Myalgic Encephalopathy/Chronic Fatigue Syndrome Longitudinal Outcomes

Pilot Study Report

"I just find this illness frustrating and misunderstood"
study participant comment

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CONTENTS

1. MAIN REPORT

i. INTRODUCTION

Myalgic Encephalopathy/Chronic Fatigue Syndrome (ME/CFS) is a not uncommon medical disorder (1) characterised by severe disabling fatigue, cognitive dysfunction, and post-exertional malaise.

ME/CFS is a recognised medical condition, and the WHO classifies it as a neurological disorder. However, its aetiology, patho-physiology, management and prognosis is still poorly understood. (2). Although there are no routine confirmatory diagnostic test(s) for the condition, a number of biological and genetic markers have been identified in research studies.

ME/CFS affects mainly younger individuals, with women affected at least twice as much as men. It is associated with a wide range of painful and debilitating symptoms that can severely affect quality of life for a prolonged duration. There is also a significant financial and social impact on family or carers.

There is no known cure for ME/CFS. A systematic review of the interventions for the treatment and management of CFS concluded that only cognitive behavioural therapy and graded exercise therapy showed promising results from published trials. (3). However, there are difficulties in assessing the effectiveness of these interventions because the trials included in the review used varying diagnostic criteria and outcome measures, as well as short follow up periods. (3). It has been suggested that the outcome measures used in future studies should be standardised, to allow proper comparison between studies and conclusions to be drawn. Outcome measures could also be more meaningful, e.g. an increase in time spent in employment or social activities may be more accurate than a perceived improvement which may reflect reduced expectations. (3) Added to the difficulties in interpreting results from studies / trials is the significant tension that still exists between a purely psychological (e.g.attribution theory) and biomedical models of ME/CFS, and the fact that biomedical research has been poorly funded. This results in confusion and biases amongst healthcare providers, which often negatively impacts on the optimal management and outcomes for patients (2). However, over the last few years, ME/CFS research is becoming much more focussed on the biomedical and genetic aspects, and this should lead (with additional funding) to a much better understanding of the disorder and its management. Nonetheless, a biopsychosocial approach to the management of ME/CFS is warranted, as this has proven to be beneficial for all known chronic medical conditions.

Longitudinal studies undertaken in the US and UK have characterised the natural history and prognosis of ME/CFS and identified an intermittent pattern of relapse and partial remission. (4,5) Studies to date have identified the following predictors of poor outcome in CFS: more severe and longstanding illness (4,5,6,7), older age (5,8), higher fatigue levels (4,6,9), and having a comorbid psychological disorder (5,9). Children are reported to have a better prognosis than adults. (5,10). A longitudinal study of outcome of CFS has been undertaken in Australia (11), but this study did not examine different interventions as potential predictors of outcome. However, the recent Dubbo study (funded by CDC Atlanta) is promising, though the number of patients involved is small (15).

We believe there is a need for a more comprehensive longitudinal study of ME/CFS patients in Australia, to gain a better understanding of the factors that may influence outcomes. A key component of any longitudinal study is the establishment of a patient register, with clear entry criteria and valid data collection methods.

A patient register will also be an important resource for further ME/CFS research and clinical service development. Overtime, it can provide comprehensive details of the characteristics, natural history and impact of this disorder on a large group of patients. Such a register would enable the investigation of possible links between interventions and patient characteristics / symptoms, for a variety of different interventions. Interventions that are beneficial to particular groups of patients may be identified and further studied. The longitudinal study would also enable the identification of any predictors of long term outcome for ME/CFS patients, as well as their health service needs and utilisation. Some of the predictors of interest are age, sex, gradual or rapid onset of illness, duration, severity, management approaches and psychological co-morbidities. The outcomes measures of most interest would be changes in the SF-36, David Bell Disability scores, and other relevant health status measures.

As this is only a pilot study, it will focus on developing the methods and questionnaires required to implement a usable ME/CFS patient register, including data base design requirements and data analysis potential. It will also be used to identify methods to both scale up the register and ensure effective follow-up methods and longitudinal studies.

The main outcome of this pilot study was to create a South Australian register of about 120 ME/CFS patients, with comprehensive data relating to their management and symptoms, impact on quality of life, and to identify treatments of benefit to date. The pilot register would also be made available as a resource for further ME/CFS research and clinical service development. Future enhancements and expansion of this pilot register would enable a proper longitudinal study of outcomes for patients with ME/CFS.

ii. METHODOLOGY

a. **Literature review**: A literature review was undertaken to establish the most appropriate diagnostic criteria, data elements/outcome indicators to be collected and health survey tools/questionnaires to use. The review also used as a guide, the clinical consensus document produced in South Australia in 2004: ME/CFS Management Guidelines for General Practitioners, SA Department of Human Services (16).

b. **Survey tools:** A range of survey tools/questionnaires were designed and formatted for data collection from patients (see appendix B). The questionnaires are as follows:

- Personal Details Form: including date of birth, gender, occupation/employment status, marital status, residential postcode, country of origin, education level reached, whether they receive a government disability benefit, whether they drink and/ or smoke or have a carer.

- ME/CFS History Form: Including date and nature of onset (gradual or acute), whether they have experienced a gradually deteriorating, gradually improving or a relapsing illness, suspected triggers and causes of relapse, family members with the illness, changes due to pregnancy and menstrual cycles, situation prior to and after becoming ill including employment and marital status, overall level of functioning, physical and mental illnesses and exercise tolerance.

- Therapy/Management Checklist: Current management details in the form of a therapy checklist including pharmacological, non-pharmacological, dietary supplements, self-management and other treatments.

- David Bell Disability Scale

- Krupp Fatigue Severity Scale

- Lloyd/Hickie Symptom Checklist

- SF-36 Quality of Life questionnaire.

- Hospital Anxiety and Depression Scale (HADS)

While the list of questionnaires seem long and may be difficult for some patients to complete, we wished to identify a minimum data set to ensure we have reliable, valid and usable data for the purposes of a longitudinal study and future use of the data in other ME/CFS research / clinical trials.

It was planned to send each patient a similar set of questionnaires 6 months later, to test follow up procedures and detect any changes in the natural history of the condition. This follow up period was considered too short for the purpose of this pilot study and given the many delays experienced (see below) it was therefore not undertaken. A more realistic timeframe would be 12 to 18 months or more.

b. Recruitment:

Patients meeting the Canadian ME/CFS criteria (2003) were selected to participate in the pilot study. The aim was to recruit 120 patients to the study by approaching two Adelaide clinicians with a special interest in ME/CFS and who have had a collaborative approach to the diagnosis and management of ME/CFS patients - Dr Peter Del Fante (General Practitioner) and Dr Richard Burnet (Endocrinologist). This would also allow for consistency with information collection. These clinicians also treat a very large proportion of the cohort of ME/CFS patients in Adelaide, and we believed this method of recruitment would result in a fairly representative sample of ME/CFS patients that are able to attend the clinics in question. However, it is acknowledged that patients with more severe ME/CFS (e.g. bed ridden) would clearly be under represented in this pilot study.

100 of Dr Del Fante's patients who met the entry criteria were sent a letter of invitation to be involved in the register with an information sheet and consent form to be signed and returned (see appendix A). The information sheet outlined the purpose of the study, benefits, eligibility, what is required of the patient, their rights and confidentiality issues. The initial letters were all sent out from his clinic to respect

confidentiality. Upon recruitment to the study patients received the questionnaires, by mail, for data collection.

The same process was repeated with Dr Burnet's patients with 46 letters of invitation sent out.

Where appropriate, patients from both doctors were followed up by phone in regards to any missing data or questionnaires to ensure completeness of data wherever possible.

d. **Data base design**: The database / register was designed by The Data Management and Analysis Centre (DMAC, Departments of General Practice and Public Health, University of Adelaide). Data from 75 sets of questionnaires was entered into the database by the DMAC team. A statistician from the Department of General Practice produced frequencies for each question, as well as statistics relating to the HADS tool and the SF36 Quality of Life questionnaire.

e. **Ethics:** An application was submitted and ethics approval was obtained from The University of Adelaide Human Research Ethics Committee (see appendix A).

iii. RESULTS (overall)

a. Response rate, data design and data entry

Of the 100 letters of invitation sent out to Dr Del Fante's patients, 56 questionnaires were returned – a response rate of 56%.

Of the 46 letters of invitation sent out to Dr Burnet's patients, 19 questionnaires were returned - a response rate of 41%.

In total 146 invitations were sent and 75 sets of questionnaires returned, reflecting an overall response rate of just over 51%.

A small number of patients from both doctors were followed up by phone in regards to questions that had not been answered to ensure completeness of data wherever possible.

There were significant delays experienced in the recruitment phase. It was originally planned to have questionnaires from both sets of patients returned by November and data entered into database in December 2005. These delays were attributed to delays with patient recruitment from Dr Burnet's clinic and delays in the data base design and programming. This put the pilot study up to 6 months behind schedule.

Data base design was completed by April 2006 and data entry occurred during May 2006. As a result of these delays it was decided to not send out the six month follow up questionnaires as was originally proposed.

b. Demographics

A total of 75 subjects were enrolled into the pilot study. Of these 57 (or 76%) were female, 18 (or 24%) were male. The female to male ratio was approximately 3 to 1.

The average age of participants was relatively young at 39 years of age (with range from 18 to 65 years).

The average age of women in the study was 37.5 years (range 18 to 65 years) and that of the men was 45 years (range 20 to 65 years).

83% of subjects were born in Australia, and the remainder were born overseas. None of the subjects were Aboriginal or Torres Strait Islander.

Only one patient's highest level of education was primary. 28% completed only their secondary education, 16% and 22% respectively for TAFE and university. 11% had a post graduate qualification.

Most people lived with one other person (39%), with 20% living in a household of 4, 19% on their own and 15% with two other people.

A high proportion of subjects received a pension (42 subjects or 56%). Of these most received the Disability Support Pension (64% or 27 subjects).

c. Lifestyle factors:

Most people do not smoke (91%), while 44% of patients do drink alcohol with most (64%) consuming no more than 2 standard drinks per day.

d. Onset and duration of Illness

35% of patients had a sudden onset of illness (over days or weeks) and 59% reported a gradual onset (over several month or years).

Age of onset was mainly between the ages of 10 and 45 years of age, with the average age being 29 years. There were two peaks: one between 10 and 20 years of age, and the other between 35 and 45 years of age.

Duration of illness varied from 1 to 50 years. The average was 11 years.

Delay in diagnosis was significant. It ranged from 0 to 24 years, with the average being nearly 7 years (6.83 years to be exact).

e. Illness at Present

32% of patients report that at present their illness is stable, while 27% are relapsing, 25% are gradually improving and 16% are gradually deteriorating.

f. Triggers of Illness

The most reported triggers of illness were 68% for virus/infection, 43% for emotional stress, 27% for physical overactivity, 16% by exposure to environmental toxins, 12% due to hormonal changes, 7% to surgery and 5% to vaccination. Some respondents had more than one event triggers.

g. Causes of Relapses

Most people reported that their relapses were brought on by physical overactivity (89%), emotional stress (84%), virus/ infection (68%) and changes in the weather (58%). Other triggers for relapse were exposure to environmental toxins (31%), hormonal changes (32%), air and car travel (25% and 27% respectively), surgery (12%) and vaccination (4%). Many respondents had more than one cause for relapses.

h. Other Family Members

12% of patients have other family members with the illness; 4% have a mother and 6% have siblings with the illness. None of the patients have a father with the illness.

i. Pregnancy

9% of patients have been pregnant during the illness. Of these 86% were made worse by the illness.

j. Menstrual Cycles

56% of patients are having menstrual cycles. Of these 67% reported that their illness worsened just before and during menstruation.

The following results refer to patient responses before and after the onset of the illness.

k. Marital Status

Before the illness 53% of patients had never married, 36% were married, 8% were divorced. After the onset of the illness 47% have never married, 41% are married and 9% divorced. Overall there was little change to marital status before and since the onset of the illness.

l. Employment

Before the illness 37% were employed full-time and 15% part-time. 7% were self-employed full-time and 7% part-time. 29% were full-time students, 3% were part-time. 12% had casual employment. 1% was unemployed, no one was retired, 1% was unable to work and 12% performed home duties.

After the onset of the illness only 4% work full-time and 16% work part-time. 1% are self-employed full-time and 12% part-time. 7% are full-time students, 9% are part-time. 11% have casual employment. 1% are unemployed, 3% have retired, 43% are unable to work and 19% perform home duties. 20% are involved in volunteer activities.

The most dramatic change was from 1% unable to work prior to the illness and 43% since the onset of the illness.

m. David Bell Disability Score

Before the illness most people rated themselves as either 100 or 90 (57% and 20% respectively). After the illness most people rated themselves as 40 or 30 (31% and 28% respectively). 15% rated themselves as 50 and 12% as 20.

n. Other Medical Conditions

Before the illness 47% of patients reported having another medical condition. 16% had asthma, 7% had fibromyalgia, 3% had hypothyroidism, 1% sleep apnoea and none had coeliac disease.

After the onset of the illness 29% reported having another medical condition. 13% had asthma, 31% fibromyalgia, 5% hypothyroidism, 4% sleep apnoea and 3% had coeliac disease.

o. Mental Health Conditions

Before the illness 28% had a mental health condition. 23% had experienced depression, 8% anxiety disorder, 5% panic disorder.

After the onset of the illness 55% had a mental health condition. 47% had depression, 21% anxiety disorder and 11% panic disorder.

p. Exercise tolerance

Before the illness 76% of patients reported having a regular exercise regime. 22% performed light exercise, 21% moderate exercise and 8% heavy exercise.

After the illness, 44% have a regular exercise program. 15% are involved in light exercise, 7% moderate exercise and 1% heavy exercise.

q. Most Effective Treatments (pharmacological and non-pharmacological)

Patients were asked to rate their three most effective treatments/ways of managing their illness and most reported that diet, activity management and social/family support were the most helpful in improving their quality of life.

Treatment	**Number of patients**
Diet	30 (40%)
Activity Management/Resting	30 (40%)
Social/family support	22 (29%)
Low-dose tri-cyclic antidepressants (for sleep and pain)	13 (17%)
Exercise	13 (17%)
Sleep Hygiene	12 (16%)
Stress Reduction	12 (16%)
Vitamins/Minerals	11 (15%)
Having a passion/interest	11 (15%)
Massage	11 (15%)
Spirituality	6 (8%)

The benefits of each type of treatment is reported in the results appendices. The following is a sample of the results.

For non-pharmacological therapies:

For those who tried a healthy diet (78%) it helped over 58% of subjects to improve their condition, with only 1% reporting it made them worse. For activity management (tried by 45%) it was 78% for improving their condition and only 7% for making it worse. For those who did light exercise (70%) it was 40% for improving their condition and 30% for making them worse. For those who tried moderate levels of exercise (45%) it made far more people worse (65%) than better (24%). Of the 20% who tried heavy exercise, all were made worse.

With regards to psychological methods: For those who tried education about the illness (85%) it helped over 52% of subjects to improve their condition, with just over 1% reporting it made them worse. For stress reduction techniques (tried by 48%) it was 65% for improving their condition and 6% for making it worse. Only 16% had tried CBT and of these 44% reported improvement while none were made worse. For general psychological counselling (tried by 36%) over 66% reported improvement while 7% were made worse.

For pharmacological treatments:
For those who tried a low dose TCA (57%) it helped over 53% of subjects to improve their condition, while 28% reported it made them worse. For anti-depressants (tried by 45%) it was 65% for improving their condition and 36% for making it worse. For those who tried pain relievers (58%) it was 57% for improving their condition and only 7% for making them worse. For those who tried antibiotic regimes (19%) it was 42% for improving and 37% made worse. For hormone treatments (tried by 16%) it was 69% for improving and 19% made worse.

r. Symptom checklist

The following symptoms frequencies were reported:

Symptom	*Never*	*Resolved*	*Mild*	*Moderate*	*Severe*
Fatigue					
. Excessive muscle fatigue with minor activity	1(1.35)	9(12.16)	14(18.92)	30(40.54)	20(27.03)
. Prolonged feeling of fatigue after physical activity	1(1.35)	6(8.11)	6(8.11)	27(36.49)	33(44.59)
. Shortness of breath with minor activity	17(22.97)	10(13.51)	23(31.08)	13(17.57)	11(14.86)
Pain					
. Muscle pain (not joint pain) after activity	4(5.41)	5(6.76)	19(25.68)	27(36.49)	19(25.68)
. Muscle pain (not joint pain), even when doing nothing	9(12.16)	6(8.11)	24(32.43)	24(32.43)	11(14.86)
. Joint pain	12(16.22)	7(9.46)	29(39.19)	15(20.27)	11(14.86)
. Headache	3(4.05)	4(5.41)	22(29.73)	20(27.03)	25(33.78)
. Redness and swelling localised around joints	57(77.03)	3(4.05)	9(12.16)	3(4.05)	2(2.70)
Nervous System					
. Repetitive muscle twitching- on the face	43(58.11)	0(0.0)	18(24.32)	5(6.76)	8(10.81)
. Repetitive muscle twitching elsewhere (arms, legs)	33(44.59)	13(17.57)	19(25.68)	8(10.81)	1(1.35)

Symptom	*Never*	*Resolved*	*Mild*	*Moderate*	*Severe*
. Sudden involuntary jerking of one arm or leg- in sleep	33(44.59)	9(12.16)	23(31.08)	6(8.11)	1(1.35)
. Sudden involuntary jerking of one arm or leg- when awake	47(63.51)	7(9.46)	18(24.32)	1(1.35)	1(1.35)
. Feeling of disturbed balance	9(12.16)	6(8.11)	30(40.54)	15(20.27)	14(18.92)
. Repeated tingling sensations (fingers, toes or elsewhere	34(45.95)	10(13.51)	17(22.97)	8(10.81)	5(6.76)
. Persistent ringing in the ears	33(44.59)	13(17.57)	17(22.97)	5(6.76)	6(8.11)
Nervous System					
. Episodes of abrupt anxiety or panic	24(32.43)	13(17.57)	23(31.08)	10(13.51)	3(4.05)
Digestive System					
. Nausea	9(12.16)	11(14.86)	28(37.84)	15(20.27)	11(14.86)
. Stomach pain	19(25.68)	9(12.16)	23(31.08)	12(16.22)	11(14.86)
. Difficulty swallowing foods	51(68.92)	9(12.16)	10(13.51)	2(2.70)	2(2.70)
. Recurrent diarrhoea (more than 4 loose stools per day)	28(37.84)	11(14.86)	21(28.38)	11(14.86)	3(4.05)
Immune System					
. Repeated fevers and sweats	20(27.03)	12(16.22)	21(28.38)	13(17.57)	8(10.81)
. Painful, red eye(s)	35(47.30)	6(8.11)	24(32.43)	6(8.11)	3(4.05)
. Persistent dryness in the eyes and mouth	29(39.19)	7(9.46)	21(28.38)	11(14.86)	6(8.11)
. Tender glands- in the neck	16(21.62)	13(17.57)	28(37.84)	10(13.51)	7(9.46)
. Tender glands- elsewhere	35(47.30)	10(13.51)	20(27.03)	7(9.46)	2(2.70)
. Sore throat (without "common cold" symptoms)	17(22.97)	7(9.46)	23(31.08)	17(22.97)	10(13.51)
. Persistent cough	42(56.76)	8(10.81)	17(22.97)	6(8.11)	1(1.35)
Cognitive Dysfunction					
. Memory loss	4(5.41)	4(5.41)	26(35.14)	25(33.78)	15(20.27)
. Loss of concentrating ability	1(1.35)	0(0.0)	16(21.62)	33(44.59)	24(32.43)
. Difficulty with speech- "lost for the word"	6(8.11)	4(5.41)	23(31.08)	25(33.78)	16(21.62)
Cardiovascular System					
. Palpitations (feeling the heart racing)	19(25.68)	9(12.16)	22(29.73)	16(21.62)	8(10.81)
. Recurrent chest pain	38(51.35)	7(9.46)	16(21.62)	8(10.81)	5(6.76)
Visual Disturbance					
. Episode(s) of complete loss of vision in one or both eye	64(86.49)	0(0.0)	9(12.16)	1(1.35)	0(0.0)
. Difficulty in focusing vision	17(22.97)	5(6.76)	19(25.68)	23(31.08)	10(13.51)
Sleep Disturbance					
. Needing to sleep for long periods	1(1.35)	15(20.27)	11(14.86)	23(31.08)	24(32.43)
. Disturbed sleep or disrupted sleep pattern	4(5.41)	3(4.05)	18(24.32)	15(20.27)	34(45.95)
. Vivid dreams or nightmares	15(20.27)	7(9.46)	22(29.73)	20(27.03)	10(13.51)
Reproductive System					
. Loss of interest in sex	14(18.92)	8(10.81)	22(29.73)	11(14.86)	15(20.27)
. Loss of sexual performance	21(28.38)	8(10.81)	19(25.68)	8(10.81)	13(17.57)
Urinary System					
. Episode(s) of loss of control of the bladder or bowel	53(71.62)	6(8.11)	10(13.51)	3(4.05)	2(2.70)

s. Krupp Fatigue Severity Scale

The following percentage of participants had high levels of agreement with the following statements (i.e. a score of 5 or more on a scale of 1 to 7, where a higher value indicates agreement):

90% of participants report that their motivation is lower when they are fatigued.
83% of participants report that exercise brings on their fatigue.
88% say they are easily fatigued.
96% say that fatigue interferes with their physical functioning.
93% report that fatigue causes frequent problems for them.
90% report that fatigue prevents sustained physical functioning.
92% say that fatigue interferes with carrying out certain duties & responsibilities.
96% report that fatigue is one of their three most disabling symptoms.
94% say that fatigue interferes with their work, family and social life.

t. SF 36 Inventory

The SF36 scores and graphs (see appendix C) show a significant impact on the quality of life (QoL) for patients with the condition when compared to the normal population.

It is most pronounced for the following:

- Standardised physical component scale
- Physical functioning
- Role Physical
- Pain Index
- General Health perceptions
- Role emotional
- Social functioning
- Vitality

It was less pronounced for the following:

- Standardised mental component scale
- Mental Health perceptions

u. Hospital Anxiety and Depression Scale (HADS)

The HADS cut off score for each condition (Anxiety and Depression) was 11 or more. 23 patients (30%) had a score of 11 or more on the anxiety scale and hence very suggestive of having an anxiety disorder, while only 11 patients (15%) had a score of 11 or more on the depression scale and hence very suggestive of having depression.

v. Postcode mapping (GIS)

A map of patient postcodes in the pilot study was also produced. The use of Geographical Information Systems can assist with spatial analysis of the data, integration with other data sources such as census data, and determining proximity to health services, etc.

iv. DISCUSSION

This is the first successful attempt in Australia to pilot the development of a ME/CFS patient register containing a large amount of information. Some researchers suggest that recruitment from the community is preferable rather than through special interest ME/CFS clinics. This is important for epidemiological / population studies, but less important for studies of effective management. For the purpose of this study, this issue was not important at this stage in the development of an ME/CFS patient register. Patients who were recruited had seen one of the two study physicians and had a confirmatory diagnosis in accordance with the Canadian ME/CFS criteria 2003. However, the entire data collection was based on patients completing questionnaires on their own, apart from follow up by phone to ensure data completeness. This meant that issues such as other medical and mental health conditions were not confirmed by a physician. For example, patient self diagnosis of depression may not meet strict diagnostic criteria for depression. Nor were patient examination data collected (e.g. height, weight, BMI, blood pressure, etc) or results of investigations. The latter would normally occur in a more clinic driven data collection process as compared to this pilot study which relied on patient reporting only.

The overall response rate was reasonable. In total 146 invitations were sent and 75 sets of questionnaires returned, reflecting an overall response rate of just over 51%. It is not known why nearly half of the participants did not respond, but this could be followed up. All those invited were seen at the respective clinics over the last 12 to 18 months. Patients with severe ME/CFS are often bedridden and would clearly not be able to participate in this pilot. This highlights a need to include such patients in future expansions of the patient register. The use of an outreach nurse to go to patients homes and collect data (maybe over several interviews) would be one way forward.

This pilot study also confirmed that ME/CFS takes a huge toll on sufferers and their families. Most of the patients in this study were very ill with only 25% reporting that they are improving; the remainder were either stable, relapsing or deteriorating.

In general the findings of this study confirmed current knowledge about the illness. Even though the number of participants is moderately large, the study was not designed to check for statistical significance of results obtained.

Particular findings of interest from this study include the following:

- The ratio of females to males was 3 to 1.
- The average age of participants was relatively young at 39 years of age (with range from 18 to 65 years).
- Age of onset was mainly between the ages of 10 and 45 years of age, with the average age being 29 years. There were two peaks: one between 10 and 20 years of age, and the other between 35 and 45 years of age.
- Average duration of illness was quite high at 11 years.
- Delay in diagnosis was significant. It ranged form 0 to 24 years, with the average being nearly 7 years (6.83 years to be exact).
- 59% of participants reported a gradual onset of their illness, while 35% had a sudden onset. This is unusual because it is usually reported that 60% are acute onset. This most likely reflects the nature of the questions in the questionnaire, rather than the small sample size. Often there is an acute onset (as indicated in

the survey 68% reported a viral like illness as a trigger), but symptoms may develop over a period of 2 to 3 months or more. However, our questionnaire would have recorded this as gradual. This clearly needs to be reviewed and changes made accordingly to the questionnaire for future use.

- Interestingly, of the 9 patients reporting a family history, none had a father with the condition. While the numbers in the study are low, this would correlate with a mitochondrial dysfunction since mitochondrial DNA is only transmitted through the mother.
- The David Bell Disability Score decreased from 100 or 90 before the onset of the illness to an average 30 or 40 after the illness (this is a very significant reduction and hence level of disability)
- There is a reduction in other medical conditions of 47% before the illness compared to 29% after, and an increase in psychological conditions of 28% before the illness compared with 55% after. However, these are all self reported. Interestingly 21% self reported an anxiety disorder and 30% were detected with having significant anxiety using the HADS questionnaire. This indicates possible underreporting and it would be worthwhile correlating those self-reporting the illness with those detected. On the other hand 45% reported suffering from depression but only 15% were detected using the HADS scale. This is quite significant and indicates that while people may report feelings of depression they may not be significant enough to meet diagnostic criteria for depressive illness. The SF-36 inventory also showed that mental functioning was much less affected by the illness when compared to its significant impact on physical and social functioning.
- The range of symptoms clearly indicates that ME/CFS is a multi-system medical condition, with significant symptoms relating to brain dysfunction.
- What seemed to be most effective for people in improving their well-being was activity management/pacing, healthy / low glycaemic index diet and social/family support. This results highlight the lack of really effective treatments for this condition and that many people have to rely on basic self-management strategies and psychosocial type support from carers.
- Moderate to heavy exercise makes people with this condition worsen with 22 of the 37 people who performed moderate exercise experiencing a deterioration of their condition and all of the 15 who tried heavy exercise reporting a worsening.
- The SF-36 showed a significant impact on physical and social functioning and much less impact on mental health functioning. This is in stark contrast to patients with major depression.
- The Fatigue Severity scale showed that the fatigue experienced has a very high impact (average of 90%+) on a person's ability to function.

Interestingly, one patient reported no impact on their daily functioning due to fatigue (Fatigue Severity Scale). On further review they had moderately severe fatigue reported through other instruments (eg David Bell Scale). This highlights the possibility of the fatigue scale (1 to 7) being misused (ie coding 1 instead of 7). It also shows that some system of internal validation is possible (ie comparing with results from other questionnaires) and hence warranted in any patient register to ensure data accuracy.

Another patient reported a high level (100) of functioning before and after onset of illness on the David Bell scale. Again this may be an error in patient coding , and if not an error, then the patient should be reassessed to see if they actually met the entry criteria. Again this is possible by phone by using the Canadian criteria

checklist or through a face to face patient review if a clinic based assessment process is used.

All the questionnaires that were used in this study proved to be effective and will be helpful for ensuring consistency in responses (internal validation). However for a future database the new CDC Symptom Inventory (17) may be useful instead of the Lloyd Hickie Symptom Checklist. The comparison of data before and after onset of illness proved to be particularly useful. Again it showed a significant impact on employment (and hence financial impact) as well as on exercise tolerance. Interestingly, there appears to be minimal impact on family structure / marital status after onset of the illness. However, anecdotally, there is evidence of significant strain on families, partners, and carers. Future studies may consider appropriate questions to probe this area, as well as obtaining information from carers, partners or other family members. Often, they also need support to cope with a loved one with ME/CFS.

The pilot study also allowed participants to express in free text their view on a range of matters and this provided a rich source of qualitative data. Although this was entered into the database, there was little time left to analyse this data further.

The study experienced significant delays beyond our control which resulted in less than the 120 patients originally expected. This also meant that we were unable to trial the use of a follow up survey 6 months later.

Other issues to consider prior to setting up a larger database include investigating ways of increasing response rates, changing particular questions in some of the questionnaires to make them less ambiguous (e.g. gradual vs acute onset) and possibly recording physical indicators such as height, weight, blood pressure etc.

A better strategy for recruiting patients for a future database would be to recruit from the general population instead of directly from doctors' clinics. The ME/CFS society could be used for this purpose and a nurse employed to screen patients to determine whether they fit the required criteria and to collect baseline physical data and any investigation results. An assessment by a physician would also be required to confirm co-morbidities. Other researchers have suggested that the best approach would be to randomly contact the population and invite those that meet the criteria to come in for further assessment to confirm the diagnosis before entry into a patient register (Reeves, CDC). This approach may lead to a more representative sample, but again the issue of getting data from severe CFS patients would require an outreach service.

The pilot study has collected a rich source of data and the analysis has only just begun. A considerable amount of further analyses can be undertaken on just the pilot data collected so far (e.g. more in depth statistical analyses and correlations with normal populations (age-sex standardised)). However, expanding the patient data base numbers and designing further studies with controls will make statistical analyses more robust

v. CONCLUSION

The aim of the study was to pilot the development of a ME/CFS patient register and to determine the ease and usefulness of collecting various data relating to patient

symptoms and management. It was also planned that the patient register would serve as a future resource for ME/CFS research and clinical service development. Therefore the basic requirements or outcomes of the pilot study have been achieved.

This pilot study also confirmed that ME/CFS takes a huge toll on sufferers and their families. Most of the patients in this study were very ill with only 25% reporting that they are improving; the remainder were either stable, relapsing or deteriorating.

Some of the comments recorded in this study reflect this:

"The muscle pain makes me cry and the fatigue is awful"

"You should ask my kids how much this (CFS) impacts on their lives and how much they hate hearing 'Sorry mummy is too tired' or 'I have to lie down". It is ruining my life."

It is hoped that the success of establishing a patient register for ME/CFS, which is the only one of its kind so far in Australia, will create a better understanding of this debilitating condition and stimulate further research into its cause and appropriate treatments. Already there are three separate groups of researchers who are interested in accessing the database for ME/CFS related projects. These are looking at: Cognitive dysfunction and its impact on QoL; Brain imaging and orthostatic intolerance; and Assessing health service needs for SA ME/CFS patients. This shows that the concept of a patient register is worthwhile and that it could be easily expanded into a larger ongoing database of 300-400 patients with further funding.