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**Evaluation of a prospective randomized
controlled exercise program for people
recovering from severe acute respiratory
syndrome (SARS)**

Herman Mun Cheung LAU

A Dissertation Submitted to
the Hong Kong Polytechnic University in Partial
Fulfillment for the Degree of Master of Philosophy in
the
Department of Rehabilitation Sciences

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STATEMENT OF SOURCES

The idea and planning of the present study were resulted from the discussions between the author and Prof. Gabriel NG, Prof. Alice JONES, and the Physiotherapists in the Prince of Wales Hospital, Hong Kong.

All experiments in the present study were completed solely by the author except otherwise stated in the text.

The author declares that the work presented in this thesis is, to the best of the author's knowledge, original, except as acknowledged in the text, and that the material has not been submitted, either in whole or in part, for a degree at this or any other university.

Herman Mun-cheung LAU

May 2006

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PUBLICATIONS RELATED TO THIS STUDY

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- Lau, H.M., Lee, E.W., Ng, G.Y., Jones, A.Y., Siu, E.H. & Hui, D.S. A randomized controlled trial of the effectiveness of an exercise training program in patients recovering from severe acute respiratory syndrome. *Aust J Physiother* 2005, 51, 213-9.

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- Lau, H.M., Lee, E.W., Siu, E.H., Wong, C.N., Tsui, A.Y., Chiang, W.K., Hui, D.S. & Chan, K.M. To investigate the effectiveness of a prospective randomized controlled exercise training program for post-SARS patients. *Hospital Authority Convention* May 2004.

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LIST OF ABBREVIATIONS

6MWT	Six-minute walk test
ARDS	Acute Respiratory Distress Syndrome
BP	Bodily Pain
COPD	Chronic Obstructive Pulmonary Disease
GH	General Health
HRQoL	Health Related Quality of Life
ICU	Intensive Care Unit
MH	Mental Health
PF	Physical Functioning
PTCOC	Coordinating Committee of Physiotherapy
PWH	Prince of Wales Hospital
QoL	Quality of Life
RE	Role Emotional
RP	Role Physical
RPD	Ratings of Perceived Dyspnoea
SARS	Severe Acute Respiratory Syndrome
SF	Social Functioning
SF36	Medical outcomes study 36-item short-form health survey
VCD	Video Compact Disc
VO _{2max}	Maximal Oxygen Uptake
VT	Vitality

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ABSTRACT

This thesis reported the outcome of a prospective epidemiological cohort study by comparing the physical fitness and the health-related quality of life (HRQoL) status between the subjects with normal health and the patients who survived from Severe Acute Respiratory Syndrome (SARS). The second phase of the study included a randomized clinical controlled trial which aimed to evaluate the effect of a 6-week supervised training program at both short-term (immediately after completion of the exercise program) and at 6-month post-training on their physical and HRQoL status.

A total of 171 post-SARS patients discharged from the Prince of Wales Hospital (PWH) in Hong Kong were recruited for the first part of the study. The mean age of these patients was 37.36 ± 12.65 years and their averaged length of hospitalization was 21.79 ± 9.93 days. 133 of them were then recruited into a randomized controlled trial. They were randomized into two groups, namely, the supervised exercise group and the home-based control group. Patients in the home-based control group received a standardized educational session from the physiotherapists on general exercise advice and an exercise VCD for performing the exercises at home while patients in the supervised exercise group were arranged to join a 6-week training program conducted in the physiotherapy department of PWH in addition to the general advice and the exercise VCD. Follow up assessment was arranged for both groups of patients six months after the 6-week training. A total of 98 subjects completed all the evaluation procedures.

The physical outcomes of the patients were measured by a series of tests which included a 6-minute walk test, a Chester step test (for predicted maximal

oxygen consumption), testing of the handgrip strength and proximal muscles strength of both the upper and lower limbs, 1-minute curl-up and push-up tests, and a SF-36 questionnaire for measuring the HRQoL status.

The test results revealed that the 6-minute walk distance, the predicted VO_{2max} , the large and small muscle strength, and the scores in SF-36 for the post-SARS patients were significantly lower than the normative value ($p<0.05$).

After the 6-week training program, the supervised exercise group significantly demonstrated greater improvement than the home-based control group in the 6-minute walk test. Their results were 77.44m (13.11%) vs 20.71m (3.37%), $p<0.001$. For the predicted VO_{2max} , the figures were 3.57ml/kg/min (10.16%) vs 0.97ml/kg/min (2.57%), $p=0.036$. For the musculoskeletal performance, the supervised group also had more significant improvement than the control group. Left handgrip: 4.15kgf (16.14%) vs 2.19kgf (8.59%), $p<0.05$, right handgrip: 4.69kgf (16.99%) vs 1.71 kgf (6.09%), $p<0.05$. Curl-up test: 7.06 counts (52.8%) vs 3.56 counts (25.34%), $p<0.05$ and push-up test: 8.59 counts (90.61%) vs 3.61 counts (37.10%), $p<0.05$. The HRQoL status of the two groups, however, did not reveal any significant difference.

Differences in the result between the two groups were also noted at the 6-month follow-up assessment, the supervised exercise group improved more significantly than the control group in the 6-minute walk test. The figures were: 59.62m (10.09%) vs 18.64m (3.03%), $p=0.022$. For the predicted VO_{2max} , the differences were 6.92ml/kg/min (16.70%) vs 3.41ml/kg/min (9.02%), $p=0.049$. Curl-up test: 6.23 counts (46.60%) vs 3.02 counts (21.49%), $p<0.037$ and push-up tests: 6.98 counts (73.63%) vs 3.37 counts (34.64%). The handgrip improvement was not

significant. Left handgrip: 1.07kgf (4.16%) vs 2.39kgf (8.51%) and right handgrip: 1.76kgf (6.37%) vs 1.57kgf (5.59%). For SF-36, none of the domains showed any prominent difference between the two groups at 6 months post-training.

In conclusion, SARS survivors demonstrated deficits in the cardiopulmonary and musculoskeletal performances as well as the HRQoL status after hospital discharge. The 6-week intensive exercise training program supervised by the physiotherapists was shown to be effective in improving both their cardio-respiratory and musculoskeletal performances. Nevertheless, physical training during the intervention period had no impact on HRQoL. At the 6-month post-training follow-up, similar results were obtained which proved that the training program could provide long-term physical benefits to the post-SARS patients.

CHAPTER 1

INTRODUCTION

1.1 Background of SARS and its impacts on patients

In March 2003, an outbreak of atypical pneumonia presented with symptoms of fever plus one or more respiratory symptoms such as cough, shortness of breath and difficulty in breathing (Donnelly et al, 2003; Hui and Sung, 2003; Lee et al, 2003) was defined by the World Health Organization as severe acute respiratory syndrome (SARS) (World Health Organization, 2003). Chest radiographs and tomography of these patients revealed various degrees of lung injury characterized by multiple areas of peripheral ground-glass appearances and consolidation (Lee et al, 2003; Wong et al, 2003). The disease soon turned into a global outbreak with majority of the cases happened in a few cities in China, Hong Kong, Toronto, and some scattered cases in other parts of the world. The epidemic in Hong Kong lasted for 3 months until June 2003. There were a total of 1755 reported SARS cases in Hong Kong with a death toll of 299.

It was then the policy in Hong Kong that patients of SARS were to be treated in a few major hospitals in the territory and the Prince of Wales Hospital (PWH) was one of the designated hospitals. The average length of hospitalization of these patients was approximately 3 weeks and all patients discharged from PWH were followed up by a newly established 'SARS review clinic'. The purpose of that clinic was to monitor the medical management and to evaluate the physical and pulmonary functions of the SARS survivors. It was observed that many patients encountered various degrees of complaints such as tremor in the hands, general muscle weakness, tachycardia, and exertional dyspnoea at the follow-ups (Donnelly et al, 2003). These

patients complained of difficulty in coping with their activities of daily living such as walking (on level ground or uphill), climbing stairs and simple housework. Many of them received short bursts of high dose systemic steroid during hospitalisation (Lee et al, 2003) and most of them could not wean off prednisolone due to residual lung opacities on radiographic examinations (Antonio et al, 2003).

It was proposed that these post SARS symptoms could be a consequence of prolonged bed-rest, steroid myopathy (Decramer, 1996; Nakago et al, 1999), residual disease pathologies such as atelectasis, ongoing alveolitis, pulmonary fibrosis, deconditioning of the cardiopulmonary and musculoskeletal systems or a combination of these factors. To assist patients to regain their physical capacity, physiotherapy programmes were designed. As SARS was a new global epidemic condition, neither the physical status of these patients after hospital discharge, nor the effectiveness of physical training on these patients was ever reported. The aims of this study were to evaluate the functional profiles of these patients upon discharge from the hospital and to determine the immediate and long-term effectiveness of a 6-week supervised physical rehabilitation program on these SARS survivors.

CHAPTER 2

LITERATURE REVIEW

2.1 History of the SARS epidemic

While sporadic human cases might have occurred in earlier times (Weiss and McLean, 2004), SARS was the first newly emergent communicable disease epidemic of the 21st century. During the first epidemic of this new pathogen, 29 countries were affected. The first human case was identified in Guangdong, China, in November 2002 (Zhong et al, 2003).

The urbanization and increase in wealth amongst the Guangzhong population in China has led to a rapidly expanding market for exotic animal food in the recent years. The resurgence of SARS was distinctly possible given its uncertain origins and the likely existence of an animal reservoir, the palm civet cat (Guan et al, 2003), was suspected to be a possible cause for SARS. “The Guangdong government and Department of Public Health subsequently took strong actions of: (1) strict control of the wildlife market, including a ban on the rearing, sales, transporting, slaughtering and food processing of small wild mammals (civet cats in particular), and (2) four “early” steps (early identification, early report, early isolation and early management) to stop transmission from human to human” (Zhong, 2004).

In Hanoi, where the epidemic was first reported, the disease was noted to have an alarming high rate of transmission at 63% among healthcare workers (HCW). In Hong Kong, where the health care system is relatively advanced and the resources are considered abundant, transmissions among HCW still acquired an alarming high rate of 46%. In Singapore, an official surveillance indicated that 76% of infections were acquired in a healthcare facility and a similarly high rate of transmission was

observed in Toronto (Centers for Disease Control and Prevention, 2003a; 2003b)

2.2 SARS in Hong Kong

SARS was carried into Hong Kong and transmitted to three vacationing Singaporeans (including the “index” case), apparently while they were waiting for a hotel elevator along with a SARS-infected person (Lim et al, 2004). It was reported that among all the SARS patients (1755) in Hong Kong, 49.3% were infected in clinics, hospitals, elderly or nursing homes, while 18.8% were from an outbreak in a residential area (the Amoy Gardens cluster) (Leung et al, 2004). The ratio of women to men among the infected individuals was 5:4. Healthcare workers accounted for 23.1% of all reported cases. The estimated mean incubation period was reported to be 4.6 days, and the mean time from onset to discharge was 26.5 days. Increasing age, male sex, atypical presenting symptoms from SARS (such as dyspnoea, persistent cough and fever), presence of co-morbid conditions, and high lactate dehydrogenase enzyme level on admission were associated with an increasing risk for death (Leung et al, 2004).

Rehabilitation was significantly affected by the extremely contagious nature of SARS, because strict infection control measures were instigated which contradicted the rehabilitation principles such as multidisciplinary interactions, patients learning from each other, and close physical contact between therapists and patients during therapy (Lim et al, 2004).

The amount of physical, occupational, or speech therapy that each patient received was significantly reduced (Lim et al, 2004). In Singapore, group therapy and patients using therapy gymnasiums in relatively close quarters were prohibited in

order to avoid the spreading of the virus. Rehabilitation equipment, such as parallel bars, step platforms, therapy balls, and assistive walking devices, were distributed to individual health care centres because the therapy gymnasiums were closed (Lim et al, 2004). In addition, the number of patients presenting for out-patient evaluations and follow-ups in Singapore dropped dramatically because the public avoided hospitals whenever possible (Lim et al, 2004).

Since the outbreak of SARS in March, 2003, there had been a weekly decline in out-patient clinic attendance of otolaryngology health services by 59%, the number of operations performed by 79%, the average ward bed occupancy rate by 79% and the daily admission rate by 84%. A dramatic increase of 300% in the number of patients defaulting on their out-patient appointments were also recorded (Vlantis et al, 2004).

2.3 What is SARS

SARS is the acronym for severe acute respiratory syndrome. “The most common symptoms included cough (83%), dyspnoea (80.6%), malaise (69.4%) and fever (61%). Less common symptoms included headache (38.9%), diarrhea (38.9%), dizziness (30.6%), myalgia (25%), chills (19.4%), nausea and vomiting (19.4%) and rigor (the occurrence of a sensation of hot-and-cold and shivering in addition to teeth chattering and bed shaking) (8.3%)” (Tiwari et al, 2003). Other common laboratory findings were lymphopenia (69.6%), thrombocytopenia (44.8%), and elevated lactate dehydrogenase and creatine kinase levels (71.0% and 32.1%) (Lee et al, 2003). Microscopic examination of nasopharyngeal aspirates from most patients showed paramyxovirus-like and coronavirus-like viral particles (Lee et al, 2003).

Based on the nasopharyngeal and serum samples of patients, the infective agent implicated was a novel coronavirus (Drosten et al, 2003; Peiris et al, 2003). The name severe acute respiratory syndrome (SARS), adopted for this infection, was an appropriate recognition of its nature and virulence (Lim et al, 2004).

Among the reported SARS cases in Hong Kong, all the patients had abnormal chest radiographs, which showed air-space consolidation. Of the 108 patients in the study of Lee et al (2003), 59 (54.6%) had unilateral focal involvement, 49 (45.4%) had either unilateral multifocal or bilateral involvements and 100% of them had eventually developed air-space opacities during the course of the disease. “The typical finding on thoracic CT images was ill-defined, ground-glass opacification in the periphery of the affected lung parenchyma, usually in a subpleural location” (Lee et al, 2003). The experience in Guangzhou showed that there was bone necrosis (femur and knee) (4%) after corticosteroid therapy at 9 months follow-up period (Zhong, 2004). The study also showed that 20-30% of patients with critical SARS received non-invasive facial / nasal mask ventilation (mainly continuous positive airway pressure), which enabled improvement of oxygenation in early stages and prevented patients from requiring intubation (Zhong, 2004).

Patients in Hong Kong were admitted to the intensive care unit (ICU) when severe respiratory failure developed as evidenced by (1) failure to maintain an arterial oxygen saturation of at least 90% while receiving supplemental oxygen of 50% and / or (2) respiratory rate > 35 breaths/min (Sung et al, 2004).

In cases where intubation and assisted mechanical ventilation were required, patients would be transferred to the SARS ICU where negative pressure room and closed suction system were available to prevent air leaks (Tiwari et al, 2003).

Among the patients admitted to the ICU (32 in PWH), dramatic increases in lung opacity, shortness of breath, and hypoxemia occurred at a median of 6.5 days (range 3 to 12) after contracting the disease. These symptoms progressed rapidly which had led to their admission to the ICU (Lee et al, 2003).

2.4 Medical management of patients with SARS in Hong Kong

Patients with SARS in Hong Kong were treated for the first 2 days with broad spectrum antibiotics for community acquired pneumonia according to the American Thoracic Society guidelines (American Thoracic Society, 2001). Ribavirin, a broad spectrum antiviral agent previously shown to be efficacious against both RNA and DNA viruses had also been used (Drosten et al, 2003; Lee et al, 2003). If fever persisted after 48 hours, patients were given a combination of ribavirin and “low dose” corticosteroid therapy commencing on day 3-4 (oral ribavirin as a loading dose of 2.4g stat followed by 1.2g three times daily and prednisolone 0.5-1mg/kg body weight per day), whereas those with dyspnoea were treated with intravenous ribavirin (400mg every 8 hours) combined with hydrocortisone (100mg every 8 hours). Steroid was used in order to control the severe inflammatory reaction and persistent high fever during the onset of SARS symptoms.

Pulses of high dose methylprednisolone (0.5g intravenous infusion for three consecutive days) were given to post-SARS patients. Such kind of steroid administration was given as a response to persistence or recurrence of fever and radiographic progression of lung opacity with or without hypoxaemia despite initial combination therapy (Sung et al, 2004)

2.5 Effects of SARS on patients

The long-term effects of SARS on the pulmonary and physical conditions remain uncertain. Results from other studies showed that the long-term effects of pulmonary and physical conditions of severe lung disease, obstructive and restrictive lung function remained commonly up to 3 years after acute respiratory distress syndrome (ARDS) (Neff et al, 2003). Elliott and his colleagues (1981) found that there was an impaired pulmonary gas transfer during exercise. Whilst in the study by Davidson and colleagues (1999), patients complained of generalized muscle weakness and dyspnoea on exertion even at one year after recovering from severe ARDS.

On the psychological aspect, the isolation policy imposed by the Hong Kong government on SARS patients prevented visits from family members while the use of personal protective equipment (masks and goggles) created a barrier to communication between patients and Healthcare workers. These had aggravated the patient's distress caused by the sudden catastrophe (Tiwari et al, 2003).

2.6 Effects of exercise training on physical and health-related quality of life

In order to restore the physical fitness and independence of daily living for people recovering from major illnesses, a key component in the rehabilitation program is exercise training [American College of Sports Medicine (ACSM), 1998]. Physical fitness is defined as the ability to perform occupational, recreational and daily activities without undue fatigue (ACSM, 1998). Cardio-respiratory fitness is related to the ability to perform large muscle, dynamic, moderate-to-high intensity exercise for prolonged periods. Performance of such exercise depends on the

functional status of the respiratory, cardiovascular and musculoskeletal systems. Muscular fitness has been used to describe the integrated status of muscular strength and endurance (Graves et al, 1998). It has also become increasingly important to review Health related Quality of Life (HRQoL) as an outcome measure for health interventions (Schelling et al, 2000).

The documented benefits of cardio-respiratory and strength exercise training, 3-5 weekly exercise sessions, for 6-12 weeks (Gigliotti et al, 2003), in patients with respiratory diseases included an increase in exercise capacity (endurance) (Casaburi et al, 1997), peripheral muscle strength (O' Donnell et al, 1998), maximal muscle strength (Simpson et al, 1992) and functional status, decrease in the severity of dyspnoea, and improvement in HRQoL (Donner and Howard, 1992).

The results of the critical review by Cambach et al (1999) showed that after pulmonary rehabilitation training in asthma and COPD patients, there were significant improvements shown in terms of the exercise capacity and the HRQoL status. However, significant improvements were found up to 9 months post training for maximal exercise capacity and walking distance only.

The study by Casaburi et al (1991) showed the effects of exercise on the delay in anaerobic threshold in COPD patients with moderate airway obstruction and indicated that there was a physiological training response. Another study by Maltais et al (1996) showed that exercise training increase skeletal muscle lactate threshold, citrate synthase and 3-hydroxyl-acyl CoA dehydrogenase in which reduction in lactic acidosis was inversely related to changes in activity of citrate synthase and 3-hydroxyl-acyl CoA dehydrogenase.

Exercise training improved COPD patients exercise tolerance by increasing

their muscle strength with minimal decrease or unchanged CO₂ output. Increase in muscle strength also decreased dynamic hyperinflation thereby increased tidal volume (VT) and decreased dead space (VD) to VT ratio (VD/VT). Decrease in respiratory rate with the unchanged CO₂ output also lowered minute ventilation (Gigliotti et al, 2003).

As SARS was a newly identified disease, there was no information available on the rehabilitation of the survivors and their physical fitness and HRQoL status. In 2003, most patients with SARS were only given general advices on medical and personal care upon discharge. The present health care system in Hong Kong does not have sufficient resources to provide a comprehensive follow up assessment of the cardiopulmonary performance or physical capacity of these patients.

Since SARS is a new disease, there are no reports on its effect on the physical fitness and quality of life (QoL) of its survivors. This information is important because knowing the effects of SARS on these parameters may guide the design of the rehabilitation programs and the assessment for these patients.

2.7 Objectives

The objectives of the present study were to (1) establish the physical profile and the HRQoL status of the patients upon discharge in comparison with the local age / gender matched able-bodied normative figures; (2) investigate into the effect of a 6-week physical rehabilitation program on the post-discharged SARS patients; (3) evaluate the effect of such training program over a 6-month follow-up period. Specific aims were to investigate into their physical fitness in the perspectives of cardio-respiratory, musculoskeletal, and HRQoL.

2.8 Null hypothesis of the study

(1) There was no significant difference in terms of the physical fitness and the HRQoL status between the discharged SARS patients and the normal healthy individuals. (2) There was no significant difference between the post-SARS patients in physical and the HRQoL status with or without a 6-week supervised physiotherapy training program and for up to 6 months post training.

CHAPTER 3

METHODOLOGY

3.1 Subjects

All patients followed up at the SARS review clinic of PWH, Hong Kong Special Administrative Region, between May to July 2003 were invited to participate in the study. Patients who were haemodynamically unstable (fluctuating blood pressure and resting heart rate), poorly motivated, uncooperative, unable to communicate, poor pre-SARS mobility, suffering from unstable medical conditions (e.g. known cardiopulmonary disorder, or musculoskeletal conditions which would affect mobility such as rheumatoid arthritis and avascular necrosis) were excluded from the study. Fiscal compensation associated with SARS contraction was not an issue aroused among those healthcare workers during the study period.

Approval to conduct the study was obtained from the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (Appendix A) and informed written consent was obtained from the subjects (Appendix B & C). A total of 171 subjects met the inclusion criteria during the studied period. Baseline assessment of the cardio-respiratory, musculoskeletal function and the HRQoL status for each subject was conducted at 2 weeks after discharge from the hospital (approximately 5 weeks after the onset of the symptoms). Patients with average or below normal performances in comparison to the same age range of healthy subjects were recruited into the second phase of the study. Details of inclusion and exclusion criteria were listed in Appendix D.

3.2 Study design

Phase I of the study was an epidemiological study followed by Phase II, a prospective randomized controlled clinical trial. The physical fitness and the HRQoL status of all the post-SARS patients recruited in Phase I were assessed before they were invited to Phase II of the study. The data collected from Phase I was compared with those obtained from a cohort of able-bodied subjects matched with age and gender (Normative data of physical fitness parameters; Lam et al, 1999)

After the initial assessment of 171 subjects, 38 patients dropped out from the study. The remaining patients (133) were divided into 2 groups, namely, the supervised exercise group and the home-based control group by random assignment with a computer program. Details of the study were listed in Figure 1.

Patients in the control group received a standardized educational session from the physiotherapists on general exercise advice and an exercise VCD (Figure 2). Each patient was phone contacted by a different physiotherapist on a twice weekly basis to monitor their compliance to the exercise program. The problems encountered by the patients were discussed with their attending physiotherapists (not the phone follow-up therapist). Their baseline physical profile and the HRQoL status were assessed.

After baseline assessment, patients in the exercise group underwent a 6-week supervised exercise training program in the physiotherapy department of PWH on top of receiving the same advice on exercise and the VCD as the control group. Their baseline physical profile and the HRQoL status were also assessed.

Cardio-respiratory and musculoskeletal fitness training were provided and monitored by the physiotherapists. This intensive exercise program started with a

warm-up and stretching exercise for about 10 minutes followed by the core training part including both the cardio-respiratory / endurance and the musculoskeletal strength training.

The cardio-respiratory and endurance training consisted of low-impact / non-weight bearing type exercises such as arm-cranking, cycling and stepping machines for 30 minutes per session (Pollock et al, 1977). The initial exercise intensity was based on the result of the cardio-respiratory assessment and the ratings of perceived exertion (RPE). Training zone was determined as 60-75% of predicted maximum heart rate (ACSM, 1998) (from the Chester step test) and progressed according to the heart rate and RPE (4-6) – “somewhat hard” (Dishman, 1994) during exercises (ACSM, 1998).

The resistance musculoskeletal strength training consisted of a circuit weight training program with moderate weight of 10-15 repetitions maximum per set of exercise (performing efforts to volitional fatigue for older and frailer persons such as post-SARS patients). The circuit weight training involved major muscle groups such as arms, shoulders, chest, abdomen, back, hips and legs. Weight training program included free weights shoulder press for shoulders, arm-curl and push-up for arms, curl-up for abdomen, back extension exercise for back, semi-squatting / lunges for hips and legs. Each exercise was performed for 3 consecutive sets based on ACSM (1998) recommendations. The exercise was progressed by increasing the weight so that 10-15 repetition maximum was maintained in each successive session (progressive overload principle) (ACSM, 1998).

Training frequency of the training program was 5 times per week in order to improve VO_{2max} and cardio-respiratory endurance (Pollock, 1977). The weight

training exercise of each major muscle group was performed 2 to 3 times per week (ACSM, 1998). Of the 5-day per week training program, 3 days were performed in the physiotherapy department and the rest were done in the subjects' own environment.

The training exercises performed in the unsupervised sessions were replicated by a self-administered exercise log book with diagrams given to the participating patients. Their progress was evaluated by the physiotherapists regularly during the training program. Telephone follow-ups were made twice weekly to all subjects in order to reinforce their compliance on the home exercise regime. It was hypothesized that once the patients in the exercise group were taught how to improve their physical and cardiopulmonary fitness level, they could regain a better physical profile and HRQoL than those in the control group (Gauchard et al, 2003).

Follow-up assessment procedures for both groups of patients were conducted at 6 weeks after recruitment (i.e. at the end of training for the exercise group) and again at 6 months after completion of the exercise training program, by an independent assessor who was blinded to the groupings. Exercise compliance (intensity, frequency and duration) of each patient throughout the 6-month period was also evaluated by the physiotherapists.

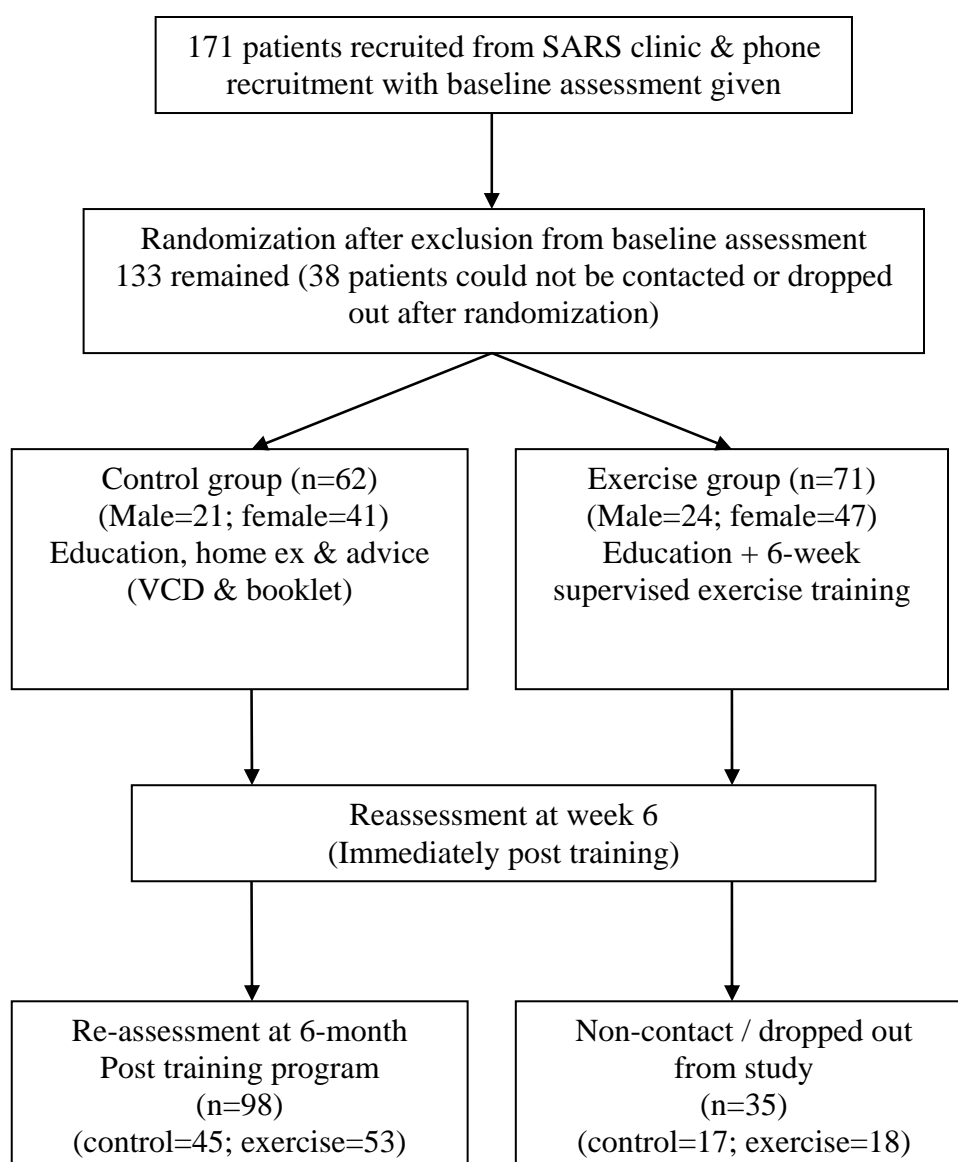


Figure 1. Flow chart illustrating the study design (Randomization of the exercise training program)



Figure 2. Self-exercised VCD and pamphlet

3.3 Outcome measures

3.3.1 Cardio-respiratory fitness

Maximal oxygen uptake (VO_{2max}) was used to measure cardio-respiratory endurance (ACSM, 1998). However, the use of maximal exercise test to determine VO_{2max} was not feasible as the subjects had to exercise to the point of volitional fatigue during the VO_{2max} testing and such a maximal level of exercise might be risky for the SARS survivors. In view of the above consideration, cardio-respiratory fitness was assessed by a 6-minute walk test (American Thoracic Society, 2002; Donner and Howard, 1992) and the Chester step test (Sykes, 1998) was used as an alternative to determine and predict the cardio-respiratory fitness of the patients (ACSM, 1998).

3.3.1.1 Chester step test

Chester step test was a popular and convenient method to predict VO_{2max} (Stevens and Sykes, 1996). A recent study (Sykes and Roberts, 2004) revealed that there was a high correlation ($r=0.92$) between VO_{2max} and Chester step test ($p<0.001$) and confirmed the face validity of step test as a predictor of VO_{2max} . The Chester step test was an incremental test with five levels of difficulties, commencing at the relatively slow pace of 15 steps per minute at the step height of 20 cm and increasing every two minutes to 20, 25, 30 and 35 steps per minute (Figure 3). The test was terminated when approximately 80% of maximum heart rate or ratings of perceived dyspnoea (RPD) of 6 (moderately hard) of the subject was reached. The VO_{2max} could then be predicted by drawing a graph of the corresponding heart rate at different step levels with a minimum of 3 points (level 3). (Sykes, 1998) The VO_2 prediction form was displayed in Appendix E.

3.3.1.2 Six-minute walk test

The 6-minute walk test was a simple functional assessment that had been used in some long-term follow up studies of patients with chronic obstructive pulmonary disease (COPD) (Berry et al, 2003; Scirba et al, 2003; Yoshikawa et al, 2001) and survivors of acute respiratory distress syndrome (ARDS) (Herridge et al, 2003; Hodgev et al, 2003; Neff et al, 2003; Schelling et al, 2000). The subjects were required to walk at their own pace on a 100-ft hallway accompanied by a physiotherapist who measured the distance covered with a rolling meter. The subjects were allowed to stop and rest during the test. The outcome measurement was the farthest distance that the subjects covered in 6 minutes (American Thoracic Society, 2002; Brooks et al, 2003; Enright PL, 2003; Scirba et al, 2003; Troosters et al, 2002) (Figure 4).



Figure 3. Chester step test



Figure 4. Six-minute walk test
(A therapist is using a rolling meter to measure the total distance the patient has walked during the test).

3.3.2 Musculoskeletal fitness

3.3.2.1 Isometric muscle strength

Clinically, many SARS survivors presented with some degrees of muscle weakness, in particular, the large muscles of the trunk and limbs. Therefore, the isometric strength of the anterior deltoid and gluteus maximus muscles were assessed with a digital hand-held dynamometer (Nicholas manual muscle tester; model 01160; Lafayette Instrument) (Figure 5) as a representation of the muscle strength of upper and lower limb respectively (Bohannon, 1999; 2001a; van Wilgen et al 2003; Wang et al 2002). The strength was measured with the subject holding an isometric contraction while the researcher pushed against the measured body part with the dynamometer to break the contraction (Bohannon, 1997).

Each subject assumed a sitting position and held their dominant arm in 90 degrees flexion to resist the downward push of the examiner for testing the strength of the anterior deltoid muscle bilaterally (Figure 6). The strength of gluteus maximus was tested with the subjects in prone lying and the hip extended with the knee straightened on each leg. The examiner pushed the thigh into flexion and the force was recorded on the dynamometer (Figure 7).

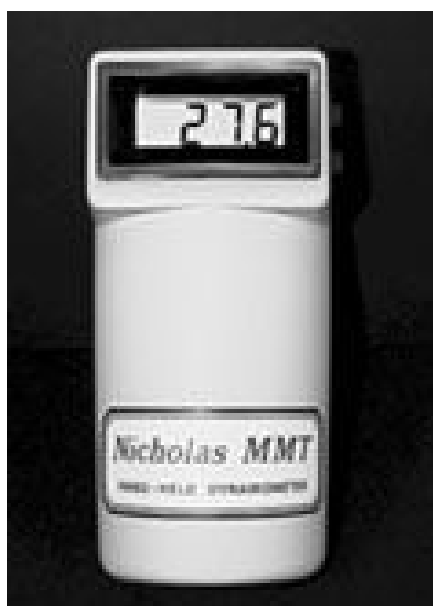


Figure 5. Handheld dynamometer



Figure 6. Isometric anterior deltoid muscle strength test



Figure 7. Isometric gluteus maximus muscle strength test

3.3.2.2 Handgrip strength

A JAMAR handheld dynamometer (Rolyan, Sammons Preston, Inc) was used to measure the handgrip (distal muscle) strength (Bellace et al, 2000; Bohannon 2001a; 2001b; Hamilton et al, 1994; Humphreys et al, 2002; Mathiowertz et al, 1984; Peolsson et al, 2001) (Figure 8). Each subject was asked to make a maximum grip on the dynamometer with the dominant hand in a sitting position whilst keeping the elbow flexed at 90° with the upper arm held against the trunk (Figure 9).

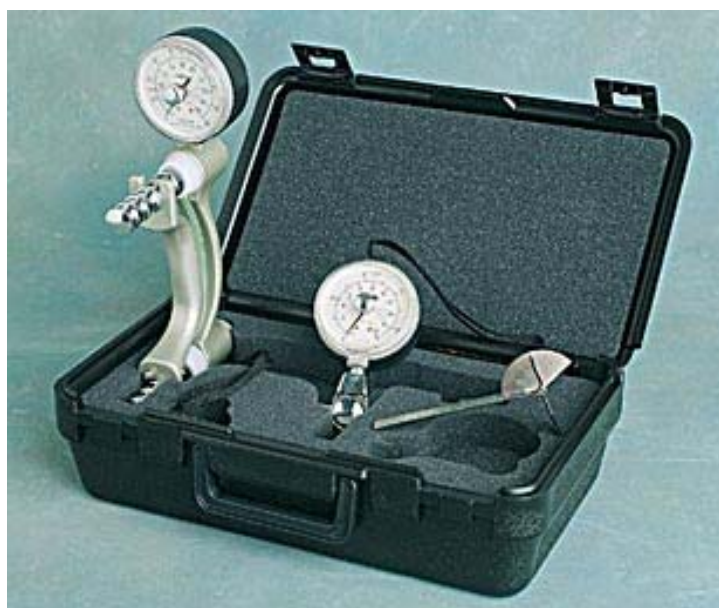


Figure 8. JAMAR handheld dynamometer



Figure 9. Handgrip test using a JAMAR handheld dynamometer

3.3.2.3 Curl-up & push-up tests

All patients were required to perform 1-minute curl-up and push-up tests (Figure 10 & 11). For the curl-up test, each subject was asked to cross his arms and try to curl his torso up until his shoulder blades (scapulae) lifted and cleared from the mattress. His elbows then reached and touched his thighs with his buttocks on the mattress.

For the push-up test, the subject was asked to keep his back and hip in a neutral position while facing the mattress as shown in Figure 11. His hands supported his upper body on the mattress at shoulder-width apart. The action involved bending both elbows to a point where his elbows were at right angles and the upper arms parallel to the mattress and then pushed up. The torso should be kept in upright at all times during the test as well. The number of curl-ups per minute and the maximum number of push-ups per trial were recorded to reflect the endurance of his abdominal and upper limb muscles (Berger, 1966; Diener et al, 1995; Faulkner et al, 1989; Fortier et al, 2001; Heyward, 2002; Sakamaki, 1983; Szasz et al, 2002). One assessor was assigned to undertake all measurements to avoid inter-tester variance.



Figure 10. Curl-up test



Figure 11. Push-up test

3.3.3 Health related quality of life status

3.3.3.1 SF-36 Questionnaire (Appendix F)

The medical outcomes study 36-item short-form health survey (SF-36) (Standard version 1) (Lam et al, 1998; Ware et al, 2000) was used to evaluate the subjects' HRQoL status. The SF-36 comprises 36 questions with eight subscales including physical functioning (PF), role physical (RP), role emotional (RE), bodily pain (BP), social functioning (SF), general health (GH), mental health (MH) and vitality (VT). A score between 0 and 100 was assigned to each domain, with higher scores representing better health status (Lam et al, 1998). Yet the "GH, VT & MH scales are bipolar in that they measure a wide range of health status from the very poor to the very good, and the majority of subjects, even without any limitations or disability, would score in the middle range" (Ware et al, 2000). In addition, the Chinese version of SF-36 adopted in the present study has been culturally validated by backward and forward translation for its cultural relevance (Lam et al, 1998). The Internal Reliability Coefficients (R_{TT}) were above the standard of 0.7 for all except the SF scale (PF – 0.78, RP – 0.83, BP – 0.87, GH – 0.71, VT – 0.74, SF – 0.65, RE – 0.77, MH – 0.77) which satisfied the scaling assumption on reliable and interpretable scale scores (Lam et al, 1998).

3.4 Data Analysis

Data collected before the exercise training formed the baseline references for comparison. The data included the mean, median, standard deviation, 95% confidence interval, and floor (proportion of subjects with the lowest possible score) and ceiling (proportion of subjects with the highest possible score) effect. Unpaired t-test was adopted to compare the baseline data with the normative data matched for

age and gender. As only the pre-training (baseline) and post-training values were compared for each outcome variable, there was no multiple comparisons for any individual outcome variable (i.e. VO_{2max} , 6MWT, handgrip, push-up, curl-up, MMT and SF-36) across other variables. Hence it was unnecessary to apply the Bonferroni correction for multiple comparisons for alpha adjustment. Differences in data scores from baseline to 6 weeks and 6 months for each group were computed. Independent t-tests were adopted to detect between-group differences in the changes between baseline and after the 6-week exercise training; baseline and 6-month follow-up for the following outcomes: 6-minute walk distance, predicted VO_{2max} , strength in anterior deltoid, gluteus maximus and handgrip, and the number of curl-ups and push-ups. Paired t-tests were adopted to detect within-group differences in the changes of the above outcomes throughout the study.

Scores from the SF-36 were calculated using the standard scoring algorithm (Ware et al, 2000). Missing values were treated with SPSS means series correction. Stepwise linear regression was used to examine the relationship between groups (control and exercise) and the differences between baseline measurements and the 6-week exercise training, as well as baseline and the 6-month post-training for the outcomes as mentioned. The following potential confounders were entered into the initial models as independent variables: gender, age, number of days of hospitalization, post-SARS duration and total dosage of prednisolone administered. A stepwise regression procedure was used to select the final model for each of the outcomes, with variables eliminated from the model until all remaining variables were significant at $p < 0.10$ level. An independent variable was considered statistically significant at $p < 0.05$.

CHAPTER 4

RESULTS

4.1 Baseline measurements

4.1.1 Demographic and baseline characteristics

There were a total of 258 SARS patients admitted to PWH between the period of March and May 2003. 31 patients (12.02%) were not accessible, 54 (20.93%) refused to participate in the study and 2 (0.78%) died. Of the remaining 171 (60 male and 111 female) patients (66.28%) who consented to join the study, their mean hospitalization was 21.8 days with ICU admission from 0-120 days (n=24, mean = 2.63 ± 11.2 days). The demographic data of all the subjects were listed in Table 1.

Table 1. Demographic data and cardio-respiratory fitness profile of the 171 patients

Characteristics / Sex	Male	Female	All Patients
No. of patients	60	111	171
Age (range from 17-89 yrs.)	38.72±14.21	36.63±11.72	37.36±12.65
Days of hospitalization	24.05±13.73	20.60±6.97	21.79±9.93
Post SARS duration (days)	84.36±17.99	80.45±18.64	81.79±18.46
Resting heart rate	86.10±12.42	86.91±12.50	86.63±12.44
Resting rate of perceived dyspnoea*	0.5	0.5	0.5
Resting SpO₂ (%)	97.73±1.07	98.36±1.14	98.14±1.16
Resting respiratory rate (breath/min)	18.52±4.47	19.39±4.35	19.08±4.40
Currently still receiving medications †	53.30%	51.40 %	52%
Steroid	45.00 %	45.90 %	45.6%
Others	1.70 %	2.70%	2.4%
<u>6-minute walk distance</u>			
Distance covered (meters)	624.32±119.03 n=60	583.66±94.34 n=111	597.92±105.14 n=171
<u>Chester step test</u>			
1. Predicted VO_{2max} (ml/kg/min)	38.47±7.39 n=43	36.19±7.42 n=91	36.92±7.46 n=134
2. No. of patients completed 5 levels of test (%)	24 (56%)	46 (51%)	70 (52%)

All values are mean ± standard deviation except denoted below

* median

† steroid / or other medications taken in the post discharge phase

Rate of perceived dyspnoea was based on a modified Borg scale from 0 to 10

4.1.2 Cardio-respiratory fitness

4.1.2.1 Six-minute walk test

The 6-minute walking distance covered by the subjects was presented in Table 2. The data revealed that the distance of the 6-minute walk declined with age, from 667.57 ± 57.13 m for male subjects (age 20-29 years) to 402.43 ± 166.33 m for the same gender of age over 60 years. For the female subjects, the mean distance covered by those of 20-29 years old was 636.64 ± 93.08 m while those aged over 60 years covered only 467.43 ± 75.05 m in 6 minutes. When compared with the normative data matched with age (Coordinating Committee for Physiotherapy, Hospital Authority, Hong Kong, 2003), there was a significant decrease in the mean performance of our subjects across different age groups ($p < 0.05$) (Table 2). Further analysis demonstrated that the distance of the 6-minute walk was significantly correlated with the post-SARS duration but negatively correlated with the number of hospitalization days (Table 3).

Table 2. Comparison (independent t-test) of 6-minute walking distance between SARS patients and normative data [†]

Age group	Patients	Mean ± SD	P-value	95% CI
1 <20	SARS (n=1)	N/A	N/A	N/A
2 20-29	SARS (n=56)	644.37 ± 86.10	P= 0.0053*	621.31 – 667.43
	Norm	698.00 ± 76.00		
3 30-39	SARS (n=51)	623.53 ± 91.22	P= 0.0003*	597.87-649.19
	Norm	698.00 ± 76.00		
4 40-49	SARS (n=35)	563.90 ± 84.17	P= 0.0002*	534.99-592.82
	Norm	635.00 ± 57.00		
5 50-59	SARS (n=21)	517.88 ± 91.62	P= 0.0001*	476.18-559.59
	Norm	635.00 ± 57.00		
6 >60	SARS (n=7)	430.29 ± 130.07	P= 0.0038*	309.99-550.58
	Norm	512.00 ± 79.00		

All values are mean ± standard deviation (m) except denoted below

N/A = not applicable (for age group with less than 5 patients)

* Statistically significant at p<0.05 for independent t-test

[†] Normative data provided by Coordinating Committee for Physiotherapy, Hospital Authority, 2003 ¹⁹

Table 3. Relationship between dependent variables and post-SARS duration, total dosage of medication and days of hospitalization (by linear regression)

	HR	6MWT	VO₂ max	Push up	Curl up	GM	AD	SF-36 (physical)	SF-36 (mental)
Post SARS duration	.621 (-2.8E-03)	.009* (.17)	.608 (-1.9E-03)	.056 (6.2E-02)	.328 (-4.3E-02)	.021* (.17)	.021* (.16)	.007* (.20)	.824 (-1.1E-02)
Total dosage of medication	.399 (1.8E-03)	.943 (-1.1E-03)	.007* (-.24)	.966 (5.8E-05)	.014* (.18)	.46 (-1.5E-03)	.361 (-1.2E-03)	.079 (-3.5E-03)	.378 (1.6E-03)
Days of hospitalizat ion	.022* (.18)	.03* (-.15)	.699 (-3.3E-02)	.093 (-9.4E-02)	.119 (-.118)	.75 (-.175)	.006* (-.19)	.005* (-.22)	.465 (6.5E-02)

* Statistically significant at $p < 0.05$

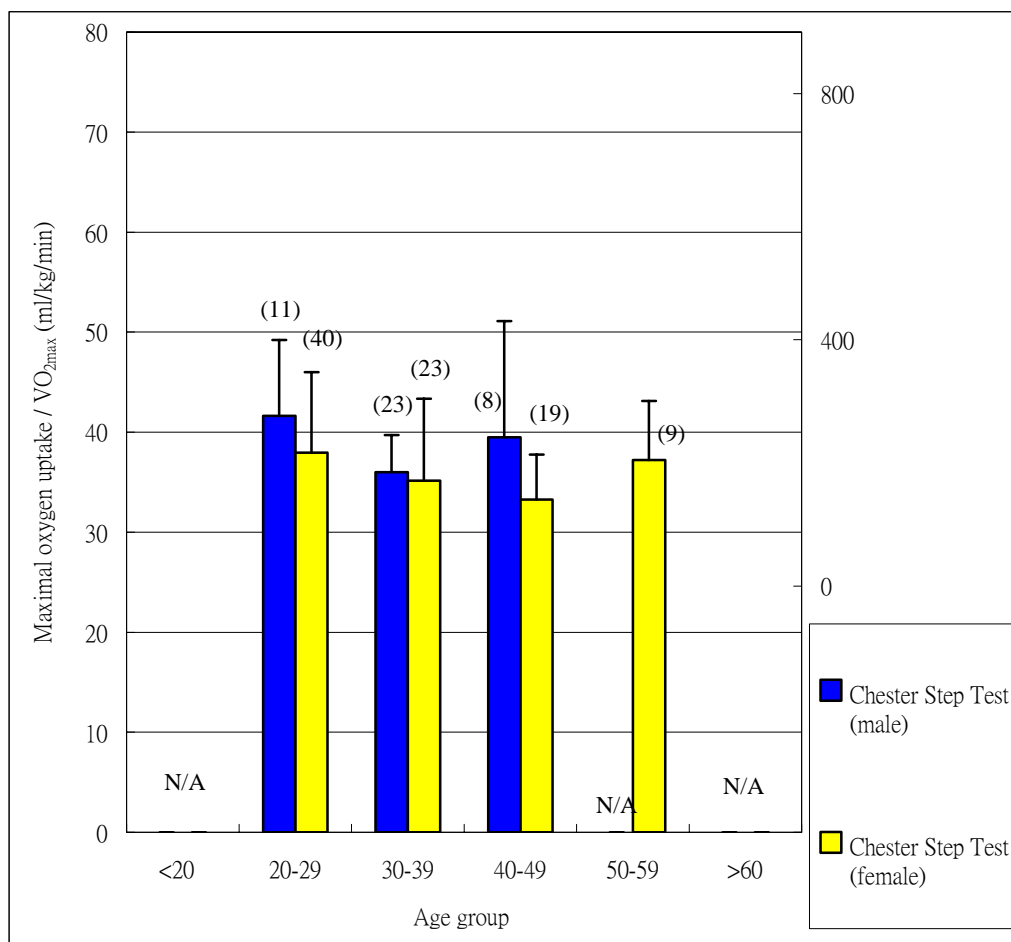
NS= not significant

() = standardized β coefficient

HR = heart rate; 6MWT = six-minute walk test; VO_{2max} = maximal oxygen uptake; GM = gluteus maximus strength; AD = anterior deltoid strength

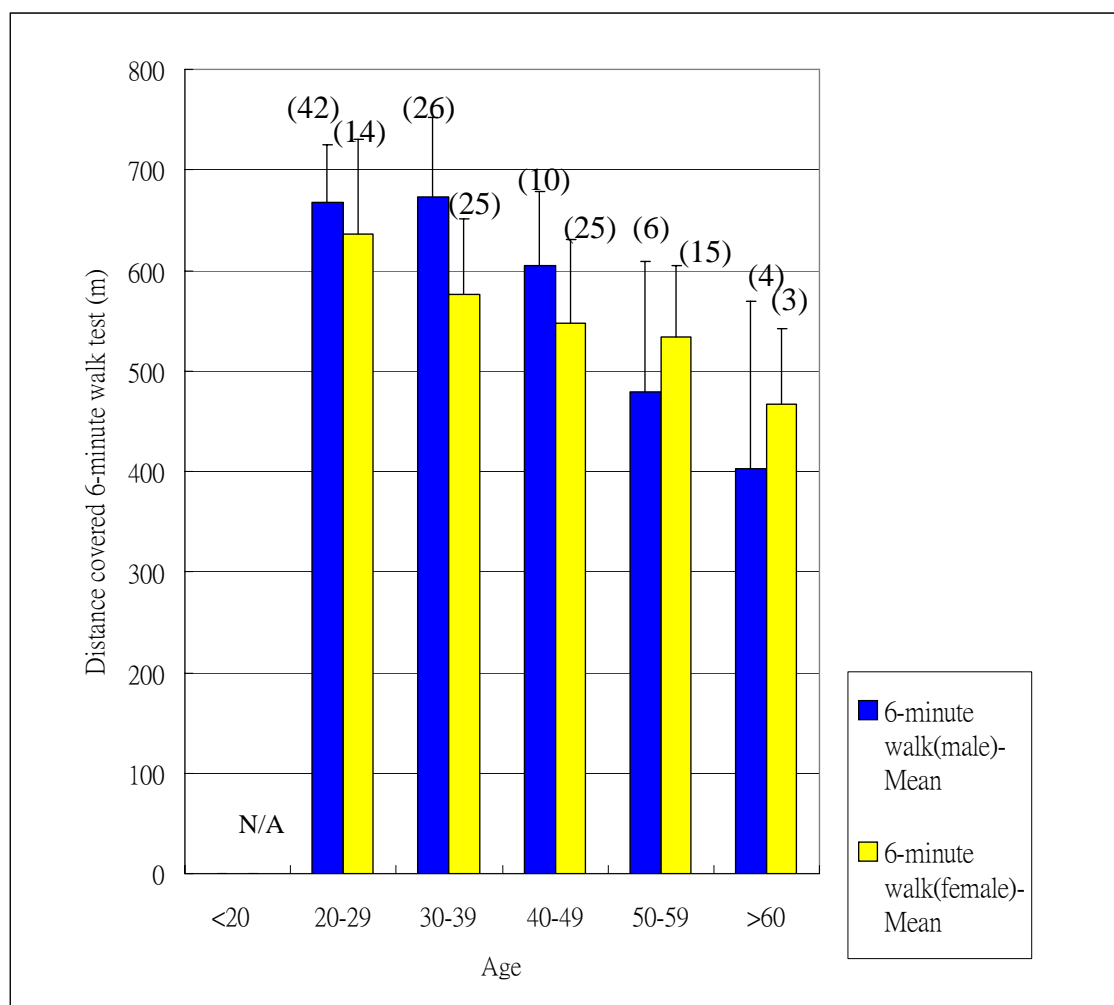
4.1.2.2 Chester step test

For male patients aged 20-29 years, the mean predicted VO_{2max} was 41.63 ± 7.57 ml/kg/min, while that of those aged 40-49 years was 39.50 ± 11.60 ml/kg/min. For female patients, the mean predicted VO_{2max} was 37.94 ± 8.05 ml/kg/min for the younger age group of 20-29 years, and that of those aged 50-59 yrs was 37.22 ± 5.88 ml/kg/min (Figure 12). Further analysis showed that the predicted VO_{2max} was negatively correlated with the total dosage of prednisolone administered, whilst the resting heart rate was positively correlated with the number of days of hospitalization ($p=0.022$) (Table 3). In addition, of the 171 patients, there were only 24 male patients (40%) and 46 female patients (41%) completed all five levels of the Chester step test (overall 41%). Sixty-six patients who completed 3 to 4 levels of the Chester step test were used to provide data for calculation of oxygen uptake. As only 133 patients out of 171 had completed 3 to 5 level of Chester step test, the predicted VO_{2max} from the Chester step test was probably an over estimation of the group fitness.



() = number of subjects; N/A= not applicable (for age group with less than 5 patients)

Figure 12. Gender comparison at different age groups for VO_{2max} predicted by the Chester step test performance. Data in means and standard deviations.



() = number of subjects; N/A= not applicable (for age group with less than 5 patients)

Figure 13. Gender comparison at different age groups for the six-minute walk test. Data in means and standard deviations.

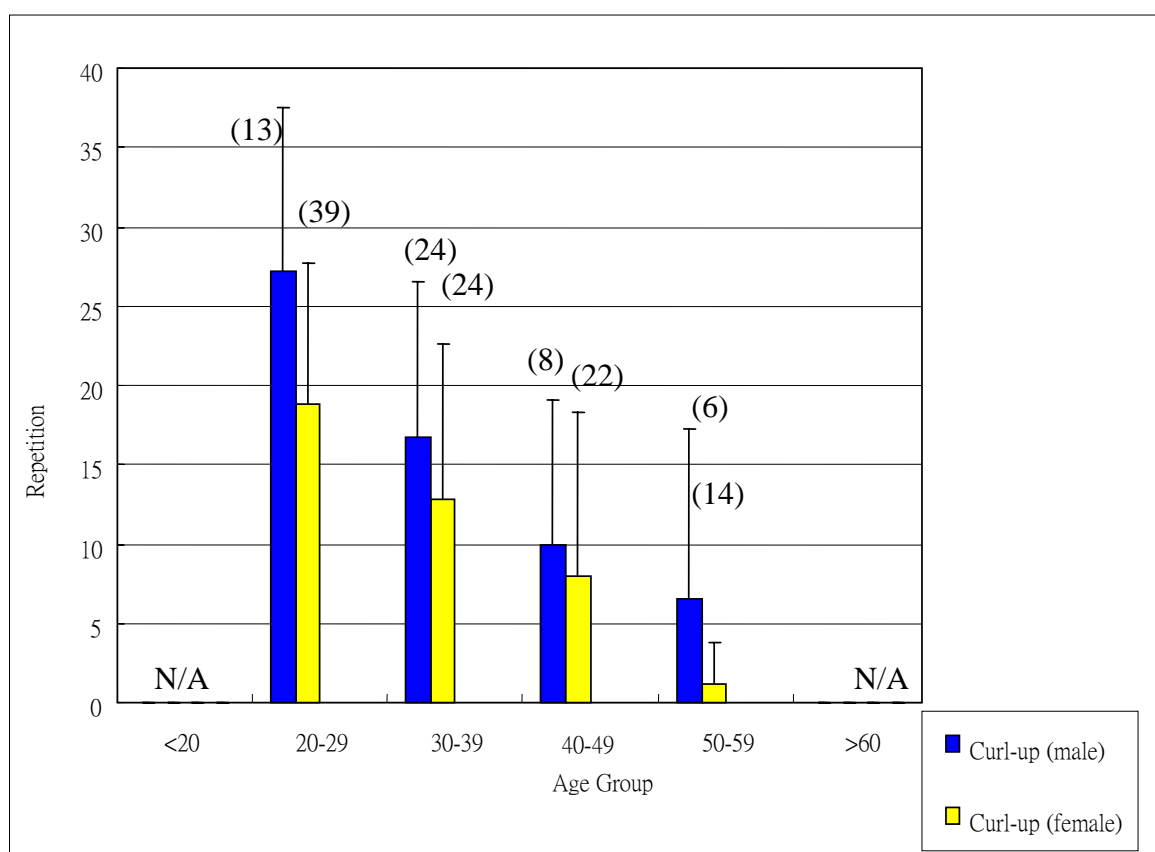
4.1.3 Musculoskeletal fitness

When compared with data of the normal subjects matched with gender and age (Normative data of physical fitness parameters), the performance in handgrip strength was diminished whilst the curl-up and push-up performances were “below average” to “poor”. There was no normative data for the strength of gluteus maximus and anterior deltoid muscles (summation of both sides) for comparison with the present study (Table 4 and Figures 14 & 15). However, only 157 patients completed the push-up and curl-up tests. In addition, male subjects generally performed better in muscle strength and endurance tests than female.

Table 4. Muscle strength and endurance profile of post-SARS patients

Outcomes / Sex	Male	Female
Anterior deltoid strength (kgf)	26.50 ± 10.32	17.37 ± 5.99
Gluteus maximus strength (kgf)	33.98 ± 15.43	24.24 ± 11.84
Handgrip strength (kgf)	69.25 ± 18.81	45.04 ± 12.89
Curl-up (repetitions in one minute)	16.41 ± 12.58	13.74 ± 11.49
Push-up maximum number of repetitions in one trial)	10.59 ± 8.86	8.71 ± 6.46

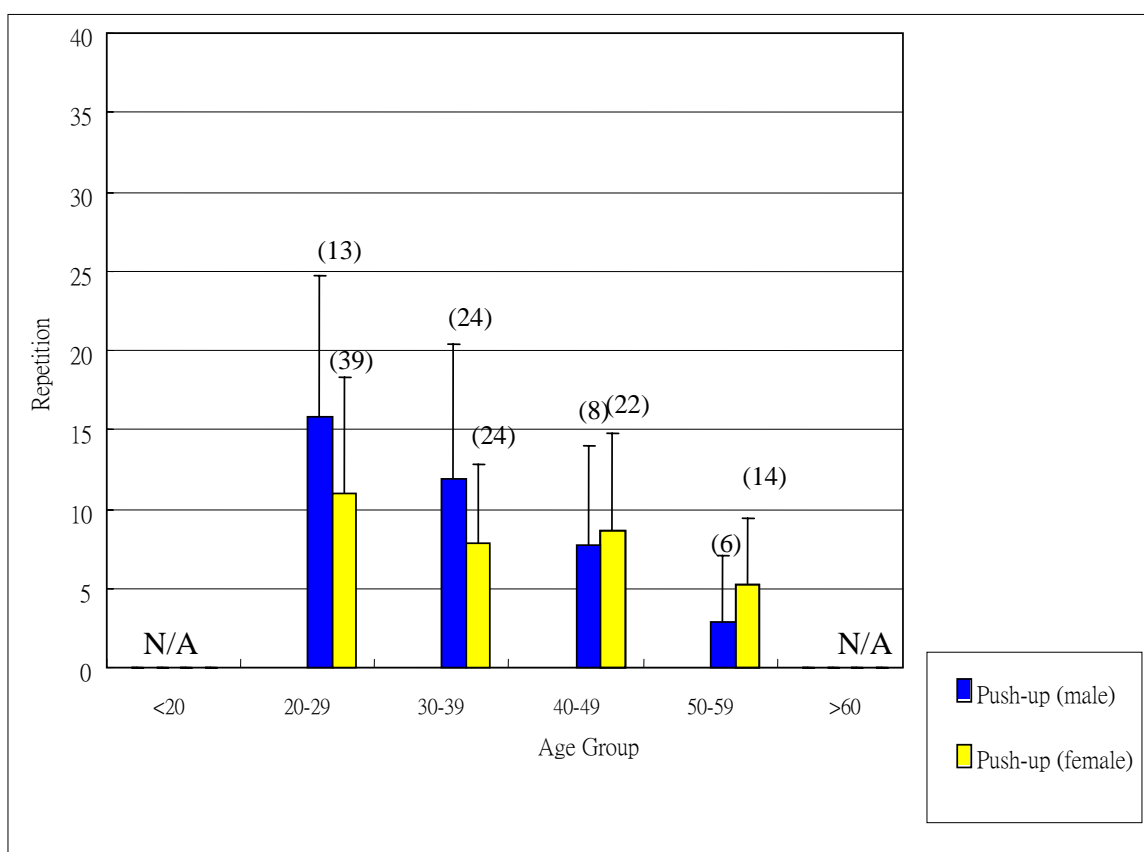
All values are means ± standard deviations



() = number of subjects

Curl-up = repetitions per minute

Figure 14. Means and standard deviations of number of curl-ups stratified by sex and age groups (157 out of 171 patients)



() = number of subjects

Push-up = maximum number of repetitions per trial

Figure 15. Means and standard deviations of number of push-ups stratified by sex and age groups (157 out of 171 patients)

4.1.4 Health related quality of life (HRQoL) status

A total of 164 (95.91%) subjects completed the SF-36. The scores for each domain were shown in Table 5. Analyses of the scores revealed a significantly lower score in every domain of the HRQoL status (total sub-scores of male and female subjects) compared to the norms of Hong Kong (Lam et al, 1999). In particular, for the RP aspect, which deals with problems with work or other daily activities as a result of physical health (Ware and Sherbourne, 1992), over 50% of the patients scored at the lowest score within the domain. In addition, the percentage of floor and ceiling effect of RP and RE were high (as shown in Table 5c). Possible explanation was that there were only 3 (RP) and 4 (RE) questions within those two domains respectively, thus most of the replies from those questions were either at low or high percentage within those domains (Ware and Sherbourne, 1992).

Table 5a. Comparison of health related quality of life outcomes between SARS patients and subjects with normal health (male) †

Scale	Sample	Mean ± SD	% Floor	% Ceiling	p value	95% CI
PF	Male	n=55 74.36 ± 22.20	0	9.09	p<0.0001*	68.35-80.37
	Norm	94.02 ± 10.88				
RP	Male	n=55 37.27 ± 41.63	47.27	23.64	p<0.0001*	26.01-48.53
	Norm	85.31 ± 28.38				
BP	Male	n=55 76.36 ± 23.38	0	33.36	p<0.0001*	70.04-82.69
	Norm	87.07 ± 18.98				
GH	Male	n=55 55.89 ± 20.90	1.82	1.82	P=0.2027	50.24-61.54
	Norm	59.32 ± 19.43				
VT	Male	n=55 58.09 ± 19.09	0	0	P=0.1422	52.93-63.25
	Norm	61.67 ± 17.59				
SF	Male	n=55 68.41 ± 23.31	0	18.18	P<0.0001*	62.10-74.72
	Norm	91.45 ± 16.00				
RE	Male	n=55 56.36 ± 45.30	34.55	45.45	P=0.0025*	44.11-68.62
	Norm	72.34 ± 37.88				
MH	Male	n=55 72.51 ± 19.26	0	12.73	P=0.8010	67.30-77.72
	Norm	73.07 ± 15.93				

All values are mean ± standard deviation except denoted below

% floor (proportion of subjects with the lowest possible score)

% ceiling (proportion of subjects with the highest possible score)

* statistically significant at p<0.05

† normative data referring to the study conducted by Lam, 1999 ²¹

n = number of SARS patients

PF = physical functioning; RP = role physical; RE = role emotional; BP = bodily pain; SF = social functioning; GH = general health; MH = mental health; VT = vitality

Table 5b. Comparison of health related quality of life outcomes between SARS patients and subjects with normal health (female) †

Scale	Sample	Mean ± SD	% Floor	% Ceiling	p value	95% CI
PF Female	n=108	67.08 ± 20.98	0	3.70	p<0.0001*	63.07-71.09
	Norm	89.82 ± 14.19				
RP Female	n=108	29.40 ± 38.95	57.41	14.81	p<0.0001*	21.96-36.84
	Norm	79.79 ± 32.96				
BP Female	n=108	64.94 ± 25.15	0	23.15	p<0.0001*	60.14-69.74
	Norm	81.14 ± 23.91				
GH Female	n=108	48.00 ± 20.99	0	0	P=0.0164*	43.99-52.01
	Norm	52.92 ± 20.38				
VT Female	n=108	45.74 ± 17.43	0.93	0.93	p<0.0001*	42.41-49.07
	Norm	59.00 ± 19.48				
SF Female	n=108	59.14 ± 23.90	0	12.96	P<0.0001*	54.58-63.70
	Norm	90.96 ± 17.08				
RE Female	n=108	43.21 ± 41.08	37.96	26.85	p<0.0001*	35.37-51.05
	Norm	71.04 ± 38.80				
MH Female	n=108	64.11 ± 17.97	0	2.77	p<0.0001*	60.68-67.54
	Norm	72.53 ± 17.13				

All values are mean ± standard deviation except denoted below

% floor (proportion of subjects with the lowest possible score)

% ceiling (proportion of subjects with the highest possible score)

* statistically significant at p<0.05

† normative data referring to the study conducted by Lam, 1999 ²¹

n = number of SARS patients

PF = physical functioning; RP = role physical; RE = role emotional; BP = bodily pain; SF = social functioning; GH = general health; MH = mental health; VT = vitality

Table 5c. Comparison of health related quality of life outcomes between SARS patients and subjects with normal health (total) †

Scale	Sample	Mean ± SD	% Floor	% Ceiling	p value	95% CI
PF	Total	n=163 69.54 ± 21.61	0	5.52	p<0.0001*	66.23-72.85
	Norm	91.83 ± 12.89				91.32-92.35
RP	Total	n=163 32.06 ± 39.92	53.99	17.79	p<0.0001*	25.95-38.17
	Norm	82.43 ± 30.97				81.19-83.67
BP	Total	n=163 68.79 ± 25.09	0	27.61	p<0.0001*	64.95-72.63
	Norm	83.98 ± 21.89				83.11-84.85
GH	Total	n=163 50.66 ± 21.23	0.61	0.61	P=0.0011*	47.41-53.91
	Norm	55.98 ± 20.18				55.17-56.79
VT	Total	n=163 49.91 ± 18.88	0.61	0.61	p<0.0001*	47.02-52.80
	Norm	60.27 ± 18.65				59.53-61.02
SF	Total	n=163 62.27 ± 24.04	0	14.72	p<0.0001*	58.59-65.95
	Norm	91.19 ± 16.57				90.53-91.82
RE	Total	n=163 47.65 ± 42.87	36.81	33.13	p<0.0001*	41.09-54.21
	Norm	71.66 ± 38.36				70.13-73.19
MH	Total	n=163 66.95 ± 18.78	0	6.13	p<0.0001*	64.08-69.82
	Norm	72.79 ± 16.57				72.13-73.45

All values are mean ± standard deviation except denoted below

% floor (proportion of subjects with the lowest possible score)

% ceiling (proportion of subjects with the highest possible score)

* statistically significant at p<0.05

† normative data referring to the study conducted by Lam, 1999²¹

n = number of SARS patients

PF = physical functioning; RP = role physical; RE = role emotional; BP = bodily pain; SF = social functioning; GH = general health; MH = mental health; VT = vitality

4.2 Phase II - Post six-week study period - Post training program period

A total of 171 patients were invited to participate in the second phase of the study, 29 were unable to join the study due to personal reasons. In all the 142 patients who had participated in the study, 9 in the control group withdrew after the randomization process, thus leaving 62 in the control group and 71 in the exercise group. Both groups did not differ in the baseline readings for age, days of hospitalization, post-SARS duration, total dosage of prednisolone given, distance of the 6-minute walk, muscle strength, muscle endurance and the SF-36 scores (Table 6). However, the predicted VO_{2max} was higher in the control group.

Variables recorded before and at the end of the 6-week exercise training were summarized in Table 7 and Figure 16. There were significant differences in the 6-minute walk test, the VO_{2max} , handgrip strength and the curl-up and push-up performances between the control and exercise groups. Though both groups showed improvements in certain physical parameters, the exercise group showed more significant improvement than the other group in the 6-minute walk test: 77.44m (13.11%) vs 20.71m (3.37%), $p < 0.001$, predicted VO_{2max} 3.57ml/kg/min (10.16%) vs 0.97ml/kg/min (2.57%), $p = 0.036$. For the musculoskeletal performance, the supervised group also had more significant improvement than the control group, left handgrip 4.15kgf (16.14%) vs 2.19kgf (8.59%), $p < 0.05$, right handgrip 4.69kgf (16.99%) vs 1.71 kgf (6.09%), $p < 0.05$, curl-up 7.06 (52.8%) vs 3.56 counts (25.34%), $p < 0.05$ and push-up 8.59 (90.61%) vs 3.61 counts (37.10%), $p < 0.05$. However, there was no significant difference in gluteal muscle strength and any of the domains in the SF-36 questionnaire. In addition, more than 80% of the patients in both groups had resumed normal work duties after the 6-week exercise program.

Table 6. Baseline characteristics of the patients in the Control and Exercise groups (n= 133)

	Control (n=62)	Exercise (n=71)	P value
Age	38.31 ± 11.20	35.93 ± 9.33	0.184
Days of hospitalization	22.05 ± 10.89	23.16 ± 11.29	0.568
Days of post-SARS duration before the program	87.51 ± 15.90	88.10 ± 22.18	0.062
Total dosage of prednisolone (mg)	435.33 ± 465.11	555.92 ± 428.96	0.124
6-minute walk distance (m)	614.30 ± 95.14	590.74 ± 89.29	0.143
Predicted VO_{2max} (ml/kg/min)	37.80 ± 8.23	35.13 ± 5.52	0.046*
Anterior deltoid strength (total) (kgf)	20.39 ± 7.75	19.50 ± 8.79	0.526
Gluteus maximus strength (total) (kgf)	28.60 ± 13.18	26.24 ± 13.70	0.322
Handgrip strength (right) (kgf)	28.08 ± 11.16	27.61 ± 9.83	0.795
Handgrip strength (left) (kgf)	25.48 ± 10.02	25.71 ± 9.24	0.891
Curl-up (repetitions in one minute)	14.05 ± 11.12	13.37 ± 11.46	0.738
Push-up (maximum number of repetitions in one trial)	9.73 ± 7.38	9.48 ± 8.09	0.857
SF-36 (physical)	36.94 ± 12.35	35.21 ± 12.03	0.419
SF-36 (mental)	44.39 ± 10.48	46.06 ± 9.86	0.358
Return to work	43.90%	35.70%	

Values are means ± standard deviations. * Statistically significant at p<0.05

Table 7. Physical functions and SF-36 scores for patients in the Control and Exercise groups before and after the 6-week program (n=133)

	Control (n=62) (post-pre)	Exercise (n=71) (post-pre)	P value for group differences
6-minute walk distance (m)	20.71 ± 98.60	77.44 ± 71.28	0.000*
Predicted VO_{2max} (ml/kg/min)	0.97 ± 7.32	3.57 ± 5.40	0.036*
Handgrip strength (right) (kgf)	1.71 ± 5.22	4.69 ± 6.03	0.003*
Handgrip strength (left) (kgf)	2.19 ± 4.80	4.15 ± 5.88	0.039*
Curl up (repetitions in one minute)	3.56 ± 5.68	7.06 ± 9.61	0.013*
Push up (maximum number of repetitions in one trial)	3.61 ± 5.48	8.59 ± 6.82	0.000*
SF-36			
PF	3.39 ± 23.45	5.49 ± 23.16	0.604
RP	13.31 ± 39.65	15.85 ± 44.78	0.729
BP	-3.72 ± 25.91	-0.1 ± 25.09	0.469
GH	-2.52 ± 21.52	0.23 ± 21.95	0.895
VT	2.26 ± 17.76	2.71 ± 21.78	0.625
SF	13.31 ± 27.80	13.92 ± 26.11	0.895
RE	6.99 ± 43.58	3.29 ± 43.34	0.420
MH	0.77 ± 18.89	-0.79 ± 15.14	0.603

Values are means ± standard deviations

* Statistically significant at p<.05

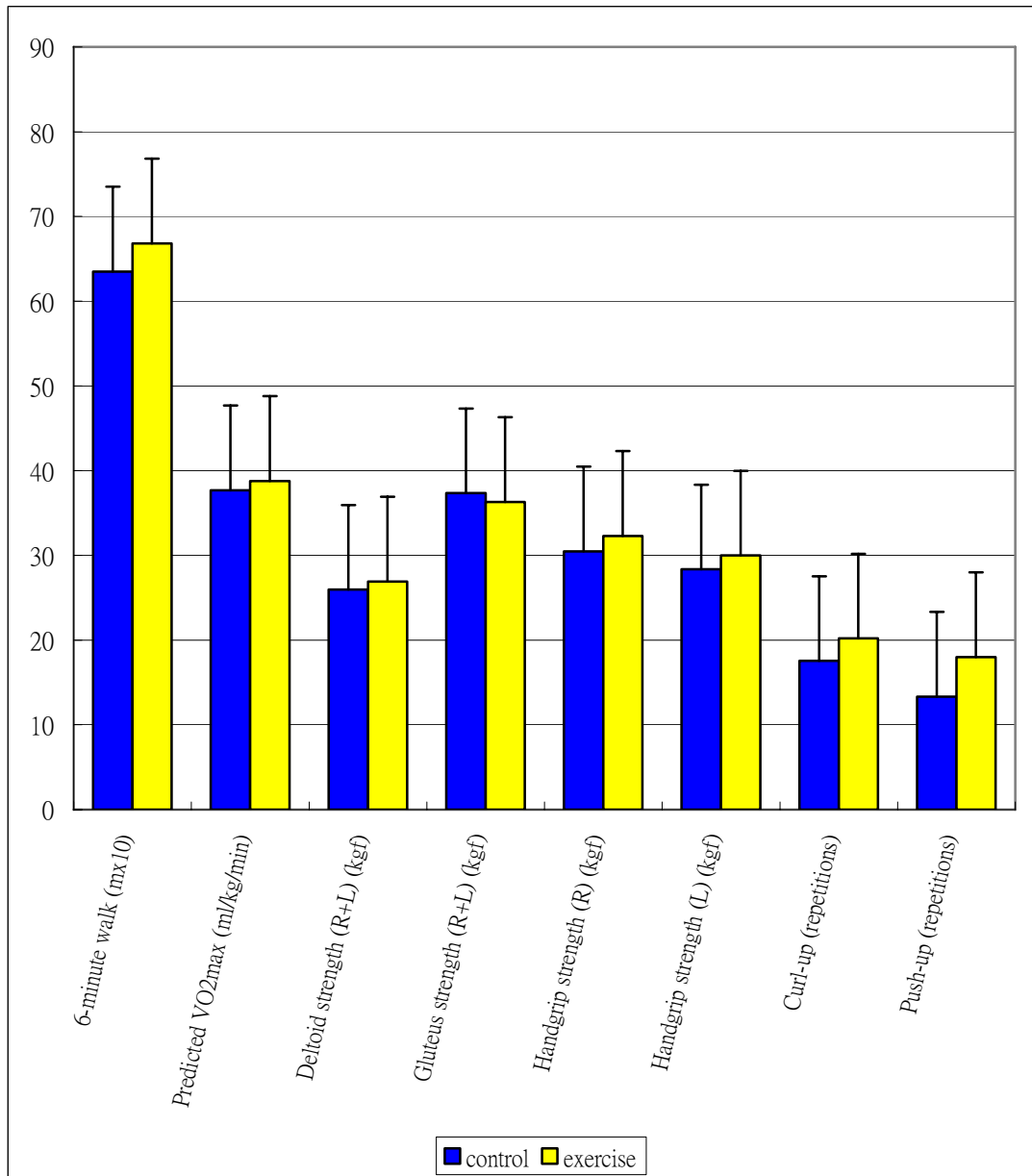


Figure 16. Mean group differences (after 6-week training) in various outcome measures

Table 8 shows the predictors (covariates) of the physical fitness outcomes and the domains in the SF-36. The effect of grouping (control vs exercise) was shown to have a positive effect on the 6-minute walk test, the predicted VO_{2max} , the deltoid strength, the handgrip strength, and the curl-up and push-up performances. Moreover, the subjects' sex, age, post-SARS duration, and return to previous work also contributed to varying degrees of the physical function outcomes and the domains in SF-36. SARS survivors who experienced longer post-SARS duration and with longer delay in starting the exercise program demonstrated weaker left handgrip strength. Elderly patients showed lower scores in RP, GH and MH in general. In addition, patients who had not resumed previous duties experienced lower scores in PF, RP, SF, RE, GH, VT and MH than those who had already returned to work. Also, it was found that male performed better in VO_{2max} , left handgrip strength and RP than female in both groups.

Table 8. Stepwise linear regression models for change in physical functions and SF-36 scores including non-standardized β coefficients, standard error, R square and p value

6-week change in the variable	Predictor	Non-standardized β coefficients	Standard error	R²	P value
6-minute walk distance	Group	49.62	15.32	0.123	0.002
	Post-SARS duration	-0.80	0.40		0.048
VO_{2max}	Group	2.68	1.26	0.04	0.035
Anterior deltoid strength (total)	Sex	-5.31	1.51	0.09	0.001
Gluteus maximus strength (total)	NS	-	-	-	-
Handgrip strength (right)	Group	3.18	1.01	0.07	0.002
Handgrip strength (left)	Post-SARS duration	-6.649E-02	0.03	0.05	0.009
Curl-up	Group	3.56	1.47	0.05	0.017
Push-up	Group	5.21	1.13	0.15	<0.0005
PF	Return to work	-12.12	5.89	0.03	0.042
RP	Sex	-25.15	7.46	0.15	0.001
	Age	-0.69	0.34		0.045
	Return to work	-32.64	10.76		0.003
BP	NS	-	-	-	-
GH	Age	-0.42	0.18	0.07	0.021
	Return to work	-12.47	5.57		0.027
VT	Return to work	-14.33	5.10	0.06	0.006
SF	Return to work	-20.65	6.91	0.07	0.003
RE	Sex	-19.29	7.74	0.09	0.014
	Return to work	-28.20	11.13		0.012
MH	Age	-0.32	0.13	0.08	0.016
	Return to work	-10.35	4.12		0.013

Variables entered: group (1=control, 2=exercise), sex (1=male, 2=female), age (years), post SARS duration (no of days before the program), total dosage of prednisolone (mg), resume duty (1=no, 0=yes), NS - all covariates excluded

* Statistically significant at $p < .05$

4.3 Six-month post-training period

There were 133 subjects participated in the 6-week training program. Out of these subjects, 98 (73.7%) completed the 6-month follow-up assessment. Among them, 45 subjects were in the control group and 53 the exercise group. The 35 subjects who did not return to the 6-month follow-up were those who had returned to work and were not available for the re-assessment.

The mean and standard deviation for the outcome variables by groups (control and exercise) of baseline measurements were shown in Table 9. There was no significant difference in the baselines between the two groups. The mean difference and comparison of the cardiopulmonary and musculoskeletal performances, the SF-36 between both groups from baseline to 6-week and baseline to 6-month were summarized in Table 10.

Table 9. Baseline characteristics of the patients who completed the assessment at 6 months (n= 98)

	Control (n=45)	Exercise (n=53)	P value
Age (yrs)	39.29 ± 10.95	36.30 ± 9.48	0.151
Days of hospitalization	22.31 ± 9.50	24.04 ± 11.86	0.436
Days of post-SARS duration before the program	108.07 ± 136.73	99.53 ± 127.63	0.750
Total dosage of prednisolone (mg)	466.76 ± 440.08	569.06 ± 437.48	0.256
6-minute walk distance (m)	616.36 ± 106.44	591.83 ± 92.48	0.225
Predicted VO_{2max} (ml/kg/min)	37.61 ± 6.66	35.19 ± 5.81	0.087
Anterior deltoid strength (total) (kgf)	19.69 ± 7.97	20.32 ± 8.62	0.714
Gluteus maximus strength (total) (kgf)	27.06 ± 13.77	27.65 ± 14.18	0.836
Handgrip strength (right) (kgf)	28.09 ± 11.58	28.45 ± 9.84	0.867
Curl-up (repetitions in one minute)	12.53 ± 11.33	13.80 ± 11.55	0.596
Push-up (maximum number of repetitions in one trial)	9.21 ± 7.58	10.68 ± 8.69	0.390
SF36			
Physical Functioning	68.77 (20.38)	70.34 (20.67)	0.709
Role Physical	27.83 (39.12)	35.23 (36.69)	0.343
Body Pain	64.81 (24.78)	67.07 (25.44)	0.660
General Health	52.21 (21.89)	48.25 (21.61)	0.375
Vitality	50.94 (20.00)	47.50 (16.76)	0.366
Social Functioning	58.65 (24.82)	60.51 (23.65)	0.710
Role Emotional	40.88 (42.18)	46.21 (41.43)	0.534
Mental Health	65.81 (17.88)	64.09 (17.26)	0.633

Values are means ± standard deviations

* Statistically significant at p<0.05

Table 10. Mean difference in physical functions and SF-36 at 6 weeks (n=133) and 6 months (n=98) and the results of t-tests for comparison between and within the two groups

		Control (post-pre)	Exercise (post- pre)	P value
6-minute walk distance (m)	6-week	20.71 ± 98.60	77.44 ± 71.28	0.000*
	6-month	18.64 ± 98.63	59.62 ± 75.81	0.022*
	p value	0.892	0.177	
Predicted VO_{2max} (ml/kg/min)	6-week	0.97 ± 7.32	3.57 ± 5.40	0.036*
	6-month	3.41 ± 6.95	6.92 ± 6.57	0.049*
	p value	<0.0005*	0.061	
Handgrip strength (right) (kgf)	6-week	1.67 ± 5.26	4.69 ± 6.03	0.003*
	6-month	0.25 ± 5.25	2.55 ± 4.66	0.026*
	p value	0.015*	0.007*	
Curl up (repetitions in one minute)	6-week	3.56 ± 5.68	7.06 ± 9.61	0.013*
	6-month	3.02 ± 5.87	6.23 ± 8.51	0.037*
	p value	0.168	0.160	
Push up (maximum number of repetitions in one trial)	6-week	3.61 ± 5.48	8.59 ± 6.82	0.000*
	6-month	3.37 ± 7.50	6.98 ± 7.76	0.026*
	p value	0.332	0.360	
SF-36				
PF	6-week	3.66 ± 15.42	3.67 ± 16.13	0.999
	6-month	5.28 ± 15.91	2.67 ± 20.45	0.495
	p value	0.235	0.574	
RP	6-week	14.44 ± 40.24	14.58 ± 37.19	0.983
	6-month	11.32 ± 40	7.39 ± 36.8	0.616
	p value	0.129	0.177	
BP	6-week	0.042 ± 24.94	-5.02 ± 24.06	0.241
	6-month	-4.21 ± 21.99	-12.86 ± 21.92	0.056
	p value	0.185	0.05*	
GH	6-week	-0.76 ± 17.53	-2.52 ± 18.6	0.581
	6-month	-4.70 ± 20.4	-8.44 ± 17.18	0.332
	p value	0.136	0.165	
VT	6-week	1.34 ± 17.95	2.50 ± 14.22	0.680
	6-month	-5.09 ± 16.48	-2.84 ± 17.60	0.520
	p value	0.003*	0.04*	
SF	6-week	12.86 ± 22.82	14.17 ± 24.19	0.753
	6-month	14.42 ± 23.14	9.09 ± 24.76	0.282
	p value	0.609	0.331	
RE	6-week	1.88 ± 38.17	8.89 ± 42.01	0.323
	6-month	6.29 ± 41.37	2.27 ± 45.69	0.654
	p value	0.900	0.168	
MH	6-week	-1.75 ± 11.73	-0.33 ± 16.91	0.583
	6-month	-3.32 ± 14.92	-3.27 ± 17.79	0.989
	p value	0.378	0.376	

Values are means ± standard deviations

* Statistically significant at p<0.05 (independent t-test)

At the 6-month follow-up assessment, similar results were shown between the exercise and the control groups. The former improved more significantly in the 6-minute walk test: 59.62m (10.09%) vs 18.64m (3.03%), $p=0.022$, the predicted VO_{2max} 6.92ml/kg/min (16.70%) vs 3.41ml/kg/min (9.02%), $p=0.049$, the curl-up test: 6.23 counts (46.60%) vs 3.02 counts (21.49%), $p<0.037$, the push-up tests: 6.98 counts (73.63%) vs 3.37 counts (34.64%); the left handgrip strength: 1.07kgf (4.16%) vs 2.39kgf (8.51%) and the right handgrip strength: 1.76kgf (6.37%) vs 1.57kgf (5.59%), (though handgrip improvement was not significant). Besides, the deltoid and gluteal muscle strength were also higher in the exercise group but this was not statistically significant.

Prominent differences were also noted when comparing the changes from 6 weeks to 6 months in the deltoid, gluteal muscles and the handgrip strength. Both the control and exercise groups demonstrated a further improvement in the deltoid and gluteal strength but with a mild decrease in the handgrip strength after 6 months. There was no other differences when comparing the physical functions of the 6-week with the 6-month follow-up data.

The 6-month follow-up assessment on the SF-36 evaluation revealed no significant difference in any of the SF-36 domains from the 6-week assessment between the exercise and the control groups (both within and between groups). However, significant declines in vitality (VT) were found for both groups when comparing the changes from 6 weeks to 6 months, otherwise, most of the other domains showed a small decline in score but there was no significant difference.

The results of analyses of the changes from baseline to 6 months in the outcome variables as dependent variable were summarized in Table 11. The effects of

covariates other than the 6-week exercise training (sex, age, days of hospitalization, total dosage of prednisolone used, etc) were analyzed. The effect of grouping (control vs exercise) was shown to have a positive effect on the 6-minute walk test, the predicted VO_{2max} , the handgrip strength and the curl-up test. For the outcomes of which, sex and age were retained in the final model, it showed that male and the younger patients had significantly better improvements than female and the older ones.

Besides, sex, age and days of hospitalization also contributed to the physical functions. SARS survivors with a longer length of hospitalization and having received a higher dosage of prednisolone demonstrated greater improvement in the 6-minute walk test and the push-up counts respectively. In addition, a higher total dosage of prednisolone, longer post-SARS duration showed better bodily pain, physical function and role emotional respectively.

The results fulfilled the objectives and rejected the null hypotheses of the current study. There was a significant difference in the physical fitness and the HRQoL status between the discharged post-SARS patients and the normal healthy individuals. In addition, it was revealed that after a 6-week supervised physiotherapy training program, the physical fitness of the post-SARS patients showed noticeable difference which lasted up to 6 months post training.

Table 11. Stepwise linear regression models for change in physical functions and SF-36 at 6-month follow-up including non-standardized β coefficients, standard error, R^2 and p value

6-month change in the variable	Predictor	Non-standardized β coefficients	Standard error	R^2	P value
6-minute walk distance Predicted	Days of hospitalization	2.348	0.800	0.132	0.004*
	Group	36.981	17.364		0.036*
	Group	3.703	1.763	0.072	0.040*
VO_{2max}					
Anterior deltoid strength (total)	Sex	-6.896	2.221	0.165	0.003*
Handgrip strength (right)	Group	2.338	1.033	0.053	0.026*
Curl-up	Group	3.163	1.581	0.044	0.049*
Push-up	Age	-0.307	0.080	0.216	0.000*
	Days of hospitalization	0.215	0.073		0.004*
	Total dosage of prednisolone	0.004	0.002		0.042*
PF	Age	-0.490	0.176	0.096	0.006*
RP	Age	-0.939	0.317	0.108	0.012*
	Sex	-17.336	7.871		0.030*
BP	Total dosage of prednisolone	0.0165	0.005	0.145	0.001*
	Group	10.946	4.306		0.036*
GH	Age	-0.399	0.187	0.047	0.036
RE	Sex	-23.740	8.909	0.104	0.009*
	Post SARS duration	0.098	0.045		0.033*
MH	NS				

Variables entered: group (1=control, 2=exercise), sex (1=male, 2=female), age (years), days of hospitalization, total dosage of prednisolone (g), resume duty (0=no, 1=yes), clinical psychologist intervention (0=no, 1=yes) * Statistically significant at $p < 0.05$ (stepwise linear regression)

CHAPTER 5

DISCUSSION

From the results of the current study, deficits in both the physical and psychological aspects of the post-SARS patients were shown at the baseline assessment up to 6 months post-intervention. With a 6-week physiotherapist supervised training program, certain physical fitness aspects of these patients' (including the cardiopulmonary and musculoskeletal endurance) improved and these improvements lasted for 6 months after the training. However, the training did not affect the HRQoL status for either the physical or mental domain. Possible explanations for these observations will be discussed in the following sessions.

5.1 Baseline assessments

SARS is a highly infectious disease with formidable morbidity and mortality rates. Many patients who recovered from SARS presented with a considerable decline in their physical fitness with major complaints of body tremors, dyspnoea, fatigue and emotional distress (Hui and Sung, 2003; Wong et al, 2003). Palpitation in the form of tachycardia at rest became more marked during mild exertion which was noted amongst patients recovering from SARS. Possible causes include deconditioning (Raven et al, 1998), impaired pulmonary function, impaired cardiac function, cardiac arrhythmia, thyroid dysfunction, anaemia, autonomic nervous dysfunction (Hasser and Moffitt, 2001) and anxiety state (Lau et al, 2005a) had been suggested.

A recently published SARS study in Hong Kong (Lau et al, 2005a) showed that the resting heart rate from a 12-lead electrocardiogram (ECG) ranged from 90 to

109 bpm. Various blood tests (complete cell count), erythrocyte sedimentation rate, liver function test (LFT), lactate dehydrogenase (LDH), creatine kinase (CK), creatine phosphate as well as results of clinical assessments, suggested that ongoing active pathology of SARS was unlikely. Normal thyroid function tests also excluded thyrotoxicosis (Lau et al, 2005a). Normal troponin I, echocardiography and other negative investigations from various blood tests also excluded myocarditis and cardiomyopathy. Only mild residual chest X-ray changes and minor lung function impairments were found. These together with a normal blood gas level suggested that pulmonary defect was unlikely due to a significant cause of sinus tachycardia during normal activity in those SARS patients. The prolonged hospitalization of 18-54 days together with confinement at convalescence could lead to physical deconditioning thus the resulting physical weaknesses (Lau et al, 2005a).

Since the SARS patients had an elevated baseline heart rate, which increased steadily and slowly during the Chester step test, the curve plotted from the data sheet of the test would be flattened and the predicted VO_{2max} would be higher when compared with a lower baseline heart rate. Thus some of the SARS patients achieved an excellent VO_{2max} according to the rating system (Sykes, 1998) despite their failure to complete 5 levels of the test and subjective complaints of distress and lower limb weakness.

Although the present study showed significant correlations on the total dosage of prednisolone administered, days of hospitalization and post-SARS duration to several dependent outcome measures, yet the coefficient of correlations were low (Table 3). Thus the chances of causal relationship between the above factors and the outcome measures were low.

The present study revealed that the cardio-respiratory and musculoskeletal functions of the patients surviving from SARS during the early recovery phase were substantially lowered than the normative data of the age and gender matched groups. The exercise performance of these patients recovering from SARS, however, was superior to those with COPD as evident by a further 6-minute walk distance covered by post-SARS patients (597.9m) compared to those with COPD (473.5m) (Berry et al, 2003).

The predicted VO_{2max} in patients with SARS admitted to the ICU was 36ml/kg/min, which was higher than those recovering from ARDS discharged from ICU (24ml/kg/min) (Neff et al, 2003) as well as that in patients with COPD (12.4ml/kg/min) (Yoshikawa et al, 2001). As the impaired physical fitness in SARS patients was believed to be caused by deconditioning from prolonged hospitalization and steroid-induced short-term myopathy and tachycardia (which was not as chronic as in COPD patients) (Yoshikawa et al, 2001), early rehabilitation for their lung functions might help in preventing deterioration of symptoms as in COPD patients.

It was not surprising that SARS patients who had been hospitalized for a mean period of 3 weeks demonstrated a decrease in cardio-respiratory and musculoskeletal function. At the time of this study (82 ± 19 days from disease onset), 78 patients (45.61%) were still undertaking steroid therapy (<0.5 mg/kg/day of prednisolone) for residual ground-glass opacities (Antonio et al, 2003). The cause of the decreased function was believed to be multifactorial, including immobility, anxiety, drug-induced hemolytic anemia from ribavirin treatment, steroid induced myopathy and underlying lung pathologies such as atelectasis and alveoli fibrosis (Hui and Sung, 2003; Lee et al, 2003; Wong et al, 2003).

The QoL scores in post-SARS patients were reported to be impaired in the domains of physical and psychological well-being (Lau et al 2005b). SARS was a new disease and there was no previous report on the disease profile of patients suffering from this condition, the present findings suggested that the physical and cardio-respiratory impairments in post-SARS patients were comparable to the patients with ARDS. Despite moderate impairment of the cardio-respiratory and musculoskeletal functions, the reported SF-36 score reflected relatively lower HRQoL, particularly in the RP domain where over 50% of the patients showed a 'floor' effect. These patients had lower RP (32.1), RE (47.7) and SF (62.3) scores as compared to patients with ARDS [RP (65), RE (75) and SF (81)] (Rothenhausler et al, 2001; Schelling et al, 2000). This result suggested that SARS had a greater impact on the physical than the psycho-mental aspect, and the effects were more profound on female than male.

The high mortality, media publicity and resultant social stigma of SARS could have caused undue stress, anxiety and vulnerability to the patients during the acute phase of their illnesses thus leading to clinical deterioration. As each patient required an average length of hospitalization of more than 3 weeks (Hui and Sung, 2003; Lee et al, 2003; Wong et al, 2003), visits from relatives and friends would inevitably increase the chance for them to contact the disease. In order to avoid the spread of the virus, it was the hospital policy that patients were banned from visits by their relatives and friends. This would naturally result in the low SF-36 scores. Thus the patients surviving from SARS demonstrated greater subjective physical, psychological and social deficits than the patients with ARDS, despite having better performance in exercise testing and higher predicted VO_{2max} levels.

Feelings of extreme vulnerability, uncertainty and threat to their lives were generally reported among the health care workers, which probably led to significantly high psychiatric morbidity from such acute stress syndrome of SARS (Chong et al, 2004). In addition, anxiety was most common while the infection was rapidly spreading, whereas depression and avoidance were prominent when it was being brought under control (Chong et al, 2004), this most probably explained the low baseline score in most of the SF-36 domains in our SARS patient cohort.

5.2 Six-week post-study period

Patients recruited in the first phase of the study were all re-assessed at 6 weeks after the baseline assessment. Within the control group, 85.5% had returned to work while 88.5% in the exercise group had returned to work at the time of re-assessment. This prospective, single-blinded, controlled study showed that a 6-week exercise training program, designed, conducted and supervised by the physiotherapists for the SARS survivors, had resulted in a greater improvement in the 6-minute walk test, the VO_{2max} , and the musculoskeletal performance than those receiving home exercise program only (see Table 6). In addition, those patients with longer post-SARS duration walked less in the 6-minute walk test. It was probably due to the more deconditioning during the 6 weeks after the initial baseline assessment.

The muscular performance of the exercise group also improved significantly when compared with the control group after 6 weeks of intensive training as listed in Table 8. It had shown that the skeletal muscle capacity (muscle strength), exercise tolerance (6-minute walk distance) and HRQoL improved significantly after 8 weeks

of endurance training (Magnusson et al 1996; McKelvie et al 1995; Tyni-Lenne et al 1998). The major training effects suggested was due to peripheral adaptations (Clark et al, 1996; Sullivan et al, 1991; Sylven, 1997). However, there was no association between the gender and the outcomes. It was hypothesized that the decrease in isometric muscle strength in the control group might be due to the effect of de-conditioning and poor compliance to home exercises after discharge from hospital. In light of that, the training program adopted in the current study was necessary and effective in improving the cardiopulmonary and musculoskeletal performances in post-SARS patients and it might prevent further de-conditioning after they were discharged from the hospital.

Apart from improvement in maximal oxygen uptake, a study by Klocek et al (2005) demonstrated that patients with congestive heart failure, after 6 weeks (twice weekly) of progressive resistance training, demonstrated significant improvements in HRQoL (psychological well-being). However, this study was unable to demonstrate a difference in any domains of the HRQoL questionnaire (SF-36) between the exercise training and the control group.

A study by Rudkin et al (1997) comparing the effectiveness of hospital-based group rehabilitation program for COPD to a home-based unsupervised self-managed program. The results showed that there was significant improvement in the endurance walk (shuttle walk distance) at 3 months and 6 months post-training program whereas the home-based program only showed improvement until 6 months post-training. However, the improvement showed in home-based program was significantly less than the hospital-based program. In addition, SF36 (social functioning) was also improved in hospital group at 3 months and 6 months post-

training (Rudkin et al, 1997).

As improvements in physical domains usually lead to improvements in psychological domains (Klocek et al, 2005; Tyni-Lenne et al, 1998), the latter was not improved despite improvements in physical domains in the post-SARS patients as shown in the current study. Possible reasons included the impact of loss of family members and anxiety induced from the media and the disease itself, in which the patients could not participate more actively in their social lives as their physical conditions improved. In addition, the tragic loss of families could not be compensated by improvement in physical fitness!

This study showed that patients who were health care workers but had not yet resumed duties had a lower score in almost all physical and mental domains (except BP) than those who had resumed duties before the end of the training program. It might be that the resumption of normal work duties had helped restore self-esteem through social support, collegial interactions and job satisfaction. A study by Preau et al (2004) also found that the employment and work status were associated independently with high physical subscales of HRQoL.

Results of HRQoL from the post-SARS patients – RP, RE and SF improved over the 6-week period irrespective of the exercise training. Despite the improvements were not statistically significant, these results might be suggestive that the resumption of daily activities and social functions for post-SARS patients had improved their ratings in the relevant domains. In addition, SF was not lower in post-SARS patients as compared to survivors of ARDS (Herridge et al, 2003; Rothenhausler et al, 2001; Schelling et al, 2000) which implied that post-SARS patients still had a subjective deficit in their physical and emotional states during 6

weeks after baseline assessment.

5.3 Six-month post-study period

Data from this study demonstrated that the physical performance of the SARS survivors had not only improved with the 6-week supervised exercise training program. The benefits were maintained for 6 months after the training program. These were important findings because the benefits achieved with exercise training usually began to fade when the training had stopped and decline in exercise capacity could occur within 1 to 2 weeks with most of the training effects lost after 6 months of detraining (Harpa et al, 2005).

A study by Wallace et al (1999) on 6-week supervised rehabilitation training for COPD patients showed that the walking performance was significantly improved than control group at 6 months post training. On HRQoL aspect, SF, VT and GH were also improved at 6 months post-training. However, the present study did not reveal any post-training effect on HRQoL aspect over a 6 months period.

There were some other reports on the exercise effects for patients with severe lung diseases after a period of training (Strijbos et al, 1996; Wijkstra et al, 1996a; 1996b). After long-term follow up, the results of these studies varied. Some studies (Ries et al, 1995; Wijkstra et al, 1996b) revealed physical deconditioning at a few months after the exercise program. This might be explained by the lack of continuity and poor home exercise compliance of these patients after cessation of the training program (Ries et al, 1995; Wijkstra et al, 1996a; 1996b).

It was revealed that patients who were hospitalized for longer durations and those who received higher dosage of steroid had poorer performances in the 6-minute

walk test and the push-up test at the 6-month post-training assessment (Table 11). These findings suggested that prolonged de-conditioning and steroid induced myopathy were associated with reduced exercise capacity.

The 6-week exercise training program was supervised by the physiotherapists who provided regular feedback specific to the patient's individual progress. This had ensured the program to achieve its original objectives and maximum compliance of the patients. Besides, this tailor-made program had provided an excellent means for the therapists to gauge the clients' perception of exercise. Once the patients perceived an improvement in the physical well being, they would be motivated to continue the exercise regime. In addition, further motivational strategies (e.g. illustrated exercise record sheet, the exercise pamphlet, VCD on exercise advice and education, feedback of the 6-week follow-up of their physical status) were adopted to increase their adherence to the exercise program.

This supervised exercise training program had also nurtured the patients to develop more positive attitudes and beliefs in active life-style. Consequently, they could become more physically active as reflected by their 6-week self-exercised log book records. This attitude and habit towards exercise could explain why the training effects were maintained at the 6-month follow-up period. Dishman (1991) showed that up to 50% of individuals who started an aerobic exercise program had dropped-out within the first 6 months. The main reason for dropout was poor exercise compliance towards such program. The success of the present exercise program was further reflected by the remarkable nil drop-out rate.

There was no significant difference in the 8 domains of HRQoL (SF-36) between the exercise group and the control group at the 6-month follow-up

assessment. This finding was similar to that of the 6-week follow-up. The SF-36 results revealed trends of improvements in some domains after 6 months of rehabilitation irrespective of the grouping, but the results were not statistically significant. There were two domains that had worsened over time, which included bodily pain ($p < 0.05$) and vitality ($P < 0.05$). Ng (2004) also reported that bodily pain worsened over time in a group of SARS patients. The reason for the increase in bodily pain might be due to the subjects being subsequently diagnosed with avascular necrosis (AVN) of the bones, which might be a side effect of high dose of steroid therapy.

Age was also a main factor that would affect the outcome of some of the domains (PF, RP, GH) in the SF-36 questionnaire while aging was found to have a negative relationship with the domains of PF, RP and GH ($P < 0.05$) in this study. The current results were in line with the report of Hui (2004) that the patients requiring intensive care unit admission were older and presented with higher peak levels of lactate dehydrogenase (LDH), they also required longer stay in the hospital and higher total dose of steroid therapy. In addition, Chan and Huak (2004) also commented that age and co-morbidity were consistently independent predictors of various adverse outcomes in SARS. Concerning the posttraumatic stress disorder (PTSD) on patients without severe neuro-trauma (blunt, penetrating injury and burn mainly), at 6-month follow-up, 42.3% of injured adults after trauma was related to female gender, poor mental health, older age and prior illnesses (Michaels et al, 1999)

In the present study, male subjects had higher scores in the role physical (RP) and role emotion domains of SF-36 when compared with female patients. In a study in Sweden on the epidemiology and HRQoL of patients with musculoskeletal pain

(Bingefors and Isacson, 2004), it was shown that the physical dimensions of HRQoL (SF-36) were more affected by headache in men, whereas psychological dimensions were more affected in women. Among persons reporting pain conditions, women scored lower than men on all the eight dimensions except on general health (GH) perceptions. For those who had not reported any pain, there were differences between men and women with respect to the dimensions bodily pain (BP), vitality (VT), social function (SF), emotional role function (RE) and mental health (MH) (Bingefors and Isacson, 2004).

5.4 Implications of study

This prospective controlled study involved serial assessments of the cardiopulmonary, physical fitness and the HRQoL for patients recovered from SARS for up to 7.5 months after discharge from the hospital. Residual physical disability for the patients who recovered from the acute phase of SARS was documented and the effectiveness of the supervised physical training program was demonstrated. The 6-week supervised training program by the physiotherapists was shown to have positive impacts on the physical aspects of post-SARS patients up to 6 months post-training. As SARS had caused several physical and psychological impacts on patients, the key of supervised training program in the rehabilitation/ recovery of the post-SARS patients was crucial.

5.5 Limitations

This study had only been able to recruit 171 of the 258 SARS survivors (66.28%) in the administrating hospital. These findings might therefore be biased

and not representative of the entire spectrum of these patients. Due to limited resources and there was a concern that many patients might be too weak to perform maximal stress tests, submaximal exercise tests were performed to determine and predict the cardio-respiratory fitness of the patients. In addition, as 38 of the 171 patients (22%) recruited after baseline assessment did not participate in the current study and a further 35 patients dropped out at the 6-month follow-up period, the power of this study would have inevitably been compromised. Some of the patients in this study (both the control and exercise groups) might have received some other contemporary treatments, such as traditional Chinese medicine or acupuncture, in addition to the prescribed exercise program which might have affected their performances in the outcome measures.

CHAPTER 6

CONCLUSION

This study showed that SARS survivors demonstrated deficits in both the cardiopulmonary and musculoskeletal performances. In addition, their HRQoL status appeared to be significantly impaired. A 6-week intensive exercise training program supervised by the physiotherapists was shown to be effective in improving both the respiratory and musculoskeletal performances. Nevertheless, the physical training during the intervention period had no impact on HRQoL, which was seemingly improved with resumption of normal work duties. Follow-up assessments at 6 months post-training showed that the improved physical status was maintained, which implied that the exercise training program had provided long-term benefits to post-SARS patients for as long as 6 months after termination of the exercise program.

The results of this study suggested that it was worthwhile to invest resources in providing a comprehensive supervised rehabilitation program to SARS survivors by appropriate health professionals such as the physiotherapists.

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APPENDIX A – Ethical Approval



香港中文大學醫學院
Faculty Of Medicine
The Chinese University Of Hong Kong



醫院管理局
新界東醫院聯網
Hospital Authority
New Territories East Cluster

Joint The Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee

香港中文大學—新界東醫院聯網 臨床研究倫理 聯席委員會

Secretary of the Clinical Research Ethics Committee c/o Centre for Epidemiology and Biostatistics,
Faculty of Medicine, The Chinese University of Hong Kong, 5th Floor, Postgraduate Education Centre, Prince of Wales Hospital.

Tel : (852) 2252 8717 Fax : (852) 2645 3098

To: Mr. Herman Lau (Principal Investigator)
Manager, Physiotherapy Department
Prince of Wales Hospital

19 September 2003

Ethics Approval of Research Protocol

CREC Ref. No.: CRE-2003.283
Date of Approval: 19 September 2003*
Protocol Title: To Investigate the Effectiveness of a Prospective Randomized Controlled Exercise Training Program for Post SARS Patients
Investigator(s): Herman LAU, Edwin LEE, Eddy SIU, Alan TSUI, Wendy CHIANG, Caroline WONG, Sammi HO, David HUI, K.M. CHAN and Jamie LAU

I write to inform you that ethics approval has been given to you to conduct the captioned study in accordance with the following document(s) submitted:

- Protocol
- Patient Informed Consent Form in English and Chinese Version

This ethics approval* will be valid for 12 months. Application for further renewal can be made by submitting the Renewal and Research Progress Report Form to the CREC. It will be much appreciated if the completion of the project will be reported to the Committee in due course.

The Joint CUHK-NTEC Clinical Research Ethics Committee serves to ensure that research complies with the Declaration of Helsinki, ICH GCP Guidelines, local regulations, HA and University policies.

(Prof. Joseph Lau)
Secretary, Joint CUHK-NTEC
Clinical Research Ethics Committee

APPENDIX B – Consent form (Chinese version)**威爾斯親王醫院物理治療部
關於嚴重急性呼吸道綜合症 SARS 復康療程研究****病人同意書**

由於在嚴重急性呼吸道綜合症 SARS 的康復過程中，病人可能會有不同程度的肌肉乏力、氣喘或未能如常工作及日常生活等。故此威爾斯親王醫院物理治療部現正推行一個 SARS 後期復康療程，以協助所有病人重建體力及心肺功能。

本部門現邀請閣下接受初步體適能測試，需時大概 90 分鐘，測試後閣下可能會有短暫性的輕微氣喘，心跳加速，或少許肌肉酸疼。之後，你會被隨機分配入運動班或對照班。運動班中的病人會在物理治療師的指導下參加每星期兩次，為期六星期的運動訓練。對照組的病人則會按物理治療師的建議進行家居運動鍛鍊。兩組病人均有一光碟來指導他們進行運動及於六星期及六個月後我們將會重覆體適能測試。

療程所有記錄將會絕對保密，而其中的數據將會用作醫學研究之用途。

本人_____將 *會/不會 參加威爾斯親王醫院物理治療部的嚴重急性呼吸道綜合症 SARS 復康療程。

病人姓名：
病人簽署：
身份証號碼：
日期：

見証人姓名：
見証人簽署：
日期：

*請刪除不適用之選擇

APPENDIX C – Consent form (English version)

**Physiotherapy Department of the Prince of Wales Hospital
The Rehabilitation Program Study for
the Severe Acute Respiratory Syndrome
Patient's Consent Form**

On the recovery from Severe Acute Respiratory Syndrome (SARS), patients may experience various degrees of physical weakness, such as muscle weakness, feeling short of breath or unable to perform activities that they used to do well. The Physiotherapy Department of the Prince of Wales Hospital now offers a post SARS rehabilitation program that hopes to assist all patients to regain their physical strength and fitness.

The Department would invite you to participate in an initial screening assessment, which comprises of a range of physical tests. The entire assessment lasts for approximately 90 minute. During the test, you may experience shortness of breath within a reasonable range, an increase in heart rate and mild to moderate muscle soreness. After the initial assessment, you will be randomized into either the exercise training or control group. In the exercise group, physiotherapists will monitor the intensity of the exercise during the training, which will be held twice per week for six weeks continuously. For the control group, the subject will be required to follow the instructions on home exercise given by the physiotherapist. Subjects from both groups will be given a VCD about the instruction of the exercise and will be arranged for a reassessment in week 6 and 6 months afterwards.

Your records will be kept confidentially for medical research authorised only by the Department.

I, _____, *will / will not participate in the post SARS rehabilitation program assessed by the Physiotherapy Department of the Prince of Wales Hospital.

Name of patient: _____

Signature of patient: _____

HK ID Card: _____

Date: _____

Name of witness: _____

Signature of witness: _____

Date: _____

****please delete as appropriate.***

APPENDIX D – Inclusion and exclusion criteria

Inclusion criteria

1. Post SARS diagnosis over at least 5 weeks AND
2. Stable medical and haemodynamic status AND
3. At least a supervised walker in ambulatory status AND
4. Baseline assessment with 6-minute walk test results / VO_{2max} fitness rating at average or below average level OR
5. Muscle endurance test (push-up, curl-up, standing heel raise) at average norm level or below average OR
6. Subjective compliant of physical deconditioning OR
7. Inadequate physical fitness for ADL / job demand / recreation OR

Exclusion criteria

1. Main problems not related to SARS
2. Patients receiving concurrent rehabilitation other than physiotherapy
3. Poor motivation/compliance in participation of training program
4. Impaired ability in communication and comprehension
5. Feverish, diarrhea or unstable medical conditions
6. Uncooperative or significantly demented patients who may have high risk of cross infection
7. Major mental or physical disease that prevents from rehabilitation

Precautions

1. Heart problems
2. On steroid medications
3. Osteoporosis
4. Psychologically / emotionally unstable
5. SARS induced DM
6. Patients having treatments from Chinese Medicine

APPENDIX E – VO_{2max} prediction (Chester step test) assessment form

VO_{2max} prediction – Chester step test (Sykes, 1998)

30cm (12”) – Normal subjects, 25-15cm (10”) – Age > 50 or obese subjects

Name: Age: HRmax: 80%HRmax:

Heart rates (bpm)

210																				
200																				
190																				
180																				
170																				
160																				
150																				
140																				
130																				
120																				
110																				
100																				
90																				
80																				
70																				
60																				
50																				

mlsO₂/kg/min 14 17 20 23 26 29 32 35 38 41 44 47 50 53 56 59 62 65 68 71

Step Level I II III IV V

Step Level I 15 steps / minute

Step Level II 20 steps / minute

Step Level III 25 steps / minute

Step Level IV 30 steps / minute

Step Level V 35 steps / minute

VO_{2max}:

Fitness Rating:

Norms for Aerobic Capacity (VO_{2max})

Male (Age group)

Female (Age group)

Fitness rating	15-19	20-29	30-39	40-49	50+	15-19	20-29	30-39	40-49	50+
Excellent	60+	55+	50+	46+	44+	55+	50+	46+	43+	41+
Good	48-59	44-54	39-49	37-45	35-43	44-54	39-49	35-45	34-42	33-40
Average	39-47	35-43	32-38	30-36	27-34	36-43	32-38	29-34	27-33	26-32
Below Average	30-38	28-34	22-31	24-29	22-26	29-35	27-31	24-28	22-26	20-25
Poor	<30	<28	<26	<24	<22	<29	<27	<24	<22	<20

APPENDIX F – SF-36 Questionnaire

簡明健康狀況調查表（SF-36） - 第一版

The Chinese (Hong Kong) SF-36 – Standard Version 1

編號_____

簡明健康狀況調查表 (SF-36)

說明：這項調查是詢問您對自己健康狀況的了解。此項資料記錄您的自我感覺和日常生活的情況。

請您按照說明回答下列問題。如果您對某一個問題不能做出肯定的回答，請按照您的理解選擇最合適的答案。

1. 總括來說，您認為您的健康狀況是：

(只圈出一個答案)

- | | | |
|----|-------|---|
| 極好 | ----- | 1 |
| 很好 | ----- | 2 |
| 好 | ----- | 3 |
| 一般 | ----- | 4 |
| 差 | ----- | 5 |

2. 和一年前相比較，您認為您目前全面的健康狀況如何？

(只圈出一個答案)

- | | | |
|---------|-------|---|
| 比一年前好多了 | ----- | 1 |
| 比一年前好一些 | ----- | 2 |
| 和一年前差不多 | ----- | 3 |
| 比一年前差一些 | ----- | 4 |
| 比一年前差多了 | ----- | 5 |

3. 下列各項是您日常生活中可能進行的活動。以您目前的健康狀況，您在進行這些活動時，有沒有受到限制？如果有的話，程度如何？

(每項只圈出一個答案)

活動	有很大限制	有一點限制	沒有任何限制
a. 劇烈活動，比如跑步，搬重物，或參加劇烈的體育活動	1	2	3
b. 中等強度的活動，比如搬桌子，使用吸塵器清潔地面，玩保齡球或打太極拳	1	2	3
c. 提起或攜帶蔬菜，食品或雜貨	1	2	3
d. 上幾層樓梯	1	2	3
e. 上一層樓梯	1	2	3
f. 彎腰，跪下，或俯身	1	2	3
g. 步行十條街以上（一公里）	1	2	3
h. 步行幾條街（幾百米）	1	2	3
i. 步行一條街（一百米）	1	2	3
j. 自己洗澡或穿衣服	1	2	3

4. 在過去四個星期裏，您在工作或其它日常活動中，會不會因為身體健康的原因而遇到下列的問題？

(每項只圈出一個答案)

	會	不會
a. 減少了工作或其它活動的時間	1	2
b. 實際做完的比想做的要少	1	2
c. 工作或其它活動的種類受到限制	1	2
d. 進行工作或其它活動時有困難（比如覺得更為吃力）	1	2

5. 在過去的四個星期裏，您在工作或其它日常活動中，會不會由於情緒方面的原因（比如感到沮喪或焦慮）遇到下列的問題？

(每項只圈出一個答案)

	會	不會
a. 減少了工作或其它日常活動的時間	1	2
b. 實際做完的比想做的要少	1	2
c. 工作時或從事其它活動時不如往常細心了	1	2

6. 在過去四個星期裏，您的身體健康或情緒問題在多大程度上妨礙了您與家人、朋友、鄰居或社團的日常社交活動？

(只圈出一個答案)

- 毫無妨礙 ----- 1
 有很少妨礙 ----- 2
 有一些妨礙 ----- 3
 有較大妨礙 ----- 4
 有極大妨礙 ----- 5

7. 在過去四個星期裏，您的身體有沒有疼痛？如果有的話，疼痛到什麼程度？

(只圈出一個答案)

- 完全沒有 ----- 1
 很輕微 ----- 2
 輕微 ----- 3
 有一些 ----- 4
 劇烈 ----- 5
 非常劇烈 ----- 6

8. 在過去四個星期裏，您身體上的疼痛對您的日常工作（包括上班和家務）有多大影響？

(只圈出一個答案)

毫無影響	-----	1
有很少影響	-----	2
有一些影響	-----	3
有較大影響	-----	4
有極大影響	-----	5

9. 下列問題是有關您在過去四個星期裏您覺得怎樣和您其它的情況。針對每一個問題，請選擇一個最接近您的感覺的答案。

在過去四個星期裏有多少時間：

(每項只圈出一個答案)

	常常如此	大部分時間	相當多時間	有時	偶爾	從來沒有
a. 您覺得充滿活力？	1	2	3	4	5	6
b. 您覺得精神非常緊張？	1	2	3	4	5	6
c. 您覺得情緒低落，以致於沒有任何事能使您高興起來？	1	2	3	4	5	6
d. 您感到心平氣和？	1	2	3	4	5	6
e. 您感到精力充足？	1	2	3	4	5	6
f. 您覺得心情不好，悶悶不樂？	1	2	3	4	5	6
g. 您感到筋疲力盡？	1	2	3	4	5	6
h. 您是個快樂的人？	1	2	3	4	5	6
i. 您覺得疲倦？	1	2	3	4	5	6

10. 在過去四個星期裏，有多少時間由於您的身體健康或情緒問題妨礙了您的社交活動（比如探親、訪友等）？

(只圈出一個答案)

常常有妨礙 ----- 1

大部分時間有妨礙	-----	2
有時有妨礙	-----	3
偶爾有妨礙	-----	4
完全沒有妨礙	-----	5

11. 如果用下列的句子來形容您，您認為有多正確？

(每項只圈出一個答案)

	肯定對	大致對	不知道	大致不對	肯定不對
a. 您好像比別人更容易生病	1	2	3	4	5
b. 您好像所有您認識的人一樣健康	1	2	3	4	5
c. 您覺得自己的身體狀況會變壞	1	2	3	4	5
d. 您的健康極好	1	2	3	4	5

APPENDIX G – Raw data collected in the study**Keys:**

Abbreviation	Description	Remarks
PHYA	Physio number	
GP	Group	
Age	Age	
Sex	Sex	
ST	Start date	
Mbase	Medication at baseline	
M6W	Medication at 6 th week	
HD	Days of hospital stay	
ICU	Days of ICU stay	
PSARS	Post SARS duration	
RD	Resume duty	
0/1/D	Baseline/ 6 th week / 6 th month	
Six0/1/D	Six-minute walk test	
V0/1/D	VO _{2max}	
JL0/1/D	Left hand grip by Jamar	
JR0/1/D	Right hand grip by Jamar	
JT0/1/D	Total Hand grip by Jamar	
GL0/1/D	Left Gluteal Maximus strength	
GR0/1/D	Right Gluteal Maximus strength	
GT0/1/D	Total Gluteal Maximus strength	
FL0/1/D	Left front deltoid strength	
FR0/1/D	Right front deltoid strength	
FT0/1/D	Total front deltoid strength	
P0/1/D	Push up repetition in 1 minute	
CU0/1/D	Curl up repetition in 1 minute	
PF0/1/D	Physical Functioning	
RP0/1/D	Role-physical	
BP0/1/D	Bodily pain	
GH0/1/D	General health	
VT0/1/D	Vitality	
SF0/1/D	Social functioning	
RE0/1/D	Role-emotional	
MH0/1/D	Mental health	

PHYA	GP	age	sex	ST	Mbase	M6W	HD	ICU	PSARS	RD	six0	six1	sixD	V0	V1	VD
0313572M	1	56	1	18.06.03	350	140	18	0	64	0	610.0	565.0	718.0	999	32	42
0313300M	2	57	1	14.06.03	665	105	26	0	85	0	517.0	613.2	606.0	999	40	51
0313867P	1	59	2	26.06.03	760	500	14	31	104	0	329.6	493.0	377.0	999	999	999
0313649O	2	54	1	23.06.03	0	350	79	65	89	0	465.0	608.1	670.6	999	27	26
0313746Q	1	58	2	24.06.03	875	0	18	0	94	0	506.8	600.0	400.0	35	31	999
0313472Q	1	58	2	18.06.03	30	0	23	0	93	0	575.1	615.0	615.0	39	57	57
0313885N	1	56	2	26.06.03	420	0	23	0	94		534.9	601.8	601.8	46	55	55
0313442O	2	50	1	17.06.03	977.5	20	20	0	68	0	483.0	697.0	523.0	999	999	999
0313234V	1	40	1	11.06.03	1770	35	13	0	92	1	560.0	551.0	584.0	54	49	60
0313233M	2	41	2	10.06.03	262.5	0	41	0	90	0	502.0	568.5	677.0	34	36	30
0313422U	2	40	2	16.06.03	842.5	280	24	2	70	0	463.0	631.7	607.0	37	40	43
0313470U	1	39	2	18.06.03	705	5	33	9	98	1	652.0	712.9	713.0	39	35	38
0313526T	2	37	1	25.06.03	590	20	5	0	77	1	600.4	736.7	999	38	41	999
0314034N	1	36	2	05.07.03	418	0	16	0	999	1	627.1	601.2	632.7	38	39	38
0313440S	1	36	1	17.06.03	410	0	19	0	75	1	644.0	753.0	691.0	42	44	48
0313505Q	1	36	1	19.06.03	525	35	19	0	68	1	692.0	733.0	697.0	31	34	63
0313748M	2	35	2	02.07.03	352.5	0	14	0	115	1	656.8	707.1	644	33	43	50
0313530R	1	33	2	20.06.03	1205	378	20	0	86	0	583.0	691.0	690.0	37	35	35
0313610T	1	32	2	14.07.03	0	0	19	0	74		618	655		38	35	
0313486Q	2	32	2	18.06.03	285	0	16	0	59	0	544.0	626.2		35	37	
0313993V	1	32	1	02.07.03	0	0	34	0	83	1	653.4	718.0	669.0	33	33	36
0313656R	1	50	2	25.06.03	515	0	23	0	86	0	514.0	522.5		29	37	
0313424Q	2	49	1	16.06.03	852.5	145	18	6	88	1	639.0	725.5	670.0	999	32	40
0313413V	2	47	2	14.06.03	1560	515	43	6	92	0	495.0	552.0	574.0	30	34	33
0313508V	1	54	2	19.06.03	35	0	29	0	69	0	577.2	514.9	599.0	44	38	47
0313420N	1	41	2	16.06.03	1410	865	24	4	63	0	509.0	524.2	621.0	38	40	42
0313349P	2	42	2	14.06.03	980	690	43	17	82	0	398.0	601.6	617.7	36	31	30
0313199T	2	37	1	13.06.03	1255	465	24	7	68	0	715.0	801.0		35	36	
0313437S	2	43	2	17.06.03	720	390	43	20	65	0	572.0	624.0	572.0	27	27	999
0313685V	2	42	2	21.06.03	550	70	22	0	73	0	556.0	634.7	999	999	53	999
0313588T	2	35	2	18.06.03	300	0	14	0	97	1	600.0	656.3		32	32	
0313268P	2	33	1	14.06.03	1145	260	15	7	91	1	650.0	717.0	723.0	40	40	37
0313515N	1	57	2	20.06.03	210	0	24	0	95	1	590.4	630.9	591.0	999	27	30
0314237V	2	55	2	11.07.03	0	0	29	0	41	0	500	613.1	620	32	32	
0313674P	2	53	2	21.06.03	1263	190	28	0	84	0	570.0	591.0	520.0	999	33	999
0313694U	1	53	2	21.06.03	125	0	14	0	91	0	478.0	351.4	999.0	999	999	999
0313227S	1	52	2	09.06.03	540	0	15	0	59	0	492.0	440.0	999	999	999	999
0313513R	2	51	2	19.06.03	125	0	24	0	83	0	570.0	570.0	539.0	31	36	999
0313992M	1	51	1	07.07.03	0	0	16	0	81	0	644	555.4		27	25	
0315403O	2	51	2	26.08.03	290	0	51	37	136	0	582.8	630		31	34	
0313244S	2	49	2	11.06.03	1015	610	18	0	56	0	563.0	649.7	669.0	26	29	35
0313229O	2	49	2	09.06.03	585	265	30	0	92	0	458.0	555.0	622.8	999	48	45
0315500Q	2	47	2	27.08.03	0	0	35	0	146	0	618.7	681.7	620	27	29	33
0313580N	1	47	1	26.06.03	415	215	42	15	80	0	659.4	739.0	665.0	31	34	45
0313225W	2	42	1	09.06.03	805	0	21	0	82	0	489.0	734.8	779.0	38	37	36
0313441Q	1	46	1	17.06.03	420	315	57	6	96	0	644.6	675.0	663.7	61	37	44
0313615U	2	39	1	25.06.03	310	335	14	0	57	1	825.1	831.9	855.0	34	36	39
0313750O	2	46	1	24.06.03	725	420	21	0	108	0	485.5	563.8		33	42	
0313512T	1	43	2	19.06.03	999	999	17	0	97	2	641.0	604.3	638.0	999	36	33
0313839U	2	41	1	25.06.03	852.5	0	17	6	109	1	681.6	747.0	724.0	34	36	36

PHYA	GP	age	sex	ST	Mbase	M6W	HD	ICU	PSARS	RD	six0	six1	sixD	V0	V1	VD
0313769P	1	42	2	27.06.03	685	120	20	0	100	0	621.4	592.4	678.0	999	24	999
0313936W	1	38	2	10.07.03	175	0	14	0	102	2	744	640	583	40	47	999
0313318P	1	45	2	14.06.03	262.5	0	14	0	97	1	622.0	682.3	676.9	34	39	39
0313700S	2	44	2	23.06.03	645	20	15	0	43	0	303.7	577.2	338.0	999	46	999
0313232O	2	38	2	10.06.03	825	505	20	0	83	0	671.0	723.0	999	35	35	999
0313475V	2	36	1	18.06.03	230	805	45	16	58	0	609.0	737.7	651.3	28	34	999
0313695S	1	61	2	21.06.03	270	373	48	0	69	0	468.2	525.0	661.0	999	999	999
0313527R	1	37	2	25.06.03	0	0	17	0	103	1	654.5	651.2	697.0	31	30	28
0313583S	2	42	2	21.06.03	1258	0	22	0	70	0	559.7	679.4	636.3	23	30	50
0313248V	1	35	1	11.06.03	1155	403	18	0	74		790.0	549.0	549.0	40	61	61
0313756N	2	35	2	26.06.03	860	0	19	0	77	0	646.0	708.3	677.3	31	41	43
0313519Q	1	41	2	20.06.03	950	0	18	0	80	0	541.0	587.6	578.0	30	32	31
0313205R	1	34	1	13.06.03	840	0	13	0	93	1	695.0	794.4	786.2	34	38	37
0313652O	1	44	1	24.06.03	120	0	19	0	95	1	661.8	654.4	999	29	31	999
0313444V	2	41	2	17.06.03	245	0	16	0	74	0	594.2	670.9	670.0	36	34	40
0313696Q	1	34	1	21.06.03	525	0	20	4	66	0	571.1	695.3	700.0	33	36	43
0313606V	2	34	1	23.06.03	0	0	999	0	999	1	699.0	757.1	745.0	36	36	37
0313520U	2	34	1	26.06.03	645	0	20	0	74	1	587.3	688.2	999	39	64	999
0313758U	1	33	2	28.07.03	196	0	20	0	129	0	658	672.3	707	33	35	64
0313239W	2	31	1	14.06.03	470	0	20	0	92	0	656.0	672.5	711.1	34	36	37
0313417N	1	31	1	23.06.03	471	0	15	0	52	0	705.8	698.7	615.0	39	33	46
0313760W	2	32	2	24.06.03	445	0	23	5	95	1	578.1	681.0	628.0	38	46	42
0313933R	2	44	1	02.07.03	175	0	16	0	109	1	664.3	672.0	691.3	36	44	44
0313994T	1	53	1	02.07.03	105	0	20	0	114	1	561.1	508.5	510.0	999	999	999
0313535S	1	34	1	23.06.03	1470	0	75	25	95	0	604.0	623.0		999	999	
0313714S	2	36	1	21.06.03	595	0	24	10	100	1	626.2	695.7	683.0	37	38	37
0313611R	1	33	2	10.07.03	237.5	0	16	0	109	1	600	650.5	646	36	33	33
0313415R	1	31	1	14.06.03	0	0	20	0	93	1	704.0	714.4	620.0	40	50	57
0313079S	2	31	2	09.06.03	402.5	228	10	0	28	0	414.0	711.0		999	34	
0313608R	2	31	2	23.06.03	0	0	21	0	105	1	618.5	652.7	999	32	38	999
0313351R	2	31	2	14.06.03	455	0	31	0	63	0	621.0	675.0	662.9	36	54	43
0314121S	1	30	1	07.07.03	210	0	20	0	120	1	546	668.3	999	47	45	999
0313754R	2	30	2	25.06.03	262.5	0	18	0	107		573.4	514.5	600.0	39	39	35
0313237P	2	30	2	10.06.03	350	0	17	0	69	0	562.0	613.0	591.0	999	40	47
0313252T	2	30	2	12.06.03	50	0	21	0	66	0	604.0	705.1		41	48	
0313645W	2	30	2	20.06.03	1453	4480	21	0	74	1	644.2	662.5		24	30	
0313529N	1	30	1	21.06.03	1340	543	25	0	88	0	652.2	569.4	759.0	36	39	46
0313612P	2	29	2	24.06.03	0	0	20	0	95	1	719.0	652.6	750.0	38	35	34
0313747O	2	29	1	26.06.03	1070	651	44	7	97	0	643.0	733.0	733.0	27	43	31
0313502W	2	29	1	18.06.03	105	0	15	0	96	1	644.0	727.0	691.0	53	57	44
0313573V	2	29	2	19.06.03	0	0	18	0	89	1	594.0	680.0	637.0	39	43	63
0313425O	1	29	1	16.06.03	1795	420	22	5	66	0	650.0	732.0	999	47	37	999
0313675N	1	28	2	21.06.03	537.5	0	19	0	73	0	566.6	620.0	664.0	38	45	50
0313650S	2	28	1	28.06.03	1350	120	19	0	58	0	659.0	698.0	618.4	36	47	40
0313895V	1	28	2	26.06.03	0	0	17	0	103	1	694.4	638.5	999	37	31	999
0313692N	1	28	2	21.06.03	695	0	13	0	69	1	684.1	700.7		39	41	
0313504S	2	28	2	19.06.03	700	0	27	0	89	0	650.0	583.5	682.0	41	48	38
0313724P	1	28	2	24.06.03	175	0	13	0	71	1	560.8	616.2	999	23	41	999
0313528P	1	27	2	18.06.03	0	0	19	0	86	1	693.9	733.3	696.1	32	32	39
0313249T	2	27	2	12.06.03	550	0	26	0	76	0	620.0	623.5	575.4	38	38	39

PHYA	GP	age	sex	ST	Mbase	M6W	HD	ICU	PSARS	RD	six0	six1	sixD	V0	V1	VD
0313474M	1	38	2	18.06.03	245	0	23	0	73	0	515.2	601.7	619.0	999	29	42
0313258S	2	34	2	13.06.03	710	0	31	13	91	0	423.2	578.6	574.0	28	28	31
0313961M	1	27	2	30.06.03	0	0	20	0	97	1	617.3	650.5		43	45	
0313546N	1	26	2	17.06.03	420	0	17	0	84	1	560.0	663.0	640.0	32	31	32
0313500P	2	26	2	18.06.03	1040	345	15	0	51	0	644.0	623.0	699.0	28	30	31
0313255N	2	26	1	12.06.03	770	0	15	0	58	0	735.0	768.6	640.0	36	37	46
0313428T	2	26	2	17.06.03	200	0	19	0	91	1	635.0	727.9	776.2	37	43	40
0313080W	2	26	2	16.06.03	655	0	23	0	51	0	462.9	664.1		999	41	
0313484U	1	25	2	25.06.03	0	0	17	0	73	0	543.2	539.6	595.0	39	999	43
0313443M	1	24	2	17.06.03	0	0	20	0	94	1	1038.8	665.0	665.0	48	40	40
0311066P	2	25	2	04.07.03	250	0	20	0	109	1	606.7	615.8	592	999	38	57
0313436U	2	25	2	17.06.03	462.5	0	16	0	56	0	603.0	633.0	618.6	39	39	46
0313260U	2	25	2	13.06.03	150	0	18	0	95	1	654.0	684.2		34	39	
0313532N	1	25	1	20.06.03	210	0	21	0	70	1	580.0	933.0	999	40	43	999
0313928V	2	25	2	28.06.03	225	0	20	4	97	1	644.0	614.7		41	40	
0313931V	1	24	2	28.06.03	25	0	20	0	105		666.9	663.0		70	61	
0313228Q	2	24	2	09.06.03	487.5	0	15	0	66	1	640.0	690.2	770.0	37	38	37
0313655T	1	24	2	24.06.03	25	0	17	0	103	0	617.3	851.0	706.0	36	36	41
0313423S	1	23	2	16.06.03	687.5	105	22	8	98	0	795.0	746.5	725.0	36	37	54
0313999U	1	36	2	02.07.03	0	0	8	0	116	0	580.7	586.8	554.4	34	31	34
0313533W	2	45	2	20.06.03	1505	70	20	0	71	0	517.0	583.5	615.0	36	40	33
0314033P	1	40	2	03.07.03	497.5	0	20	0	80	0	594.9	632.6	600.0	33	32	38
0313590V	2	39	1	18.06.03	1208	0	26	16	100	0	537.0	714.5	762.0	38	35	37
0313501N	1	59	2	18.06.03	0	0	17	0	93		582.3	583.3		999	26	
0313757W	1	39	1	30.06.03	90	0	43	0	76	0	584.0	674.0	667.0	28	32	40
0313507M	2	37	2	19.06.03	0	0	21	0	103	0	537.0	619.2	567.0	33	38	41
0313518S	1	25	2	20.06.03	1003	0	21	0	94	0	612.8	617.3	655.0	38	40	38
0313523O	2	23	1	16.06.03	350	0	21	0	84	1	662.3	783.2	620.0	42	45	58
0313251V	2	23	1	11.06.03	0	0	20	0	43	0	727.0	751.0	800.0	49	52	50
0313236R	2	22	2	11.06.03	910	0	15	0	60	1	692.0	859.2		42	32	
0314320M	2	22	2	14.07.03	100	0	13	0	109	1	632	709	704	42	48	54
0313576P	2	22	2	20.06.03	0	0	10	0	43	0	630.1	657.9	604.0	31	33	35
0313419U	1	21	2	16.06.03	0	0	19	0	93	999	612.7	598.6		33	37	

PHYA	JL0	JR0	JT0	JL1	JR1	JT1	JLD	JRD	JTD	GL0	GR0	GT0	GL1	GR1	GT1	GLD	GRD	GTD
0313769P	28	26	54	25	20	45	22	22	44	19.1	22.6	41.7	11.0	17.3	28.3	20.1	20.3	40.4
0313936W	18	28	46	26	28	54	16	20	36	13.5	15.6	29.1	13.2	15.3	28.5	16.7	16.8	33.5
0313318P	24	26	50	30	32	62	25	24	49	10.1	10.9	21.0	23.7	24.5	48.2	23.7	19.6	43.3
0313700S	21	21	42	30	31	61	22	22	44	8.3	9.2	17.5	13.1	14.3	27.4	18.3	18.4	36.7
0313232O	25	30	55	25	27	52	999	999	999	23.1	21.1	44.2	16.1	18.0	34.1	999	999	999
0313475V	38	34	72	42	44	86	32	40	72	11.2	12.2	23.4	26.4	26.3	52.7	15.8	17.6	33.4
0313695S	16	16	32	20	20	40	18	18	36	2.5	2.2	4.7	10.0	11.0	21.0	17.2	16.3	33.5
0313527R	28	30	58	30	32	62	30	28	58	7.6	8.9	16.5	17.8	19.8	37.6	21.6	22.0	43.6
0313583S	30	25	55	33	28	61	32	30	62	999.0	999.0	999.0	15.3	15.0	30.3	24.0	20.0	44.0
0313248V	32	38	70	36	44	80	36	44	80	11.3	12.5	23.8	31.2	31.6	62.8	31.2	31.6	62.8
0313756N	26	29	55	28	30	58	28	32	60	17.2	19.0	36.2	18.9	19.2	38.1	21.3	21.5	42.8
0313519Q	20	16	36	24	22	46	12	18	30	10.3	11.2	21.5	10.5	11.7	22.2	16.6	18.2	34.8
0313205R	44	58	102	56	60	116	50	55	105	10.2	13.6	23.8	31.0	31.0	62.0	23.0	23.0	46.0
0313652O	40	40	80	38	40	78	999	999	999	13.1	15.8	28.9	23.0	22.0	45.0	999	999	999
0313444V	20	24	44	22	31	53	25	28	53	10.9	11.9	22.8	14.0	15.2	29.2	18.4	22.4	40.8
0313696Q	41	43	84	42	44	86	44	42	86	21.2	26.6	47.8	24.0	29.0	53.0	28.6	28.0	56.6
0313606V	42	44	86	45	43	88	44	42	86	24.0	25.0	49.0	28.0	29.0	57.0	21.9	24.7	46.6
0313520U	12	13	25	48	50	98	999	999	999	5.5	7.2	12.7	26.0	29.0	55.0	999	999	999
0313758U	36	40	76	36	38	74	38	38	76	12.8	13.6	26.4	21.9	21.9	43.8	21.7	23.9	45.6
0313239W	19	20	39	24	26	50	26	30	56	7.2	8.4	15.6	12.2	13.2	25.4	16.0	15.3	31.3
0313417N	26	32	58	38	40	78	35	40	75	14.2	17.1	31.3	24.3	26.5	50.8	24.8	24.4	49.2
0313760W	12	8	20	17	17	34	18	18	36	3.2	6.1	9.3	6.0	11.8	17.8	8.4	8.0	16.4
0313933R	32	30	62	34	36	70	36	34	70	24.9	26.0	50.9	28.0	23.0	51.0	26.3	28.4	54.7
0313994T	21	36	57	28	32	60	22	32	54	999.0	999.0	999.0	17.5	16.4	33.9	15.6	13.9	29.5
0313535S	32	32	64	31	32	63				11.5	14.0	25.5	10.0	13.0	23.0			
0313714S	44	43	87	48	52	100	40	46	86	36.2	37.3	73.5	28.2	33.4	61.6	31.1	29.4	60.5
0313611R	18	18	36	22	24	46	18	22	40	20.9	19.7	40.6	23	31	54.0	23.6	20.3	43.9
0313415R	44	44	88	46	48	94	48	50	98	14.0	16.2	30.2	17.0	17.6	34.6	25.4	25.2	50.6
0313079S	6	15	21	32	36	68				9.8	11.3	21.1	14.0	16.2	30.2			
0313608R	20	20	40	20	25	45	999	999	999	16.0	14.2	30.2	17.3	19.3	36.6	999	999	999
0313351R	24	28	52	27	30	57	24	30	54	6.7	7.2	13.9	12.8	13.0	25.8	12.5	13.0	25.5
0314121S	36	38	74	40	42	82	999	999	999	13.5	15.4	28.9	28.3	25.2	53.5	999	999	999
0313754R	14	20	34	22	26	48	18	22	40	12.0	13.3	25.3	13.5	14.0	27.5	19.3	11.4	30.7
0313237P	21	22	43	28	30	58	18	22	40	14.1	12.6	26.7	23.0	22.1	4.0	21.1	19.6	40.7
0313252T	20	24	44	22	26	48				7.6	8.2	15.8	7.2	8.6	15.8			
0313645W	24	23	47	25	23	48				10.1	8.1	18.2	13.3	12.1	25.4			
0313529N	46	38	84	44	43	87	46	40	86	28.0	31.0	59.0	29.8	32.3	62.1	25.3	24.9	50.2
0313612P	26	28	54	24	26	50	28	30	58	18.0	21.0	39.0	20.0	18.8	38.8	20.0	19.0	39.0
0313747O	38	42	80	43	45	88	42	52	94	15.3	16.5	31.8	22.6	24.4	47.0	32.5	34.5	67.0
0313502W	34	44	78	40	48	88	36	48	84	11.6	13.2	24.8	20.1	25.5	45.6	23.5	24.6	48.1
0313573V	28	30	58	28	30	58	26	28	54	12.0	13.0	25.0	22.4	23.6	46.0	18.9	18.1	37.0
0313425O	28	32	60	26	30	56	999	999	999	12.8	13.2	26.0	13.8	16.8	30.6	999	999	999
0313675N	22	20	42	22	24	46	22	25	47	16.2	14.6	30.8	16.0	20.0	36.0	20.0	20.8	40.8
0313650S	36	40	76	32	35	67	32	40	72	26.3	30.8	57.1	31.0	32.9	63.9	22.9	26.6	49.5
0313895V	13	16	29	22	24	46	999	999	999	24.8	23.1	47.9	20.0	22.6	42.6	999	999	999
0313692N	30	28	58	28	30	58		0	15.9	19.6	35.5	12.4	13.6	26.0			.0	
0313504S	23	22	45	28	28	56	28	26	54	11.2	13.0	24.2	10.9	11.2	22.1	20.9	19.1	40.0
0313724P	24	28	52	25	31	56	999	999	999	15.8	16.7	32.5	23.1	31.0	54.1	999	999	999
0313528P	22	30	52	22	25	47	25	28	53	14.2	15.3	29.5	13.8	14.5	28.3	20.8	23.5	44.3
0313249T	25	28	53	26	28	54	28	32	60	8.0	9.0	17.0	11.3	12.0	23.3	13.0	14.2	27.2
0313474M	22	20	42	32	30	62	30	32	62	7.9	9.2	17.1	10.2	10.4	20.6	15.1	14.5	29.6

PHYA	FL0	FR0	FT0	FL1	FR1	FT1	FLD	FRD	FTD	P0	P1	PD	CU0	CU1	CUD
0313572M	11.6	12.0	23.6	14.0	16.9	30.9	14.0	17.0	31.0	6	10	7	27	30	26
0313300M	9.3	11.2	20.5	12.4	15.2	27.6	14.0	18.2	32.2	0	8	5	10	10	12
0313867P	7.7	6.7	14.4	6.8	7.2	14.0	11.3	13.3	24.6	0	0	999	0	0	999
0313649O	2.9	3.2	6.1	8.9	11.6	20.5	21.1	24.0	45.1	0	0	16	0	0	4
0313746Q	6.2	8.3	14.5	8.6	11.6	20.2	6.7	8.1	14.8	6	13	6	0	6	6
0313472Q	7.1	8.9	16.0	12.4	15.7	28.1	12.4	15.7	28.1	2	1	1	0	0	0
0313885N	5.1	5.3	10.4	14.9	12.9	27.8	14.9	12.9	27.8	5	6	6	0	8	8
0313442O	13.0	12.6	25.6	13.1	12.7	25.8	11.7	12.2	23.9	1	5	1	0	0	0
0313234V	5.4	4.5	9.9	20.5	26.0	46.5	30.0	27.1	57.1	999	0	0	999	10	18
0313233M	8.4	5.4	13.8	8.2	8.4	16.6	11.0	13.3	24.3	9	9	13	6	17	20
0313422U	6.4	8.3	14.7	11.4	12.8	24.2	15.0	12.9	27.9	3	30	22	10	27	24
0313470U	8.2	10.1	18.3	11.4	12.8	24.2	14.5	15.1	29.6	12	17	18	24	29	32
0313526T	16.5	15.8	32.3	20.4	22.2	42.6	999	999	999	10	9	999	0	31	999
0314034N	7.6	7.6	15.2	7.4	7.2	14.6	11.2	10.4	21.6	10	15	18	13	20	21
0313440S	13.5	12.9	26.4	16.3	14.5	30.8	22.6	23.4	46.0	6	10	8	15	23	16
0313505Q	15.2	16.6	31.8	16.0	17.6	33.6	22.5	22.0	44.5	27	36	45	17	28	25
0313748M	11.4	11.8	23.2	11.8	13.4	25.2	10	10	20	12	25	9	0	21	17
0313530R	9.6	8.9	18.5	14.5	11.5	26.0	19.2	18.0	37.2	6	16	20	16	23	18
0313610T	6.5	6.3	12.8	8.8	10.1	18.9			.0	5	5		15	18	
0313486Q	9.3	11.6	20.9	11.0	13.2	24.2			.0	2	13		7	0	
0313993V	20.4	24.5	44.9	26.2	28.6	54.8	33.6	30.0	63.6	12	20	15	7	19	24
0313656R	9.2	8.9	18.1	6.2	5.6	11.8			.0	6	18		0	0	
0313424Q	12.8	11.6	24.4	16.5	17.1	33.6	23.2	29.3	52.5	6	15	18	2	28	31
0313413V	11.2	13.0	24.2	12.3	14.5	26.8	11.6	13.0	24.6	10	8	12	10	0	0
0313508V	6.0	7.7	13.7	4.4	5.7	10.1	9.0	3.0	12.0	6	10	0	0	0	0
0313420N	4.2	5.1	9.3	7.8	8.8	16.6	12.2	10.5	22.7	3	4	9	0	7	10
0313349P	8.0	9.9	17.9	14.5	16.5	31.0	20.0	21.6	41.6	3	10	20	10	10	3
0313199T	8.9	10.1	19.0	18.3	18.2	36.5				6	14		20	28	
0313437S	5.7	6.5	12.2	6.9	8.1	15.0	4.7	9.8	14.5	0	7	0	0	0	0
0313685V	2.2	2.4	4.6	11.0	11.0	22.0	999	999	999	9	20	999	0	11	999
0313588T	10.2	11.5	21.7	13.1	12.9	26.0				3	22		19	25	
0313268P	10.8	12.5	23.3	14.2	15.7	29.9	24.6	24.6	49.2	7	16	13	13	28	24
0313515N	9.2	8.9	18.1	9.3	8.8	18.1	11.4	9.4	20.8	16	16	7	0	0	0
0314237V	4.3	5.6	9.9	18.3	15.4	33.7	19.8	19.1	38.9	0	20	10	0	0	0
0313674P	3.4	3.2	6.6	6.8	8.9	15.7	8.1	8.1	16.2	1	3	1	0	0	0
0313694U	9.3	9.8	19.1	4.3	4.7	9.0	5.3	5.3	10.6	1	2	1	0	0	0
0313227S	9.1	9.7	18.8	5.0	6.2	11.2	999	999	999	999	999	999	999	999	999
0313513R	8.6	9.9	18.5	11.2	9.8	21.0	12.1	9.5	21.6	2	5	0	0	0	0
0313992M	15	19.7	34.7	16.1	18	34.1			.0	10	7		14	16	
0315403O	4.2	4.6	8.8	8.5	8.7	17.2				0	0		0	0	
0313244S	3.8	3.5	7.3	12.4	14.1	26.5	16.2	15.2	31.4	999	21	16	999	18	0
0313229O	12.5	13.0	25.5	11.3	12.0	23.3	17.8	17.3	35.1	999	10	11	999	0	0
0315500Q	15	13.2	27.7	14.2	16.3	30.5	13.5	16.8	30	19	31	29	0	0	2
0313580N	11.2	13.7	24.9	12.3	14.0	26.3	17.3	17.3	34.6	4	12	10	19	22	20
0313225W	10.4	13.8	24.2	999	999	999	15.0	18.1	33.1	20	30	7	10	20	25
0313441Q	9.7	10.2	19.9	18.8	22.1	40.9	19.0	22.3	41.3	4	13	19	5	12	14
0313615U	17.9	20.0	37.9	18.1	19.8	37.9	19.0	21.4	40.4	16	20	17	22	25	24
0313750O	6.1	13.2	19.3	12.1	13.1	25.2			.0	6	21		3	23	
0313512T	12.0	13.5	25.5	15.0	18.6	33.6	13.7	17.0	30.7	12	20	18	19	19	20
0313839U	18.0	20.2	38.2	19.8	20.3	40.1	26.6	25.7	52.3	15	17	20	25	26	25

PHYA	FLO	FRO	FTO	FL1	FR1	FT1	FLD	FRD	FTD	P0	P1	PD	CU0	CU1	CUD
0313769P	11.1	12.5	23.6	8.1	9.3	17.4	10.4	12.9	23.3	11	11	5	0	0	0
0313936W	4.4	6.7	11.1	10	10.1	20.1	9.8	10.2	20.0	6	16	0	5	7	1
0313318P	6.7	8.4	15.1	12.7	12.7	25.4	18.6	16.6	35.2	20	30	20	22	24	24
0313700S	8.0	8.6	16.6	16.3	17.9	34.2	13.4	15.0	28.4	8	30	23	6	33	23
0313232O	7.4	7.0	14.4	10.1	12.8	22.9	999	999	999	10	14	999	24	28	999
0313475V	10.1	11.2	21.3	17.1	17.6	34.7	12.1	13.2	25.3	0	26	17	7	22	21
0313695S	2.1	2.9	5.0	8.7	8.1	16.8	12.9	15.5	28.4	0	0	0	0	0	0
0313527R	6.2	7.5	13.7	11.1	10.6	21.7	13.6	13.0	26.6	7	6	4	7	13	7
0313583S	999	999	999	14.2	15.0	29.2	20.2	22.4	42.6	9	27	27	11	30	23
0313248V	9.2	8.7	17.9	26.8	29.1	55.9	26.5	29.1	55.6	999	50	50	999	21	21
0313756N	11.3	10.2	21.5	12.6	13.7	26.3	14.1	14.8	28.9	16	20	28	30	36	43
0313519Q	6.5	7.4	13.9	10.1	11.3	21.4	13.5	15.4	28.9	8	20	16	12	23	10
0313205R	10.3	11.8	22.1	22.0	19.0	41.0	23.0	23.0	46.0	2	10	10	25	21	21
0313652O	18.0	18.9	36.9	21.0	18.8	39.8	999	999	999	20	23	999	16	29	999
0313444V	6.9	7.2	14.1	8.6	9.1	17.7	18.2	22.4	40.6	4	999	15	17	33	27
0313696Q	16.6	20.8	37.4	22.0	17.5	39.5	22.5	23.3	45.8	15	32	30	33	20	33
0313606V	22.0	24.0	46.0	23.8	24.8	48.6	27.2	23.0	50.2	29	26	30	24	34	30
0313520U	7.6	8.2	15.8	17.5	18.1	35.6	999	999	999	9	31	999	16	35	999
0313758U	11	12.6	23.9	12.2	11.8	24.0	16.4	12.3	28.7	13	20	15	31	30	31
0313239W	5.1	8.4	13.5	7.6	8.2	15.8	9.8	10.2	20.0	19	26	14	3	24	24
0313417N	5.1	7.2	12.3	18.4	20.4	38.8	27.0	25.9	52.9	2	10	8	25	27	19
0313760W	4.2	4.4	8.6	8.1	8.4	16.5	7.0	7.2	14.2	2	3	5	0	7	7
0313933R	15.7	16.6	32.3	20.0	17.0	37.0	16.4	17.3	33.7	2	10	5	10	3	4
0313994T	999	999	999	13.9	14.0	27.9	13.0	11.9	24.9	10	8	3	0	5	0
0313535S	11.0	10.2	21.2	10.0	9.0	19.0				0	0		15	12	
0313714S	13.0	14.7	27.7	24.1	25.3	49.4	28.4	30.6	59.0	2	20	13	10	15	15
0313611R	11	11.3	21.9	12.4	15.1	27.5	13.9	12.5	26.4	30	30	10	7	10	0
0313415R	11.2	13.6	24.8	12.1	13.3	25.4	25.4	25.4	50.8	19	30	30	21	37	28
0313079S	999	999	999	11.2	13.4	24.6				999	14		999	26	
0313608R	10.5	12.0	22.5	12.5	10.7	23.2	999	999	999	14	24	999	13	22	999
0313351R	7.0	7.9	14.9	8.1	8.3	16.4	8.1	9.0	17.1	15	30	19	35	30	26
0314121S	12	12.3	24.2	20.1	20.2	40.3	999	999	999	5	12	999	23	30	999
0313754R	9.0	9.3	18.3	11.6	9.8	21.4	13.3	9.9	23.2	4	12	12	11	14	15
0313237P	10.9	12.4	23.3	15.2	17.6	32.8	17.9	18.3	36.2	7	10	10	3	28	22
0313252T	4.5	5.8	10.3	6.0	6.3	12.3				10	16		19	24	
0313645W	6.2	8.3	14.5	7.5	9.2	16.7				0	12		20	21	
0313529N	6.5	8.5	15.0	12.7	15.4	28.1	18.4	20.0	38.4	7	11	15	26	35	39
0313612P	8.3	8.9	17.2	9.4	13.2	22.6	18.0	15.8	33.8	19	26	20	12	16	17
0313747O	16.5	17.6	34.1	20.6	22.0	42.6	22.1	23.9	26.0	30	45	41	31	40	38
0313502W	11.0	13.0	24.0	18.8	20.1	38.9	27.5	29.6	57.1	19	33	31	25	32	30
0313573V	8.2	9.0	17.2	12.8	13.8	26.6	11.6	14.8	26.4	11	21	35	10	21	19
0313425O	7.7	9.2	16.9	14.6	17.8	32.4	999	999	999	10	22	999	23	20	999
0313675N	16.2	14.6	30.8	11.7	9.5	21.2	13.0	14.1	27.1	30	30	36	24	21	22
0313650S	14.3	16.0	30.3	15.5	18.0	33.5	17.1	18.6	35.7	13	20	23	34	33	29
0313895V	8.1	8.4	16.5	10.6	12.8	23.4	999	999	999	11	2	999	15	22	999
0313692N	9.4	9.6	19.0	6.9	7.2	14.1			.0	16	10		16	18	
0313504S	9.6	11.2	20.8	10.0	11.2	21.2	15.8	17.8	33.6	8	11	16	19	22	26
0313724P	9.6	10.5	20.1	11.1	12.1	23.2	999	999	999	15	11	999	19	22	999
0313528P	10.0	12.0	22.0	9.5	10.6	20.1	16.5	14.5	31.0	7	10	21	37	42	37
0313249T	4.5	6.5	11.0	7.5	8.6	16.1	9.7	10.0	19.7	999	16	17	999	21	25
0313474M	5.6	7.2	12.8	5.8	9.2	15.0	10.4	9.9	20.3	7	6	16	10	5	10
PHYA	FLO	FRO	FTO	FL1	FR1	FT1	FLD	FRD	FTD	P0	P1	PD	CU0	CU1	CUD
0313258S	3.2	3.9	7.1	9.6	11.7	21.3	11.0	12.1	23.1	5	11	17	1	17	0
0313961M	11.7	12.3	24.0	13.9	14.7	28.6			.0	22	24		17	27	
0313546N	8.9	9.2	18.1	10.5	9.5	20.0	7.9	12.3	20.2	2	14	10	4	14	13

PHYA	PF0	RP0	BP0	GH0	VT0	SF0	RE0	MH0	PF1	RP1	BP1	GH1	VT1	SF1	RE1	MH1
0313572M	85	50	41	60	50	75	67	60	75	100	41	75	45	100	100	64
0313300M	40	0	44	30	55	25	0	64	55	0	41	25	30	50	0	48
0313867P	25	0	100	15	25	25	33	88	65	0	100	20	30	75	100	80
0313649O	60	0	74	50	65	25	0	44	30	0	52	35	50	38	0	48
0313746Q	50	0	42	40	45	62.5	0	64	999	999	999	999	999	999	999	999
0313472Q	75	75	74	57	50	100	33	64	85	50	62	35	70	75	33	52
0313885N	65	0	52	55	45	50	0	56	55	0	52	25	40	50	0	52
0313442O	55	0	42	30	20	25	0	40	70	0	31	35	45	38	0	36
0313234V	80	100	100	65	70	87.5	100	92	85	100	84	57	75	100	100	84
0313233M	60	0	41	35	50	50	33	44	70	0	52	20	50	75	0	52
0313422U	35	0	41	25	25	25	0	40	30	0	41	20	35	25	0	40
0313470U	90	75	100	67	75	100	100	76	80	0	74	37	60	75	67	84
0313526T	100	0	74	67	80	62.5	0	72	85	0	100	57	60	63	0	72
0314034N	80	75	100	77	60	50	0	64	90	75	100	77	70	100	100	92
0313440S	95	50	74	37	65	62.5	100	80	85	100	100	67	70	88	100	72
0313505Q	95	75	100	82	70	87.5	67	72	95	100	100	87	65	100	100	80
0313748M	100	100	100	82	60	100	100	76	75	0	74	40	35	88	67	52
0313530R	80	50	84	45	35	87.5	100	68	70	100	41	40	40	75	100	60
0313610T	60	0	64	37	50	37.5	0	64	60	0	64	37	40	63	0	64
0313486Q	95	100	84	75	65	62.5	100	88	65	50	84	55	55	100	67	64
0313993V	85	50	84	40	75	75	100	80	80	100	72	45	85	100	100	80
0313656R	70	50	31	52	35	100	67	68	60	0	10	15	15	75	0	52
0313424Q	80	50	100	72	80	87.5	33	80	90	50	84	82	80	100	100	84
0313413V	50	0	32	92	60	37.5	33	72	20	0	41	57	60	38	0	68
0313508V	30	0	22	45	40	37.5	0	40	25	0	22	20	35	38	0	52
0313420N	40	0	52	10	35	50	0	44	45	0	52	10	30	25	0	40
0313349P	65	0	62	35	75	75	0	76	75	0	100	42	80	75	0	84
0313199T	70	25	41	50	60	50	0	64	80	0	64	45	50	88	33	68
0313437S	60	0	51	15	50	62.5	33	44	65	0	74	35	45	88	33	60
0313685V	65	0	52	45	40	37.5	0	60	70	0	41	57	35	50	0	56
0313588T	95	75	84	60	50	100	100	72	90	100	72	55	50	100	67	76
0313268P	90	25	100	55	50	62.5	33	64	100	100	100	62	60	100	100	68
0313515N	75	75	41	85	70	25	33	72	100	100	61	55	50	100	100	60
0314237V	75	0	74	77	65	75	0	76	75	0	41	60	55	63	0	68
0313674P	55	0	41	35	25	50	0	64	50	0	41	35	25	50	0	48
0313694U	50	0	41	45	30	12.5	0	28	65	25	0	20	5	25	0	20
0313227S	55	0	100	20	15	25	0	24	45	0	22	20	15	50	0	20
0313513R	55	50	74	67	30	50	33	44	55	50	41	50	40	75	67	56
0313992M	75	0	41	45	45	50	0	64	70	50	41	40	35	63	0	52
0315403O	50	25	64	30	30	37.5	67	72	90	75	74	52	80	75	100	84
0313244S	70	0	52	47	75	75	33	72	70	25	74	47	65	75	67	68
0313229O	60	50	100	47	40	87.5	0	48	65	25	51	52	55	88	0	48
0315500Q	85	75	51	57	50	100	67	88	90	100	74	62	65	100	100	80
0313580N	90	25	74	72	60	75	67	100	100	100	100	82	80	100	100	100
0313225W	100	100	100	77	80	62.5	100	72	100	100	84	87	80	75	100	76
0313441Q	60	0	84	45	40	25	100	80	85	50	100	30	35	75	100	76
0313615U	95	75	100	65	55	75	100	64	95	100	84	87	55	88	100	60
0313750O	45	0	62	40	45	50	0	36	50	0	62	20	30	50	0	32
0313512T	999	999	999	999	999	999	999	999	90	50	74	60	55	63	0	68
0313839U	95	100	100	72	70	100	67	88	100	100	100	82	80	100	100	88

PHYA	PF0	RP0	BP0	GH0	VT0	SF0	RE0	MH0	PF1	RP1	BP1	GH1	VT1	SF1	RE1	MH1
0313769P	35	0	31	25	25	25	0	56	30	0	31	40	30	38	0	48
0313936W	85	75	41	67	60	87.5	67	88	85	50	41	70	55	88	33	80
0313318P	40	0	74	25	35	37.5	0	48	55	0	41	35	35	50	33	44
0313700S	15	0	41	40	40	25	0	60	40	0	31	35	45	25	0	36
0313232O	70	0	74	40	50	75	67	72	75	0	74	40	25	75	0	72
0313475V	65	0	62	42	65	62.5	100	96	95	25	84	57	65	75	100	92
0313695S	85	0	100	52	50	50	0	68	85	100	100	37	65	100	100	84
0313527R	95	100	100	72	60	100	100	76	90	100	100	72	85	100	100	88
0313583S	65	0	42	25	45	50	0	60	60	0	41	30	40	63	0	68
0313248V	80	0	100	45	40	37.5	0	32	90	0	51	25	40	50	0	52
0313756N	80	0	74	45	50	50	0	48	100	100	84	97	95	100	100	60
0313519Q	70	0	100	45	65	62.5	100	92	55	25	52	42	70	75	67	60
0313205R	70	0	62	25	20	62.5	0	64	70	0	51	37	25	75	0	56
0313652O	100	100	100	82	75	100	100	88	95	100	84	82	70	100	100	80
0313444V	75	25	52	65	45	62.5	0	80	55	0	31	10	20	50	33	52
0313696Q	80	0	74	67	80	75	100	84	85	50	74	52	70	88	67	68
0313606V	90	100	100	87	40	87.5	100	76	100	100	74	82	55	88	100	76
0313520U	45	0	41	35	15	37.5	0	48	55	0	41	20	20	38	0	36
0313758U	90	75	100	42	30	37.5	67	60	90	100	100	35	35	100	67	52
0313239W	80	0	100	42	50	37.5	67	88	90	100	84	32	65	100	100	60
0313417N	75	0	74	35	45	75	0	44	75	100	62	30	70	75	100	72
0313760W	50	0	41	10	0	25	33	64	45	75	41	30	25	88	67	76
0313933R	50	25	22	52	70	50	0	72	35	0	62	30	50	63	0	56
0313994T	35	0	32	0	10	50	0	44	25	0	41	40	50	75	0	48
0313535S	25	0	70	20	45	62.5	33	88	80	25	100	15	70	63	33	84
0313714S	50	0	52	55	45	62.5	0	56	60	25	80	67	60	63	0	72
0313611R	85	100	74	57	55	87.5	33	56	70	100	62	67	40	75	100	52
0313415R	85	50	80	50	50	75	33	64	90	100	84	52	55	50	100	56
0313079S	60	0	21	50	35	37.5	100	92	95	100	100	82	90	100	100	100
0313608R	75	25	84	72	55	75	67	100	80	25	51	67	60	75	33	96
0313351R	85	0	84	50	45	75	33	52	90	100	62	47	55	88	33	72
0314121S	70	0	62	30	40	37.5	67	36	100	100	100	67	80	100	100	72
0313754R	85	50	62	35	75	75	100	76	65	0	22	30	50	63	0	60
0313237P	85	100	72	97	100	100	100	64	90	50	52	62	55	63	33	52
0313252T	60	0	100	30	45	75	0	60	75	0	51	35	40	63	0	60
0313645W	75	0	51	30	50	75	33	68	75	0	41	35	40	75	0	76
0313529N	60	0	74	60	60	50	0	64	90	75	74	67	55	75	67	64
0313612P	85	100	84	75	70	100	100	88	95	100	62	72	70	100	100	92
0313747O	35	0	31	35	30	12.5	0	60	80	100	72	45	85	100	100	80
0313502W	100	100	84	72	70	62.5	100	80	95	100	100	62	75	75	100	76
0313573V	30	0	41	20	35	37.5	0	36	35	0	31	30	25	25	0	24
0313425O	75	0	74	45	45	62.5	67	68	75	25	74	47	40	88	100	72
0313675N	25	0	31	15	25	25	0	52	80	50	74	57	50	88	100	80
0313650S	65	0	74	25	35	50	0	48	80	0	41	15	25	25	0	24
0313895V	80	75	100	20	25	87.5	33	32	95	100	100	45	50	100	100	52
0313692N	85	100	74	62	70	62.5	100	92	75	100	100	72	75	100	100	92
0313504S	85	25	100	77	45	75	33	64	85	25	100	77	45	75	33	64
0313724P	90	0	41	30	30	37.5	0	52	85	0	41	35	25	50	67	72
0313528P	95	25	52	87	65	75	0	68	80	75	100	70	70	88	0	72
0313249T	60	0	74	50	25	37.5	100	72	55	25	41	30	20	75	0	64

PHYA	PFD	RPD	BPD	GHD	VTD	SFD	RED	MHD
0313572M	50	25	51	40	45	100	67	64
0313300M	40	0	41	25	35	50	0	52
0313867P	65	25	22	20	40	50	67	60
0313649O	55	0	74	27	30	50	33	36
0313746Q	25	0	22	0	15	12.5	0	32
0313472Q	85	50	62	35	70	75	33	52
0313885N	55	0	52	25	40	50	0	52
0313442O	45	0	22	15	15	37.5	33	28
0313234V	80	50	64	47	65	75	33	64
0313233M	75	0	51	35	40	75	0	56
0313422U	40	0	22	25	35	50	0	52
0313470U	85	25	74	42	80	87.5	33	72
0313526T	-50	-100	999	-25	-20	-25	-100	-20
0314034N	90	100	100	87	35	87.5	100	92
0313440S	85	50	52	25	40	62.5	100	72
0313505Q	100	100	100	92	80	100	100	80
0313748M	75	25	100	35	55	100	0	72
0313530R	65	100	41	35	35	75	100	56
0313610T	-50	-100	999	-25	-20	-25	-100	-20
0313486Q	-50	-100	999	-25	-20	-25	-100	-20
0313993V	75	50	41	35	80	75	100	76
0313656R	-50	-100	999	-25	-20	-25	-100	-20
0313424Q	90	100	100	72	80	100	100	88
0313413V	30	25	22	20	15	50	33	64
0313508V	35	0	12	40	20	25	0	60
0313420N	45	0	52	20	45	75	0	52
0313349P	75	25	74	67	80	87.5	0	80
0313199T	-50	-100	999	-25	-20	-25	-100	-20
0313437S	35	0	52	20	10	50	0	12
0313685V	-50	-100	999	-25	-20	-25	-100	-20
0313588T	-50	-100	999	-25	-20	-25	-100	-20
0313268P	100	100	62	72	35	87.5	100	48
0313515N	75	75	51	45	20	62.5	0	44
0314237V	70	0	52	60	65	62.5	33	68
0313674P	45	0	41	40	20	50	0	48
0313694U	50	0	22	10	20	25	0	32
0313227S	-50	-100	999	-25	-20	-25	-100	-20
0313513R	45	50	41	35	20	62.5	0	44
0313992M	-50	-100	999	-25	-20	-25	-100	-20
0315403O	-50	-100	999	-25	-20	-25	-100	-20
0313244S	80	0	41	57	55	75	33	64
0313229O	80	0	74	42	65	87.5	0	60
0315500Q	90	50	74	67	70	100	33	68
0313580N	70	0	41	60	50	50	33	88
0313225W	100	100	62	87	75	75	100	76
0313441Q	85	100	74	67	65	100	100	80
0313615U	65	25	74	55	45	62.5	33	56
0313750O	-50	-100	999	-25	-20	-25	-100	-20
0313512T	90	0	74	67	45	62.5	0	60
0313839U	100	100	84	77	75	100	67	84

PHYA	PFD	RPD	BPD	GHD	VTD	SFD	RED	MHD
0313769P	10	0	22	15	10	25	0	48
0313936W	70	50	41	65	30	87.5	33	48
0313318P	45	0	41	20	20	50	0	-20
0313700S	50	0	31	10	40	25	0	84
0313232O	-50	-100	999	-25	-20	-25	-100	76
0313475V	85	0	41	35	50	75	100	80
0313695S	85	0	52	42	40	87.5	0	60
0313527R	95	100	100	77	70	100	100	52
0313583S	60	0	42	30	35	50	0	84
0313248V	90	0	51	25	40	50	0	56
0313756N	95	100	62	92	80	87.5	67	48
0313519Q	35	0	41	35	50	50	0	-20
0313205R	80	0	51	25	30	75	0	76
0313652O	-50	-100	999	-25	-20	-25	-100	80
0313444V	85	0	52	35	35	50	67	84
0313696Q	80	50	74	52	80	100	100	-20
0313606V	90	100	74	82	45	100	100	36
0313520U	-50	-100	999	-25	-20	-25	-100	84
0313758U	999	100	100	10	10	100	100	76
0313239W	100	100	84	37	70	100	100	28
0313417N	75	100	74	30	50	87.5	100	40
0313760W	50	0	10	10	0	37.5	0	52
0313933R	50	25	64	30	60	62.5	67	-20
0313994T	45	0	41	15	55	50	0	72
0313535S	-50	-100	999	-25	-20	-25	-100	24
0313714S	85	25	74	40	50	87.5	33	56
0313611R	60	0	41	35	25	37.5	0	-20
0313415R	65	75	62	40	60	87.5	100	-20
0313079S	-50	-100	999	-25	-20	-25	-100	68
0313608R	-50	-100	999	-25	-20	-25	-100	-20
0313351R	95	100	100	57	60	100	100	48
0314121S	-50	-100	999	-25	-20	-25	-100	56
0313754R	60	0	22	20	35	37.5	0	-20
0313237P	80	25	74	40	55	50	33	-20
0313252T	-50	-100	999	-25	-20	-25	-100	60
0313645W	-50	-100	999	-25	-20	-25	-100	84
0313529N	90	100	62	57	55	75	100	60
0313612P	95	100	72	72	75	100	100	80
0313747O	70	0	22	35	25	50	0	68
0313502W	100	100	100	72	60	100	100	-20
0313573V	50	0	52	47	40	62.5	0	76
0313425O	-50	-100	999	-25	-20	-25	-100	40
0313675N	80	0	41	35	35	50	100	-20
0313650S	75	0	41	35	30	62.5	33	-20
0313895V	-50	-100	999	-25	-20	-25	-100	76
0313692N	-50	-100	999	-25	-20	-25	-100	-20
0313504S	85	50	62	72	55	100	67	68
0313724P	-50	-100	999	-25	-20	-25	-100	60
0313528P	95	50	62	67	75	50	0	76
0313249T	60	25	62	30	0	100	33	64

