clear correlations between cytokine levels and these cognitive disturbances.

Although further work is required to define the relationship between PTP and physiological disturbance, this study has confirmed that there is a relationship worth studying.

4.4.5 Metabolic Markers vs Outcomes & Trauma Scores

Having defined the relationship between psychological disturbance and both physical impairment and physiological disturbance, it was logical to take the analysis a further step. This involved assessing the correlation between the physiological disturbance and physical impairment. This relationship is illustrated in Fig 4.1 below.

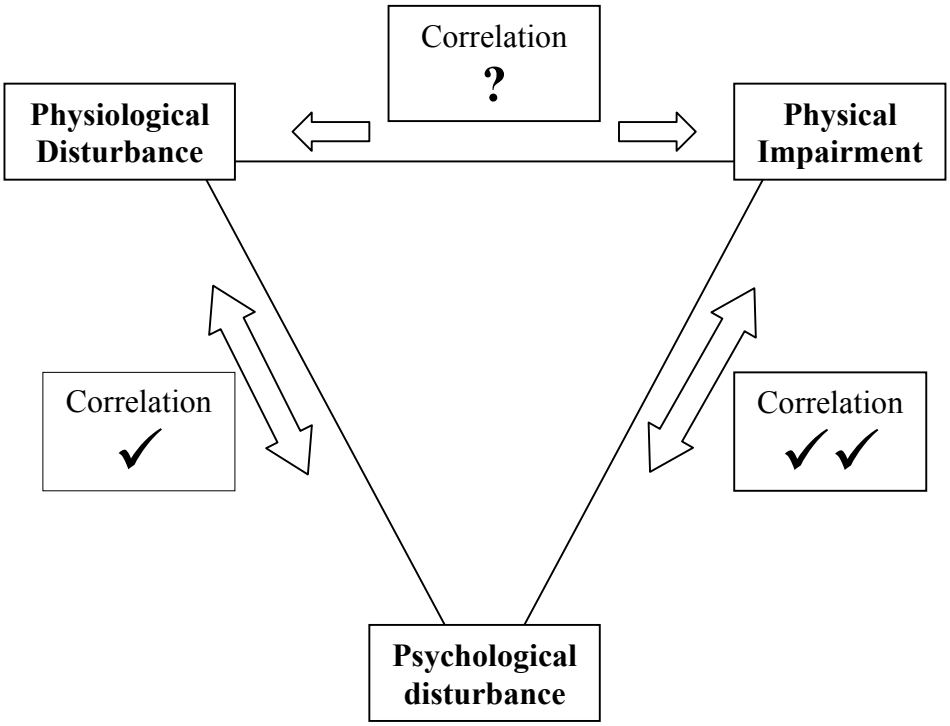


Fig 4.1 The possible relationships between psychological disturbance, physical impairment and physiological disturbance.

The analysis of the relationship between GHQ caseness and the outcomes measures total scores suggested that there were some significant correlations. Assessment of the scatterplots of these relationships revealed that the correlations were not real, and were due to outliers that were skewing the data. Similarly, apparent correlations between the metabolic markers and initial trauma scores were distorted by outliers. When the correlation analysis was repeated with the outliers excluded, the

correlations were not significant. The exception was that initial CRP correlated with both ISS and TRISS. This indicates that it is the best indicator of the extent of the initial injury of the markers studied, and is in keeping with previous work on multiply-injured patients (Mimoz *et al*. 1998). It did not have any predictive value with regard to physical recovery from the injury. The exact timing of individual samples with reference to the actual injury was quite variable (generally 12-72 hours after the injury), and this may affect the relationship between cytokine levels and trauma scores. There is some indication that IL-6 levels may be predictive of survival after trauma (Nast-Kolb *et al*. 1997; Gebhard *et al*. 2000), but there is no work on the function of the survivors.

In summary, this study has shown that there are relationships between PTP and both physiological disturbance and physical impairment. These relationships are not affected by any correlations between physiological disturbance and physical impairment, or between physiological disturbance and injury severity.

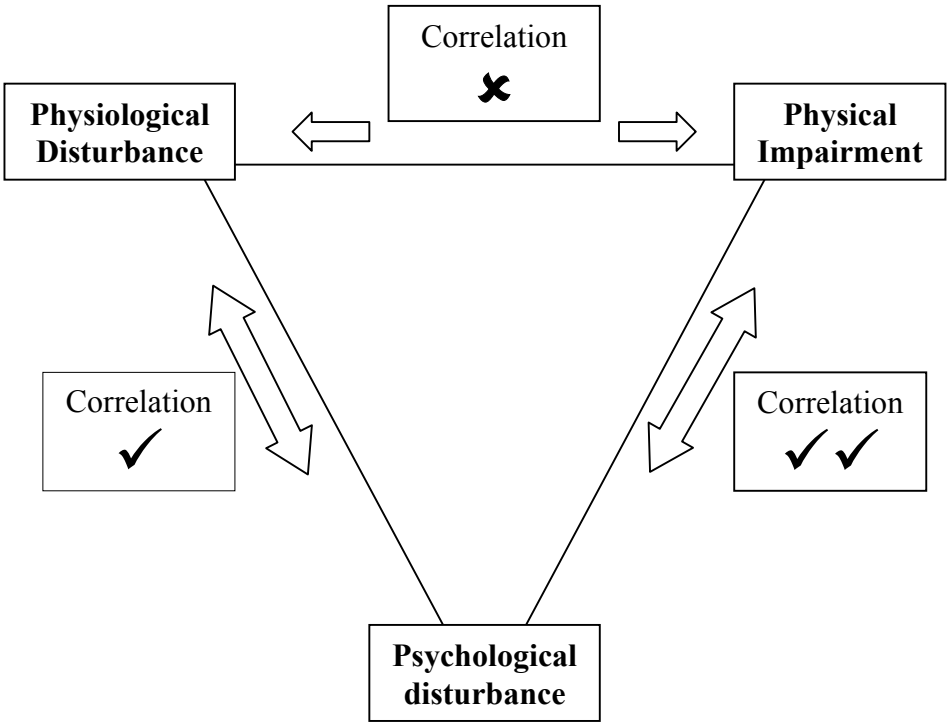


Fig 4.2 The relationships between psychological disturbance, physical impairment and physiological disturbance.

4.5 STRENGTHS OF GRAMPIAN TRAUMA OUTCOMES STUDY

This is a prospective study of an unselected group of 200 patients with a miscellany of injuries, representing the every-day workload of the Grampian Orthopaedic Trauma Unit. Follow up rates over the six months have been high (75% for the main group).

The most widely used methods of assessing injury severity have been used, so that the extent of injuries sustained in this group can be compared to those in other studies. Of particular interest has been the fact that the ISS, a purely anatomical system, has given the best prediction of outcome.

The study utilised established measures of psychological disturbance (GHQ-28) and physical and psychosocial outcome (SF-36 and SIP). We have also used a USA-validated orthopaedic outcome measure (MFA). In this way, there is a great deal of detailed follow-up data on these patients.

The study has also examined established pro-inflammatory markers (IL-6, sIL-6r and TNF-α) and the widely used acute-phase protein CRP in order to characterise the inflammatory response both soon after injury, and over time.

The use of such well established tools to study this group of patients with everyday trauma, has enabled a novel but robust approach to the assessment of the interaction of physical and psychological recovery after physical trauma.

4.6 WEAKNESSES

By insisting upon entry to the study within 72 hours, the study has recruited few patients who had multiple injuries or who required Intensive Therapy Unit treatment.

The facts that the author was responsible for most of the recruitment further means that many eligible patients were missed at weekends or during leave periods. The population may not accurately reflect the whole spectrum of patients admitted to the Orthopaedic Trauma Unit of Aberdeen Royal Infirmary. In spite of the absence of polytraumatised patients, we have seen a great deal of PTP, and the effect of this upon physical and physiological outcome is clear.

4.7 CONCLUSIONS

In order to finalise the conclusions of this study, it is perhaps helpful to re-address the questions that the thesis set out to address (see Section 1.7).

1) *That PTP is an important problem in the treatment of patients with common musculoskeletal injuries.*

YES:

This study has shown a very clear increase in psychological disturbance two months after the injury, with a fall towards, but not reaching normal at six months. These results are recalled in Table 4.1.

	GHQ cases ***(n=200)***
Initial	11
2 months	46***
6 months	22***

Table 4.1 Analysis of GHQ caseness at standard and high thresholds for GTOS main group (***p<0.001; Wilcoxon signed ranks test).

2) That the presence of PTP is associated with impaired physical recovery, as assessed by validated outcome instruments.

YES:

The three outcomes measured used in the study (SF-36, SIP and MFA) have all shown physical and psychosocial impairment that is worse in those patients defined as cases by the GHQ. Those with psychological disturbance are healing less well physically, or those who are healing less well physically are psychologically disturbed; it is not possible to say which from the results presented here.

The relationship between GHQ caseness and the totals of each of the outcomes

measures is indicated in Fig 4.3.

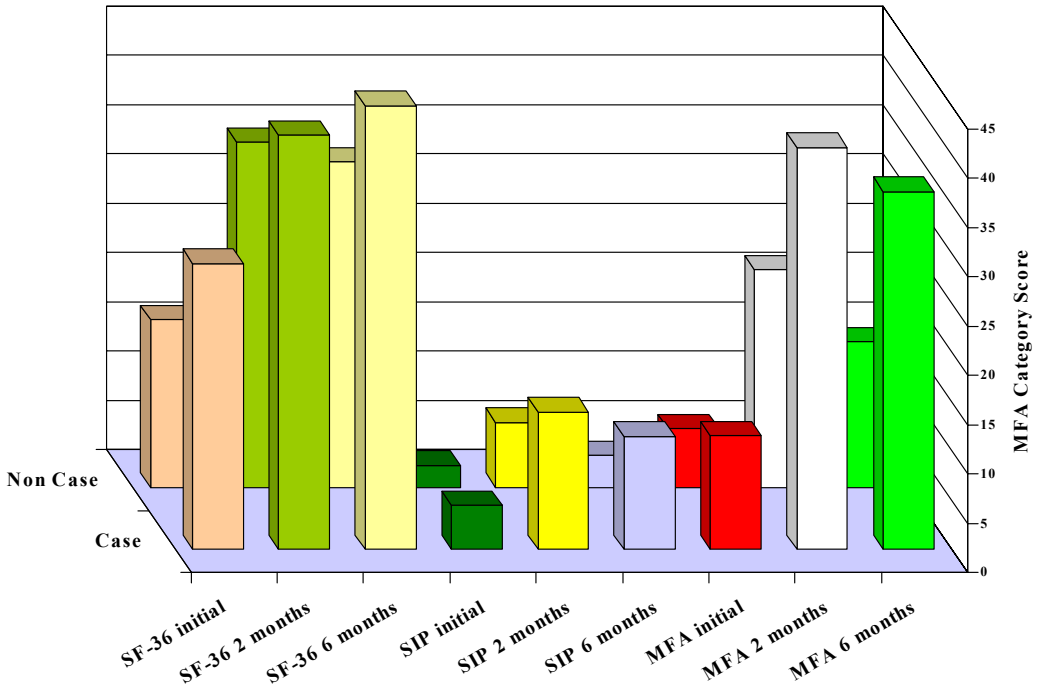


Fig 4.3 Analysis of outcomes scores (Short Form-36, Sickness Impact Profile, Musculoskeletal Function Assessment) at each follow-up point against GHQ caseness GTOS main group.

NB SF-36 scores have been reversed (such that minimal dysfunction scores 0 rather than the normal 100) for ease of comparison with the other measures.

3) *That biochemical markers, such as IL-6, sIL-6r, TNF and CRP, can be used to monitor the physiological disturbance in the victims of physical trauma with PTP.*

PERHAPS:

The finding that caseness at two months was associated with higher IL-6 levels and caseness at six months with higher sIL-6r and TNF-α levels, this study has confirmed the presence of a disturbance in pro-inflammatory cytokines in PTP. This relationship requires further study.

4.8 FURTHER WORK

A number of possible future projects have developed from this work:

1) Work is already in progress in Aberdeen to develop a screening tool that would allow early prediction of those most at risk of PTP.
2) Study of early intervention for PTP, targeting those patients at highest risk. This project is already underway.
3) Further work is required to characterise the metabolic response to injury, both prospectively on a new group of patients, but also using spare blood samples already in store from this study.

4.9 DISSEMINATION

It is expected that the work will yield three direct papers and at least two offshoot papers that will be submitted for publication and presentation:

Direct:

1) Study of prediction of psychological disturbance in trauma patients
2) Study of psychological disturbance and physical impairment in trauma patients
3) Study of psychological disturbance and physiological disturbance in trauma patients

Indirect

1) Use of trauma severity scoring in prediction of physical impairment in trauma survivors – the use of the New Injury Severity Score (NISS).
2) Validation of MFA for use in a UK setting.

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APPENDICES

APPENDIX 1
PATIENT INFORMATION SHEETS AND CONSENT FORMS

UNIVERSITY OF **ABERDEEN**

Grampian Trauma Outcomes (Biological Markers) Study

Patient Information Sheet

An accident causing serious injury is very stressful, but it has become clear that some people cope better with the stress than others. It may be that those people who cope well mentally with the aftermath of an accident may heal more quickly than those that do not. It is our intention to monitor a large group of patients who have been involved in accidents, using a series of questionnaires to assess how well they are coping and how well they are healing. Most of the questionnaires that we are using have been used many times in the past, and are of proven worth, but we are also testing out a new questionnaire from the USA to see if it can provide us with further useful information.

We very much hope that you will be kind enough to participate in this study, which is part of a research project designed to promote medical knowledge, even though it may be of no benefit to you personally.

If you agree to take part, you will be asked to complete these questionnaires during the first day or two after admission, and then again two months and six months after your accident. We expect that each set of forms will take 30-40 minutes to fill, and should require little or no input from medical staff.

In addition to the questionnaires, we will be asking a smaller group of patients to allow us to take blood samples. These samples, approximately 10ml (2 teaspoons), will be tested for a series of substances in order to see if they can be of value in monitoring progress after injuries. These samples will also be taken soon after your admission, and will be repeated two months and six months after your injury.

Other than giving the blood samples, this study will not affect your treatment in any way, and you will continue to be given the best possible care. If you decide not to participate, or you wish to withdraw once you have begun taking part in the study, then this will again have no effect on your treatment.

Thank you for taking the time to read this and to discuss the study.

AG Sutherland FRCSEd, Clinical Lecturer
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Polwarth Building
Foresterhill
Aberdeen AB9 2ZD
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e-mailort025@abdn.ac.uk

UNIVERSITY OF **ABERDEEN**

Grampian Trauma Outcomes Study

Patient Information Sheet

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Thank you for taking the time to read this and to discuss the study.

AG Sutherland FRCSEd, Clinical Lecturer
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UNIVERSITY OF **ABERDEEN**

Grampian Trauma Outcomes (Biological Markers) Study

CONSENT BY PATIENT/VOLUNTEER TO PARTICIPATE

Name of patient/Volunteer.....

Principal Investigator: ***Mr AG Sutherland***

I have read the patient/volunteer information sheet on the above study and have had the opportunity to discuss the details with .....
and ask questions. The doctor has explained to me the nature and purpose of the tests to be undertaken. I understand fully what is proposed to be done.

I have agreed to take part in the study as it has been outlined to me, but I understand that I am completely free to withdraw from the study or any part of the study at any time I wish and that this will not affect my continuing medical treatment in any way.

I understand that these trials are part of a research project designed to promote medical knowledge, which has been approved by the Joint Ethical Committee of Grampian Health Board and the University of Aberdeen, and may be of no benefit to me personally. The Joint Ethical Committee may wish to inspect the data collected at any time as part of its monitoring activities.

I hereby fully and freely consent to participate in the study which has been fully explained to me.

Signature of Patient/Volunteer: .....

Date:
.....

I confirm that I have explained to the patient/volunteer named above, the nature and purpose of the tests to be undertaken.
Signature of Investigator: .....

Date : .....

Please note: This form must be kept in Section A of the patient's notes.

UNIVERSITY OF **ABERDEEN**

Grampian Trauma Outcomes Study

CONSENT BY PATIENT/VOLUNTEER TO PARTICIPATE

Name of Patient/Volunteer: .....

Principal Investigator: ***Mr AG Sutherland***

I have read the patient/volunteer information sheet on the above study and have had the opportunity to discuss the details with .....
and ask questions. The doctor has explained to me the nature and purpose of the tests to be undertaken. I understand fully what is proposed to be done.

I have agreed to take part in the study as it has been outlined to me, but I understand that I am completely free to withdraw from the study or any part of the study at any time I wish and that this will not affect my continuing medical treatment in any way.

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I hereby fully and freely consent to participate in the study which has been fully explained to me.

Signature of Patient/Volunteer: .....

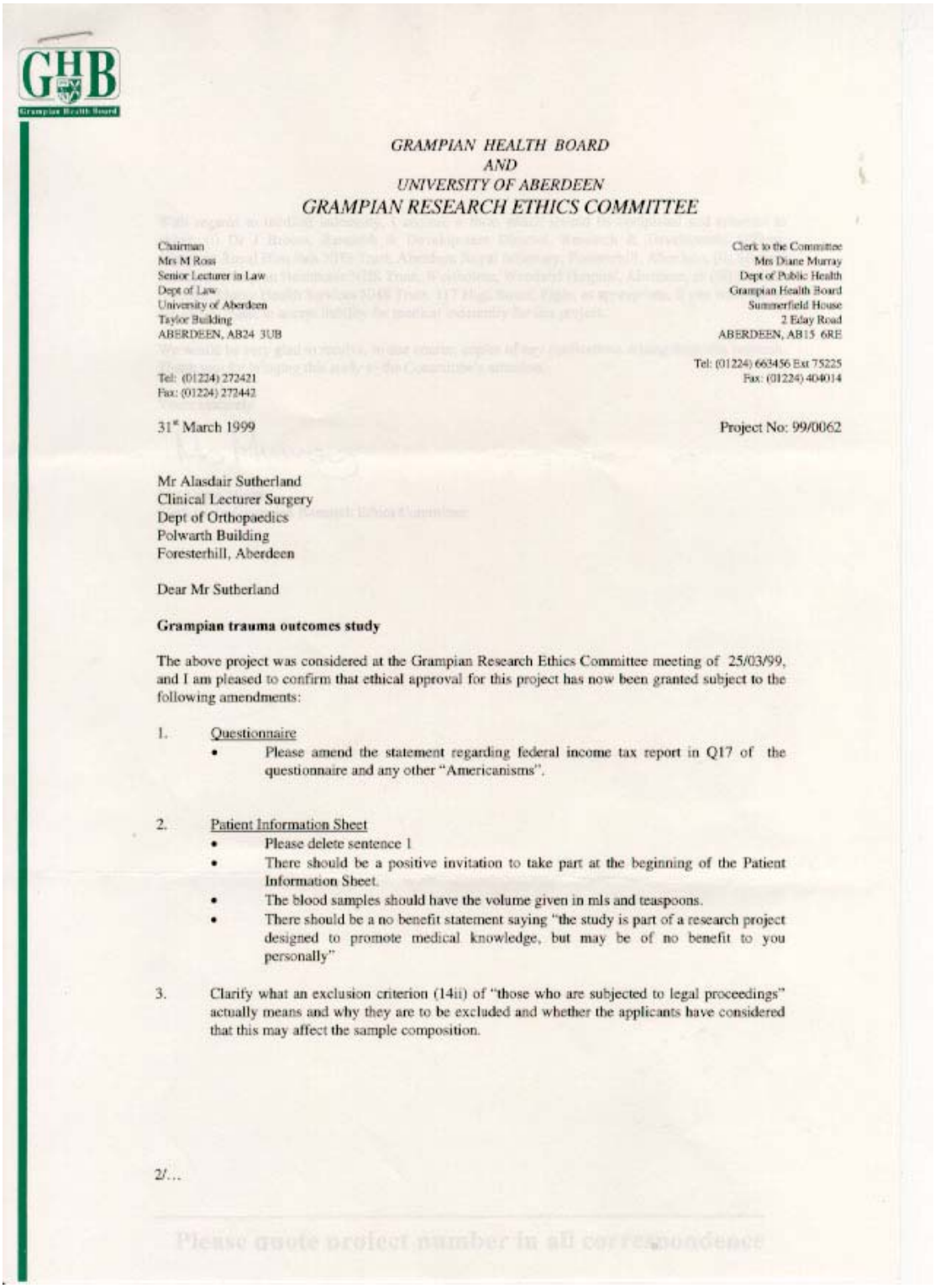
Date:
.....

I confirm that I have explained to the patient/volunteer named above, the nature and purpose of the tests to be undertaken.
Signature of Investigator: .....

Date : .....

Please note: This form must be kept in Section A of the patients notes.

APPENDIX 2
ETHICAL COMMITTEE APPROVAL



GHB
Grampian Health Board

GRAMPIAN HEALTH BOARD
AND
UNIVERSITY OF ABERDEEN
GRAMPIAN RESEARCH ETHICS COMMITTEE

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Clerk to the Committee
Mrs Diane Murray
Dept of Public Health
Grampian Health Board
Summerfield House
2 Eday Road
ABERDEEN, AB15 6RE

Tel: (01224) 663456 Ext 75225
Fax: (01224) 404014

31st March 1999

Project No: 99/0062

Mr Alasdair Sutherland
Clinical Lecturer Surgery
Dept of Orthopaedics
Polwarth Building
Foresterhill, Aberdeen

Dear Mr Sutherland

Grampian trauma outcomes study

The above project was considered at the Grampian Research Ethics Committee meeting of 25/03/99, and I am pleased to confirm that ethical approval for this project has now been granted subject to the following amendments:

1. Questionnaire
   - Please amend the statement regarding federal income tax report in Q17 of the questionnaire and any other "Americanisms".

2. Patient Information Sheet
   - Please delete sentence 1
   - There should be a positive invitation to take part at the beginning of the Patient Information Sheet.
   - The blood samples should have the volume given in mls and teaspoons.
   - There should be a no benefit statement saying "the study is part of a research project designed to promote medical knowledge, but may be of no benefit to you personally"

3. Clarify what an exclusion criterion (14ii) of "those who are subjected to legal proceedings" actually means and why they are to be excluded and whether the applicants have considered that this may affect the sample composition.

2/...

2

With regards to medical indemnity, I enclose a form which should be completed and returned to either; (i) Dr J Broom, Research & Development Director, Research & Development Offices, Aberdeen Royal Hospitals NHS Trust, Aberdeen Royal Infirmary, Foresterhill, Aberdeen, (ii) Medical Director, Grampian Healthcare NHS Trust, Westholme, Woodend Hospital, Aberdeen, or (iii) Medical Director, Moray Health Services NHS Trust, 317 High Street, Elgin, as appropriate, if you wish one of the above Trusts to accept liability for medical indemnity for this project.

We would be very glad to receive, in due course, copies of any publications arising from this research. Thank you for bringing this study to the Committee's attention.

Yours sincerely

Mrs Murray

Mrs Diane Murray
Clerk to the Grampian Research Ethics Committee

Please quote project number in all correspondence

C084

UNIVERSITY OF **ABERDEEN**

Professor of Orthopaedic Surgery
James D Hutchison PhD FRCSEd

Clinical Lecturer in Orthopaedics
Alasdair G Sutherland FRCSEd

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13th April 1999

Mrs Diane Murray
Clerk to Grampian Research Ethics Committee
Dept Public Health
Grampian Health Board
Summerfield House
2 Eday Road
Aberdeen AB 15 6RE

Dear Mrs Murray

Grampian Trauma Outcomes Study, Project No 99/0062

Thank you for your letter of 31st March about the granting of ethical approval for the above study. I have dealt with the points raised in your letter, and I very much hope that the amendments made are satisfactory.

1) Questionnaire
All parts of the questionnaire have been again scoured to remove any remaining "Americanisms", and the statement regarding federal income tax has been removed.

2) Patient information sheet
Sentence 1 has been deleted, and a positive invitation to take part has been substituted.
The blood sample volume is now in ml and teaspoons.
A no benefit statement has been added, as recommended.

3) Exclusion criterion 14 ii "those who are subjected to legal proceedings"
In previous research by Professor Alexander and Professor Hutchison, there have been occasions when legal proceedings involving research subjects have led to data being frozen, and lengthy involvement by the research team in the legal proceedings have resulted. We wish to avoid this, and so chose to exclude the small number of potential subjects that this involves. The vast majority of trauma victims remain eligible.

I have completed and passed on the medical indemnity form to the R&D Office at ARI.

We have now completed preparation of the patient questionnaires in the form of initial assessment, 2 month and 6 months assessments, with all Americanisms removed. The only change that this involves to the forms submitted with the original application is that the initial assessment forms ask for baseline information from the patient about how they were before their injury. I enclose copies of all three sets of questionnaires.

We hope that this answers your questions satisfactorily, and that we can proceed.

Yours sincerely

Alasdair Sutherland
Clinical Lecturer in Orthopaedics

GHB
Grampian Health Board

GRAMPIAN HEALTH BOARD
AND
UNIVERSITY OF ABERDEEN

GRAMPIAN RESEARCH ETHICS COMMITTEE

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Project No: 99/0062

29th April 1999

Mr Alasdair Sutherland
Clinical Lecturer Surgery
Dept of Orthopaedics
Polwarth Building
Foresterhill
Aberdeen

Dear Mr Sutherland

Grampian trauma outcomes study

Thank you for your letter of the 13th of April 1999, enclosing the revised questionnaires, Patient Information Sheet and clarification to (14ii). I am now pleased to confirm that full ethical approval has now been granted for the above study.

Yours sincerely

Mrs Murray.

Mrs Diane Murray
Clerk to the Grampian Research Ethics Committee

APPENDIX 3
ASSESSMENT DOCUMENTS

GRAMPIAN TRAUMA OUTCOMES STUDY

INITIAL ASSESSMENT DOCUMENTS

Principal Investigator
AG Sutherland FRCSEd
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Grampian Trauma Outcomes Study

Patient Details

Patient ID Sex M / F Marital status

S/E Class **I** Professional **II** Managerial **IIINM** skilled non manual **IIIM** skilled manual **IV** Semi-skilled **V** Non-skilled

Nature of trauma

Injuries

ISS ^{2}+ ^{2}+ ^{2} =

RTS	**GCS**	13-15	*4*	**Sys BP**	>89	*4*	**Resp Rate**	10-29	*4*
		9-12	*3*		76-89	*3*		>29	*3*
		6-8	*2*		50-75	*2*		6-9	*2*
		4-5	*1*		1-49	*1*		1-5	*1*
		3	*0*		0	*0*		0	*0*

	Score	**Value**	**Weight**	**Value x Weight**
GCS			0.9368	
Sys BP			0.7326	
Resp Rate			0.2908	_____
			Total	

TRISS Survival Score

Surgery Initial admission

Subsequent admissions

PMH **Drugs**

Past Mental Health Services Contact

Alcohol **units/week**

Cigarettes **/day**

Illicit drug Use

TRAUMA SCREENING SCALE

For each question, circle the appropriate response

1.To what extent were you frightened just before the trauma?	*Not at all*	*To some extent*	*Considerably*	*Greatly*
2.At any time during the trauma, did you think you might die?	*Not at all*	*Rarely*	*Sometimes*	*Often*
3. To what extent during the trauma, did you think you might die?	*Not at all*	*To some extent*	*Considerably*	*Greatly*
4. At any time during the trauma, did you think you might be seriously injured?	*Not at all*	*Rarely*	*Sometimes*	*Often*
5. To what extent during the trauma, did you think you might be seriously injured?	*Not at all*	*To some extent*	*Considerably*	*Greatly*
6. At the time of the trauma, were there moments when you had difficulty making sense of what was happening?	*Not at all*	*Rarely*	*Sometimes*	*Often*
7. To what extent during the trauma, did you have difficulty making sense of what was happening?	*Not at all*	*To some extent*	*Considerably*	*Greatly*
8. Were you trapped?	*Yes*	*No*		
If "Yes", for what length of time were you trapped?_____*minutes*				
Were you alone, or with others, while you were trapped?	*Alone*	*With others*		
9. Do you tend to have mood swings?	*Not at all*	*Rarely*	*Sometimes*	*Often*
10. Do you tend to be a worrier?	*Not at all*	*Rarely*	*Sometimes*	*Often*
11. Do you tend to be lively and talkative?	*Not at all*	*Rarely*	*Sometimes*	*Often*
12. Do you tend to bottle up your feelings?	*Not at all*	*Rarely*	*Sometimes*	*Often*

***SCORE*_____**

THE
GENERAL HEALTH
QUESTIONNAIRE

We would like to know if you have had any medical complaints and how your health has been in general, *over the past few weeks before your injury.* Please answer ALL the questions on the following pages simply by circling the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Have you recently				
Al — been feeling perfectly well and in good health?	*Better than usual*	*Same as usual*	*Worse than usual*	*Much worse than usual*
A2 —been feeling in need of a good tonic?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A3 — been feeling run down and out of sorts?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A4 — felt that you are ill?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A5 — been getting any pains in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A6 — been getting a feeling of tightness or pressure in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A7 — been having hot or cold spells?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
Have you recently				
B1— lost much sleep over worry?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B2 — had difficulty in staying asleep once you are off?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B3 — felt constantly under strain?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B4 — been getting edgy and bad-tempered?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B5 — been getting scared or panicky for no good reason?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B6 — found everything getting on top of you?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B7 — been feeling nervous and strung-up all the time?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*

Have you recently

Cl — been managing to keep yourself busy and occupied?	*More so than usual*	*Same as usual*	*Rather less than usual*	*Much less than usual*
C2 — been taking longer over the things you do?	*Quicker than usual*	*Same as usual*	*Longer than usual*	*Much longer than usual*
C3 — felt on the whole you were doing things well?	*Better than usual*	*About the same*	*Less well than usual*	*Much less well*
C4 — been satisfied with the way you've carried out your task?	*More satisfied*	*About same as usual*	*Less satisfied than usual*	*Much less satisfied*
C5 — felt that you are playing a useful part in things?	*More so than usual*	*Same as usual*	*Less useful than usual*	*Much less useful*
C6 — felt capable of making decisions about things?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less capable*
C7 — been able to enjoy your normal day-to-day activities?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less than usual*

Have you recently

Dl — been thinking of your self as a worthless person?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D2 — felt that life is entirely hopeless?	*Not than usual*	*No more at all*	*Rather more than usual*	*Much more than usual*
D3 — felt that life isn't worth living?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D4 — thought of the possibility that you might do away with yourself?	*Definitely Not*	*I don't think so*	*Has crossed my mind*	*Definitely have*
D5 — found at times you couldn't do anything because your nerves were too bad?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D6 — found yourself wishing you were dead and away from it all?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D7 — found that the idea of taking your own life kept coming into your mind?	*Definitely not*	*I don't think so*	*Has crossed my mind*	*Definitely have*

A	B	C	D	TOTAL
___	____	____	____	_____

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MUSCULOSKELETAL FUNCTION ASSESSMENT

PART I: INSTRUCTIONS

We are interested in finding out how you were managing in your daily life in the week before your injury, so that we can see how you progress during your recovery.

Please answer "YES" or "NO" to each question by putting a cross in the box next to the question. If the question is true for you, choose "YES". If the question is not true for you, choose "NO".

If you wish to comment on any of the questions, please use the space in the margins. Please answer all questions, even though some of the questions may not apply to you.

PLEASE WRITE IN TODAY'S DATE: _____

ACTIVITIES USING YOURARMS or LEGS

This first set of questions is about changes or problems you may have using your arms or legs to do such things as reaching, walking, and carrying.

During the week before your injury:		**YES**	**NO**
1.	Were you unable to walk?	☐	☐
2.	Did you feel unsteady on your feet?	☐	☐
3.	Was it difficult for you to reach up high?	☐	☐
4.	Could you straighten or bend your arm(s) completely?	☐	☐
5.	Could you straighten or bend your leg(s) completely?	☐	☐
6.	Could you pivot on one leg?	☐	☐
7.	Could you climb up and down ladders?	☐	☐
8.	Did you have to rest often when walking?	☐	☐
9.	Did you avoid stairs?	☐	☐
10.	Could you stand for long periods of time?	☐	☐
11.	Was it hard for you to get moving after you have been sitting or lying down?	☐	☐
12.	Did you always walk with a limp?	☐	☐
13.	Did your leg sometimes lock or give-way?	☐	☐
14.	Did you have trouble getting in or out of a low chair?	☐	☐
15.	Did you have trouble getting in or out of bed?	☐	☐

		YES	NO
16.	Could you kneel?	□	□
17.	Could you pick up things from the floor?	□	□
18.	Could you run at all?	□	□
19.	Did you have trouble getting in or out of a car?	□	□
20.	Could you use public transport?	□	□

How much were you bothered by problems you were having using your arms or legs during the week before you injury? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

ACTIVITIES USING YOUR HANDS

The following questions are about activities using your hands. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Did you have difficulty squeezing things?	□	□
2.	Did you have difficulty making a tight fist?	□	□
3.	Was it hard for you to put your hand in your pocket?	□	□
4.	Did you have difficulty turning handles or levers (for example, opening doors, rolling down car windows)?	□	□
5.	Did you have trouble holding a book?	□	□
6.	Did you have difficulty writing or typing?	□	□
7.	Did you have trouble opening medicine bottles or jars?	□	□

How much were you bothered by problems you were now having using your hands? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK AROUND YOUR HOME

These questions are about activities around your home, including such things as cooking, cleaning, maintenance, or repairs. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Did you need help with housework or work in the garden?	□	□
2.	Did you do as much housework or work in the garden as usual?	□	□
3.	Could you do household chores but find that it took more effort?	□	□
4.	Could you mop or sweep or vacuum?	□	□
5.	Was scrubbing a pan or dish difficult?	□	□
6.	Did you need someone to cook for you?	□	□
7.	Did it take you longer to do household chores than ususal?	□	□
8.	Was it difficult for you to shop for groceries or other things?	□	□
9.	Had you stopped doing car, house, or maintenance repairs because of your health?	□	□

How much were you bothered by problems you were having doing work around your home? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SELF CARE ACTIVITIES

The following questions are about taking care of yourself. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Did you wear things that are easier to get into?	□	□
2.	Did you sometimes need help from others to get dressed?	□	□
3.	Did you struggle with buttons, snaps, hooks, zips?	□	□
4.	Did you have trouble pulling clothes on over your head?	□	□
5.	Was it difficult for you to put on shoes, socks, or stockings?	□	□
6.	Was it a chore for you to dress because it takes so long?	□	□
7.	Was it difficult to brush your teeth?	□	□

		YES	NO
8.	Did you have difficulty cutting your fingernails?	□	□
9.	Did you need help keeping yourself clean after going to the bathroom?	□	□
10.	Was it difficult for you to get on or off the toilet?	□	□
11.	Was it hard for you to get in or out of the bath or shower?	□	□
12.	Did you sit while showering?	□	□
13.	Did you need help washing yourself?	□	□
14.	Did you need help eating?	□	□
15.	Was it hard for you to cut food?	□	□
16.	Were you stuck at home?	□	□
17.	Had you stopped going out by yourself?	□	□
18.	Had you stopped driving because of your health?	□	□

How much were you bothered by problems you were having caring for yourself during the week before your injury? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SLEEP and REST

These questions are about changes or problems you may have experienced with sleep and rest. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Were you tired all of the time?	□	□
2.	Did you have trouble falling asleep at night?	□	□
3.	Did you have difficulty sleeping the whole night?	□	□
4.	Was it hard for you to get comfortable to sleep?	□	□
5.	Did you wake up sooner than you would like?	□	□
6.	Did you have disturbing dreams?	□	□

How much were you bothered by problems you were having with sleep and rest during the week before your injury? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

LEISURE AND RECREATIONAL ACTIVITIES

We would also like to know about problems you may have had with leisure time or recreational activities. These activities may include such things as hobbies, sports, crafts, gardening, aerobics, or volunteering. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Was your physical fitness worse because of your health?	□	□
2.	Did you do less of your usual physical recreational activities?	□	□
3.	Had you stopped doing all of your usual physical recreational activities?	□	□
4.	Were you doing fewer leisure activities (such as hobbies, crafts, gardening, card playing, going out with friends)?	□	□

How much were you bothered by problems you were having with leisure and recreational activities during the week before your injury? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

RELATIONSHIPS:

FAMILY and FRIENDS

These questions are about your relationships with family, friends, and other important people in your life. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Was there a strain in your relationships with either your friends or family?	□	□
2.	Did you feel you just don't want to be around anybody?	□	□
3.	Was it hard for you to get either your family or friends to help you do things?	□	□
4.	Were you lonely?	□	□

		YES	NO
5.	Did you feel that either your friends or family have shied away from you?	□	□
6.	Were you irritable toward those around you (for example, snap at people, give sharp answers, criticise easily)?	□	□
7.	Did you miss being with either your friends or family?	□	□
8.	Did you feel like being less intimate?	□	□
9.	Had your sexual life changed?	□	□
10.	Did you enjoy sex less?	□	□

How much were you bothered by problems you were now having with your friends, family, and other important people in your life during the week before your injury? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

THINKING

At times, people may have difficulty with thinking, concentrating, or remembering as a result of their health. If the question was true for you, please check "YES". If the question was not true for you, please check "NO".

During the week before your injury:		**YES**	**NO**
1.	Did it take you longer to figure things out?	□	□
2.	Did you have problems with concentration?	□	□
3.	Were you more confused and scattered?	□	□
4.	Were you more forgetful?	□	□

How much were you bothered by problems you were having thinking, concentrating, and remembering during the week before your injury? *(Please check one.)*

□	□		□	□ □
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK ACTIVITIES

Were you working before your injury?

NO---------> Was this because of your health? NO

YES

YES

PART II: INSTRUCTIONS

In this section of the survey some questions are answered with a **"YES"** or "NO". Others have a number of choices. Please indicate your choice by putting a check in the box that is true for you.

HEALTH and DAILY ACTIVITIES

These questions are about your health and daily activities before your injury. Please try to answer each question as accurately as you can.

1. Do you have any of the following conditions?

(Check one answer for each condition.)	**YES**	**NO**
Heart Problems (heart attack, angina, congestive heart failure)	☐	☐
Lung Problems (including bronchitis or emphysema)	☐	☐
Blindness or Trouble Seeing, even when wearing glasses	☐	☐
Deafness or Trouble Hearing	☐	☐
Bad Headaches or Migraines	☐	☐
Depression, Anxiety or other Mental Troubles	☐	☐
Allergies	☐	☐
Diabetes	☐	☐
Asthma	☐	☐
Stomach Problems	☐	☐
Arthritis	☐	☐
Menstrual or Female Problems	☐	☐
Back Problems	☐	☐
Seizures or Convulsions or fits	☐	☐
High Blood Pressure or Hypertension	☐	☐
Stroke	☐	☐
Kidney Disease	☐	☐

Cancer (not including skin cancer)	☐	☐
Other	☐	☐

2. Were you using any of the following aids?

(Check one answer for each item)

	YES	**NO**
Sling	☐	☐
Brace Or Splint	☐	☐
Cast	☐	☐
Walking Stick	☐	☐
Crutches	☐	☐
Walking Frame (Zimmer Frame)	☐	☐
Wheelchair	☐	☐
Electric Wheelchair Or Buggy	☐	☐
Other *(Please write in)* _____	☐	☐

3. People sometimes have good days and sometimes have bad days. How were you doing the day before your injury?

(Check one)

VERY BAD	☐
BAD	☐
AVERAGE OR TYPICAL DAY	☐
GOOD	☐
VERY GOOD	☐

4. In the <u>week before your injury</u>, how much were you bothered by pain?

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

5. How would you describe your current use of cigarettes? *(Check one)*

NEVER SMOKED	☐
FORMER SMOKER	☐
SMOKE 1-10 CIGARETTES A DAY	☐
SMOKE 11-20 CIGARETTES A DAY	☐
SMOKE MORE THAN 20 CIGARETTES A DAY	☐

6. How often do you drink alcoholic drinks, such as beer, wine or spirits?

(Check one)

ONCE A MONTH OR LESS □

2-3 TIMES A MONTH □

1-2 TIMES A WEEK □

3-4 TIMES A WEEK □

DAILY OR ALMOST DAILY □

I DON'T DRINK □

7. When you drink, how much do you drink on the average?

(Check one)

1 DRINK □

2 DRINKS □

3-4 DRINKS □

5 OR MORE DRINKS □

I DON'T DRINK □

THE SICKNESS IMPACT PROFILE

We are interested in the effect of your general health on your daily activities before your injury. In each section mark only those statements that describe you before your injury, and were related to your state of health then. Once you have read each section and marked the appropriate statements, put a mark in the box at the end of the section.

Section A

Please mark only those statements that you are *sure* described you before your injury and are related to your state of health.

1) I spent much of the day lying down in order to rest ☐
2) I sat during much of the day ☐
3) I slept or dozed most of the time—day and night ☐
4) I lay down more often during the day in order to rest ☐
5) I sat around half-asleep ☐
6) I slept less at night, for example, woke up too early, don't fall asleep for a long time, woke up frequently ☐
7) I slept or napped more during the day ☐

Mark here when you have read all statements in this section ☐

Section B

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I said how bad or useless I was, for example, that I was a burden on others ☐
2) I laughed or cried suddenly ☐
3) I often moaned and groaned in pain or discomfort ☐
4) I had attempted suicide ☐
5) I was nervous or restless ☐
6) I kept rubbing or holding areas of my body that hurt or were uncomfortable ☐
7) I was irritable and impatient with myself, for example, talked badly about myself, swore at myself, blamed myself for things that happened ☐
8) I talked about the future in a hopeless way ☐
9) I got sudden frights ☐

Mark here when you have read all statements in this section ☐

Section C

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I made certain moves with help, for example, getting into or out of cars, bathtubs ☐
2) I could not move into or out of bed or chair by myself but was moved by a person or mechanical aid ☐
3) I could stand only for short periods of time ☐
4) I could not maintain balance ☐
5) I moved my hands or fingers with some limitation or difficulty ☐
6) I could stand up only with someone's help ☐
7) I could kneel, stoop, or bend down only by holding on to something ☐
8) I was in a restricted position all the time ☐
9) I was very clumsy in body movements ☐
10) I could get in and out of bed or chairs by grasping something for support ☐
11) I stayed lying down most of the time ☐
12) I changed position frequently ☐
13) I had to hold on to something to move myself around in bed ☐
14) I could not bathe myself completely; for example, require assistance with bathing ☐
15) I could not bathe myself at all, but am bathed by someone else ☐
16) I used a bedpan with assistance ☐
17) I had trouble getting shoes, socks, or stockings on ☐
18) I did not have control of my bladder ☐
19) I could not fasten my clothing, for example, require assistance with buttons, zips, shoelaces ☐
20) I spent most of the time partly undressed or in pyjamas ☐
21) I did not have control of my bowels ☐
22) I could dress myself, but did so very slowly ☐
23) I could get dressed only with someone's help ☐

Mark here when you have read all statements in this section ☐

Section D

This group of statement has to do with any work that you usually did in caring for your home or garden. Considering just those things that you did, please mark *only* those statements that you are *sure* described you before your injury and were related to your state of health.

1) I did work around the house only for short periods of time or rested often □
2) I did *less* of the regular daily work around the house than I would usually do □
3) I could not do *any* of the regular daily work around the house that I would usually do □
4) I could not do *any* of the maintenance or repair work that I would usually do in my home or yard □
5) I could not do *any* of the shopping that I would usually do □
6) I could not do *any* of the house cleaning that I would usually do □
7) I had difficulty doing handwork, for example, turning taps, using kitchen gadgets, sewing □
8) I could not do *any* of the clothes washing that I would usually do □
9) I could not do heavy work around the house □
10) I had given up taking care of personal or household business affairs, for example, paying bills, banking, working on budget □

Mark here when you have read all statements in this section □

Section E

Please mark *only* those statements that you are *sure* described you before your injury and were related to your state of health.

1) I was getting around only within one building □
2) I stayed within one room □
3) I stayed in bed more □
4) I stayed in bed most of the time □
5) I could not use public transportation □
6) I stayed at home most of the time □
7) I only went to places with toilets nearby □
8) I could not go into town □

Mark here when you have read all statements in this section □

Section F

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I went out less to visit people □
2) I did not go out to visit people at all □
3) I showed less interest in other people's problems, for example, didn't listen when they tell me about their problems, didn't offer to help □
4) I often acted irritable toward those around me, for example, snap at people, give sharp answers, criticise easily □
5) I showed less affection □
6) I did fewer social activities with groups of people □
7) I cut down the length of visits with friends □
8) I avoided social visits from others □
9) My sexual activity was decreased □
10) I often expressed concern over what might be happening to my health □
11) I talked less with those around me □
12) I was demanding, for example, insisted that people do things for me, tell them how to do things□
13) I stayed alone much of the time □
14) I acted disagreeably to family members, for example, I was spiteful or stubborn □
15) I had frequent outbursts of anger at family members, for example, struck at them, screamed, threw things at them □
16) I isolated myself as much as I could from the rest of the family □
17) I am paid less attention to the children □
18) I refused contact with family members, for example, turned away from them □
19) I could not do the things I usually did to take care of my children or family □
20) I could not joke with family members as I usually did □

Mark here when you have read all statements in this section □

Section G

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I walked shorter distances or stop to rest more often □

2) I could not walk up or down hills □
3) I could use stairs only with mechanical support, for example, handrail, stick, crutches □
4) I could walk up or down stairs only with assistance from someone else □
5) I got around in a wheelchair □
6) I could not walk at all □
7) I could walk by myself but with some difficulty, for example, limp, stumble, have stiff leg □
8) I could walk only with help from someone □
9) I went up and down stairs more slowly, for example, one step at a time, stop often □
10) I could not use stairs at all □
11) I could get around only by using a walker, crutches, stick, walls, or furniture □
12) I walked more slowly than usual □

Mark here when you have read all statements in this section □

Section H

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I was confused and started several actions at a time □
2) I had more minor accidents, for example, dropped things, tripped and fell, bumped into things □
3) I reacted slowly to things that were said or done □
4) I could not finish things I started □
5) I had difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things □
6) I sometimes behaved as if I were confused or disoriented in place or time, for example, where I was, who was around, directions, what day it was □
7) I forgot a lot, for example, things that happened recently, where I put things, appointments □
8) I could not keep my attention on any activity for long □
9) I made more mistakes than usual □
10) I had difficulties doing activities involving concentration and thinking □

Mark here when you have read all statements in this section □

Section I

Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I had trouble writing or typing □
2) I communicated mostly by gestures, for example, moving my head, pointing, sign language □
3) My speech was understood by only a few people who know me well □
4) I often lost control of my voice when I talked, for example, my voice got louder or softer trembled, changed unexpectedly □
5) I couldn't write except to sign my name □
6) I could carry on a conversation only when very close to the other person, or looking at them □
7) I had difficulty speaking, for example, got stuck, stuttered, stammered, slurred my words □
8) I was understood only with difficulty □
9) I could not speak clearly when I was under stress □

Mark here when you have read all statements in this section □

Section J

The next group of statements has to do with any work you usually did other than managing your home. By this we mean anything that you regard as work that you did on a regular basis.

Did you usually do work other than managing your home?

Yes □ No □

If you answered yes, go on to section K

If you answered no:

Are you retired? Yes □ No □

If you are retired, was your retirement related to your health? Yes □ No □

If you are not retired, but are not working, is this related to your health? Yes □ No □

Now skip to section L.

Mark here when you have read all statements in this section □

Section K

Now consider the work you do and mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I was not working at all □

(If you checked this statement, skip to section L.)

2) I was doing part of my job at home □
3) I was not accomplishing as much as usual at work □
4) I often acted irritable toward my work associates, for example, snap at them, gave sharp answers, criticised easily □
5) I was working shorter hours □
6) I was doing only light work □
7) I worked only for short periods of time or took frequent rests □
8) I was working at my usual job but with some changes, for example, using different tools or special aids, trading some tasks with other workers □
9) I could not do my job as carefully and accurately as usual □

Mark here when you have read all statements in this section □

Section L

This group of statements has to do with activities you usually did in your free time. These activities are things that you might do for relaxation, to pass the time, or for entertainment. Please mark only those statements that you are *sure* described you before your injury and were related to your state of health.

1) I did my hobbies and recreation only for short periods of time □
2) I went out for entertainment less often □
3) I had cut down on *some* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading □
4) I was not doing *any* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading □
5) I was doing more inactive pastimes in place of my other usual activities □
6) I was doing fewer community activities □

7) I had cut down on *some* of my usual physical recreation or activities □
8) I could not do any of my usual physical recreation or activities □

Mark here when you have read all statements in this section □

Section M

Please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I was eating much less than usual □
2) I could feed myself but only by using specially prepared food or utensils □
3) I had to eat special or different food, for example, soft food, bland diet, low-salt, low-fat, low-sugar □
4) I could eat no food at all but could take fluids □
5) I just picked or nibbled at my food □
6) I drank less fluids □
7) I fed myself with help from someone else □
8) I could not feed myself at all, but had to be fed □
9) I could eat no food at all, nutrition was taken through tubes or intravenous fluids □

Mark here when you have read all statements in this section □

SHORT FORM 36

We are interested in finding out about your health, feelings and general activities over the four weeks before your injury. For each question, please mark the most appropriate answer.

Overall Health

1) In general, would you say that your health before your injury was:

Excellent □ Very Good □ Good □ Fair □ Poor □

2) Compared to one year ago, how would you rate your health over the four weeks before your injury?

Much better than a year ago □	Somewhat better than a year ago □	About the same □	Somewhat worse than a year ago □	Much worse than a year ago □

Health and Daily Activities

2) The following questions are about activities you might do during a typical day over the four weeks before your injury. Did **your health** limit you on these activities? If so, how much

	Yes, limited a lot	Yes, limited a little	No, not limited
a) **Vigorous activities,** such as running, lifting heavy objects, participating in strenuous sports	□	□	□
b) **Moderate activities,** such as moving a table, pushing a vacuum cleaner, bowling or playing golf	□	□	□
c) Lifting of carrying groceries	□	□	□
d) Climbing **several** flights of stairs	□	□	□
e) Climbing **one** flight of stairs	□	□	□
f) Bending, kneeling or stooping	□	□	□
g) Walking **more than one mile**	□	□	□
h) Walking **half a mile**	□	□	□
i) Walking **100 yards**	□	□	□
j) Bathing and dressing	□	□	□

4) During **the four weeks before your injury**, how much of the time did you have any of the following problems with your work or other regular daily activities **as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like to	□	□	□	□	□
c) Were limited in the **kind** of work or other activities	□	□	□	□	□
d) Had **difficulty** performing the work or other activities (eg took more effort)	□	□	□	□	□

5) During the **4 weeks before your injury**, how much time did you have any of the following problems with your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like	□	□	□	□	□
c) Did work or other activities **less carefully** than usual	□	□	□	□	□

6) During the **4 weeks before your injury**, to what extent did your physical health or emotional problems interfere with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

7) How much bodily pain did you have during the **4 weeks before your injury**?

None	Very mild	Mild	Moderate	Severe	Very severe
□	□	□	□	□	□

8) During the **4 weeks before your injury**, how much did **pain** interfere with your normal work (both outside the house and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

Your Feelings

9) These questions are about how you felt and how things were with you **during the month before your injury**. For each question please give the answer that comes closest to the way you have been feeling.

How much **during the month before your injury**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Did you feel full of life?	□	□	□	□	□
b) Were you very nervous?	□	□	□	□	□
c) Did you felt so down in the dumps that nothing could cheer you up?	□	□	□	□	□
d) Did you feel calm and peaceful?	□	□	□	□	□
e) Did you have a lot of energy?	□	□	□	□	□
f) Did you feel worn out?	□	□	□	□	□
g) Were you happy?	□	□	□	□	□
h) Did you feel tired?	□	□	□	□	□

10) **During the 4 weeks before your injury** how much of your time did your physical health or emotional problems interfere with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
□	□	□	□	□

Health in General

11) How TRUE or FALSE was **each** of the following statements to you **during the 4 weeks before your injury**?

	Definitely true	Mostly true	Not true	Mostly false	Definitely false
a) I seemed to get ill more easily than other people	□	□	□	□	□
b) I was as healthy as anybody I know	□	□	□	□	□
c) I expected my health to get worse	□	□	□	□	□
d) My health was excellent	□	□	□	□	□

GRAMPIAN TRAUMA OUTCOMES STUDY

2 MONTH ASSESSMENT DOCUMENTS

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UNIVERSITY OF **ABERDEEN**

Grampian Trauma Outcomes Study

Patient Information Sheet

Hopefully you will remember helping us out with this study when you were in hospital after your injury, and filling in the initial assessment forms. It is now time to ask you to fill in the first set of follow-up forms. These forms ask a series of questions in quite specific ways, in order to see how you are recovering from your injuries. You may notice some overlap between the forms, and some of the questions may not seem relevant to you - please answer all of the questions as they apply to you.

An accident causing serious injury is very stressful, but it has become clear that some people cope better with the stress than others. It may be that those people who cope well mentally with the aftermath of an accident may heal more quickly than those that do not. It is our intention to monitor a large group of patients who have been involved in accidents, using a series of questionnaires to assess how well they are recovering. Most of the questionnaires that we are using have been used many times in the past, and are of proven worth, but we are also testing out a new questionnaire from the USA to see if it can provide us with further useful information.

This study will not affect your treatment in any way, and you will continue to be given the best possible care. If you decide not to participate, or you wish to withdraw once you have begun taking part in the study, then this will again have no effect on your treatment.

If you have any questions at all, please feel free to call me. My contact numbers are on the front sheet of this booklet, and if I am not there to answer straight away, please leave a message and I will call you back.

Thank you for taking the time to read this and to complete the enclosed forms

Alasdair Sutherland
Lecturer in Orthopaedics

GRAMPIAN TRAUMA OUTCOMES STUDY

2 MONTH ASSESSMENT

These questions relate to any changes in your home and work circumstances since your injury, whether they are related to your injury or not. For each question, please check the box which most closely applies to you.

1. What is your marital status? **(***Check one)*

- Married or living as married ☐
- Widowed ☐
- Divorced ☐
- Separated ☐
- Never married ☐

2. Do you live alone or with someone else? *(Check all that apply)*

- Alone ☐
- With another adult ☐
- With a child/children (7-17 years old) ☐
- With -a child/children (birth to 6 years old) ☐

3. Are your daily activities or work...? *(Check one)*

- The same as before your injury or arthritis ☐
- Different due to your injury ☐
- Different, but not due to your injury ☐

4. Are you now...? *(Check one)*

- Employed full-time (35 or more hours a week) ☐
- Employed part-time, because of your health ☐
- Employed part-time, for reasons other than health ☐
- Employed, but on sick-leave ☐
- Retired, because of your health ☐
- Retired, for reasons other than health ☐
- Laid-off or unemployed, because of health ☐
- Laid-off or unemployed, for reasons other than health ☐
- Full-time housewife ☐
- Other *(please write in)*

  _____ ☐

5. If you are not currently working, when do you plan to return to work?

	(Check one)
Within 1 month	☐
Within 2-4 months	☐
Within 5-8 months	☐
Within 9-12 months	☐
I plan to work sometime later	☐
I have no plans to work	☐
I am currently working	☐

6. Are you involved in legal action because of your injury?

	(Check one)
NO	☐
YES	☐

7. Are you receiving or applying for any disability compensation for your injury?

	(Check one)	
NO	☐	—> *(Please go to Question 15)*
YES	☐	

8. What type of disability compensation are you receiving or applying for?

	(Check all that apply)
DHSS disability benefit	☐
Personal injury claim	☐
Private disability insurance	☐
Other *(please write in)*_____	☐

9. How has your household income changed because of your injury or arthritis?

	(Check one)
Unchanged	☐
Decreased	☐
Increased	☐

10. Do you have private health insurance that is covering the care for your injury?

YES ☐ NO ☐

THE
GENERAL HEALTH
QUESTIONNAIRE

We would like to know if you have had any medical complaints and how your health has been in general, *over the past few weeks.* Please answer ALL the questions on the following pages simply by circling the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Have you recently				
Al — been feeling perfectly well and in good health?	*Better than usual*	*Same as usual*	*Worse than usual*	*Much worse than usual*
A2 —been feeling in need of a good tonic?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A3 — been feeling run down and out of sorts?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A4 — felt that you are ill?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A5 — been getting any pains in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A6 — been getting a feeling of tightness or pressure in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A7 — been having hot or cold spells?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
Have you recently				
B1— lost much sleep over worry?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B2 — had difficulty in staying asleep once you are off?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B3 — felt constantly under strain?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B4 — been getting edgy and bad-tempered?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B5 — been getting scared or panicky for no good reason?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B6 — found everything getting on top of you?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B7 — been feeling nervous and strung-up all the time?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*

Have you recently				
Cl — been managing to keep yourself busy and occupied?	*More so than usual*	*Same as usual*	*Rather less than usual*	*Much less than usual*
C2 — been taking longer over the things you do?	*Quicker than usual*	*Same as usual*	*Longer than usual*	*Much longer than usual*
C3 — felt on the whole you were doing things well?	*Better than usual*	*About the same*	*Less well than usual*	*Much less well*
C4 — been satisfied with the way you've carried out your task?	*More satisfied*	*About same as usual*	*Less satisfied than usual*	*Much less satisfied*
C5 — felt that you are playing a useful part in things?	*More so than usual*	*Same as usual*	*Less useful than usual*	*Much less useful*
C6 — felt capable of making decisions about things?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less capable*
C7 — been able to enjoy your normal day-to-day activities?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less than usual*
Have you recently				
Dl — been thinking of your self as a worthless person?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D2 — felt that life is entirely hopeless?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D3 — felt that life isn't worth living?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D4 — thought of the possibility that you might do away with yourself?	*Definitely Not*	*I don't think so*	*Has crossed my mind*	*Definitely have*
D5 — found at times you couldn't do anything because your nerves were too bad?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D6 — found yourself wishing you were dead and away from it all?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D7 — found that the idea of taking your own life kept coming into your mind?	*Definitely not*	*I don't think so*	*Has crossed my mind*	*Definitely have*

A	B	C	D	TOTAL
___	____	____	____	_____

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MUSCULOSKELETAL FUNCTION ASSESSMENT

PART I: INSTRUCTIONS

We are interested in finding out how you are managing with your injury this week.
Please answer "YES" or "NO" to each question by putting a cross in the box next to the question. If the question is true for you and is related to your injury, choose "YES". If the question is not true for you and is not related to your injury, choose "NO".

If you wish to comment on any of the questions, please use the space in the margins. Please answer all questions, even though some of the questions may not apply to your injury.

PLEASE WRITE IN TODAY'S DATE: _____

1 ACTIVITIES USING YOURARMS or LEGS

This first set of questions is about changes or problems you may have using your arms or legs to do such things as reaching, walking, and carrying.

This week, because of your injury	**YES**	**NO**
1. Are you unable to walk?	☐	☐
2. Do you feel unsteady on your feet?	☐	☐
3. Is it difficult for you to reach up high?	☐	☐
4. Can you straighten or bend your arm(s) completely?	☐	☐
5. Can you straighten or bend your leg(s) completely?	☐	☐
6. Can you pivot on one leg?	☐	☐
7. Can you climb up and down ladders?	☐	☐
8. Do you have to rest often when walking?	☐	☐
9. Do you avoid stairs?	☐	☐
10 Can you stand for long periods of time?	☐	☐
11 Is it hard for you to get moving after you have been sitting or lying down?	☐	☐
12 Do you always walk with a limp?	☐	☐
13. Does your leg sometimes lock or give-way?	☐	☐
14. Do you have trouble getting in or out of a low chair?	☐	☐
15. Do you have trouble getting in or out of bed?	☐	☐
16. Can you kneel?	☐	☐
17. Can you pick up things from the floor?	☐	☐

	YES	NO
19. Do you have trouble getting in or out of a car?	☐	☐
20. Have you stopped using public transport because of your injury?	☐	☐

How much are you bothered by problems you are now having using your arms or legs? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	Extremely Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered

ACTIVITIES USING YOUR HANDS

The following questions are about activities using your hands. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury..		**YES**	**NO**
1.	Do you have difficulty squeezing things?	☐	☐
2.	Do you have difficulty making a tight fist?	☐	☐
3.	Is it hard for you to put your hand in your pocket?	☐	☐
4.	Do you have difficulty turning handles or levers (for example, opening doors, rolling down car windows)?	☐	☐
5.	Do you have trouble holding a book?	☐	☐
6.	Do you have difficulty writing or typing?	☐	☐
7.	Do you have trouble opening medicine bottles or jars?	☐	☐

How much are you bothered by problems you are now having using your hands? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK AROUND YOUR HOME

These questions are about activities around your home, including such things as cooking, cleaning, maintenance, or repairs. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you need help with housework or work in the garden?	□	□
2.	Can you do as much housework or work in the garden as before your injury?	□	□
3.	Can you manage household chores but find that it takes more effort?	□	□
4.	Can you mop or sweep or vacuum?	□	□
5.	Is scrubbing a pan or dish difficult?	□	□
6.	Do you need someone to cook for you?	□	□
7.	Does it take you longer to do household chores?	□	□
8.	Is it difficult for you to shop for groceries or other things?	□	□
9.	Have you stopped doing car, house, or maintenance repairs because of your injury?	□	□

How much are you bothered by problems you are now having doing work around your home? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SELF CARE ACTIVITIES

The following questions are about taking care of yourself. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you wear things that are easier to get into?	□	□
2.	Do you sometimes need help from others to get dressed?	□	□
3.	Do you struggle with buttons, snaps, hooks, zips?	□	□
4.	Do you have trouble pulling clothes on over your head?	□	□
5.	Is it difficult for you to put on shoes, socks, or stockings?	□	□
6.	Is it a chore for you to dress because it takes so long?	□	□
7.	Is it difficult to brush your teeth?	□	□

		YES	NO
8.	Do you have a difficult time cutting your fingernails?	□	□
9.	Do you need help keeping yourself clean after going to the bathroom?	□	□
10.	Is it difficult for you to get on or off the toilet?	□	□
11.	Is it hard for you to get in or out of the bath or shower?	□	□
12.	Do you sit while showering?	□	□
13.	Do you need help washing yourself?	□	□
14.	Do you need help eating?	□	□
15.	Is it hard for you to cut food?	□	□
16.	Are you stuck at home?	□	□
17.	Have you stopped going out by yourself?	□	□
18.	Have you stopped driving because of your injury?	□	□

How much are you bothered by problems you are now having caring for yourself? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SLEEP and REST

These questions are about changes or problems you may be experiencing with sleep and rest. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Are you tired all of the time?	□	□
2.	Do you have trouble falling asleep at night?	□	□
3.	Do you have difficulty sleeping the whole night?	□	□
4.	Is it hard for you to get comfortable to sleep?	□	□
5.	Do you wake up sooner than you would like?	□	□
6.	Do you have disturbing dreams?	□	□

How much are you bothered by problems you are now having with sleep and rest? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

LEISURE AND RECREATIONAL ACTIVITIES

We would also like to know about changes or problems you are having with leisure time or recreational activities. These activities may include such things as hobbies, sports, crafts, gardening, aerobics, or volunteering. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Is your physical fitness worse because of your injury?	☐	☐
2.	Do you do less of your usual physical recreational activities?	☐	☐
3.	Have you stopped doing all of your usual physical recreational activities?	☐	☐
4.	Are you doing fewer leisure activities (such as hobbies, crafts, gardening, card playing, going out with friends)?	☐	☐

How much are you bothered by problems you are now having with leisure and recreational activities? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

RELATIONSHIPS:

FAMILY and FRIENDS

These questions are about your relationships with family, friends, and other important people in your life. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury...		**YES**	**NO**
1.	Is there a strain in your relationships with either your friends or family?	☐	☐

		YES	NO
2.	Do you feel you just don't want to be around anybody?	□	□
3.	Is it hard for you to get either your family or friends to help you do things?	□	□
4.	Are you lonely?	□	□
5.	Do you feel that either your friends or family have shied away from you?	□	□
6.	Are you often irritable toward those around you (for example, snap at people, give sharp answers, criticise easily)?	□	□
7.	Do you miss being with either your friends or family?	□	□
8.	Do you feel like being less intimate?	□	□
9.	Has your sexual life changed?	□	□
10.	Do you enjoy sex less?	□	□

How much are you bothered by problems you are now having with your friends, family, and other important people in your life? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

THINKING

At times, people may have difficulty with thinking, concentrating, or remembering as a result of their injury. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Does it take you longer to figure things out?	□	□
2.	Do you have problems with concentration?	□	□
3.	Are you more confused and scattered?	□	□
4.	Are you more forgetful?	□	□

How much are you bothered by problems you are now having thinking, concentrating, and remembering? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

LIFE CHANGES and FEELINGS

These questions are about day to day adiustments you may be making because of your injury and about feelings you may be having about your experiences. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you sometimes use your injuries as an excuse not to do things?	□	□
2.	Do you have to concentrate when using your injured limb?	□	□
3.	Do you avoid using your injured limb?	□	□
4.	Do you protect your injured limb?	□	□
5.	Do you think everything will work out well in the long run?	□	□
6.	Do you accept your current situation?	□	□
7.	Do you feel everything is back to normal?	□	□
8.	Do you feel your life has changed quite a bit?	□	□
9.	Are you getting worse[7]	□	□
10.	If you do too much in one day, does it affect what you do the next day?	□	□
11.	Do you feel disabled, even though you may look fine to others?	□	□
12.	Do you feel useless?	□	□
13.	Do you feel unattractive?	□	□
14.	Does your injury make you feel less capable?	□	□
15.	Do you feel sorry for your self?	□	□
16.	Do you feel like you complain a lot?	□	□
17.	Do you have to ask for help a lot?	□	□
18.	Do you feel angry or frustrated that you have this injury?	□	□

How much are you bothered by the day to day adjustments you are making in your life and the feelings you are now experiencing, because of your injury?

(Please check one.)

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK ACTIVITIES

Are you working now?

□ **NO----------**> Are you unable to work because of your injury?

□ **NO** *(Please skip to Part II)*

□ **YES** *(Please skip to Part II)*

□ **YES----------**> *(Please answer questions below)*

Please answer these questions as they describe your experiences at work. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Are you making changes in your job?	□	□
2.	Is it more difficult for you to do your job now?	□	□
3.	Are you slower at your job?	□	□
4.	Do you take more breaks?	□	□

How much are you bothered by problems you are **now** having with work activities, because of your injury or arthritis? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

PART II: INSTRUCTIONS

In this section of the survey some questions are answered with a **"YES"** or "**NO**". Others have a number of choices. Please indicate your choice by putting a check in the box that is true for you.

2 HEALTH and DAILY ACTIVITIES

These questions are about your health and daily activities. Please try to answer each question as accurately as you can.

1. Do you have any of the following conditions?

(Check one answer for each condition.)	**YES**	**NO**
Heart Problems (heart attack, angina, congestive heart failure)	☐	☐
Lung Problems (including bronchitis or emphysema)	☐	☐
Blindness or Trouble Seeing, even when wearing glasses	☐	☐
Deafness or Trouble Hearing	☐	☐
Bad Headaches or Migraines	☐	☐
Depression, Anxiety or other Mental Troubles	☐	☐
Allergies	☐	☐
Diabetes	☐	☐
Asthma	☐	☐
Stomach Problems	☐	☐
Arthritis	☐	☐
Menstrual or Female Problems	☐	☐
Back Problems	☐	☐
High Blood Pressure or Hypertension	☐	☐
Stroke	☐	☐
Kidney Disease	☐	☐
Cancer (not including skin cancer)	☐	☐
Other	☐	☐

2. Are you now using any of the following aids?

	(Check one answer for each item)	
	YES	**NO**
Sling	□	□
Brace or splint	□	□
Cast	□	□
Walking stick	□	□
Crutches	□	□
Walking frame (zimmer frame)	□	□
Wheelchair	□	□
Electric wheelchair or buggy	□	□
Oother *(please write in)* _____	□	□

3. How much has your injury changed your life?

(Check one)

Not at all	□
A little	□
Somewhat	□
Quite a bit	□
Completely	□

4. **People sometimes have good days and sometimes have bad days. How are you doing today?**

(Check one)

Very bad	□
Bad	□
Average or typical day	□
Good	□
Very good	□

5. In the <u>past week</u>, how much were you bothered by pain?

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

6. Rate the overall quality of care you have received for your injury

(Check one)

Poor	□
Fair	□
Good	□
Very good	□
Excellent	□

7. How would you describe your current use of cigarettes? *(Check one)*

Never smoked	□
Former smoker	□
Smoke 1-10 cigarettes a day	□
Smoke 11-20 cigarettes a day	□
Smoke more than 20 cigarettes a day	□

8. How often do you drink alcoholic drinks, such as beer, wine or spirits?

(Check one)

Once a month or less	□
2-3 times a month	□
1-2 times a week	□
3-4 times a week	□
Daily or almost daily	□
I don't drink	□

9. When you drink, how much do you drink on the average?

(Check one)

1 drink	□
2 drinks	□
3-4 drinks	□
5 or more drinks	□
I don't drink	□

THE SICKNESS IMPACT PROFILE

We are interested in the effect of your injury on your health and daily activities. In each section mark only those statements that describe you today, and are related to your state of health. Once you have read each section and marked the appropriate statements, put a mark in the box at the end of the section.

Section A

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I spend much of the day lying down in order to rest ☐
2) I sit during much of the day ☐
3) I sleep or doze most of the time—day and night ☐
4) I lie down more often during the day in order to rest ☐
5) I sit around half-asleep ☐
6) I sleep less at night, for example, wake up too early, don't fall asleep for a long time, wake up frequently ☐
7) I sleep or nap more during the day ☐

Mark here when you have read all statements in this section ☐

Section B

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I often say how bad or useless I am, for example, that I am a burden on others ☐
2) I laugh or cry suddenly ☐
3) I often moan and groan in pain or discomfort ☐
4) I have attempted suicide ☐
5) I am nervous or restless ☐
6) I keep rubbing or holding areas of my body that hurt or are uncomfortable ☐
7) I am irritable and impatient with myself, for example, talk badly about myself, swear at myself, blame myself for things that happen ☐
8) I talk about the future in a hopeless way ☐
9) I get sudden frights ☐

Mark here when you have read all statements in this section ☐

Section C

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I make difficult moves with help, for example, getting into or out of cars, bath □
2) I cannot move into or out of bed or chair by myself but am moved by a person or mechanical aid □
3) I can stand only for short periods of time □
4) I cannot maintain balance □
5) I move my hands or fingers with some limitation or difficulty □
6) I can stand up only with someone's help □
7) I can kneel, stoop, or bend down only by holding on to something □
8) I am in a restricted position all the time □
9) I am very clumsy in body movements □
10) I get in and out of bed or chairs by grasping something for support or using a stick or frame □
11) I stay lying down most of the time □
12) I change position frequently □
13) I hold on to something to move myself around in bed □
14) I cannot bathe myself completely; for example, require assistance with bathing □
15) I cannot bathe myself at all, but am bathed by someone else □
16) I use a bedpan with assistance □
17) I have trouble getting shoes, socks, or stockings on □
18) I do not have control of my bladder □
19) I cannot fasten my clothing, for example, require assistance with buttons, zips, shoelaces □
20) I spend most of the time partly undressed or in pyjamas □
21) I do not have control of my bowels □
22) I can dress myself, but do so very slowly □
23) I can get dressed only with someone's help □

Mark here when you have read all statements in this section □

Section D

This group of statement has to do with any work that you usually do in caring for your home or garden. Considering just those things that you do, please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I can do work around the house only for short periods of time or rest often ☐
2) I am doing *less* of the regular daily work around the house than I would usually do ☐
3) I cannot do *any* of the regular daily work around the house that I would usually do ☐
4) I cannot do *any* of the maintenance or repair work that I would usually do in my home or yard ☐
5) I cannot do *any* of the shopping that I would usually do ☐
6) I cannot do *any* of the house cleaning that I would usually do ☐
7) I have difficulty doing handwork, for example, turning taps, using kitchen gadgets, sewing, carpentry ☐
8) I can not do *any* of the clothes washing that I would usually do ☐
9) I cannot do heavy work around the house ☐
10) I have given up taking care of personal or household business affairs, for example, paying bills, banking, working on budget ☐

Mark here when you have read all statements in this section ☐

Section E

Please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I can get around only within one building ☐
2) I stay within one room ☐
3) I am staying in bed more ☐
4) I am staying in bed most of the time ☐
5) I cannot now use public transportation ☐
6) I stay at home most of the time ☐
7) I can only go to places with toilets nearby ☐
8) I do not go into town ☐

Mark here when you have read all statements in this section ☐

Section F

Please mark only those statements that you are *sure* descr1be you today and are related to your state of health.

1) I go out less to visit people □
2) I do not go out to visit people at all □
3) I show less interest in other people's problems, for example, don't listen when they tell me about their problems, don't offer to help □
3) I often act irritable toward those around me, for example, snap at people, give sharp answers, criticise easily □
5) I show less affection □
6) I do fewer social activities with groups of people □
7) I have cut down the length of visits with friends □
8) I avoid social visits from others □
9) My sexual activity is decreased □
10) I often express concern over what might be happening to my health □
11) I talk less with those around me □
12) I make many demands, for example, insist that people do things for me, tell them how to do things

13) I stay alone much of the time □
14) I am disagreeable to family members, for example, I am spiteful, I am stubborn □
15) I have frequent outbursts of anger at family members, for example, strike at them, scream, throw things at them □
16) I isolate myself as much as I can from the rest of the family □
17) I pay less attention to the children □
18) I refuse contact with family members, for example, turn away from them □
19) I do not do the things I usually do to take care of my children or family □
20) I do not joke with family members as I usually do □

Mark here when you have read all statements in this section □

Section G

Please mark only those statements that you are *sure* descr1be you today and are related to your state of health.

1) I walk shorter distances or stop to rest more often □
2) I cannot walk up or down hills □
3) I can use stairs only with mechanical support, for example, handrail, stick, crutches □

4) I can walk up or down stairs only with assistance from someone else □
5) I get around in a wheelchair □
6) I cannot walk at all □
7) I can walk by myself but with some difficulty, for example, limp, wobble, stumble, have stiff leg□
8) I can walk only with help from someone □
9) I go up and down stairs more slowly, for example, one step at a time, stop often □
10) I cannot use stairs at all □
11) I can get around only by using a walker, crutches, stick, walls, or furniture □
12) I walk more slowly □

Mark here when you have read all statements in this section □

Section H

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I am confused and start several actions at a time □
2) I have more minor accidents, for example, drop things, trip and fall, bump into things □
3) I react slowly to things that are said or done □
4) I do not finish things I start □
5) I have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things □
6) I sometimes behave as if I were confused or disoriented in place or time, for example, where I am, who is around, directions, what day it is □
7) I forget a lot, for example, things that happened recently, where I put things, appointments □
8) I do not keep my attention on any activity for long □
9) I make more mistakes than usual □
10) I have difficulties doing activities involving concentration and thinking □

Mark here when you have read all statements in this section □

Section I

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I am having trouble writing or typing □

2) I communicate mostly by gestures, for example, moving my head, pointing, sign language □
3) My speech is understood by only a few people who know me well □
4) I often loose control of my voice when I talk, for example, my voice gets louder or softer trembles, changes unexpectedly □
5) I cannot write except to sign my name □
6) I carry on a conversation only when very close to the other person, or looking at them □
7) I have difficulty speaking, for example, get stuck, stutter, stammer, slur my words □
8) I am understood only with difficulty □
9) I do not speak clearly when I am under stress □

Mark here when you have read all statements in this section □

Section J

The next group of statements has to do with any work you usually do other than managing your home. By this we mean anything that you regard as work that you do on a regular basis.

Do you usually do work other than managing your home?

Yes □ No □

If you answered yes, go on to section k

If you answered no:

Are you retired? Yes □ No □

If you are retired, was your retirement related to your health? Yes □ No □

If you are not retired, but are not working, is this related to your health? Yes □ No □

Now skip to section L.

If you are not working and it is *not* because of your health, please **skip to section L.**

Mark here when you have read all statements in this section □

Section K

Now consider the work you do and mark only those statements that you are *sure* describe you today and are related to your state of health. (If today is a Saturday or Sunday or some other day that you would usually have off, please respond as if today were a working day.)

1) I am not working at all ☐

(If you checked this statement, skip to section L.)

2) I am doing part of my job at home ☐
3) I am not accomplishing as much as usual at work ☐
4) I am often irritable toward my work associates, for example, snap at them, give sharp answers, criticise easily ☐
5) I am working shorter hours ☐
6) I am doing only light work ☐
7) I work only for short periods of time or take frequent rests ☐
8) I am working at my usual job but with some changes, for example, using different tools or special aids, trading some tasks with other workers ☐
9) I do not do my job as carefully and accurately as usual ☐

Mark here when you have read all statements in this section ☐

Section L

This group of statements has to do with activities you usually do in your free time. These activities are things that you might do for relaxation, to pass the time, or for entertainment. Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I do my hobbies and recreation for shorter periods of time ☐
2) I go out for entertainment less often ☐
3) I have cut down on *some* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading ☐
4) I do not do *any* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading ☐
5) I do more inactive pastimes in place of my other usual activities ☐
6) I do fewer community activities ☐
7) I have cut down on *some* of my usual physical recreation or activities ☐
8) I am not doing any of my usual physical recreation or activities ☐

Mark here when you have read all statements in this section □

Section M

Please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I am eating much less than usual □
2) I feed myself but only by using specially prepared food or utensils □
3) I eat special or different food, for example, soft food, bland diet, low-salt, low-fat, low-sugar □
4) I eat no food at all but am taking fluids □
5) I just pick or nibble at my food □
6) I am drinking less fluids □
7) I feed myself with help from someone else □
8) I do not feed myself at all, but must be fed □
9) I am eating no food at all, nutrition is taken through tubes or intravenous fluids □

Mark here when you have read all statements in this section □

SHORT FORM 36

We are interested in finding out about your health, feelings and general activities over the four weeks. For each question, please mark the most appropriate answer.

Overall Health

1) In general, would you say that your health before your injury was:

Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐

2) Compared to one year ago, how would you rate your health over the four weeks?

Much better than a year ago ☐	Somewhat better than a year ago ☐	About the same ☐	Somewhat worse than a year ago ☐	Much worse than a year ago ☐

Health and Daily Activities

3) The following questions are about activities you might do during a typical day over the four weeks. Did **your health** limit you on these activities? If so, how much

	Yes, limited a lot	Yes, limited a little	No, not limited
a) **Vigorous activities,** such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
b) **Moderate activities,** such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
c) Lifting of carrying groceries	☐	☐	☐
d) Climbing **several** flights of stairs	☐	☐	☐
e) Climbing **one** flight of stairs	☐	☐	☐
f) Bending, kneeling or stooping	☐	☐	☐
g) Walking **more than one mile**	☐	☐	☐
h) Walking **half a mile**	☐	☐	☐
i) Walking **100 yards**	☐	☐	☐
j) Bathing and dressing	☐	☐	☐

4) During **the past four weeks**, how much of the time did you have any of the following problems with your work or other regular daily activities **as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the timetime	None of the
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like to	□	□	□	□	□
c) Were limited in the **kind** of work or other activities	□	□	□	□	□
d) Had **difficulty** performing the work or other activities (eg took more effort)	□	□	□	□	□

5) During the past **4 weeks**, how much time did you have any of the following problems with your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like	□	□	□	□	□
c) Did work or other activities **less carefully** than usual	□	□	□	□	□

6) During the past **4 weeks**, to what extent did your physical health or emotional problems interfere with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

7) How much bodily pain did you have during the past **4 weeks**?

None	Very mild	Mild	Moderate	Severe	Very severe
□	□	□	□	□	□

8) During the **4 weeks before your injury**, how much did **pain** interfere with your normal work (both outside the house and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

Your Feelings

9) These questions are about how you felt and how things were with you **during the past month**. For each question please give the answer that comes closest to the way you have been feeling.

How much **during the past month**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Did you feel full of life?	□	□	□	□	□
b) Were you very nervous?	□	□	□	□	□
c) Did you felt so down in the dumps that nothing could cheer you up?	□	□	□	□	□
d) Did you feel calm and peaceful?	□	□	□	□	□
e) Did you have a lot of energy?	□	□	□	□	□
f) Did you feel worn out?	□	□	□	□	□
g) Were you happy?	□	□	□	□	□
h) Did you feel tired?	□	□	□	□	□

10) **During the past 4 weeks** how much of your time did your physical health or emotional problems interfere with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
□	□	□	□	□

Health in General

11) How TRUE or FALSE was **each** of the following statements to you **during the past 4 weeks**?

	Definitely true	Mostly true	Not true	Mostly false	Definitely false
a) I seemed to get ill more easily than other people	□	□	□	□	□
b) I was as healthy as anybody I know	□	□	□	□	□
c) I expected my health to get worse	□	□	□	□	□
d) My health was excellent	□	□	□	□	□

GRAMPIAN TRAUMA OUTCOMES STUDY

6 MONTH ASSESSMENT DOCUMENTS

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UNIVERSITY OF **ABERDEEN**

Aberdeen Trauma Outcomes Study

Patient Information Sheet

Hopefully you will remember helping us out with this study when you were in hospital after your injury, and again two months after your injury. I am sure that your injury now seems long ago, but it is now time to ask you to fill in the final set of follow-up forms. These forms again ask a series of questions in quite specific ways, in order to see how you are recovering from your injuries. You may notice some overlap between the forms, and some of the questions may not seem relevant to you - please answer all of the questions as they apply to you.

An accident causing serious injury is very stressful, but it has become clear that some people cope better with the stress than others. It may be that those people who cope well mentally with the aftermath of an accident may heal more quickly than those that do not. It is our intention to monitor a large group of patients who have been involved in accidents, using a series of questionnaires to assess how well they are recovering. Most of the questionnaires that we are using have been used many times in the past, and are of proven worth, but we are also testing out a new questionnaire from the USA to see if it can provide us with further useful information.

This study will not affect your treatment in any way, and you will continue to be given the best possible care. If you decide not to participate further in this study, then this will again have no effect on your treatment. Just let us know and no further reminders will be sent

If you have any questions at all, please feel free to call me. My contact numbers are on the front sheet of this booklet, and if I am not there to answer straight away, please leave a message and I will call you back.

Thank you for taking the time to read this and to complete the enclosed forms

Alasdair Sutherland
Lecturer in Orthopaedics

GRAMPIAN TRAUMA OUTCOMES STUDY

6 MONTH ASSESSMENT

These questions relate to any changes in your home and work circumstances since your injury, whether they are related to your injury or not. For each question, please check the box which most closely applies to you.

1. What is your marital status? **(***Check one)*

- Married or living as married ☐
- Widowed ☐
- Divorced ☐
- Separated ☐
- Never married ☐

2. Do you live alone or with someone else? *(Check all that apply)*

- Alone ☐
- With another adult ☐
- With a child/children (7-17 years old) ☐
- With -a child/children (birth to 6 years old) ☐

3. Are your daily activities or work...? *(Check one)*

- The same as before your injury or arthritis ☐
- Different due to your injury ☐
- Different, but not due to your injury ☐

4. Are you now...? *(Check one)*

- Employed full-time (35 or more hours a week) ☐
- Employed part-time, because of your health ☐
- Employed part-time, for reasons other than health ☐
- Employed, but on sick-leave ☐
- Retired, because of your health ☐
- Retired, for reasons other than health ☐
- Laid-off or unemployed, because of health ☐
- Laid-off or unemployed, for reasons other than health ☐
- Full-time housewife ☐
- Other *(please write in)*

  _____ ☐

5. If you are not currently working, when do you plan to return to work?

(Check one)

Within 1 month	☐
Within 2-4 months	☐
Within 5-8 months	☐
Within 9-12 months	☐
I plan to work sometime later	☐
I have no plans to work	☐
I am currently working	☐

6. Are you involved in legal action because of your injury?

(Check one)

NO	☐
YES	☐

7. Are you receiving or applying for any disability compensation for your injury?

(Check one)

NO	☐ —> *(Please go to Question 15)*
YES	☐

8. What type of disability compensation are you receiving or applying for?

	(Check all that apply)
DHSS disability benefit	☐
Personal injury claim	☐
Private disability insurance	☐
Other *(please write in)*_____	☐

9. How has your household income changed because of your injury or arthritis?

(Check one)

Unchanged	☐
Decreased	☐
Increased	☐

10. Do you have private health insurance that is covering the care for your injury?

YES ☐ NO ☐

THE
GENERAL HEALTH
QUESTIONNAIRE

We would like to know if you have had any medical complaints and how your health has been in general, *over the past few weeks.* Please answer ALL the questions on the following pages simply by circling the answer which you think most nearly applies to you. Remember that we want to know about present and recent complaints, not those that you had in the past.

It is important that you try to answer ALL the questions.

Have you recently				
Al — been feeling perfectly well and in good health?	*Better than usual*	*Same as usual*	*Worse than usual*	*Much worse than usual*
A2 —been feeling in need of a good tonic?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A3 — been feeling run down and out of sorts?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A4 — felt that you are ill?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A5 — been getting any pains in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A6 — been getting a feeling of tightness or pressure in your head?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
A7 — been having hot or cold spells?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
Have you recently				
B1— lost much sleep over worry?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B2 — had difficulty in staying asleep once you are off?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B3 — felt constantly under strain?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B4 — been getting edgy and bad-tempered?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B5 — been getting scared or panicky for no good reason?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B6 — found everything getting on top of you?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
B7 — been feeling nervous and strung-up all the time?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*

Have you recently				
Cl — been managing to keep yourself busy and occupied?	*More so than usual*	*Same as usual*	*Rather less than usual*	*Much less than usual*
C2 — been taking longer over the things you do?	*Quicker than usual*	*Same as usual*	*Longer than usual*	*Much longer than usual*
C3 — felt on the whole you were doing things well?	*Better than usual*	*About the same*	*Less well than usual*	*Much less well*
C4 — been satisfied with the way you've carried out your task?	*More satisfied*	*About same as usual*	*Less satisfied than usual*	*Much less satisfied*
C5 — felt that you are playing a useful part in things?	*More so than usual*	*Same as usual*	*Less useful than usual*	*Much less useful*
C6 — felt capable of making decisions about things?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less capable*
C7 — been able to enjoy your normal day-to-day activities?	*More so than usual*	*Same as usual*	*Less so than usual*	*Much less than usual*
Have you recently				
Dl — been thinking of your self as a worthless person?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D2 — felt that life is entirely hopeless?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D3 — felt that life isn't worth living?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D4 — thought of the possibility that you might do away with yourself?	*Definitely Not*	*I don't think so*	*Has crossed my mind*	*Definitely have*
D5 — found at times you couldn't do anything because your nerves were too bad?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D6 — found yourself wishing you were dead and away from it all?	*Not at all*	*No more than usual*	*Rather more than usual*	*Much more than usual*
D7 — found that the idea of taking your own life kept coming into your mind?	*Definitely not*	*I don't think so*	*Has crossed my mind*	*Definitely have*

A	B	C	D	TOTAL
___	____	____	____	_____

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MUSCULOSKELETAL FUNCTION ASSESSMENT

PART I: INSTRUCTIONS

We are interested in finding out how you are managing with your injury this week.
Please answer "YES" or "NO" to each question by putting a cross in the box next to the question. If the question is true for you and is related to your injury, choose "YES". If the question is not true for you and is not related to your injury, choose "NO".

If you wish to comment on any of the questions, please use the space in the margins. Please answer all questions, even though some of the questions may not apply to your injury.

PLEASE WRITE IN TODAY'S DATE: _____

ACTIVITIES USING YOUR ARMS or LEGS

This first set of questions is about changes or problems you may have using your arms or legs to do such things as reaching, walking, and carrying.

This week, because of your injury	**YES**	**NO**
1. Are you unable to walk?	☐	☐
2. Do you feel unsteady on your feet?	☐	☐
3. Is it difficult for you to reach up high?	☐	☐
4. Can you straighten or bend your arm(s) completely?	☐	☐
5. Can you straighten or bend your leg(s) completely?	☐	☐
6. Can you pivot on one leg?	☐	☐
7. Can you climb up and down ladders?	☐	☐
8. Do you have to rest often when walking?	☐	☐
9. Do you avoid stairs?	☐	☐
10 Can you stand for long periods of time?	☐	☐
11 Is it hard for you to get moving after you have been sitting or lying down?	☐	☐
12 Do you always walk with a limp?	☐	☐
13. Does your leg sometimes lock or give-way?	☐	☐
14. Do you have trouble getting in or out of a low chair?	☐	☐
15. Do you have trouble getting in or out of bed?	☐	☐
16. Can you kneel?	☐	☐
17. Can you pick up things from the floor?	☐	☐

	YES	NO
19. Do you have trouble getting in or out of a car?	□	□
20. Have you stopped using public transport because of your injury?	□	□

How much are you bothered by problems you are now having using your arms or legs? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	Extremely Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered

ACTIVITIES USING YOUR HANDS

The following questions are about activities using your hands. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury..		**YES**	**NO**
1.	Do you have difficulty squeezing things?	□	□
2.	Do you have difficulty making a tight fist?	□	□
3.	Is it hard for you to put your hand in your pocket?	□	□
4.	Do you have difficulty turning handles or levers (for example, opening doors, rolling down car windows)?	□	□
5.	Do you have trouble holding a book?	□	□
6.	Do you have difficulty writing or typing?	□	□
7.	Do you have trouble opening medicine bottles or jars?	□	□

How much are you bothered by problems you are now having using your hands? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK AROUND YOUR HOME

These questions are about activities around your home, including such things as cooking, cleaning, maintenance, or repairs. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you need help with housework or work in the garden?	□	□
2.	Can you do as much housework or work in the garden as before your injury?	□	□
3.	Can you manage household chores but find that it takes more effort?	□	□
4.	Can you mop or sweep or vacuum?	□	□
5.	Is scrubbing a pan or dish difficult?	□	□
6.	Do you need someone to cook for you?	□	□
7.	Does it take you longer to do household chores?	□	□
8.	Is it difficult for you to shop for groceries or other things?	□	□
9.	Have you stopped doing car, house, or maintenance repairs because of your injury?	□	□

How much are you bothered by problems you are now having doing work around your home? *(Please check one.)*

□		□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SELF CARE ACTIVITIES

The following questions are about taking care of yourself. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you wear things that are easier to get into?	□	□
2.	Do you sometimes need help from others to get dressed?	□	□
3.	Do you struggle with buttons, snaps, hooks, zips?	□	□
4.	Do you have trouble pulling clothes on over your head?	□	□
5.	Is it difficult for you to put on shoes, socks, or stockings?	□	□
6.	Is it a chore for you to dress because it takes so long?	□	□
7.	Is it difficult to brush your teeth?	□	□

		YES	NO
8.	Do you have a difficult time cutting your fingernails?	□	□
9.	Do you need help keeping yourself clean after going to the bathroom?	□	□
10.	Is it difficult for you to get on or off the toilet?	□	□
11.	Is it hard for you to get in or out of the bath or shower?	□	□
12.	Do you sit while showering?	□	□
13.	Do you need help washing yourself?	□	□
14.	Do you need help eating?	□	□
15.	Is it hard for you to cut food?	□	□
16.	Are you stuck at home?	□	□
17.	Have you stopped going out by yourself?	□	□
18.	Have you stopped driving because of your injury?	□	□

How much are you bothered by problems you are now having caring for yourself? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

SLEEP and REST

These questions are about changes or problems you may be experiencing with sleep and rest. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Are you tired all of the time?	□	□
2.	Do you have trouble falling asleep at night?	□	□
3.	Do you have difficulty sleeping the whole night?	□	□
4.	Is it hard for you to get comfortable to sleep?	□	□
5.	Do you wake up sooner than you would like?	□	□
6.	Do you have disturbing dreams?	□	□

How much are you bothered by problems you are now having with sleep and rest? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

LEISURE AND RECREATIONAL ACTIVITIES

We would also like to know about changes or problems you are having with leisure time or recreational activities. These activities may include such things as hobbies, sports, crafts, gardening, aerobics, or volunteering. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Is your physical fitness worse because of your injury?	☐	☐
2.	Do you do less of your usual physical recreational activities?	☐	☐
3.	Have you stopped doing all of your usual physical recreational activities?	☐	☐
4.	Are you doing fewer leisure activities (such as hobbies, crafts, gardening, card playing, going out with friends)?	☐	☐

How much are you bothered by problems you are now having with leisure and recreational activities? *(Please check one.)*

☐	☐	☐	☐	☐
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

RELATIONSHIPS:

FAMILY and FRIENDS

These questions are about your relationships with family, friends, and other important people in your life. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury...		**YES**	**NO**
1.	Is there a strain in your relationships with either your friends or family?	☐	☐

		YES	NO
2.	Do you feel you just don't want to be around anybody?	□	□
3.	Is it hard for you to get either your family or friends to help you do things?	□	□
4.	Are you lonely?	□	□
5.	Do you feel that either your friends or family have shied away from you?	□	□
6.	Are you often irritable toward those around you (for example, snap at people, give sharp answers, criticise easily)?	□	□
7.	Do you miss being with either your friends or family?	□	□
8.	Do you feel like being less intimate?	□	□
9.	Has your sexual life changed?	□	□
10.	Do you enjoy sex less?	□	□

How much are you bothered by problems you are now having with your friends, family, and other important people in your life? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

THINKING

At times, people may have difficulty with thinking, concentrating, or remembering as a result of their injury. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Does it take you longer to figure things out?	□	□
2.	Do you have problems with concentration?	□	□
3.	Are you more confused and scattered?	□	□
4.	Are you more forgetful?	□	□

How much are you bothered by problems you are now having thinking, concentrating, and remembering? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

LIFE CHANGES and FEELINGS

These questions are about day to day adiustments you may be making because of your injury and about feelings you may be having about your experiences. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Do you sometimes use your injuries as an excuse not to do things?	□	□
2.	Do you have to concentrate when using your injured limb?	□	□
3.	Do you avoid using your injured limb?	□	□
4.	Do you protect your injured limb?	□	□
5.	Do you think everything will work out well in the long run?	□	□
6.	Do you accept your current situation?	□	□
7.	Do you feel everything is back to normal?	□	□
8.	Do you feel your life has changed quite a bit?	□	□
9.	Are you getting worse[7]	□	□
10.	If you do too much in one day, does it affect what you do the next day?	□	□
11.	Do you feel disabled, even though you may look fine to others?	□	□
12.	Do you feel useless?	□	□
13.	Do you feel unattractive?	□	□
14.	Does your injury make you feel less capable?	□	□
15.	Do you feel sorry for your self?	□	□
16.	Do you feel like you complain a lot?	□	□
17.	Do you have to ask for help a lot?	□	□
18.	Do you feel angry or frustrated that you have this injury?	□	□

How much are you bothered by the day to day adjustments you are making in your life and the feelings you are now experiencing, because of your injury?

(Please check one.)

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

WORK ACTIVITIES

Are you working now?

□ **NO----------**> Are you unable to work because of your injury?

□ **NO** *(Please skip to Part II)*

□ **YES** *(Please skip to Part II)*

□ **YES----------**> *(Please answer questions below)*

Please answer these questions as they describe your experiences at work. If the question is true for you, please check "YES". If the question is not true for you, please check "NO".

This week, because of your injury		**YES**	**NO**
1.	Are you making changes in your job?	□	□
2.	Is it more difficult for you to do your job now?	□	□
3.	Are you slower at your job?	□	□
4.	Do you take more breaks?	□	□

How much are you bothered by problems you are **now** having with work activities, because of your injury or arthritis? *(Please check one.)*

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

PART II: INSTRUCTIONS

In this section of the survey some questions are answered with a **"YES"** or "**NO**". Others have a number of choices. Please indicate your choice by putting a check in the box that is true for you.

3 HEALTH and DAILY ACTIVITIES

These questions are about your health and daily activities. Please try to answer each question as accurately as you can.

1. Do you have any of the following conditions?

(Check one answer for each condition.)	**YES**	**NO**
Heart Problems (heart attack, angina, congestive heart failure)	☐	☐
Lung Problems (including bronchitis or emphysema)	☐	☐
Blindness or Trouble Seeing, even when wearing glasses	☐	☐
Deafness or Trouble Hearing	☐	☐
Bad Headaches or Migraines	☐	☐
Depression, Anxiety or other Mental Troubles	☐	☐
Allergies	☐	☐
Diabetes	☐	☐
Asthma	☐	☐
Stomach Problems	☐	☐
Arthritis	☐	☐
Menstrual or Female Problems	☐	☐
Back Problems	☐	☐
High Blood Pressure or Hypertension	☐	☐
Stroke	☐	☐
Kidney Disease	☐	☐
Cancer (not including skin cancer)	☐	☐
Other	☐	☐

2. Are you now using any of the following aids?

	(Check one answer for each item)	
	YES	**NO**
Sling	□	□
Brace or splint	□	□
Cast	□	□
Walking stick	□	□
Crutches	□	□
Walking frame (zimmer frame)	□	□
Wheelchair	□	□
Electric wheelchair or buggy	□	□
Oother *(please write in)* _____	□	□

3. How much has your injury changed your life?

(Check one)

Not at all	□
A little	□
Somewhat	□
Quite a bit	□
Completely	□

4. **People sometimes have good days and sometimes have bad days. How are you doing today?**

(Check one)

Very bad	□
Bad	□
Average or typical day	□
Good	□
Very good	□

5. In the <u>past week</u>, how much were you bothered by pain?

□	□	□	□	□
1	2	3	4	5
Not at All Bothered	A Little Bothered	Somewhat Bothered	Quite Bothered	Extremely Bothered

6. Rate the overall quality of care you have received for your injury

(Check one)

Poor	□
Fair	□
Good	□
Very good	□
Excellent	□

7. How would you describe your current use of cigarettes? *(Check one)*

Never smoked	□
Former smoker	□
Smoke 1-10 cigarettes a day	□
Smoke 11-20 cigarettes a day	□
Smoke more than 20 cigarettes a day	□

8. How often do you drink alcoholic drinks, such as beer, wine or spirits?

(Check one)

Once a month or less	□
2-3 times a month	□
1-2 times a week	□
3-4 times a week	□
Daily or almost daily	□
I don't drink	□

9. When you drink, how much do you drink on the average?

(Check one)

1 drink	□
2 drinks	□
3-4 drinks	□
5 or more drinks	□
I don't drink	□

THE SICKNESS IMPACT PROFILE

We are interested in the effect of your injury on your health and daily activities. In each section mark only those statements that describe you today, and are related to your state of health. Once you have read each section and marked the appropriate statements, put a mark in the box at the end of the section.

Section A

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I spend much of the day lying down in order to rest ☐
2) I sit during much of the day ☐
3) I sleep or doze most of the time—day and night ☐
4) I lie down more often during the day in order to rest ☐
5) I sit around half-asleep ☐
6) I sleep less at night, for example, wake up too early, don't fall asleep for a long time, wake up frequently ☐
7) I sleep or nap more during the day ☐

Mark here when you have read all statements in this section ☐

Section B

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I often say how bad or useless I am, for example, that I am a burden on others ☐
2) I laugh or cry suddenly ☐
3) I often moan and groan in pain or discomfort ☐
4) I have attempted suicide ☐
5) I am nervous or restless ☐
6) I keep rubbing or holding areas of my body that hurt or are uncomfortable ☐
7) I am irritable and impatient with myself, for example, talk badly about myself, swear at myself, blame myself for things that happen ☐
8) I talk about the future in a hopeless way ☐
9) I get sudden frights ☐

Mark here when you have read all statements in this section ☐

Section C

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I make difficult moves with help, for example, getting into or out of cars, bath □
2) I cannot move into or out of bed or chair by myself but am moved by a person or mechanical aid □
3) I can stand only for short periods of time □
4) I cannot maintain balance □
5) I move my hands or fingers with some limitation or difficulty □
6) I can stand up only with someone's help □
7) I can kneel, stoop, or bend down only by holding on to something □
8) I am in a restricted position all the time □
9) I am very clumsy in body movements □
10) I get in and out of bed or chairs by grasping something for support or using a stick or frame □
11) I stay lying down most of the time □
12) I change position frequently □
13) I hold on to something to move myself around in bed □
14) I cannot bathe myself completely; for example, require assistance with bathing □
15) I cannot bathe myself at all, but am bathed by someone else □
16) I use a bedpan with assistance □
17) I have trouble getting shoes, socks, or stockings on □
18) I do not have control of my bladder □
19) I cannot fasten my clothing, for example, require assistance with buttons, zips, shoelaces □
20) I spend most of the time partly undressed or in pyjamas □
21) I do not have control of my bowels □
22) I can dress myself, but do so very slowly □
23) I can get dressed only with someone's help □

Mark here when you have read all statements in this section □

Section D

This group of statement has to do with any work that you usually do in caring for your home or garden. Considering just those things that you do, please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I can do work around the house only for short periods of time or rest often □
2) I am doing *less* of the regular daily work around the house than I would usually do □
3) I cannot do *any* of the regular daily work around the house that I would usually do □
4) I cannot do *any* of the maintenance or repair work that I would usually do in my home or yard □
5) I cannot do *any* of the shopping that I would usually do □
6) I cannot do *any* of the house cleaning that I would usually do □
7) I have difficulty doing handwork, for example, turning taps, using kitchen gadgets, sewing, carpentry □
8) I can not do *any* of the clothes washing that I would usually do □
9) I cannot do heavy work around the house □
10) I have given up taking care of personal or household business affairs, for example, paying bills, banking, working on budget □

Mark here when you have read all statements in this section □

Section E

Please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I can get around only within one building □
2) I stay within one room □
3) I am staying in bed more □
4) I am staying in bed most of the time □
5) I cannot now use public transportation □
6) I stay at home most of the time □
7) I can only go to places with toilets nearby □
8) I do not go into town □

Mark here when you have read all statements in this section □

Section F

Please mark only those statements that you are *sure* descr1be you today and are related to your state of health.

1) I go out less to visit people □
2) I do not go out to visit people at all □
3) I show less interest in other people's problems, for example, don't listen when they tell me about their problems, don't offer to help □
4) I often act irritable toward those around me, for example, snap at people, give sharp answers, criticise easily □
5) I show less affection □
6) I do fewer social activities with groups of people □
7) I have cut down the length of visits with friends □
8) I avoid social visits from others □
9) My sexual activity is decreased □
10) I often express concern over what might be happening to my health □
11) I talk less with those around me □
12) I make many demands, for example, insist that people do things for me, tell them how to do things

13) I stay alone much of the time □
14) I am disagreeable to family members, for example, I am spiteful, I am stubborn □
15) I have frequent outbursts of anger at family members, for example, strike at them, scream, throw things at them □
16) I isolate myself as much as I can from the rest of the family □
17) I pay less attention to the children □
18) I refuse contact with family members, for example, turn away from them □
19) I do not do the things I usually do to take care of my children or family □
20) I do not joke with family members as I usually do □

Mark here when you have read all statements in this section □

Section G

Please mark only those statements that you are *sure* descr1be you today and are related to your state of health.

1) I walk shorter distances or stop to rest more often □
2) I cannot walk up or down hills □
3) I can use stairs only with mechanical support, for example, handrail, stick, crutches □

4) I can walk up or down stairs only with assistance from someone else □
5) I get around in a wheelchair □
6) I cannot walk at all □
7) I can walk by myself but with some difficulty, for example, limp, wobble, stumble, have stiff leg □
8) I can walk only with help from someone □
9) I go up and down stairs more slowly, for example, one step at a time, stop often □
10) I cannot use stairs at all □
11) I can get around only by using a walker, crutches, stick, walls, or furniture □
12) I walk more slowly □

Mark here when you have read all statements in this section □

Section H

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I am confused and start several actions at a time □
2) I have more minor accidents, for example, drop things, trip and fall, bump into things □
3) I react slowly to things that are said or done □
4) I do not finish things I start □
5) I have difficulty reasoning and solving problems, for example, making plans, making decisions, learning new things □
6) I sometimes behave as if I were confused or disoriented in place or time, for example, where I am, who is around, directions, what day it is □
7) I forget a lot, for example, things that happened recently, where I put things, appointments □
8) I do not keep my attention on any activity for long □
9) I make more mistakes than usual □
10) I have difficulties doing activities involving concentration and thinking □

Mark here when you have read all statements in this section □

Section I

Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I am having trouble writing or typing □
2) I communicate mostly by gestures, for example, moving my head, pointing, sign language □

3) My speech is understood by only a few people who know me well □
4) I often loose control of my voice when I talk, for example, my voice gets louder or softer trembles, changes unexpectedly □
5) I cannot write except to sign my name □
6) I carry on a conversation only when very close to the other person, or looking at them □
7) I have difficulty speaking, for example, get stuck, stutter, stammer, slur my words □
8) I am understood only with difficulty □
9) I do not speak clearly when I am under stress □

Mark here when you have read all statements in this section □

Section J

The next group of statements has to do with any work you usually do other than managing your home. By this we mean anything that you regard as work that you do on a regular basis.

Do you usually do work other than managing your home?

Yes □ No □

If you answered yes, go on to section k

If you answered no:

Are you retired? Yes □ No □

If you are retired, was your retirement related to your health? Yes □ No □

If you are not retired, but are not working, is this related to your health? Yes □ No □

Now skip to section L.

If you are not working and it is *not* because of your health, please **skip to section L.**

Mark here when you have read all statements in this section □

Section K

Now consider the work you do and mark only those statements that you are *sure* describe you today and are related to your state of health. (If today is a Saturday or Sunday or some other day that you would usually have off, please respond as if today were a working day.)

1) I am not working at all ☐

(If you checked this statement, skip to section L.)

2) I am doing part of my job at home ☐
3) I am not accomplishing as much as usual at work ☐
4) I am often irritable toward my work associates, for example, snap at them, give sharp answers, criticise easily ☐
5) I am working shorter hours ☐
6) I am doing only light work ☐
7) I work only for short periods of time or take frequent rests ☐
8) I am working at my usual job but with some changes, for example, using different tools or special aids, trading some tasks with other workers ☐
9) I do not do my job as carefully and accurately as usual ☐

Mark here when you have read all statements in this section ☐

Section L

This group of statements has to do with activities you usually do in your free time. These activities are things that you might do for relaxation, to pass the time, or for entertainment. Please mark only those statements that you are *sure* describe you today and are related to your state of health.

1) I do my hobbies and recreation for shorter periods of time ☐
2) I go out for entertainment less often ☐
3) I have cut down on *some* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading ☐
4) I do not do *any* of my usual inactive recreation and pastimes, for example, watching TV, playing cards, reading ☐
5) I do more inactive pastimes in place of my other usual activities ☐
6) I do fewer community activities ☐
7) I have cut down on *some* of my usual physical recreation or activities ☐
8) I am not doing any of my usual physical recreation or activities ☐

Mark here when you have read all statements in this section □

Section M

Please mark *only* those statements that you are *sure* describe you today and are related to your state of health.

1) I am eating much less than usual □
2) I feed myself but only by using specially prepared food or utensils □
3) I eat special or different food, for example, soft food, bland diet, low-salt, low-fat, low-sugar □
4) I eat no food at all but am taking fluids □
5) I just pick or nibble at my food □
6) I am drinking less fluids
7) I feed myself with help from someone else □
8) I do not feed myself at all, but must be fed □
9) I am eating no food at all, nutrition is taken through tubes or intravenous fluids □

Mark here when you have read all statements in this section □

SHORT FORM 36

We are interested in finding out about your health, feelings and general activities over the four weeks. For each question, please mark the most appropriate answer.

Overall Health

1) In general, would you say that your health before your injury was:

Excellent ☐ Very Good ☐ Good ☐ Fair ☐ Poor ☐

2) Compared to one year ago, how would you rate your health over the four weeks?

Much better than a year ago ☐	Somewhat better than a year ago ☐	About the same ☐	Somewhat worse than a year ago ☐	Much worse than a year ago ☐

Health and Daily Activities

3) The following questions are about activities you might do during a typical day over the four weeks. Did **your health** limit you on these activities? If so, how much

	Yes, limited a lot	Yes, limited a little	No, not limited
a) **Vigorous activities,** such as running, lifting heavy objects, participating in strenuous sports	☐	☐	☐
b) **Moderate activities,** such as moving a table, pushing a vacuum cleaner, bowling or playing golf	☐	☐	☐
c) Lifting of carrying groceries	☐	☐	☐
d) Climbing **several** flights of stairs	☐	☐	☐
e) Climbing **one** flight of stairs	☐	☐	☐
f) Bending, kneeling or stooping	☐	☐	☐
g) Walking **more than one mile**	☐	☐	☐
h) Walking **half a mile**	☐	☐	☐
i) Walking **100 yards**	☐	☐	☐
j) Bathing and dressing	☐	☐	☐

4) During **the past four weeks**, how much of the time did you have any of the following problems with your work or other regular daily activities **as a result of your physical health?**

	All of the time	Most of the time	Some of the time	A little of the timetime	None of the
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like to	□	□	□	□	□
c) Were limited in the **kind** of work or other activities	□	□	□	□	□
d) Had **difficulty** performing the work or other activities (eg took more effort)	□	□	□	□	□

5) During the past **4 weeks**, how much time did you have any of the following problems with your work or any other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Cut down on the **amount of time** you spent on work or other activities	□	□	□	□	□
b) **Accomplished less** than you would like	□	□	□	□	□
c) Did work or other activities **less carefully** than usual	□	□	□	□	□

6) During the past **4 weeks**, to what extent did your physical health or emotional problems interfere with your normal social activities with family, friends, neighbours, or groups?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

2) How much bodily pain did you have during the past **4 weeks**?

None	Very mild	Mild	Moderate	Severe	Very severe
□	□	□	□	□	□

8) During the **4 weeks before your injury**, how much did **pain** interfere with your normal work (both outside the house and housework)?

Not at all	Slightly	Moderately	Quite a bit	Extremely
□	□	□	□	□

Your Feelings

9) These questions are about how you felt and how things were with you **during the past month**. For each question please give the answer that comes closest to the way you have been feeling.

How much **during the past month**

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
a) Did you feel full of life?	□	□	□	□	□
b) Were you very nervous?	□	□	□	□	□
c) Did you felt so down in the dumps that nothing could cheer you up?	□	□	□	□	□
d) Did you feel calm and peaceful?	□	□	□	□	□
e) Did you have a lot of energy?	□	□	□	□	□
f) Did you feel worn out?	□	□	□	□	□
g) Were you happy?	□	□	□	□	□
h) Did you feel tired?	□	□	□	□	□

10) **During the past 4 weeks** how much of your time did your physical health or emotional problems interfere with your social activities (like visiting friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
□	□	□	□	□

Health in General

12) How TRUE or FALSE was **each** of the following statements to you **during the past 4 weeks**?

	Definitely true	Mostly true	Not true	Mostly false	Definitely false
a) I seemed to get ill more easily than other people	□	□	□	□	□
b) I was as healthy as anybody I know	□	□	□	□	□
c) I expected my health to get worse	□	□	□	□	□
d) My health was excellent	□	□	□	□	□

APPENDIX 4

GHQ Results for GTOS-MM subgroup

A4 GHQ Results for GTOS-MM subgroup

Table A4.1 displays the GHQ total scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 28. Statistically significant differences are noted between GHQ scores at initial and two-month assessments. The GHQ subscores at each assessment point are shown in table A4.2. Significant differences are noted between GHQ subscores at initial and two months and between scores at initial and six-month assessments.

	Number	***Mean***	***Median***	***SD***	***Range***
Initial	83	1.31	0.00	2.69	0-14
2 months	66	6.10	0.00 ***	5.98	0-24
6 months	62	3.39	0.00 ***	5.90	0-24

Table A4.1 Analysis of GHQ total scores for GTOS-MM subgroup (***p=0.001; Wilcoxon signed ranks test).

	Initial (n=83)			***2 Mo (n=68)***			***6 Mo (n=62)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
GHQ A	0.19 (0.83)	0.00	0-7	1.26 (1.62)	0.00 ***	0-6	0.92 (1.73)	0.00 ***	0-7
GHQ B	0.61 (1.23)	0.00	0-6	1.18 (1.79)	0.00 **	0-7	0.92 (1.93)	0.00	0-7
GHQ C	0.35 (1.13)	0.00	0-6	3.05 (2.28)	2.00 ***	0-7	1.39 (2.12)	0.00 ***	0-7
GHQ D	1.57 (0.63)	0.00	0-4	0.62 (1.49)	0.00 **	0-7	0.42 (1.45)	0.00	0-7

Table A4.2 Analysis of GHQ subscores for GTOS-MM subgroup (Differences between baseline and follow-up: *** $p<0.001$, ** $p\leq0.02$; Wilcoxon signed ranks test).

Results for GHQ caseness are shown in Table A4.3. Significant differences are noted in caseness between initial and two-month follow-up, and between initial and six-month follow-up. Fig A4.1 demonstrates the progress of caseness, with an increase to two months followed by a fall, though not back to initial levels, by six months.

	No of GHQ cases (%) at 4/5 Threshold
Initial	9 (11)
2 months	32 (39) ***
6 months	15 (18) **

Table A4.3 Analysis of GHQ Caseness for GTOS-MM subgroup (Differences between baseline and follow-up: *** p<0.001, ** p<0.02; Wilcoxon signed ranks test).

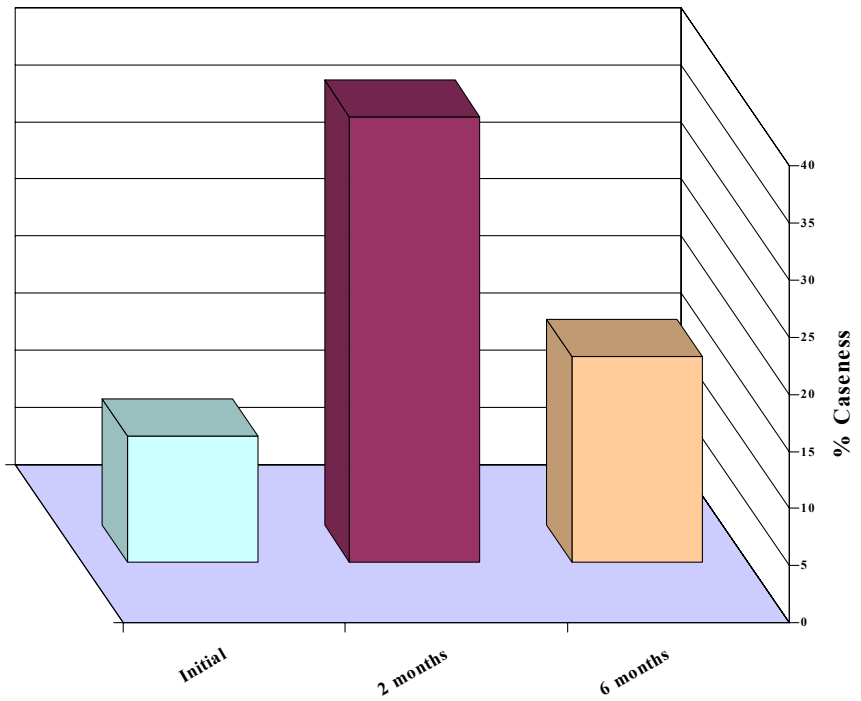

Fig A4.1 GHQ Caseness for GTOS-MM subgroup

APPENDIX 5

SF-36 Results for GTOS-MM Subgroup

A5 SF-36 Results for GTOS-MM Subgroup

Table A5.1 displays the SF-36 scale and total scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 100 (minimum dysfunction). Statistically significant differences are noted between mean SF-36 scale and total scores at initial and two months, and between scores at initial and six-month assessments. Fig A5.1 graphically shows the fall in SF-36 scores at two months and their partial recovery by six months.

SF-36 scale/total	*Initial (n=83)*			*2 Mo (n=66)*			*6 Mo (n=62)*		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Physical Function	96.40 (12.65)	100	5-100	59.92 (30.14)	65.00 ***	0-100	73.22 (25.47)	78.89 ***	0-100
Social Function	94.21 (13.20)	100	37-100	60.98 (29.21)	62.50 ***	0-100	82.71 (21.97)	100 ***	25-100
Limitation – Physical probs.	76.58 (9.96)	80.00	20-80	36.06 (24.03)	37.50 ***	0-80	56.83 (27.34)	67.50 ***	0-80
Limitation-emotional probs	76.46 (10.24)	80.00	13-80	59.70 (25.34)	66.66 ***	0-80	66.36 (20.99)	80.00 ***	13-80
Mental Health	76.34 (9.40)	80.00	45-90	69.14 (18.58)	75.00 ***	25-90	70.97 (13.75)	75.00 ***	35-90
Energy & Fatigue	68.78 (12.39)	70.00	30-90	54.14 (18.58)	50.00 ***	10-85	57.55 (17.68)	60.00 ***	15-90
Pain	94.95 (11.22)	100.00	52-100	57.05 (26.27)	51.00 ***	12-100	63.55 (27.42)	62.00 ***	12-100
General Health Perception	81.56 (17.51)	87.00	15-100	60.45 (15.30)	62.00 ***	17-96	65.13 (18.63)	67.00 ***	17-100
Change in Health	57.93 (17.51)	50.00	25-100	37.31 (21.25)	50.00 ***	0-75	42.92 (22.12)	50.00 ***	0-100

Table A5.1. Analysis of SF-36 scale and total scores for GTOS-MM subgroup. (Differences between baseline and follow-up: ***p≤0.001; Wilxcoxon signed ranks test)

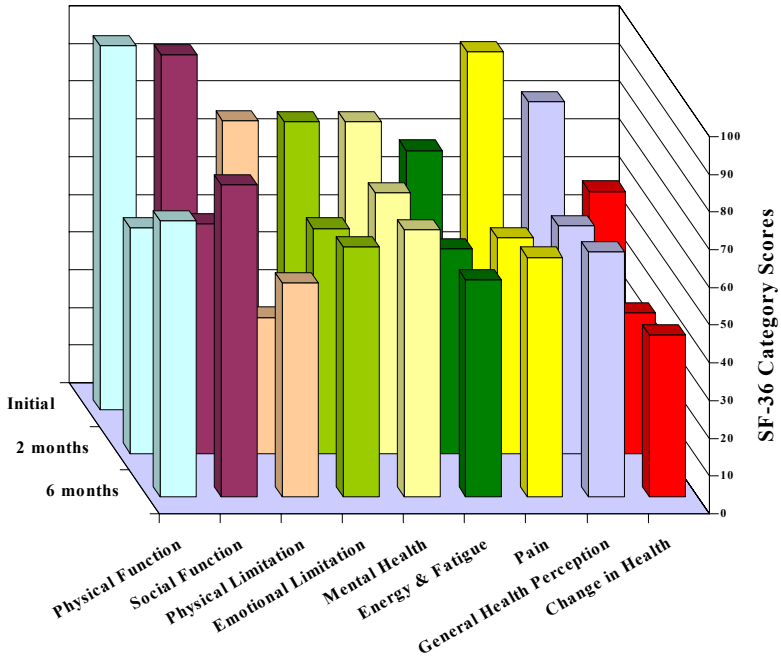

Fig A5.1. SF-36 scale and total scores for GTOS-MM subgroup.

APPENDIX 6

SIP Results for GTOS-MM Subgroup

A6 SIP Results for GTOS-MM Subgroup

Table A6.1 displays the SIP category scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 100 (maximum dysfunction). Statistically significant differences are noted between mean SIP category scores at initial and two months, and between scores at initial and six-month assessments. The SIP dimension and total scores at each assessment point are shown in table A6.2. Significant differences are noted between GHQ subscores at initial and two months and between scores at initial and six-month assessments. Figs A6.1 and A6.2 show the increase in dysfunction at two months and partial recovery by six months.

SIP Category	*Initial (n=83)*			*2 Mo (n=66)*			*6 Mo (n=62)*		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Ambulation	1.19 (5.92)	0	0-47	18.32 (16.57)	18.78 ***	0-68	9.50 (13.50)	0 ***	0-57
Mobility	0 (0)	0	0-0	4.39 (8.43)	8.43 ***	0-42	2.29 (6.65)	0 **	0-39
Body Care & Movement	0.75 (3.71)	0	0-32	6.80 (8.59)	3.60 ***	0-35	4.66 (10.22)	0 ***	0-43
Communication	4.58 (8.66)	0	0-43	3.05 (7.07)	0	0-30	1.32 (3.45)	0 **	0-11
Alertness Behaviour	1.28 (6.13)	0	0-45	5.92 (14.83)	0 **	0-74	4.15 (9.78)	0	0-47
Emotional Behaviour	1.97 (6.49)	0	0-31	8.29 (11.18)	3.27 ***	0-47	8.03 (13.90)	0 **	0-69
Social Interaction	5.04 (6.45)	2.48	0-25	9.37 (11.23)	5.90 ***	0-47	5.65 (9.95)	0	0-58
Sleep & Rest	11.50 (12.76)	9.80	0-57	7.21 (9.21)	0 ***	0-41	7.22 (9.91)	0	0-40
Eating	0 (0)	0	0-0	2.93 (6.30)	0	0-30	1.63 (4.67)	0	0-28
Work	7.14 (16.68)	0	0-79	32.63 (33.82)	16.44 ***	0-104	16.25 (26.94)	0	0-69
Home Management	1.10 (3.96)	0	0-25	16.80 (18.21)	13.20 ***	0-80	8.23 (17.81)	0 ***	082
Recreation & Pastimes	7.08 (10.01)	7.08	0-14	24.76 (18.62)	21.60 ***	0-67	11.89 (13.80)	9.48 ***	0-58

Table A6.1 Analysis of SIP category scores for GTOS-MM subgroup (Differences between baseline and follow-up: ***p<0.001, **p<0.01; Wilcoxon signed ranks test).

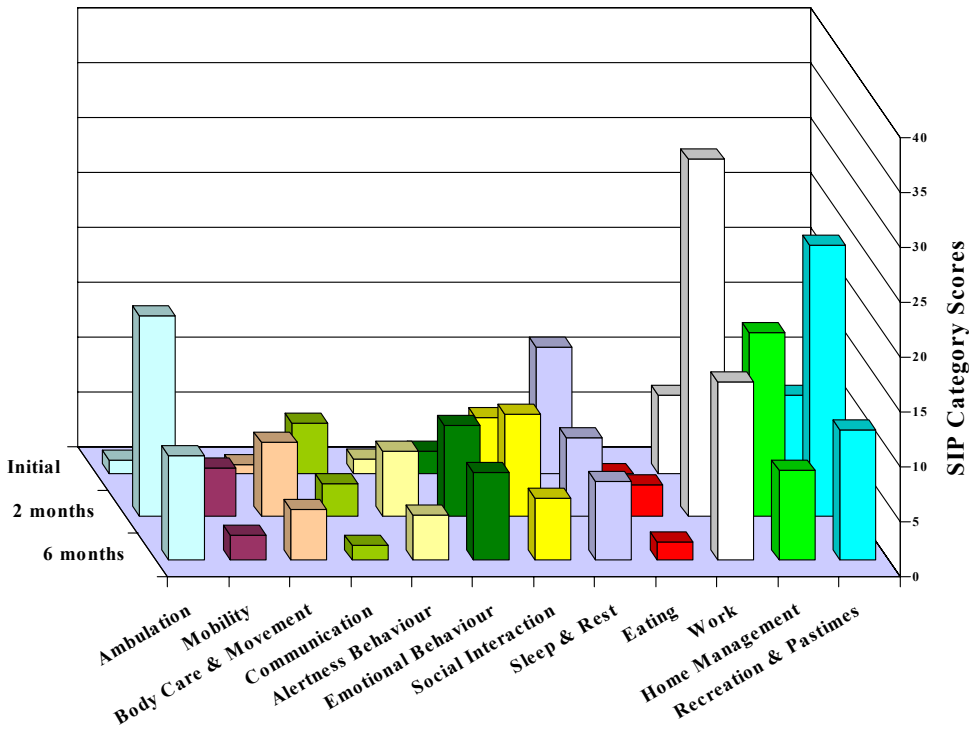

Fig A6.1 SIP category scores for GTOS-MM subgroup.

SIP Dimension/ Total	***Initial (n=83)***			***2 Mo (n=66)***			***6 Mo (n=62)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Physical	0.70 (3.29)	0	0-28	8.96 (9.15)	6.41 ***	0-34	5.28 (9.27)	1.79 ***	0-38
Psychosocial	3.50 (4.50)	2.27	0-29	7.06 (7.79)	5.55 ***	0-40	4.85 (7.56)	1.89	0-38
Total	2.49 (3.59)	1.77	0-30	10.54 (7.57)	9.75 ***	0-32	6.07 (7.90)	2.80 **	0-35

Table A6.2 Analysis of SIP dimension and total scores for GTOS-MM subgroup. (Differences between baseline and follow-up: ***p<0.001, **p<0.01; Wilcoxon signed ranks test).

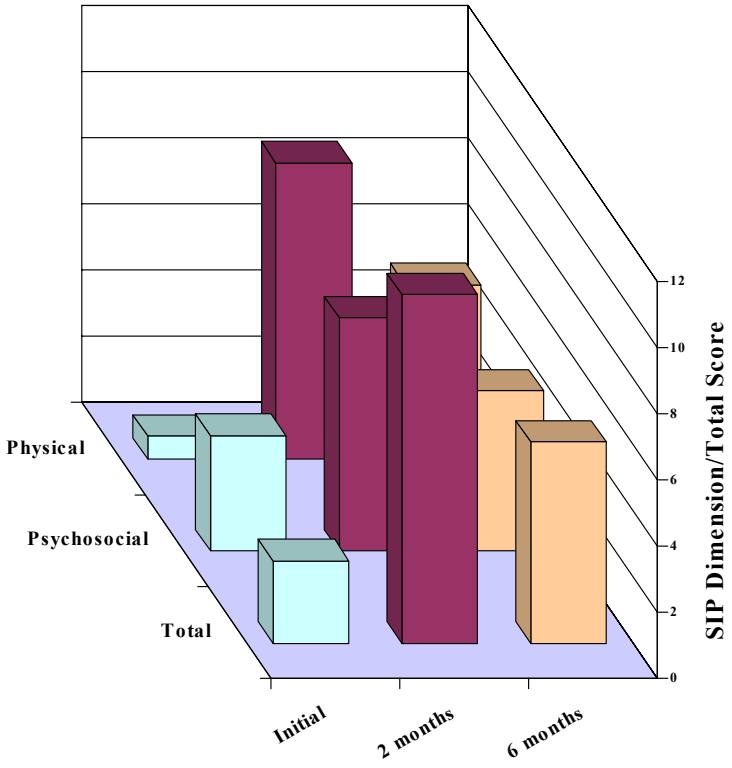

Fig A6.2 SIP dimension and total scores for GTOS-MM subgroup.

APPENDIX 7

MFA Results for GTOS-MM subgroup

A7 MFA for GTOS-MM subgroup

Table A7.1 displays the MFA total scores, and descriptive statistics, at each of the three assessment points, from a maximum possible score of 100, indicating maximal dysfunction. Statistically significant differences are noted between MFA scores at initial and two-month assessments. The MFA category scores at each assessment point are shown in table A7.2. Significant differences are noted between MFA category scores at initial and two months and between scores at initial and six-month assessments. These differences are shown graphically in fig A7.1, demonstrating the rise in dysfunction at two months and the partial recovery by six months.

	Number	***Mean***	***Median***	***SD***	***Range***
Initial	83	5.60	2.00	9.21	0-57
2 months	66	33.01	32.00 ***	16.66	0-60
6 months	62	20.82	19.50 ***	17.65	0-72

Table A7.1 Analysis of MFA total scores for GTOS-MM subgroup
(Differences between baseline and follow-up: ***p=0.001; Wilcoxon signed ranks test).

MFA Category	***Initial (n=83)***			***2 Mo (n=66)***			***6 Mo (n=62)***		
	Mean (SD)	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**	**Mean (SD)**	**Median**	**Range**
Mobility	10.84 (19.12)	0	0-65	38.71 (27.76)	40.00 ***	0-95	27.02 (24.62)	22.50 ***	0-85
Hand/Fine Motor	2.75 (10.57)	0	0-57	14.07 (27.85)	0 ***	0-100	5.30 (17.97)	0	0-86
Housework	7.36 (10.45)	0	0-33	49.66 (29.12)	55.55 ***	0-100	21.68 (25.95)	11.11 ***	0-89
Self Care	1.94 (5.37)	0	0-33	16.75 (17.55)	11.11 ***	0-61	6.00 (12.04)	0 **	0-55
Sleep/Rest	14.85 (23.43)	0	0-83	34.09 (31.13)	33.33 ***	0-100	22.84 (31.54)	0	0-100
Leisure/ Recreation	7.53 (19.80)	0	0-100	71.97 (30.85)	75.00 ***	0-100	46.37 (40.95)	50.00 ***	0-100
Family Relations	8.43 (15.89)	0	0-70	25.45 (25.00)	20.00 ***	0-100	15.00 (20.78)	5.00 **	0-80
Cognition/ Thinking	4.82 (14.85)	0	0-75	12.50 (25.66)	0 *	0-100	12.09 (27.44)	0	0-100
Emotional Adjustment	0 (0)	0	0	36.45 (20.88)	38.89 ***	0-83	29.48 (23.90)	27.77 ***	0-83
Employment /Work	0 (0)	0	0	56.82 (47.13)	87.50 ***	0-100	37.50 (45.21)	0 ***	0-100

Table A7.2 Analysis of MFA category scores for GTOS-MM subgroup (Differences between baseline and follow-up: *** $p \leq 0.001$, **$p < 0.01$, *$p < 0.05$; Wilcoxon signed ranks test).

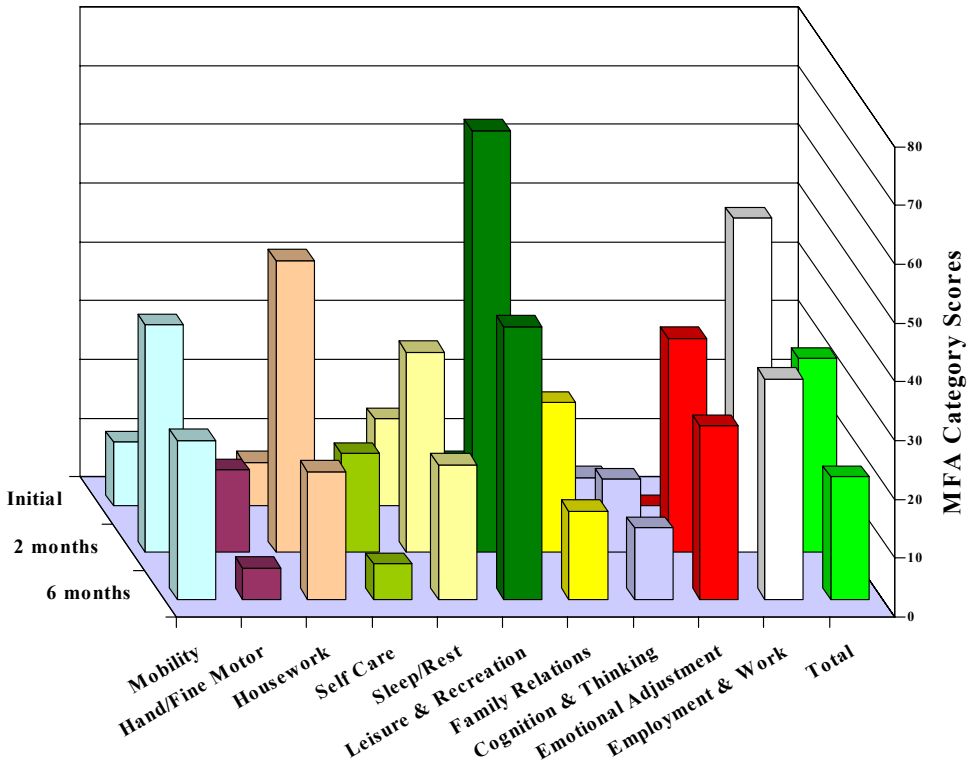

Fig A7.1 MFA category and total scores for GTOS-MM subgroup

APPENDIX 8

GHQ Caseness *vs* Demographics for GTOS-MM Subgroup

A8 GHQ Caseness *vs* Demographics for GTOS-MM Subgroup

At the initial assessment, 9 patients (11%) were cases. At the two-month assessment, 32 patients (39%) were cases, while at six months 15 patients (18%) were cases. There was no difference between cases and non-cases for the principal demographic information: age, sex, socioeconomic group, marital status, past medical history, past psychiatric history, smoking, narcotic use or alcohol use at any of the assessments.

APPENDIX 9
GHQ Caseness vs Type of Injury and Trauma Scores for GTOS-MM Subgroup

A 9 GHQ Caseness vs Type of Injury and Trauma Scores for GTOS-MM Subgroup

Table A9.1 demonstrates the analysis of trauma scores for caseness at each of the three assessments, for the GTOS-MM subgroup.

		ISS			RTS			TRISS		
		Mean (SD)	Median	Range	Mean (SD)	Median	Range	Mean (SD)	Median	Range
GHQ Initial	**Non-case**	9.62 (4.71)	9.00	4-25	7.67 (0.32)	7.84	7.11-7.84	98.91 (1.28)	99.40	93.30-99.80
	Case	8.89 (2.26)	9.00	4-13	7.70 (0.31)	7.84	6.38-7.84	98.78 (1.69)	99.40	94.30-99.60
GHQ 2 month	**Non-case**	9.15 (4.6)	9.00	4-25	7.72 (0.29)	7.84	6.81-7.84	98.92 (2.28)	99.40	94.30-99.60
	Case	10.78* (4.13)	9.00	4-25	7.72 (0.25)	7.84	7.10-7.84	98.93 (1.00)	99.40	95.60-99.60
GHQ 6 month	**Non-case**	8.80 (3.92)	9.00	4-25	7.71 (0.32)	7.84	6.38-7.84	98.86 (1.52)	99.40	93.30-99.60
	Case	11.53* (3.89)	9.00	8-18	7.61 (0.33)	7.84	7.10-7.84	98.61* (1.13)	99.40	95.60-99.40

Table A9.1. Trauma score analysis for cases and non-cases for GTOS-MM Subgroup.(Differences between baseline and follow-up: * $p<0.05$; Mann Whitney U Test)

There were no differences in mechanism of injury, ISS, RTS or TRISS between cases and non-cases at initial assessment. Similarly, were no differences in mechanism of injury, RTS or TRISS between cases and non-cases at two months. ISS score was

higher for cases (p=0.012) (Mann-Whitney U test).

At six months, cases had higher ISS scores (p=0.014), and lower (worse) TRISS survival probabilities (p=0.038), but there was no difference in RTS between cases and non-cases (Mann-Whitney U test). The victims of RTAs and falls from height were more likely, and victims of sports accidents less likely than expected to be cases (p=0.009).

APPENDIX 10

GHQ Caseness *vs* Outcomes Measures for GTOS-MM Subgroup

A10 GHQ Caseness *vs* Outcomes Measures for GTOS-MM Subgroup

Tables A10.1-3, and Figures A10.1-9 summarise the analysis of subscores and total scores of each of the three outcomes measures compared with for the GTOS-MM subgroup. At each assessment, although most clearly at two and six month follow-ups, psychological dysfunction is related to physical dysfunction.

SF-36 Scale/total scores	***Initial (n=83)*** **GHQ**		***2 months (n=66)*** **GHQ**		***6 months (n=62)*** **GHQ**	
	Non-case Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)
Physical Function	96.50 (13.06)	95.56 (9.17)	74.26 (24.03)	42.62 *** (28.15)	81.15 (20.61)	54.18 *** (23.65)
Social Function	95.38 (12.06)	84.72 ** (18.52)	72.79 (23.92)	48.44 *** (29.40)	90.34 (17.65)	64.17 *** (16.95)
Limitation – Physical probs.	77.47 (7.87)	69.44* (19.60)	45.44 (23.94)	26.09 *** (20.03)	65.34 (22.78)	35.00 *** (25.70)
Limitation-emotional probs	76.57 (10.57)	75.56 (7.45)	64.71 (70.79)	54.38 (28.79)	71.97 (15.46)	52.02 ** (26.12)
Mental Health	77.26 (8.58)	68.99* (12.69)	71.42 (14.84)	66.72 (14.62)	75.38 (11.23)	60.11 *** (12.38)
Energy & Fatigue	70.14 (11.30)	57.78 ** (15.83)	63.48 (17.10)	44.22 *** (14.65)	64.28 (13.31)	39.00 *** (15.49)
Pain	95.21 (10.88)	92.89 (14.43)	65.43 (22.56)	48.16 ** (27.34)	70.86 (25.61)	45.53 *** (21.19)
General Health Perception	82.83 (16.99)	71.33 (24.41)	64.26 (13.75)	56.40 * (16.01)	68.87 (18.01)	55.27 ** (17.02)
Change in Health	57.19 (17.42)	63.89 (18.16)	45.45 (11.62)	28.91 *** (25.44)	47.72 (16.89)	31.67 ** (29.07)

Table A10.1 Analysis of initial SF-36 scores against GHQ Caseness for GTOS-MM Subgroup (Differences between baseline and follow-up: *** $p \leq 0.001$, ** $p < 0.01$, *$p < 0.05$; Mann Whitney U Test).

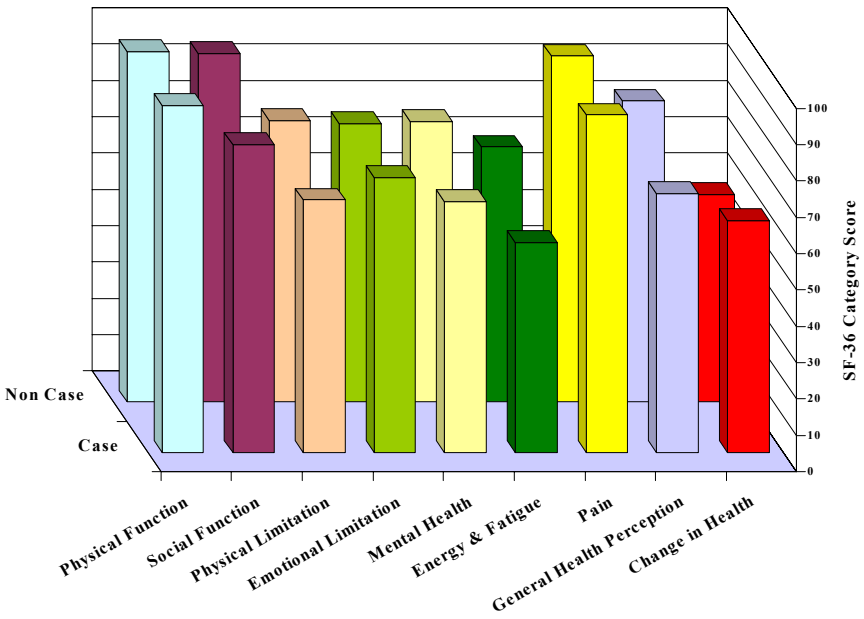

Fig A 10.1. Analysis of initial SF-36 scores against GHQ Caseness for GTOS-MM Subgroup.

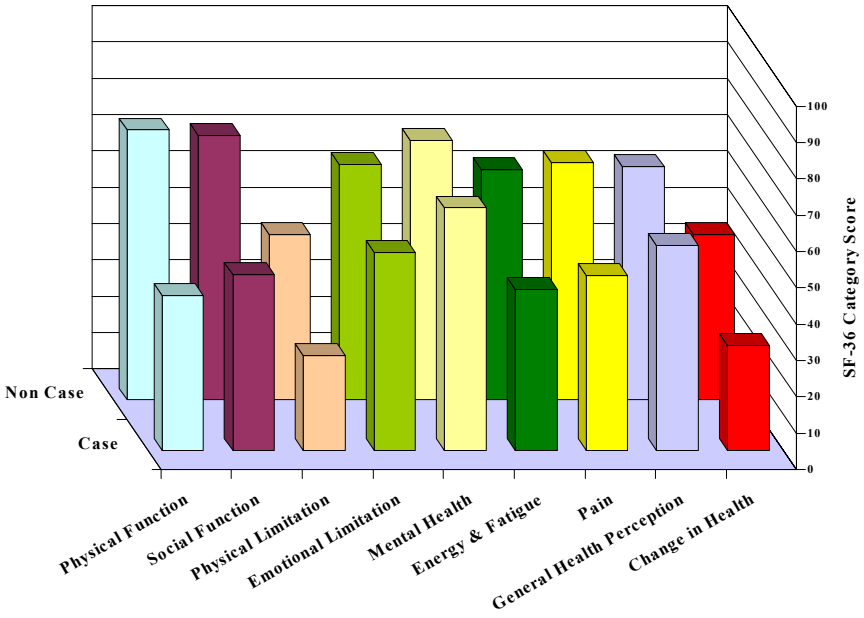

Fig A 10.2 Analysis of 2 month SF-36 scores against GHQ Caseness for GTOS-MM Subgroup.

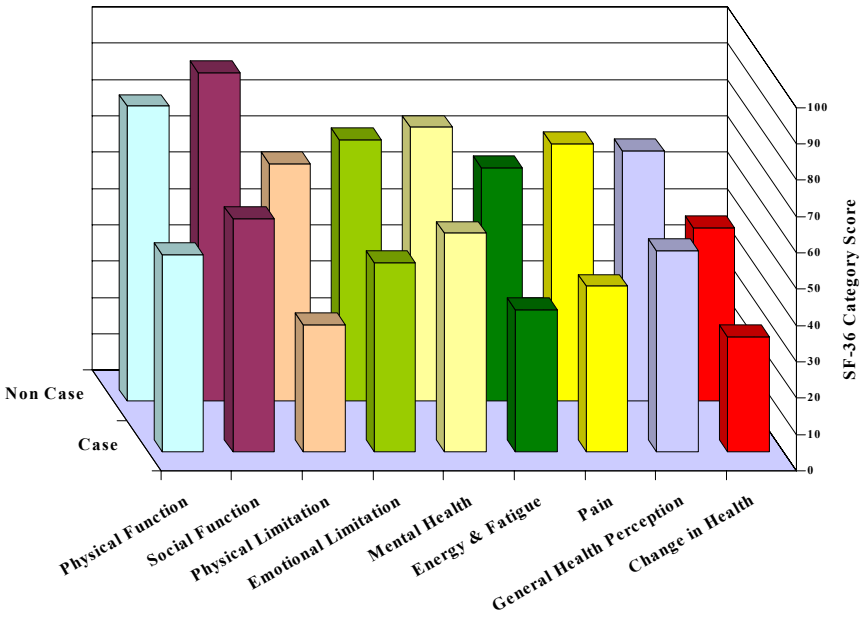

Fig A 10.3 Analysis of 6 month SF-36 scores against GHQ Caseness for GTOS-MM Subgroup.

SIP Category	*Initial (n=83)* GHQ		*2 months (n=66)* GHQ		*6 months (n=62)* GHQ	
	Non-case Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)	**Non-case** Mean (SD)	**Case** Mean (SD)
Ambulation	1.33 (6.26)	0 (0)	11.00 (14.16)	26.11 *** (15.53)	6.59 (10.96)	16.02 ** (15.51)
Mobility	0 (0)	0 (0)	2.84 (7.30)	6.04 ** (9.31)	0.84 (5.70)	5.68** (7.21)
Body Care & Movement	0.68 (3.81)	1.31 (2.84)	2.70 (5.73)	11.15 *** (9.05)	1.55 (3.38)	12.11 *** (16.06)
Communication	4.67 (8.77)	3.94 (8.15)	2.29 (6.94)	3.85 (7.23)	0.66 (2.52)	3.42 ** (5.02)
Alertness Behaviour	1.29 (6.40)	1.16 (3.47)	5.23 (13.73)	6.64 (16.11)	0.84 (2.77)	13.93 *** (15.86)
Emotional Behaviour	2.13 (6.83)	0.73 (2.17)	3.05 (7.42)	13.85 *** (11.89)	3.92 (9.10)	16.41 *** (13.53)
Social Interaction	4.91 (6.32)	6.07 (7.77)	4.93 (7.07)	14.10 * (12.90)	3.07 (5.58)	10.10 *** (9.89)
Sleep & Rest	4.46 (8.18)	5.89 (10.06)	8.21 (13.72)	19.22 *** (12.46)	6.10 (8.72)	11.72 ** (12.00)
Eating	2.04 (4.66)	7.17 ** (9.12)	2.43 (6.15)	3.46 (6.50)	0.33 (1.29)	5.69 ** (8.15)
Work	6.01 (15.82)	11.57 (23.35)	22.24 (31.87)	43.66 ** (32.75)	10.96 (23.28)	33.57 ** (31.44)
Home Management	1.04 (4.05)	1.63 (3.26)	10.20 (17.15)	23.82 *** (16.86)	3.88 (13.26)	17.74 *** (20.59)
Recreation & Pastimes	2.08 (6.71)	3.15 (9.44)	17.84 (15.45)	32.11 *** (19.09)	7.88 (10.46)	21.14 *** (13.56)
Physical Dimension	0.69 (3.45)	0.73 (1.59)	4.64 (7.35)	13.55 *** (8.72)	2.57 (4.59)	11.65 *** (13.37)
Psychosocial Dimension	3.50 (4.63)	3.51 (3.44)	4.04 (4.86)	10.27 *** (9.20)	2.26 (3.68)	10.62*** (8.46)
Total SIP	2.41 (3,67)	3.21 (2.92)	6.31 (6.07)	15.03 *** (6.35)	3.24 (4.76)	12.88 *** (8.24)

Table A10.2 Analysis of initial SIP scores against GHQ Caseness for GTOS-MM subgroup (Differences between baseline and follow-up: *** $p \leq 0.001$, ** $p < 0.01$, *$p < 0.05$; Mann Whitney U Test).

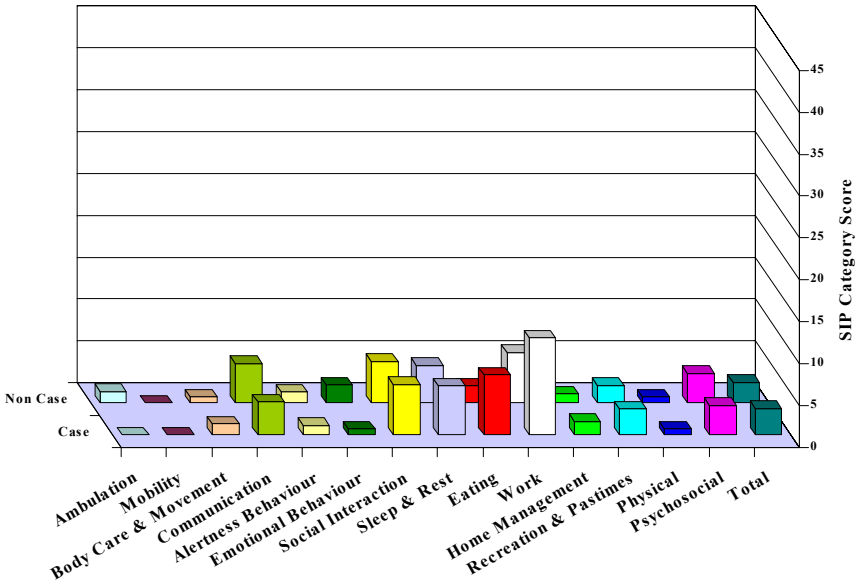

Fig A 10.4 Analysis of initial SIP scores against GHQ Caseness for GTOS-MM Subgroup.

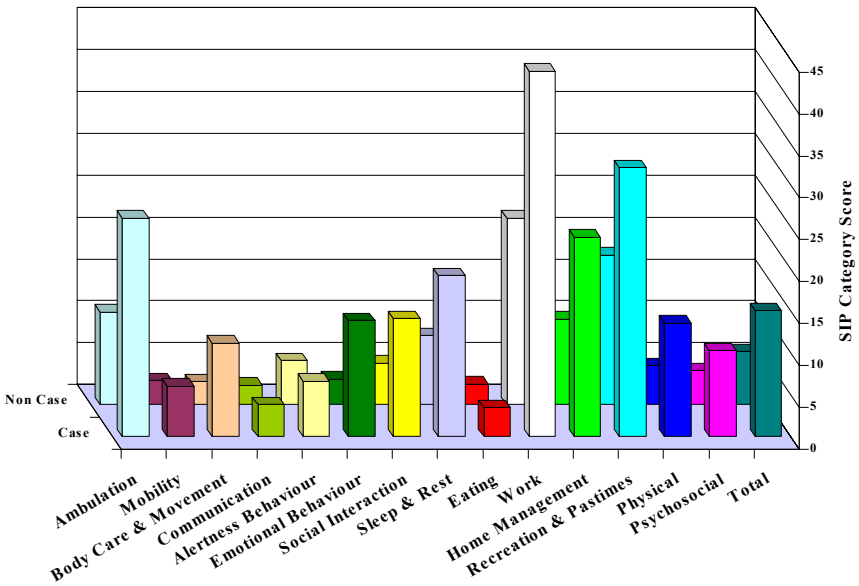

Fig A 10.5 Analysis of 2 month SIP scores against GHQ Caseness for GTOS-MM Subgroup.

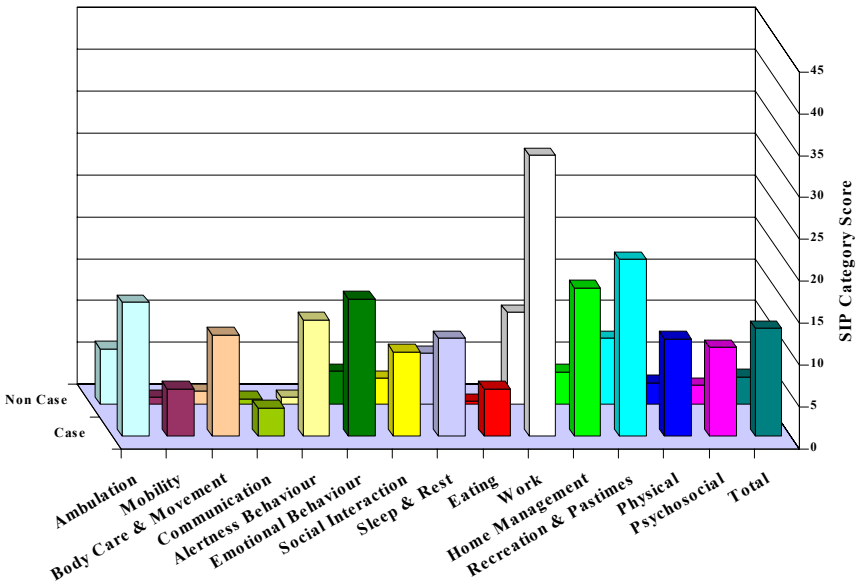

Fig A 10.6 Analysis of 6 month SIP scores against GHQ Caseness for GTOS-MM Subgroup.

MFA Category	*Initial (n=83)* GHQ		*2 months (n=66)* GHQ		*6 months (n=62)* GHQ	
	Non-case	**Case**	**Non-case**	**Case**	**Non-case**	**Case**
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Mobility	9.93	18.33 **	26.47	51.72 ***	21.30	40.67 ***
	(18.40)	(24.24)	(25.42)	(24.28)	(23.37)	(18.41)
Hand/Fine	2.32	6.35	9.66	18.75	3.11	12.38 *
Motor	(9.16)	(19.05)	9 (23.25)	(31.72)	(13.44)	(27.46)
Housework	7.21	8.64	34.31	65.97 ***	15.70	35.56 **
	(10.31)	(12.14)	(29.76)	(17.38)	(22.78)	(24.92)
Self Care	2.03	1.23	10.29	23.61 ***	2.78	13.33 ***
	(5.64)	(12.45)	(15.78)	(16.93)	(8.09)	(14.97)
Sleep/Rest	13.29	27.78 **	16.18	53.12 ***	15.94	40.00 *
	(23.08)	(23.57)	(24.44)	(25.90)	(23.03)	(43.55)
Leisure/	6.76	13.89	59.56	85.16 ***	34.24	80.00 ***
Recreation	(18.64)	(28.26)	(32.58)	(22.77)	(38.14)	(27.06)
Family	7.43	16.67	14.41	37.19 ***	9.13	28.60 ***
Relations	(14.90)	(21.80)	(21.35)	(23.45)	(13.63)	(25.88)
Cognition/	4.39	8.33 **	7.35	17.97 **	5.43	31.67 ***
Thinking	(15.12)	(12.50)	(24.25)	(26.36)	(21.02)	(35.94)
Emotional	0	0	24.67	48.96 ***	22.58	48.15 ***
Adjustment	(0)	(0)	(18.76)	(15.03)	(21.67)	(18.74)
Employment/	0	0	46.32	67.97*	21.74	81.67 ***
Work	(0)	(0)	(49.29)	(42.71)	(39.30)	(27.49)
Total	5.15	9.33 **	22.94	44.41 ***	14.78	36.27 ***
MFA	(7.03)	(4.82)	(14.32)	(10.17)	(13.87)	(14.51)

Table A10.3 Analysis of initial MFA scores against GHQ Caseness for GTOS-MM subgroup. (Differences between baseline and follow-up: *** $p \leq 0.001$, ** $p < 0.01$, *$p < 0.05$; Mann Whitney U Test).

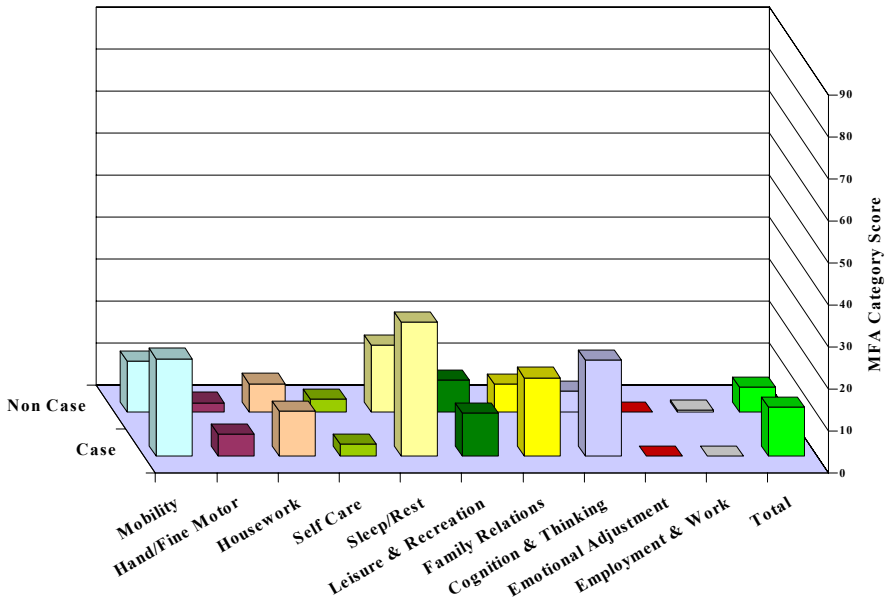

Fig A 10.7 Analysis of initial MFA scores against GHQ Caseness for GTOS-MM Subgroup.

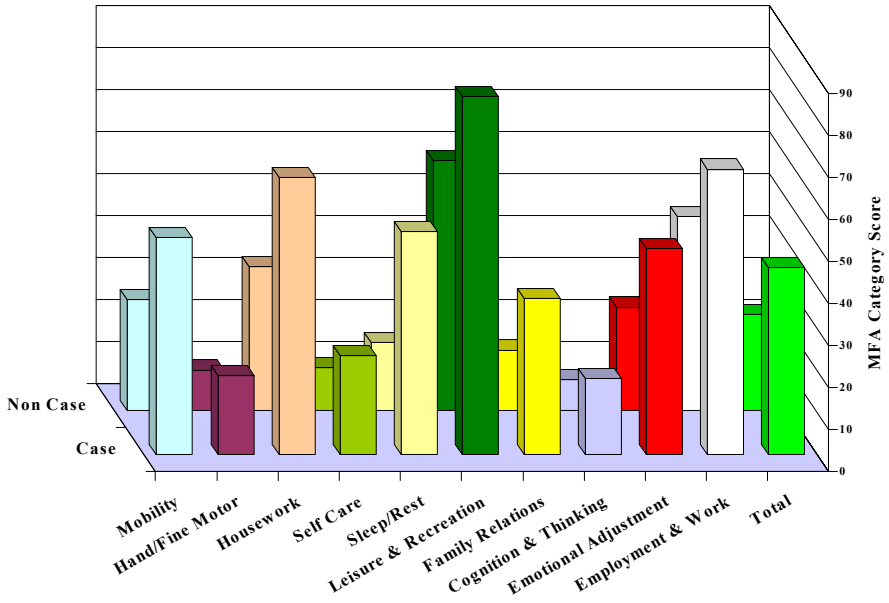

Fig A 10.8 Analysis of 2 month MFA scores against GHQ Caseness for GTOS-MM Subgroup.

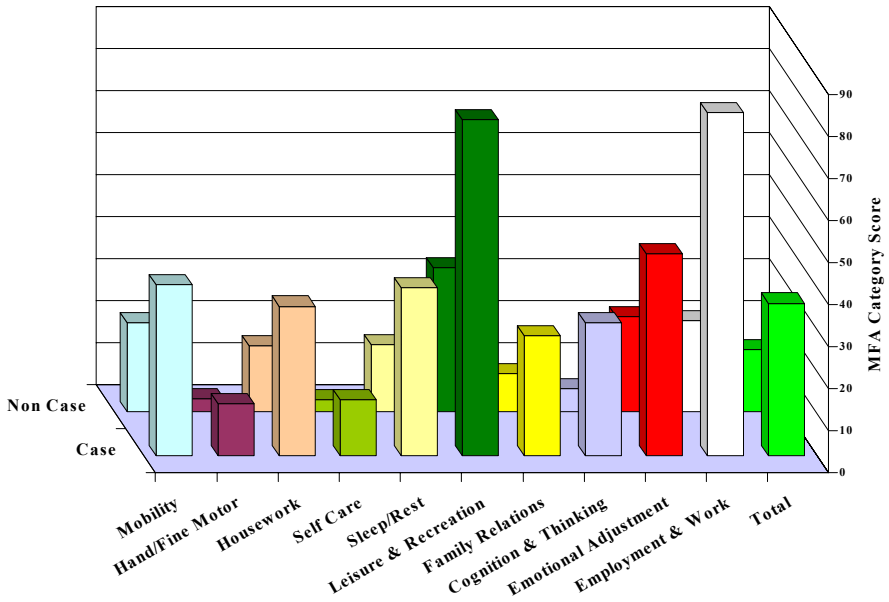

Fig A 10.9 Analysis of 6 month MFA scores against GHQ Caseness for GTOS-MM Subgroup.

APPENDIX 11

IL-6 ELISA Kit Instructions

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INTRODUCTION

Interleukin 6 (IL-6) is a multifunctional protein produced by lymphoid and non-lymphoid cells, and by normal and transformed cells, including T cells, monocyte/macrophages, fibroblasts, hepatocytes, vascular endothelial cells, cardiac myxomas, bladder cell carcinomas, myelomas, astrogliomas and glioblastomas. The production of IL-6 in these various cells is regulated, either positively or negatively, by a variety of signals including mitogens, antigenic stimulation, lipopolysaccharides, IL-1, TNF, PDGF and viruses. On the basis of its various activities, IL-6 has also been called interferon-β2 (IFN-β2), 26-kDa protein, B-cell stimulatory factor-2 (BSF-2), hybridoma/plasmacytoma growth factor, hepatocyte stimulating factor, cytotoxic T-cell differentiation factor, and macrophage-granulocyte inducing factor 2A (MGI-2A). For reviews on IL-6, see references 1-5.

The human IL-6 cDNA sequence predicts a protein of 212 amino acid residues in length with 5 potential N-glycosylation sites. The hydrophobic N-terminal 28 amino acid residue signal peptide is cleaved to produce a mature protein of 184 amino acids with four cysteine residues and a predicted molecular mass of 21 kDa (6 - 9). Mouse IL-6 cDNA sequence shows a homology of 42% at the amino acid level when compared with the human sequence (10). Sequencing of the genomic DNA for IL-6 indicates that the gene for this factor consists of five exons and four introns. On the basis of sequence similarity and gene structural motif similarity, IL-6 can be grouped in a family of cytokines that also includes OSM, G-CSF, LIF, and CNTF. All of these cytokines are predicted to have a four helix bundle structure similar to that found for growth hormone, suggesting that they all evolved from a common ancestral gene (11, 38, 39).

The effects of IL-6 on different cells are numerous and varied. The effect on B cells is stimulation of differentiation and antibody secretion (6, 12 - 15). IL-6 also affects T cells, acting as a co-stimulant with sub-optimal concentrations of PHA or Con A to stimulate IL-2 production and IL-2 receptor expression. IL-6 exhibits growth factor activity for mature thymic or peripheral T-cells and reportedly enhances the differentiation of cytotoxic T-cells in the presence of IL-2 or IFN-γ (16 - 18). It stimulates production of acute phase proteins by hepatocytes (19) and has colony-stimulating activity on hematopoietic stem cells (20, 21). IL-6 has growth factor activities and will stimulate the growth of myeloma/hybridoma/plasmacytoma cells (22, 23), EBV-transformed B cells (24), keratinocytes and mesangial cells (4, 5). Additional bioactivities attributed to IL-6 include: inhibition of the growth and induction of terminal differentiation of M1 myeloid leukemic cells (25); induction of neuronal cell differentiation (26, 27); induction of the maturation of megakaryocytes (28). Although IL-6 was also discovered as an antiviral activity produced by human diploid fibroblasts, the question of whether or not IL-6 has antiviral activity is controversial. Many groups have been consistently unable to find any antiviral activity for recombinant human IL-6.

The various activities of IL-6 described above suggest that this factor will have a major role in the mediation of the inflammatory and immune responses initiated by infection or injury. Although the exact functions of IL-6 *in vivo* are not known, elevated IL-6 levels have been reported to be associated with a variety of diseases, including autoimmune diseases such as arthritis and Castleman's disease (4, 5, 29, 30), mesangial proliferative glomerulonephritis (4, 5), psoriasis (31), inflammatory bowel disease (32), and malignancies such as plasmacytomas (4), myelomas (2, 3, 4, 33), lymphomas and leukemias (4, 34), and ovarian cancers (35). A great deal of work is in progress in order to provide a better understanding of the role of IL-6 in the modulation of normal and pathological processes (2, 5).

2

Current methods for assay of this interleukin are based on the mitogenic effects of IL-6 on appropriate cell lines, such as B9, a mouse B cell hybridoma line, or T1165.85.2.1, a mouse plasmacytoma cell line. These bioassays are time-consuming and are not completely specific for IL-6. The Quantikine IL-6 Immunoassay is a 4.5 hour solid phase ELISA designed to measure IL-6 in cell culture supernates, serum, and plasma. It contains recombinant human IL-6 and antibodies raised against recombinant human IL-6 and has been shown to accurately quantitate the recombinant factor. Results obtained using natural IL-6 showed linear curves that were parallel to the standard curves obtained using the *E. coli*-expressed Quantikine kit standards. These results indicate that the Quantikine Immunoassay kit can be used to determine relative mass values for natural IL-6.

It has been observed in our laboratories that the measurement of IL-6 is insensitive to the addition of the recombinant form of the IL-6 soluble receptor. Therefore it is probable that experimental sample measurements reflect the total amount of IL-6 present, *i.e.*, the total amount of free IL-6 plus the amount of IL-6 initially bound to soluble receptors, if any are present in the samples. High levels of high-affinity autoantibodies to IL-6 in the serum of some normal blood donors have been reported (36, 37). Such autoantibodies have the potential to interfere with the measurement of IL-6 by ELISA immunoassays.

PRINCIPLE OF THE ASSAY

This assay employs the quantitative sandwich enzyme immunoassay technique. A monoclonal antibody specific for IL-6 has been pre-coated onto a microplate. Standards and samples are pipetted into the wells and any IL-6 present is bound by the immobilized antibody. After washing away any unbound substances, an enzyme-linked polyclonal antibody specific for IL-6 is added to the wells. Following a wash to remove any unbound antibody-enzyme reagent, a substrate solution is added to the wells and color develops in proportion to the amount of IL-6 bound in the initial step. The color development is stopped and the intensity of the color is measured.

LIMITATIONS OF THE PROCEDURE

- FOR RESEARCH USE ONLY. NOT FOR USE IN DIAGNOSTIC PROCEDURES.
- The kit should not be used beyond the expiration date on the kit label.
- It is important that the Calibrator Diluent selected for the standard curve be consistent with the samples being assayed.
- If samples generate values higher than the highest standard, dilute the samples with the appropriate Calibrator Diluent and repeat the assay. If cell culture supernate samples require larger dilutions, perform an intermediate dilution with culture media and the final dilution with the appropriate Calibrator Diluent.
- As manufacturers we take great care to ensure that our products are suitable for use with all validated sample types, as designated in the product insert. However, it is possible that in some cases, high levels of interfering factors may cause unusual results.
- Any variation in standard diluent, operator, pipetting technique, washing technique, incubation time or temperature, and kit age can cause variation in binding.
- Soluble receptors or other binding proteins present in biological samples do not necessarily interfere with the measurement of ligands in samples. However, until the factors have been tested in the Quantikine Immunoassay, the possibility of interference cannot be excluded.

REAGENTS

IL-6 Microplate (Part 890045) - 96 well polystyrene microplate (12 strips of 8 wells) coated with a murine monoclonal antibody against IL-6.

IL-6 Conjugate (Part 890046) - 21 mL of polyclonal antibody against IL-6 conjugated to horseradish peroxidase, with preservatives.

IL-6 Standard (Part 890047) - 1.5 ng of recombinant human IL-6 in a buffered protein base with preservatives, lyophilized.

Assay Diluent RD1A (Part 895005) - 11 mL of a buffered protein base with preservatives.

Calibrator Diluent RD5A (Part 895010) - 21 mL of a buffered protein base with preservatives. *For cell culture supernate samples.*

Calibrator Diluent RD6F (Part 895018) - 21 mL of animal serum with preservatives. *For serum/plasma samples.*

Wash Buffer Concentrate (Part 895003) - 21 mL of a 25-fold concentrated solution of buffered surfactant with preservatives.

Color Reagent A (Part 895000) - 12.5 mL of stabilized hydrogen peroxide.

Color Reagent B (Part 895001) - 12.5 mL of stabilized chromogen (tetramethylbenzidine).

Stop Solution (Part 895032) - 6 mL of 2 N sulfuric acid.

Plate Covers - 4 adhesive strips.

STORAGE

Unopened Kit	Store at 2 - 8° C. Do not use past kit expiration date.	
Opened/ Reconstituted Reagents	Diluted Wash Buffer	May be stored for up to 1 month at 2 - 8° C.*
	Stop Solution	
	Calibrator Diluent RD5A	
	Calibrator Diluent RD6F	
	Assay Diluent RD1A	
	Conjugate	
	Unmixed Color Reagent A	
	Unmixed Color Reagent B	
	Standard	Aliquot and store for up to 1 month at ≤ - 20° C. Avoid repeated freeze-thaw cycles.*
	Microplate Wells	Return unused wells to the foil pouch containing the desiccant pack, reseal along entire edge of zip-seal. May be stored for up to 1 month at 2 - 8° C.*

*Provided this is within the expiration date of the kit.

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OTHER SUPPLIES REQUIRED

- Microplate reader capable of measuring absorbance at 450 nm, with the correction wavelength set at 540 nm or 570 nm.
- Pipettes and pipette tips.
- Deionized or distilled water.
- Multi-channel pipette, squirt bottle, manifold dispenser, or automated microplate washer.

PRECAUTIONS

Some components of this kit contain sodium azide which may react with lead and copper plumbing to form explosive metallic azides. Flush with large volumes of water during disposal.

The Stop Solution provided with this kit is an acid solution. Wear eye, hand, face, and clothing protection when using this material.

This kit contains Thimerosal, a mercury containing compound. The total amount of mercury in this kit is 2.55 mg.

SAMPLE COLLECTION AND STORAGE

Cell Culture Supernates - Remove particulates by centrifugation and assay immediately or aliquot and store samples at ≤ -20° C. Avoid repeated freeze-thaw cycles.

Serum - Use a serum separator tube (SST) and allow samples to clot for 30 minutes before centrifugation for 10 minutes at approximately 1000 x g. Remove serum and assay immediately or aliquot and store samples at ≤ -20° C. Avoid repeated freeze-thaw cycles.

Plasma - Collect plasma using EDTA, heparin, or citrate as an anticoagulant. Centrifuge at 1000 x g within 30 minutes of collection. Assay immediately or aliquot and store samples at ≤ -20° C. Avoid repeated freeze-thaw cycles.

REAGENT PREPARATION

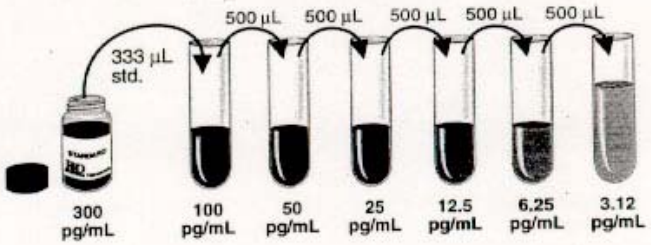
Bring all reagents to room temperature before use.

Wash Buffer - If crystals have formed in the concentrate, warm to room temperature and mix gently until the crystals have completely dissolved. Dilute 20 mL of Wash Buffer Concentrate into deionized or distilled water to prepare 500 mL of Wash Buffer.

Substrate Solution - Color Reagents A and B should be mixed together in equal volumes within 15 minutes of use. Protect from light. 200 µL of the resultant mixture is required per well.

IL-6 Standard - Reconstitute the IL-6 Standard with 5 mL of Calibrator Diluent RD5A (for cell culture supernate samples) or Calibrator Diluent RD6F (for serum/plasma samples). This reconstitution produces a stock solution of 300 pg/mL. Allow the standard to sit for a minimum of 15 minutes with gentle agitation prior to making dilutions.

Pipette 667 µL of the appropriate Calibrator Diluent into the 100 pg/mL tube and 500 µL of diluent into each remaining tube. Use the stock solution to produce a dilution series (below). Mix each tube thoroughly before the next transfer. The undiluted standard serves as the high standard (300 pg/mL). The appropriate Calibrator Diluent serves as the zero standard (0 pg/mL).



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ASSAY PROCEDURE

Bring all reagents and samples to room temperature before use. It is recommended that all samples and standards be assayed in duplicate.

1. Prepare all reagents and working standards as directed in the previous sections.
2. Remove excess microplate strips from the plate frame, return them to the foil pouch containing the desiccant pack, reseal.
3. Add 100 µL of Assay Diluent RD1A to each well.
4. Add 100 µL of Standard or sample per well. Cover with the adhesive strip provided. Incubate for 2 hours at room temperature.
5. Aspirate each well and wash, repeating the process three times for a total of four washes. Wash by filling each well with Wash Buffer (400 µL) using a squirt bottle, multi-channel pipette, manifold dispenser or autowasher. Complete removal of liquid at each step is essential to good performance. After the last wash, remove any remaining Wash Buffer by aspirating or decanting. Invert the plate and blot it against clean paper toweling.
6. Add 200 µL of IL-6 Conjugate to each well. Cover with a new adhesive strip. Incubate for 2 hours at room temperature.
7. Repeat the aspiration/wash as in step 5.
8. Add 200 µL of Substrate Solution to each well. Incubate for 20 minutes at room temperature. **Protect from light.**
9. Add 50 µL of Stop Solution to each well. If color change does not appear uniform, gently tap the plate to ensure thorough mixing.
10. Determine the optical density of each well within 30 minutes, using a microplate reader set to 450 nm. If wavelength correction is available, set to 540 nm or 570 nm. If wavelength correction is not available, subtract readings at 540 nm or 570 nm from the readings at 450 nm. This subtraction will correct for optical imperfections in the plate. Readings made directly at 450 nm without correction may be higher and less accurate.

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ASSAY PROCEDURE SUMMARY

1. Prepare reagents and standards as directed.

2. Add 100 µL Assay Diluent RD1A to each well.

3. Add 100 µL Standard or sample to each well. Incubate 2 hrs. RT

4. Aspirate and wash 4 times.

5. Add 200 µL Conjugate to each well. Incubate 2 hrs. RT

6. Aspirate and wash 4 times.

7. Add 200 µL Substrate Solution to each well. **Protect from light.** Incubate 20 min. RT

8. Add 50 µL Stop Solution to each well. Read at 450 nm within 30 min. λ correction 540 or 570 nm

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CALCULATION OF RESULTS

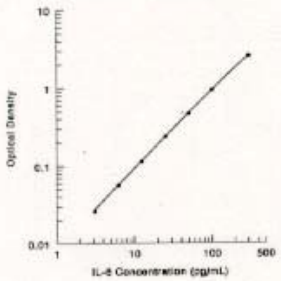
Average the duplicate readings for each standard, control, and sample and subtract the average zero standard optical density.

Create a standard curve by reducing the data using computer software capable of generating a four parameter logistic (4-PL) curve fit. As an alternative, construct a standard curve by plotting the mean absorbance for each standard on the y-axis against the concentration on the x-axis and draw a best fit curve through the points on the graph. The data may be linearized by plotting the log of the IL-6 concentrations versus the log of the O.D. and the best fit line can be determined by regression analysis. This procedure will produce an adequate but less precise fit of the data. If samples have been diluted, the concentration read from the standard curve must be multiplied by the dilution factor.

TYPICAL DATA

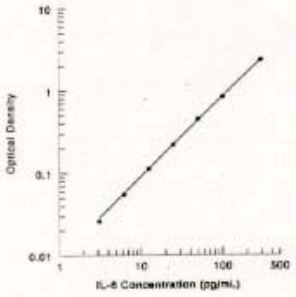
These standard curves are provided for demonstration only. A standard curve should be generated for each set of samples assayed.

Calibrator Diluent RD5A



(pg/mL)	O.D.	Average	Corrected
0	0.022 0.028	0.025	
3.12	0.050 0.052	0.051	0.026
6.25	0.078 0.078	0.078	0.053
12.5	0.134 0.136	0.135	0.110
25	0.247 0.245	0.246	0.221
50	0.472 0.465	0.468	0.443
100	0.865 0.836	0.850	0.825
300	2.524 2.515	2.520	2.495

Calibrator Diluent RD6F



(pg/mL)	O.D.	Average	Corrected
0	0.025 0.029	0.027	
3.12	0.049 0.051	0.050	0.023
6.25	0.078 0.077	0.078	0.051
12.5	0.127 0.129	0.128	0.101
25	0.236 0.236	0.236	0.209
50	0.438 0.442	0.440	0.413
100	0.780 0.773	0.776	0.749
300	2.176 2.221	2.198	2.171

TECHNICAL HINTS

- Substrate Solution should remain colorless until added to the plate. Keep the Substrate Solution protected from light. Substrate Solution should change from colorless to gradations of blue. The color developed in the wells will turn from blue to yellow upon addition of the Stop Solution.
- Stop Solution should be added to the plate in the same order as the Substrate Solution.
- When mixing or reconstituting protein solutions, always avoid foaming.
- To avoid cross-contamination, change pipette tips between additions of each standard level, between sample additions, and between reagent additions. Also, use separate reservoirs for each reagent.
- To ensure accurate results, proper adhesion of plate sealers during incubation steps is necessary.

PRECISION

Intra-assay Precision (Precision within an assay)
Three samples of known concentration were assayed twenty times on one plate to assess intra-assay precision.

Inter-assay Precision (Precision between assays)
Three samples of known concentration were assayed in twenty separate assays to assess inter-assay precision.

Serum/Plasma Assay

	Intra-assay Precision			Inter-assay Precision		
Sample	1	2	3	1	2	3
n	20	20	20	20	20	20
Mean (pg/mL)	16.8	97.7	186	17.2	101	191
Standard deviation	0.7	1.6	3.8	1.1	3.3	7.2
CV (%)	4.2	1.6	2.0	6.4	3.3	3.8

Cell Culture Supernate Assay

	Intra-assay Precision			Inter-assay Precision		
Sample	1	2	3	1	2	3
n	20	20	20	20	20	20
Mean (pg/mL)	15.8	95.6	179	16.4	98.8	188
Standard deviation	0.7	3.0	3.1	0.6	2.5	3.7
CV (%)	4.4	3.1	1.7	3.7	2.5	2.0

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RECOVERY

The recovery of IL-6 spiked to three different levels in five samples throughout the range of the assay in various matrices was evaluated.

Sample Type	Average % Recovery	Range
Cell culture media	98	94 - 103%
Serum	93	86 - 99%
EDTA plasma	95	84 - 101%
Heparin plasma	90	88 - 98%
Citrate plasma	91	82 - 95%

LINEARITY

To assess the linearity of the assay, four samples were spiked with high concentrations of IL-6 in various matrices and diluted with the appropriate Calibrator Diluent to produce samples with values within the dynamic range of the assay.

		Cell culture media	Serum	EDTA plasma	Heparin plasma	Citrate plasma
1:2	Average % of Expected	99	97	101	103	101
	Range (%)	96-101	92-100	98-105	96-109	96-106
1:4	Average % of Expected	100	101	104	106	105
	Range (%)	93-110	93-107	97-110	97-113	101-109
1:8	Average % of Expected	96	102	100	104	106
	Range (%)	92-100	96-108	86-112	93-111	101-111
1:16	Average % of Expected	94	103	99	105	101
	Range (%)	83-108	93-111	90-110	99-107	90-114

SENSITIVITY

The minimum detectable dose of IL-6 is typically less than 0.70 pg/mL.

The minimum detectable dose was determined by adding two standard deviations to the mean optical density value of twenty zero standard replicates and calculating the corresponding concentration.

CALIBRATION

This immunoassay is calibrated against a highly purified *E. coli*-expressed recombinant human IL-6 produced at R&D Systems. The NIBSC/WHO International Standard for IL-6 (89/548) (40), which was intended as a potency standard, was evaluated in this kit. The NIBSC/WHO Standard is a CHO cell-derived recombinant human IL-6.

The dose response curve of the International Standard (89/548) parallels the Quantikine standard curve. To convert sample values obtained with the Quantikine IL-6 kit to equivalent NIBSC 89/548 units, use the equation below.

NIBSC (89/548) equivalent value (IU/mL) = 0.131 x Quantikine IL-6 value (pg/mL)

SAMPLE VALUES

Serum/Plasma - Forty serum and plasma samples were evaluated for the presence of IL-6 in this assay. Thirty-three samples measured less than the lowest standard, 3.13 pg/mL. Seven samples measured between 3.13 and 12.5 pg/mL.

Cell culture supernates - Human peripheral blood mononuclear cells ($1x10^6$ cells/mL) were cultured in RPMI supplemented with 10% fetal calf serum, 50 µM β-mercaptoethanol, 2 mM L-glutamine, 100 U/mL penicillin, and 100 µg/mL streptomycin sulfate and stimulated for 1, 3, and 5 days with 10 µg/mL PHA. Aliquots of the culture supernate were removed on days 1, 3, and 5 and assayed for levels of natural IL-6. Results are listed in the following table.

Condition	Day 1 (pg/mL)	Day 3 (pg/mL)	Day 5 (pg/mL)
Unstimulated	575	311	660
Stimulated	17,130	17,520	16,340

SPECIFICITY

This assay recognizes both natural and recombinant human IL-6. The factors listed below were prepared at 50 ng/mL in Calibrator Diluent RD5A and at 100 ng/mL in Calibrator Diluent RD6F, and assayed for cross-reactivity. Preparations of the following factors at 50 ng/mL in a mid-range rhIL-6 control prepared in Calibrator Diluent RD5A and 100 ng/mL in a mid-range rhIL-6 control prepared in Calibrator Diluent RD6F were assayed for interference. No significant cross-reactivity or interference was observed.

Factors related to or associated with IL-6:

Recombinant human:	IL-12	LIF R	IL-11
IL-6 sR	CNTF	OSM	IL-12
IL-6 sR/sgp 130	G-CSF	**Recombinant mouse:**	**Other:**
IL-11	sgp130	IL-6	rrCNTF
	LIF		

Other factors:

Recombinant human:	GM-CSF	IL-5	pTGF-β1.2
IL-1α	LIF	IL-7	pTGF-β2
IL-1β	TNF-α	GM-CSF	
IL-2	TNF-β	**Other:**	
IL-3	**Recombinant mouse:**	bFGF acidic	
IL-4	IL-2	bFGF basic	
IL-7	IL-3	hPDGF	
IL-8	IL-4	pPDGF	
		hTGF-β1	

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