PROGRESSIVE RESISTANCE TRAINING DURING MAINTENANCE HEMODIALYSIS TO COUNTERACT CATABOLISM IN END STAGE RENAL DISEASE

by

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As the doctoral thesis supervisor of Birinder Singh Bobby Cheema, MSc, BHK, I certify that I consider his thesis 'Progressive resistance training during maintenance hemodialysis to counteract catabolism in end stage renal disease' to be suitable for examination.

Signed

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STATEMENT OF THE AUTHOR

I, B.S.B. Cheema, MSc, BHK, hereby declare that this submission is my own work and that it contains no material previously published or written by another person except where acknowledged in the text. Nor does it contain material which has been accepted for the award of another degree.

In addition, ethical approval from the University of Sydney Human Ethics Committee was granted for the two studies presented in this thesis. Subjects were required to read a subject information document and informed consent was gained prior to data collection.

Name: B. Cheema, MSc., BHK

Signed

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PUBLISHED ABSTRACTS


CONFERENCE PRESENTATIONS - ORAL


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DEDICATION

This thesis is dedicated to my beloved grandmother, Charan Kaur Sandhu, mother Preme Kaur Cheema, M.A. (Bastyr University, USA), and father Jaswinder Singh Cheema, MSc. (Peoples Friendship University, Russia) for their infinite support and love throughout my entire life in everything I choose to do.

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CHAPTER 1

INTRODUCTION
The purpose of this Doctor of Philosophy research experience was to evaluate the overall efficacy of delivering a progressive resistance training (PRT) intervention during routine, outpatient maintenance hemodialysis treatment in an attempt to counteract catabolism in patients with end-stage renal disease (ESRD). This experience culminated in the development and implementation of a 24-week randomized controlled clinical trial of *Progressive Exercise for Anabolism in Kidney Disease* (PEAK).

The rationale for prescribing exercise during HD treatment based on the empirical evidence to date is presented in Chapter 2: *A Rationale for Intradialytic Exercise Training as Standard Clinical Practice in End-Stage Renal Disease*, published by *The American Journal of Kidney Diseases*, 45:912-916, 2005). This article summarizes the overall safety and effectiveness of an intradialytic exercise prescription for inducing a number of favorable health-related and clinical adaptations, and the promotion of greater exercise compliance in patients receiving maintenance HD. In addition, the article includes the results of a survey of actual exercise prescription practices within the operating dialysis units in Australia in 2004.

A systematic review of the literature was performed to identify necessary gaps in the literature at this juncture, culminating in the development of Chapter 3: *Exercise Training in Patients Receiving Maintenance Hemodialysis Treatment: A Systematic Review of Clinical Trials*, published in *The American Journal of Nephrology*, 25:352-364, 2005. While a summary of the research reveals supports the clinical utility of exercise training in this cohort, no trial to date had integrated PRT directly into routine, outpatient hemodialysis treatment sessions as the sole exercise intervention.
PRT is a known anabolic stimulus in elderly and certain chronically diseased cohorts. Given the multitude of catabolic insults chronically assailing patients with ESRD, the rationale for prescribing PRT in this cohort clearly makes intuitive sense. Unfortunately, the barriers to exercise participation in this cohort are many, lending reason for the implementation of the PRT intervention within the HD treatment session itself. Chapter 4, *Progressive Resistance Training During Hemodialysis: Rationale and Method of a Randomized Controlled Trial*, provides a robust argument for applying PRT during dialysis, and the novel methodology via which such an endeavor, for the purpose of this investigation, would take place within a controlled, empirical investigation.

Outcomes of the randomized, controlled clinical trial, appropriately titled PEAK, are presented in Chapter 5 and 6. Chapter 5 presents outcomes from the initial 12 weeks of the randomized controlled trial comparing patients receiving 12 weeks of PRT to 12 weeks of usual care, while Chapter 6 presents the outcomes of the entire 24-week PEAK trial. There was one adverse event reported during the PEAK clinical trial presented in detail in Chapter 7: *Rotator Cuff Tear During Resistance Training in an Older Woman: A Case Report and Review of the Literature*, currently submitted to *Medicine & Science in Sport & Exercise*.

Overall, findings of the PEAK clinical trial reveal that intradialytic PRT is clinically safe and feasible for patients with ESRD, resulting in significant anabolic and clinically meaningful adaptations including improved quality of life (Chapter 5 and 6). Currently, there is a need for further investigation involving robust randomized controlled trials evaluating a broad spectrum of physiological, functional, psychological, and clinical outcome measures potentially ameliorable to exercise training in this cohort. These research efforts are required for the
development of comprehensive guidelines for exercise prescription in this cohort, and the application of intradialytic exercise training as standard clinical practice in ESRD. Such complete integration of exercise in the dialysis setting is a potentially favorable route by which overall health status, functioning, and quality of life can be markedly improved.
CHAPTER 2

A Rationale for Intradialytic Exercise Training as Standard

Clinical Practice in End Stage Renal Disease
ABSTRACT

The purpose of this article is to present a rationale for intradialytic exercise training in patients with end stage renal disease (ESRD) based on the empirical evidence to date, and to determine if this evidence has translated into enhanced renal rehabilitation practices throughout the world. According to the published literature, intradialytic exercise improves exercise adoption and adherence in this cohort, is safely performed, and is feasible to administer. Moreover, intradialytic exercise can improve solute removal, dialysis adequacy, intradialytic protein synthesis, muscular strength, peak oxygen consumption, nutritional status, and quality of life (QOL). Despite these findings, there are currently no policies or position stands regarding exercise prescription for HD patients in Australia. According to a telephone survey we conducted, intradialytic exercise programs are essentially nonexistent in this country. However, such programs are successfully being implemented as standard clinical practice in dialysis units in Germany, and there is reason to believe that this practice can be expanded throughout the world.

At present, further research is indicated. There is a lack of large-scale, robustly-designed randomized controlled trials of intradialytic exercise training. Such research is needed to conclusively demonstrate the clinical importance of intradialytic exercise for hemodialysis patients, which may influence current standard clinical practice among nephrologists, and as such, improve the health and QOL of this vulnerable cohort.

Keywords: Resistance Training, Aerobic Training, VO_{2peak}, Dialysis Adequacy, Survey, Australia, Health, Quality of Life, Standard of Care
INTRODUCTION

The 2003 report from the Australia and New Zealand Dialysis and Transplant Registry indicates that 12,945 individuals in Australia live with end-stage renal disease (ESRD), and 7,205 of these individuals receive maintenance hemodialysis (HD).\(^1\) Almost 2000 new patients began HD in Australia in 2002, a 5% increase over the previous year, and this number is projected to continue to rise significantly in the future.\(^1\) According to the United States Renal Data System, similar trends are occurring in the United States, where nearly 400,000 individuals currently live with ESRD.\(^2\)

Approximately 91% of patients diagnosed with ESRD will commence HD treatment as renal replacement therapy.\(^2\) While advances in dialysis techniques, and control of co-morbid diseases have extended the lifespan of HD patients, these individuals continue to suffer from significant impairments of quality of life (QOL). The reduced QOL experienced by this cohort may be attributed to: 1) physiologic alterations of the internal milieu secondary to ESRD, 2) co-morbidities, 3) biological aging, 4) lifestyle restrictions and sedentariness imposed by 12-18 hours of maintenance HD treatment per week, and 5) loss of psychological and functional health status as a direct consequence of 1 through 4. With rising incidence of ESRD and increased competition for kidney transplants, greater efforts must be directed toward improving the QOL of patients receiving maintenance HD treatment.

The numerous health-related benefits derived from engaging in appropriately structured exercise regimens have been extensively documented with sedentary adults, the frail elderly, and individuals with a wide array of chronic...
illnesses. Accordingly, the efficacy of exercise training for patients with ESRD has been investigated for the past 25 years. The rationale for prescribing exercise in this patient population is extremely strong, however the barriers to regular exercise participation are many, which may explain the persistent sedentariness of this cohort. Motivation to exercise has been reported to be problematic, particularly when the training is performed on non-dialysis days.

In an attempt to promote exercise adoption, several authors have prescribed exercise training during routine HD treatment, time typically devoted to complete idleness or sedentary pursuits such as watching television. An accumulating body of literature suggests that intradialytic exercise is safe, beneficial, feasible to administer, and enhances compliance to exercise training. Therefore, the purpose of our article is two-fold: 1) To present a rationale for the efficacy of intradialytic exercise training based on the empirical evidence to date, and 2) To determine if this evidence has translated into enhanced renal rehabilitation practices throughout the world.

A RATIONALE FOR INTRADIALYTIC EXERCISE

Health-Related Adaptations

Painter et al. conducted the first clinical trial to prescribe exercise during routine, outpatient HD treatment. Fourteen patients performed up to 30 minutes of cycling using adapted cycle ergometers, during the second or third hour of HD treatment, 3 times per week, for 6 months. Exercising patients significantly improved peak oxygen uptake (VO2peak) by 23% following the 6-month
intervention, an extremely beneficial adaptation given that VO2peak in this cohort has been reported to be 155% less than observed in healthy, sedentary age-matched individuals (p<0.001). No change in VO2peak was reported in the control group.

At least 16 additional reports available in the published literature have prescribed intradialytic exercise regimens of sufficient frequency, intensity, duration, and modality to elicit significant, beneficial adaptations. Physiological adaptations include the holistic (central and peripheral) enhancement of the cardiorespiratory system, improved blood pressure regulation, and reversal of the malnutrition-inflammation complex (Table 1). Functional adaptations include improved muscle strength, exercise capacity, habitual and fastest gait speed, and ability to perform activities of daily living such as sit-to-stand movements (Table 1). Intradialytic exercise can also induce positive psychological adaptations in this cohort by reducing symptoms of anxiety, depression, and fatigue, and enhancing various components of quality of life, including general health, vitality, and perceptions of physical functioning (Table 1). Clearly, there is evidence to suggest that the benefits of intradialytic exercise can ameliorate the physiological, functional, and psychological impairments commonly induced and/or exacerbated by the ESRD process (Table 1).

Clinical Relevance

Damaging solutes are disproportionately retained in the skeletal muscle during HD, and this gradient re-equilibrates after treatment, a process recognized as post-dialysis solute rebound. Studies have demonstrated that acute bouts of intradialytic exercise cycling can significantly reduce the post-dialysis rebound of urea, creatinine, and potassium, thereby increasing the removal of these three
solute via dialysis. Phosphate removal can also significantly increase as a result of intradialytic exercise training. Kong et al concluded that the improvement of dialysis adequacy is equivalent to extending the length of the HD treatment session by 30 minutes. The mechanism underlying this enhancement of dialysis adequacy likely includes increased blood perfusion between the working muscle and the bloodstream, thereby enabling more thorough removal of the damaging solutes via HD treatment. These benefits may also translate into the long-term enhancement of dialysis adequacy (Kt/V), although this hypothesis has not been rigorously investigated in a randomized controlled trial involving exercise training.

Muscle wasting is the most significant predictor of morbidity and mortality in hemodialysis patients. HD treatment can significantly decrease protein synthesis directly via the loss of amino acids in dialysate and may therefore be a factor contributing to the prevalent muscle catabolism in this cohort. However, Pupim et al demonstrated that just 15 minutes of intradialytic cycling at 40% of maximal heart rate combined with adequate nutritional supplementation significantly increased amino acid uptake and net protein accretion during HD treatment, as compared to nutritional supplementation alone (p<0.05). Moreover, intradialytic exercise resulted in a nearly fourfold increase in post-dialysis growth hormone levels (p<0.05). These adaptations suggest that exercise may ameliorate muscle catabolism by promoting an anabolic milieu, thereby potentially improving the clinical sequelae of sarcopenia, such as muscle weakness, falls, fractures, frailty, insulin resistance, and immune dysfunction, in hemodialysis patients.
Adherence

Konstantinidou et al\textsuperscript{11} and Kouidi et al\textsuperscript{7} investigated exercise adherence rates in HD patients by comparing training protocols performed on non-dialysis days and during dialysis. The authors demonstrated that training on non-dialysis days yielded significantly greater cardiorespiratory adaptations,\textsuperscript{7,11} however this result must be interpreted with caution given that training volume was not equal between regimens. Patients engaging in the intradialytic training program significantly improved cardiorespiratory outcomes when compared to non-exercising controls.\textsuperscript{11} Perhaps more importantly however, exercise training on non-dialysis days resulted in a higher percentage of subject attrition vs. intradialytic training at 6 months (23.8\% vs. 16.7\%, respectively),\textsuperscript{11} 1 year (20.8\% vs. 12.5\%, respectively),\textsuperscript{7} and 4 years (37.5\% vs. 21.0\%, respectively).\textsuperscript{7}

The most common reason for discontinuing exercise on non-dialysis days in 5 of 9 patients (55.5\%) who withdrew before 4 years was "a lack of motivation."\textsuperscript{7} Other commonly cited reasons included "lack of time" and "transportation difficulties."\textsuperscript{11} The authors concluded that it is difficult to persuade patients to maintain exercise programs on non-dialysis days.\textsuperscript{7,11} Therefore, exercising during HD is often recommended as a more feasible, convenient, and time-effective solution to promote exercise adherence in this cohort.\textsuperscript{4,5,7,11}

Safety

No serious exercise-induced adverse events have been reported in the 17 published trials of intradialytic exercise training conducted with HD patients\textsuperscript{5,7-22} suggesting that, in appropriately screened patients, the risks of this method of
training are low. This is notable in light of the high prevalence of cardiovascular disease, hypertension, and diabetes in this cohort. Large, long-term randomized controlled trials are required to confirm this apparent safety.

REHABILITATION PRACTICES IN HEMODIALYSIS UNITS
WORLDWIDE

Despite a strong rationale for the implementation of intradialytic exercise programs, such efforts are not being promoted by Kidney Health Australia. There are no policies or position stands regarding exercise prescription for HD patients in this country, and no discussions are currently ongoing toward this end. According to a telephone survey we conducted of all 145 HD units in Australia, only three units (2.1%) offered an exercise program to their patients and only one unit (0.68%), as an extension of a recent research study,22 prescribed exercise at a sufficient dose to induce clinical and physiological adaptations. Thus, intradialytic exercise as standard clinical practice is essentially nonexistent in Australia.

Statistics regarding the worldwide prevalence of intradialytic exercise programs are not available, however our findings for Australia stand in marked contrast to the standard of care in several other countries.

Over the past 20 years, research groups in Germany, Greece, the United States, Sweden, the Czech Republic, Japan, and several other countries have initiated exercise programs for individuals with kidney disease as outpatient training programs, or during HD.29 For example, exercise in the dialysis setting
has become part of clinical practice in the Ruhr area of Germany, where approximately 20% of all dialysis patients are involved in intradialytic exercise programs.\textsuperscript{4} However, according to these authors,\textsuperscript{4} the number of participating patients could markedly increase if more dialysis units were to establish such training programs. Currently, 50% of units in the Ruhr area are prescribing exercise.\textsuperscript{4} In several of these units, participation rates have reached 75%.\textsuperscript{4} In a recent survey of 48 nephrologists conducted at the 2003 World Congress on Nephrology in Berlin, 7 (15%) reported that intradialytic exercise programs were offered at their respective dialysis unit.\textsuperscript{30} The majority of these units were in Germany.\textsuperscript{30}

We were unable to find any evidence to suggest that intradialytic exercise has become integrated as clinical practice in other countries. Greater financial support from the German Health Care System toward intradialytic exercise programs may be the mechanism responsible for this practice of dialysis units in Germany.\textsuperscript{4,30} Support from expert advisory bodies, government-funded health care resources, private advocacy groups, industry, and the health care professional community will likely all be required if such practices are to become routine in other countries such as Australia as well.

Although research into the efficacy of exercise in ESRD has been ongoing since 1977, there is currently no American College of Sports Medicine Position Stand regarding exercise prescription for this cohort. By comparison, such position stands do exist for overweight/obesity, bone health, Type 2 diabetes, hypertension, coronary artery disease, healthy adults, and the elderly.\textsuperscript{31} This disparity may be due to the limited availability of large-scale, robustly-designed randomized controlled trials of exercise training in ESRD. Of the 17 reports of
intradialytic training we reviewed, only 6 were randomized controlled trials,\textsuperscript{7-9,11-12,17} while 5 were controlled trials,\textsuperscript{5,10,13,15-16} and 6 were uncontrolled trials.\textsuperscript{14,18-22} This paucity of hard empirical data may be responsible for the low rates of exercise counseling among nephrologists,\textsuperscript{32} the absence of position stands, and the limited involvement of health care service providers in promoting and/or financially supporting exercise programs for patients with ESRD.

Robust, long-term clinical trials are needed to identify optimal modalities and doses of exercise for this cohort for a broad range of clinical outcomes including cardiovascular morbidity and mortality, muscle catabolism, visceral obesity, the malnutrition-inflammatory complex, insulin sensitivity, depression, endothelial dysfunction, vascular access maturation and efficacy, functional independence, and QOL, among others.
REFERENCES

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31. American College of Sports Medicine Position Stands. Available at:

Table 1: Impact of ESRD can be counteracted with intradialytic exercise training*

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<td><strong>Functional Adaptations</strong></td>
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</tr>
<tr>
<td>Reduced Muscular Strength</td>
<td>Increased Muscular Strength$^{8,12,14}$</td>
</tr>
<tr>
<td>Reduced Exercise Capacity</td>
<td>Increased 6-min walk distance$^{15,20}$</td>
</tr>
<tr>
<td>Reduced Maximal Work Capacity</td>
<td>Increased Maximal Vertical Work Capacity$^5$</td>
</tr>
<tr>
<td>Functional Limitations</td>
<td>Improved Habitual and Fastest Gait Speed, and Sit-to-Stand Movement Time$^{15,16}$</td>
</tr>
<tr>
<td><strong>Psychological Adaptations</strong></td>
<td></td>
</tr>
<tr>
<td>Increased Subjective Fatigue Symptoms</td>
<td>Reduced Subjective Fatigue Symptoms$^{30}$</td>
</tr>
<tr>
<td>Poor Perception of Physical Functioning</td>
<td>Improved Perception of Physical Functioning$^{14,17}$</td>
</tr>
<tr>
<td>Poor Perception of General Health</td>
<td>Improved Perception of General Health$^{7,15-16}$</td>
</tr>
<tr>
<td>Increased Anxiety</td>
<td>Reduced Anxiety$^{10}$</td>
</tr>
<tr>
<td>Poorer Mental Health</td>
<td>Improved Mental Health$^{14}$</td>
</tr>
<tr>
<td>Greater Experience of Bodily Pain</td>
<td>Reduced Experience of Bodily Pain$^{15-16}$</td>
</tr>
<tr>
<td>Reduced Vitality</td>
<td>Increased Vitality$^{11}$</td>
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</table>

*All listed effects of intradialytic exercise training are significant according to trials to date$^{3,22}$
CHAPTER 3

Exercise Training in Patients Receiving Maintenance Hemodialysis:

A Systematic Review of Clinical Trials
ABSTRACT

Background: Exercise is not routinely advocated in patients with end stage renal disease (ESRD) receiving maintenance hemodialysis (HD), compared to best practice in other chronically diseased cohorts. Lack of widespread awareness of the exercise in HD literature may be contributing to these shortcomings of clinical practice. Therefore, our objectives are: 1) to systematically review trials of exercise training involving adult HD patients, 2) to provide empirical evidence that exercise can elicit health-related adaptations in this cohort, and 3) to provide recommendations for future investigations.

Method: A systematic review of the literature using computerized databases was performed.

Results: According to the 29 trials reviewed, HD patients can safely derive a myriad of health-related adaptations from engaging in appropriately structured exercise regimens involving aerobic and/or resistance training. However, methodological limitations within this body of literature may be partially responsible for minimal advocacy for exercise in this cohort.

Conclusions: Robustly designed RCTs with thorough, standardized reporting are required if clinical practice and quality of life of this cohort is to be enhanced through the integration of exercise training and mainstream medical practice. Future trials should demonstrate the clinical importance, and long-term feasibility and applicability of exercise training for this vulnerable patient population.

Keywords: Aerobic Training, Resistance Training, End Stage Renal Disease, Quality of Life, Health
INTRODUCTION

According to the United States Renal Data System (USRDS), the incidence of end stage renal disease (ESRD) continues to increase each year [1]. Over 100,000 new cases were reported in the USRDS 2004 report [1] and over 430,000 individuals in the United States currently live with ESRD [1]. Rising incidence and prevalence trends are being reported in many other countries maintaining renal registries [2].

Approximately 91.9% of patients diagnosed with ESRD receive maintenance hemodialysis (HD) treatment as renal replacement therapy [1]. This intervention is typically prescribed 3 times per week, 4-6 hour per session, and remains ongoing for the lifetime of the patient or until successful kidney transplantation. Although advances in HD treatment have extended the lifespan of patients with ESRD, this treatment alone does not ensure preservation of quality of life (QOL). Hemodialysis patients typically suffer from significant impairments of QOL as compared to their healthy counterparts, or those with successful kidney transplants.

Planned exercise, involving aerobic and resistance training modalities, has become well-recognized as a therapeutic intervention that can ameliorate the marked physiological, functional, and psychological deterioration which commonly accrues as a consequence of biological aging, catabolic illness, and a sedentary lifestyle, factors that may all contribute to the progressive decline of vitality and QOL commonly observed in HD patients. As such, many trials of exercise training have been conducted with HD patients over the past 3 decades. Findings from virtually all of these trials have demonstrated that prolonged exercise is safe and
beneficial for this patient population. However, recent evidence has clearly suggested that exercise is still not routinely advocated or prescribed in this cohort [3, 4], compared to best practice in other diseased populations, such as those with cardiac and pulmonary disease. The lack of widespread awareness of the exercise in HD literature may potentially be contributing to the shortcomings of clinical practice with regard to prescribing exercise.

Therefore our objectives are:

1. To systematically review trials of exercise training involving adult hemodialysis patients
2. To provide empirical evidence that exercise can counteract the marked physiological, functional, and psychological wasting associated with end-stage renal disease,
3. To provide recommendations for future investigations which may potentially lead to the integration of exercise prescription within the mainstream of medical practice for this patient population.

METHOD

A systematic, critical review rather than a meta-analytic approach has been taken as the heterogeneity of exercise modalities and dosages utilized and outcomes assessed do not lend themselves to meta-analytic methods. There are also clinically important results to discuss in some of the uncontrolled trials.
Criteria for Considering Studies

Study Designs

Randomized controlled trials (RCTs), controlled trials and uncontrolled trials were included. Abstracts and case reports were not considered.

Subjects

Subjects were adult (≥18yr) men and women receiving HD treatment for the management of ESRD. Studies involving young (<18yr) HD patients, continuous ambulatory peritoneal dialysis patients and/or pre-dialysis patients were not considered.

Interventions

Trials prescribing aerobic and/or resistance training modalities ≥5wk in duration were included. Studies investigating the effects of single, acute bouts of exercise, or studies applying interventions <5wk were excluded. Studies involving multimodal interventions (e.g. exercise combined with nutritional supplementation) were also excluded.

Outcome Measures

Outcome measures potentially responsive to exercise training, based on evidence of exercise training in other diseased and non-diseased cohorts, were considered. These outcomes included a broad spectrum of physiological, psychological, and functional measures.

Search Method

We conducted a literature review in November 2004 from yrs 1966 to 2004, limited to the English language, using computerized databases, including Medline, CINAHL, SportDiscus, Embase, and Web of Science. The search combined key
words related to HD treatment (i.e. hemodialysis, haemodialysis, dialysis, renal replacement therapy), ESRD (i.e. nephrology, nephron, kidney, renal disease, renal failure) and exercise (i.e. exercise, training, physical activity, rehabilitation, resistance training, aerobic training, strength training, muscle, endurance, VO₂peak).

Articles retrieved were examined for further relevant references.

RESULTS OF SEARCH

Study Designs and Research Quality

The search resulted in 34 articles presenting the findings of 29 trials, including: 9 uncontrolled trials (9/29, 31%) [5-15], 7 controlled trials (7/29, 24%) [16-23], and 13 RCTs (13/29, 45%) [24-38].

All 9 uncontrolled trials [5-15] involved time series investigation of a single treatment group evaluated with repeated measures collected before and after training (Table 1). One uncontrolled trial utilized the non-compliant subjects as a comparison group for statistical analyses [7], however the study was originally intended as a single treatment group design. None of the 9 uncontrolled trials mentioned the involvement of blinded outcomes assessors.

Seven controlled trials [16-23] involved a treatment (i.e. exercise) and control (i.e. non-exercise) group, consisting of HD patients but without random assignment of subjects into these two groups (Table 2). Statistical analyses performed in 4/7 trials (57%) involved repeated measures comparisons within groups only, while 3/7 trials (43%) [20-22, 27] performed statistical comparisons
between groups. None of the 7 controlled trials mentioned the involvement of blinded outcomes assessors.

Thirteen trials involved randomization of subjects (Table 3) [24-38]. Nine RCTs (9/13, 69%) assigned subjects to a treatment or non-treatment control group [24-26, 28-32, 35, 37, 38]. Three additional RCTs (3/13, 23%) randomized subjects to: (a) intradialytic vs. non-dialysis exercise interventions [36], (b) exercise vs. sham exercise (i.e. placebo) [33], or (c) exercise vs. a social support group [27]. One study (1/13, 8%) compared the effects of exercise training plus the normalization of blood hematocrit within a 4-group RCT [34]. Eleven RCTs (11/13, 85%) performed between group comparisons on repeated measures [27, 29-38] while 2 trials (2/13, 15%) [24-26, 28] reported change over time within groups only. Six RCTs (6/13, 46%) [24-26, 29, 31, 35-37] reported that randomization of subjects occurred following baseline testing. Only two RCTs (2/13, 15%) reported that partial, or complete collection of outcome measures were performed by blinded assessors [29, 33]. To date, only two RCTs (2/13, 15%) involved intention-to-treat strategy of analysis [33, 34].

Overview of the Subjects
Sample Sizes

Nine hundred and fifty-nine (n=959) patients have been enrolled in the 29 trials reviewed. Sample size ranged from 7 to 286 enrolled patients. Thirteen trials (13/29, 45%) have enrolled <20 patients, 15 trials (15/29, 52%) have enrolled 20-75 patients, and only one trial (3/29, 3%) has enrolled >75 patients (n=286) (Tables 1-3) [20, 21].
Gender

Excluding two trials that did not provide a gender breakdown (where combined n=20) [11, 16], 479 men and 460 women (51:49) have been enrolled in the trials reviewed. Excepting one trial involving 12 men only [17], all trials included men and women.

Age

Age of the sample was expressed as Mean±SD in 10 trials (10/29, 34%) [18-23, 27, 28, 33, 34, 38] in which mean age ranged from 36±3 to 60±17 [27, 38]. In 18 trials (18/29, 62%) that presented an age range [5-10, 12-17, 24-26, 29-32, 35-37] the youngest and eldest patient enrolled were 19yr [24-26] and 84yr [12], respectively. A broad age range was generally reported. One trial (1/29, 3%) did not describe the age of their sample [11].

Duration of Hemodialysis

Entry criteria typically precluded patients receiving HD treatment <3 months. Length of HD treatment ranged from 0.25-17.4yr [13,14] in trials providing these data. Three trials (3/29, 10%) did not delimit an entry criterion, or describe their sample with respect to this factor [10-12].

Etiology of Renal Failure

Sixteen trials (16/29, 55%) detailed the etiology of renal failure in their sample [5-9, 12-15, 20-22, 24-28, 33, 34, 37, 38]. Common causes of ESRD in these trials included glomerulonephritis (32%) hypertension (18.5%), and diabetes (12%). Diabetes was a prevalent predisposing factor despite the fact that 5/16 trials (31%) that described ESRD etiology precluded diabetics [7, 9, 24-27, 37].

Comorbidities
Eleven trials provided information regarding common comorbidities in their sample [5-8, 10, 17, 22, 31, 32, 35, 36, 38]. Then average prevalence of common comorbidities among these trials included hypertension (71%), cardiovascular disease (34%), and diabetes (21%). Diabetes was prevalent in 4/29 trials (14%) providing these data [17, 22, 33, 38]. However, at least 11/29 trials to date (34%), including 9/13 RCTs (69%), have excluded patients with diabetes [7, 9, 26-29, 31-34, 37, 40, 41]. Other trials have excluded patients with ischemic heart disease [8, 33, 34], and congestive heart failure [10, 24-27, 36].

Overview of the Exercise Interventions

Duration

Duration ranged from 6 weeks [30] to 4 years [36]. The majority of interventions extended for 3-6 mo. [8-16, 18-22, 27-29, 31-35, 37], with 3 trials of shorter duration [23, 30, 38] and 4 trials of longer duration [5, 6, 17, 24-26, 36]. Kouidi et al [36] have conducted the longest trial to date (4yr).

Modality

Nineteen trials (19/29, 66%) involved aerobic training as the sole exercise modality [5-8, 11, 15-19, 22-30, 34, 37, 38]. Cycle ergometer training, walking/jogging, aerobics, calisthenics, swimming, and ball games were reported among these trials. Nine trials (9/29, 31%) combined aerobic training with some form of strength training [9, 10, 12, 20, 21, 31-33, 35, 36]. Strength training interventions in these trials were generally not adequately described [9, 31, 32, 36], were of low intensity [9, 10, 12, 20, 21, 31-33, 35, 36], and/or involved lower extremity training only [12, 33, 35]. Only one trial to date [15, 16] has prescribed a progressive resistance training (PRT) intervention targeting the upper and lower
extremities performed at a relatively high intensity (10-15RM) as currently recommended for improving the musculoskeletal fitness of healthy adults and the elderly [43].

**Delivery**

- Exercise training has been prescribed:
  - In non-dialysis time at a training centre in 12/29 trials (41%) [5-7, 9, 15-18, 24-26, 28, 29, 31, 37],
  - During HD treatment in 11/29 trials (38%) [8, 10, 11, 12, 19, 22, 23, 30, 33, 34, 38],
  - In non-dialysis time at a training centre + at home in 2/29 trials (7%) [13, 14, 27],
  - During HD treatment + at home in 1/32 trial (3%) [20, 21].

  Additionally, 3 RCTs (3/29, 10%) assigned patients into treatment groups that trained in separate locations, including in non-dialysis time in a training centre [32, 35, 36], at home [32, 35] and/or during HD [32, 35, 38].

**Frequency**

Exercise training was typically prescribed 3-4 sessions/wk (Tables 1-3) [8, 9, 11, 16, 18, 19, 22, 24-36, 38]. In two RCTs (2/29, 7%), subjects randomized to home-based training were prescribed ≥5 training sessions/wk [32, 35]. Painter et al [20, 21] prescribed home based exercise 5-6 sessions/wk for 8 weeks followed by intradialytic training 3 sessions/wk for 8 wk. One trial (1/29, 3%) did not report on the frequency of exercise training [5, 6].
Intensity

Aerobic training interventions were generally of moderate intensity and progressed according to tolerance as the conditioning of the patient improved (Tables 1-3). Two trials however, prescribed and maintained aerobic training at a relatively low intensity (≤60% of maximal effort) [18, 38]. Additionally, several trials did not mention how aerobic training intensity was gauged [9, 10, 11, 22].

Strength training interventions were generally prescribed at a low to moderate intensity [9, 10, 12, 20, 21, 31-33, 35, 36], with 1 trial (1/29, 3%) prescribing higher-intensity PRT [15, 16] (Tables 1-3).

Duration of Aerobic Training Sessions

In general, the duration of aerobic training sessions ranged from 30-60 min/session, with a few trials exceeding this duration with the inclusion of warm-up and cool-down periods [32, 35, 36]. Two trials (2/29, 7%) maintained aerobic training sessions to ≤20 min/session [28, 33]. One trial (1/29, 3%) did not define the duration of aerobic training per session [5, 6].

Supervision

Eighteen trials (18/29, 62%) reported qualified health professionals including study personnel supervised exercise training sessions [5-10, 12-16, 24-26, 29, 31-37]. Nine trials did not provide details regarding supervision [11, 17, 18, 22, 23, 27, 28, 30, 38]. In one trial by Painter et al [20, 21], which combined home-based and intradialytic training, subjects trained independently in both locations. In another trial by Painter et al [19], the first half (3 mo.) of an intradialytic cycling program was directly supervised, while the latter half was not. Home-based interventions were never directly monitored however regular contact with study personnel was reported as being provided [13, 14, 20, 21, 27, 32, 35].
**Compliance**

Nine trials (9/29, 31%) provided information regarding compliance to exercise training (e.g. sessions attended). In these trials [7, 8, 13-15, 19, 22, 23, 29, 37], compliance ranged from fair (43%) [7] to excellent (99%) [23]. However, no trial to date has provided an a priori definition of “compliance” within their methods section.

**Adverse Events**

Thirteen trials (13/29, 45%) have reported that no serious complications have resulted from participation in the prescribed exercise intervention [7, 9, 10, 12-14, 22, 23, 29, 32, 34, 35, 36]. Trials have noted that hypotension has been induced by exercise training [33, 38] though not always presenting with regularity [13-15]. One trial reported an acute gastrointestinal hemorrhage in an exercising subject [16]. DePaul et al [33] reported more adverse events in exercising versus non-exercising patients, citing complaints such as fatigue (n=1), soreness (n=1), hypotension (n=1), foot ulcer (n=1) and foot pain (n=1). No other serious adverse events have been reported in the 29 trials presented in this review. However, to date, no trial has provided an a priori definition of “adverse event” within their methods section.
ADAPTATIONS TO EXERCISE TRAINING IN HEMODIALYSIS

Documented adaptations to exercise training in the 29 trials reviewed are presented in Tables 1-3. A synopsis of these findings highlights some important physiological, functional, and psychological benefits of exercise training in this cohort.

Physiological Adaptations to Exercise Training

*The Cardiorespiratory System and Aerobic Capacity*

Several trials have reported that HD patients can significantly increase peak oxygen consumption ($VO_2^{peak}$) 17-23% by performing aerobic training during non-dialysis time [16, 17, 24-27, 29], during dialysis [19], and at home [35]. By contrast, a few trials have reported no significant improvement of $VO_2^{peak}$ with aerobic training, which may perhaps be due to prescribing low intensity (<60% $VO_2^{peak}$) [24] and/or short duration (10-20 min/session) training [28]. Moreover, it has been well documented that oxygen consumption in this cohort is limited at the peripheral level (i.e. at the skeletal muscle) [40], which is not optimally enhanced with aerobic exercise training alone [8]. In support of this, the magnitude of improvement in $VO_2^{peak}$ secondary to combined (aerobic and strength) training (41-48%) [9, 31, 32, 35, 36] is notably superior to studies prescribing aerobic training only (17-23%). No studies have directly compared aerobic and strength training evaluating this outcome, or assessed $VO_2^{peak}$ after isolated strength training.

Central, intermediary and peripheral cardiorespiratory system adaptations to exercise training documented in the literature are presented in Tables 1-3.
Cardiac Functioning

Deligiannis et al [32] in a RCT demonstrated that 6-months of combined training on nondialysis days improved left ventricle mass index, ejection fraction, cardiac output index, and stroke volume index. Another RCT by the same authors [31] revealed that 6 months of combined training could significantly increase heart rate variability index and the standard deviation of the R-R interval, while reducing the prevalence of arrhythmias (Lown class>II).

Muscle Architecture and Neuromuscular Control

Kouidi et al [9] reported in an uncontrolled trial of 7 patients that cross-sectional area of type I and II muscle fibres obtained from the vastus lateralis significantly increased 2831±846 to 3565±764μm² and 2683±763 to 3319±1049μm², respectively, with 6-months of combined aerobic and strength training. Further, the ratio of type I to type II fibres improved from 54.6:45.4 to 31.6:68.4, which is reported to be near normal (1:2) for this biopsy site.

Ultrastructural analysis revealed that the muscle appeared more normal, including positive adaptations of the capillaries and mitochondria. The authors also noted activation of satellite cells and an increased number of leukocytes and natural killer cells. Motor conduction of the peroneal nerve also significantly improved (p<0.05). By contrast, Moore et al [8] observed no hypertrophy secondary to 6 months of intradialytic aerobic training, which is not unexpected given that aerobic training is not the preferred exercise modality for eliciting myogenic adaptation.

Components of Metabolic Syndrome

Miller et al [22] demonstrated that hypertensive patients could significantly reduce predialysis and postdialysis systolic blood pressure after 3 months of intradialytic cycling. The reduction in blood pressure was accompanied by a
reduction in antihypertensive medications (-36%, p<0.018) resulting in a cost savings of $885 per patient annually. Additional trials have observed reduced resting blood pressure [15, 17, 32], and blood pressure during maximal exercise [32] with >3mo of aerobic, or combined training. Other studies have expressed such findings anecdotally [5, 6, 19, 24].

Goldberg and colleagues [5, 6, 24-26] demonstrated that non-diabetic HD patients could significantly reduce fasting plasma glucose and insulin concentrations, while significantly increasing insulin binding affinity and glucose disappearance rate with 8-12 months of aerobic training. The authors [5, 6, 24-26] also reported increased fasting plasma high-density lipoprotein (HDL) cholesterol, reduced very-low-density lipoprotein (VLDL), reduced VLDL triglyceride, and reduced total plasma triglyceride secondary to aerobic exercise training.

To date there have been no studies investigating the effects of exercise training on visceral obesity in this cohort, or studies of insulin sensitivity and glucose control in diabetic patients receiving maintenance HD.

Dialysis Adequacy

One uncontrolled trials has demonstrated an improvement in dialysis adequacy (Kt/V) with 6 months of intradialytic aerobic training using cycle ergometers [11]. By contrast, two trials implementing shorter training durations (7 and 8 wk) have not observed an improvement in Kt/V [30, 38]. Evidence suggests that a single, acute bout of intradialytic cycling can significantly enhance the removal of urea, creatinine and potassium during HD by significantly reducing post-dialysis rebound of these damaging solutes [41]. Intradialytic exercise training could enhance dialysis adequacy chronically via this same mechanism [3].
However, this hypothesis has not yet been rigorously investigated within a longitudinal RCT [3].

**Functional Adaptations to Exercise Training**

*Muscular Strength*

Headley et al [13, 14] prescribed high-intensity PRT to elicit improvements in muscular strength in HD patients. Four additional trials [9, 10, 12, 33] reported improved muscular strength with regimens involving lower-intensity strength training. By contrast, Meng et al [23] reported no significant improvement of lower body strength secondary to 6 weeks of intradialytic cycling. This finding is not unexpected given that aerobic training is not the preferred modality for improving muscular strength, unlike resistance training [42].

*Functional Performance*

Hemodialysis patients can significantly improve exercise capacity (i.e. 6-minute walk distance) secondary to PRT [13] or combined training [10, 21]. Other functional performance outcomes reported include increased maximal walking speed [13, 20, 21], habitual walking speed [20, 21], and sit-to-stand movement speed [13, 20, 21].

*Disability*

Independence in activities of daily living has not specifically been measured after exercise in this cohort. However, in the longest trial of exercise training conducted with HD patients, Kouidi et al [36] demonstrated that combined training on non-dialysis days significantly improved the likelihood of returning to work after 1 and 4 years of training.
Psychological Adaptations to Exercise Training

Depression

Carney et al [27], in a RCT, showed that aerobic training alleviated depression to a greater extent than participation in a social support group in this cohort, as evaluated by the Beck Depression Inventory (BDI) [43] (p<0.05). Significantly reduced BDI scores following 3-12 months of aerobic exercise training have been observed in other trials [24, 25, 29]. Kouidi et al [29] suggested that the most severely depressed patients benefited to the greatest extent.

Quality of Life

Several trials of exercise training in HD patients have evaluated Medical Outcomes Trust Short-Form 36 (SF-36) [44] scores as health-related QOL outcome measures. Improved perceptions of 'physical functioning' have been observed secondary to 3 to 5 months of aerobic [34, 37] and combined training [12, 20, 21]. Painter et al [20, 21] reported improvements in other SF-36 QOL domains including: 'role physical' [20, 21], 'bodily pain' [20, 21], 'general health' [20, 21], 'vitality' [20], and the 'physical component scale' [20, 21], especially in patients with low baseline perceptions of physical functioning. Oh-Park [12] showed improved 'mental health' scores with combined training performed during HD. One trial did not yield improvements in any SF-36 scores [33]. The authors [33] speculated that the lack of significance could be due to the fact that their samples had high functional status at baseline and/or their study was inadequately powered. Improved measures of QOL have been ascertained in this cohort using other scales [31], including the Spitzer QOL Index (QLI) [45].
DISCUSSION

Overall, the evidence gathered in this critical review suggests that appropriately prescribed exercise involving aerobic and/or resistance training modalities, is safe and beneficial for HD patients. Planned exercise can induce a myriad of positive health and clinical adaptations in this cohort, which may be associated with enhanced quality and quantity of life. However, current limitations within this body of the literature may be partially responsible for the fact that exercise training is not routinely recommended or prescribed in this cohort by practitioners [3, 4]. Despite nearly 3 decades of research demonstrating the benefits of exercise in ESRD, advocacy for exercise has been notably absent from official position stands and policy documents until the publication of a brief supportive statement in the recent Kidney Disease Outcomes Quality Initiative (KDOQI) in April 2005 [46].

Thirteen trails (13/29, 45%) reviewed were RCTs. Several of these RCTs were methodologically limited according to current standards of reporting [47]. Limitations were evident with respect to: statistical analyses where only 2 studies mentioned utilization of intention-to-treat strategy; the limited involvement of blinded outcomes assessors; and the inadequate reporting of subject characteristics, interventions, and outcome measures, including safety and compliance. Further, the external validity of 9/13 (69%) RCTs reviewed is compromised by the fact that these trials precluded diabetics. Diabetes has become the leading cause of ESRD in the United States affecting approximately 45% of newly diagnosed patients [1]. Currently, over 35% of patients with ESRD in the US are diagnosed diabetics [1].
Thorough and standardized reporting [47] is required of future clinical trials of exercise training in HD patients. Subject characteristics should be clearly described, including the etiology of renal failure and comorbidities. Interventions should be thoroughly defined with respect to frequency, intensity, modality, session duration, delivery, and supervision. This is essential for determining the exercise prescription required to positively affect specific outcomes. Clearly, the fact that some trials we reviewed observed no effect of exercise training on certain outcomes [8, 15, 23, 28, 30, 38] does not imply that exercise, in general, is ineffective in this cohort, but rather suggests that the exercise dose and/or modality prescribed was insufficient to positively affect the desired measure. Compliance to training should be defined a priori to determine the feasibility and generalizability of prescribing exercise training in this patient population. Thorough reporting of adverse events, including a priori definitions, is necessary to determine the risk to benefit ratio of exercise training in this cohort, which is suggested to be favorable among other chronically diseased populations [42].

The documented adaptations to exercise training in the 29 trials reviewed represent important areas of benefit to the HD population. The physiological, functional, and psychological adaptations induced by exercise may be associated with reduced cardiovascular risk profile, improved QOL, and extended lifespan. At present however, robustly designed studies are required to further evaluate many of these, and other health-related and clinical outcomes, including skeletal muscle wasting, osteoporosis, the malnutrition-inflammatory complex, dialysis adequacy, metabolic syndrome, endothelial dysfunction, disability, depression, self-efficacy and QOL. Future investigations should also be conducted explicitly with targeted subpopulations within this cohort, including those suffering from clinical
depression, obesity, hypertension, and insulin resistance/diabetes. For example, there are currently no trials evaluating insulin resistance/glucose homeostasis in diabetics on HD, nor are there trials of exercise in patients with clinically diagnosed depressive illness. Additionally, few studies have specifically targeted patients >65yr, an increasingly large cohort with a greater burden of complex comorbidities which may impact on both feasibility and benefit of exercise training interventions.

Trials prescribing aerobic and resistance training modalities, independently and in combination, should be conducted. It could be hypothesized that combined interventions elicit superior adaptations of VO2peak (central and peripheral) and other health-related outcomes than either intervention on its own, however studies isolating each modality will be useful for determining which beneficial adaptations can be assigned to each modality specifically. At present, there is only one report involving PRT in this cohort [13, 14]. This is a significant gap in the literature given the risk and critically important outcomes associated with skeletal muscle wasting in patients with chronic uremia [48]. PRT may also be a more feasible exercise modality in this cohort as patients with congestive and ischemic heart disease, who cannot engage in vigorous aerobic training, may be able to perform robust PRT safely. PRT is currently widely advocated and prescribed for health benefits in various healthy, and chronically diseased cohorts [42], though not in HD patients as yet.

Various methods of exercise delivery should continue to be investigated, compared and contrasted, as recently performed by Kouidi, Konstantinidou et al [35, 36]. It should be noted however, that training volume in these trials was not equated. Thus, the greater cardiorespiratory benefits achieved by patients training on non-dialysis days could primarily be attributed to the fact that they received a
greater volume of training. Future trials should therefore equate the volume of training to determine which method of training is more feasible, and beneficial. Novel exercise equipment customized to the HD setting will likely have to be developed to investigate such hypotheses.

Long-term behavioral change is the challenge to exercise prescription in most clinical cohorts, and patients receiving maintenance HD for the management of ESRD are no exception. Only 4 trials were identified which were >6 months in duration [5, 6, 17, 24-26, 36], compliance was often not reported, and virtually no information was presented on psychological, demographic, or clinical predictors of adoption and adherence in the patients studied. Future studies can contribute to the successful dissemination of their research findings and overcome barriers to behavioral change if such analyses are conducted and compliance, as well as reasons for non-compliance, is carefully documented.

The available literature supports the clinical utility of exercise participation for HD patients. Although methodological shortcomings exist, and gaps in knowledge are clearly evident in some specific areas, there is sufficient empirical published evidence to support the addition of exercise recommendations to clinical guidelines, as recently published by the KDOQI [46]. Further research is required to advance these guidelines toward the development of position stands on exercise prescription. There is no other available medical treatment with the capacity to induce beneficial adaptations across as wide a range of physiological, functional, psychological, and clinical domains as appears possible with sufficient doses of aerobic and resistance training. In addition, it appears possible to creatively modify the sedentary, often negative, and depressing ambiance of the typical HD unit by bringing the exercise treatment directly into this medical setting. Such complete
integration of exercise and medicine is critical for its acceptance by practitioners as part of mainstream medical care, for enhancing compliance and safety, and perhaps for the actual improvement of dialysis adequacy itself.
REFERENCES


Table 1: Uncontrolled Trials of Exercise Training in Hemodialysis

<table>
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<tr>
<th>Authors (year) Country</th>
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<th>Study Groups (n)</th>
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<td>Exercise (n=7)</td>
<td>NDT AER Cycle erg, walking, jogging, calisthenics 65-75% HR_{max} To tolerance</td>
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NDT=nondialysis time; ID=intradialytic; HB=home based; AER=aerobic training; COMBO=aerobic plus lower-intensity strength training; PRT=progressive resistance training; GXT=graded exercise test; RPE=rating of perceived exertion; HR_max=maximal heart rate; SBP=systolic blood pressure; DBP=diastolic blood pressure.

Note: All p values calculated by comparing within group change over time (i.e. pretest-posttest)
<table>
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<tr>
<th>Authors (year)</th>
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NDT=nondialysis time, ID=intradialytic, HB=home based, AER=aerobic training; COMBO=aerobic plus lower-intensity strength training; AT=anaerobic threshold; GXT=graded exercise test; SBP=systolic blood pressure; DBP=diastolic blood pressure; Significant over time versus control group; Significant versus baseline value
### Table 3: Randomized Controlled Trials of Exercise Training in Hemodialysis

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NDT=nondialysis time, ID=intradialytic, HB=home based, AER=aerobic training; COMBO=aerobic plus lower-intensity strength training; PRT=progressive resistance training; QLI=Quality of Life Index; HRV=Heart Rate Variability; VE_{peak}=peak ventilation; HR_{peak}=peak heart rate; GXT=graded exercise test

*Significant change over time versus comparison group(s);
†Significant versus baseline values within group;
*Significant versus control group only;
*Significant change over time between Exercise Group 1 and Exercise Group 2.
CHAPTER 4

Progressive Resistance Training During Hemodialysis: Rationale

and Method of a Randomized Controlled Trial
ABSTRACT

Skeletal muscle wasting in hemodialysis patients has been well documented. The rationale for prescribing progressive resistance training (PRT) in this cohort in an attempt to reverse this catabolism and induce a wide spectrum of physiological, functional, and psychological health-related adaptations is extremely strong. Unfortunately, the barriers to exercise adoption in this cohort are many, which may explain the persisting sedentariness of this population, and the lack of widespread clinical programs such as are now commonplace in cardiac rehabilitation and pulmonary rehabilitation units. Current health care practices for hemodialysis patients do not address the negative health issues of inactivity and muscle wasting. Therefore, we conducted the first randomized controlled trial to prescribe PRT during maintenance hemodialysis treatment. The purpose of this paper is to describe the methodology we utilized for implementing intradialytic PRT in a conventional outpatient hemodialysis clinic, and to determine to overall perceptions of the nursing staff at this unit toward this novel endeavor. Potential areas for modification of PRT regimens in this setting are also presented.

KEYWORDS: Hemodialysis, Exercise, Muscle, Quality of Life, Health
A RATIONALE FOR RESISTANCE TRAINING DURING HEMODIALYSIS

According to the United States Renal Data System (USRDS), the national incidence and prevalence of end stage renal disease (ESRD) continues to rise each year [1]. Over 100,000 new cases of end stage renal disease (ESRD) were reported in the USRDS 2004 report, and nearly 92,000 of these individuals commenced hemodialysis treatment (HD) as renal replacement therapy [1].

Although advances in dialysis techniques have extended the lifespan of HD patients, this treatment alone does not ensure the preservation of quality of life (QOL). Patients receiving maintenance HD typically suffer significant impairment of QOL as compared to healthy individuals, and individuals with successful kidney transplants [2]. As incidence of ESRD continues to increase [1] with a concomitant rise in the competition for kidney transplants, it has become evident that greater efforts must be directed toward restoring and enhancing QOL of individuals receiving long-term hemodialysis treatment.

Among chronic illnesses, ESRD is prominently associated with skeletal muscle wasting [3]. This catabolism, with its intimate relation to the malnutrition-inflammatory complex [4,5], is the most significant predictor of mortality in this cohort [6]. The structural abnormalities of skeletal muscle at the cellular and subcellular level have been well-described [7-14]. Concomitant metabolic changes include decrements in protein synthesis, and glucose and lipid metabolism, influenced to a large extent by a catabolic milieu, reduced insulin sensitivity [3], and mitochondrial dysfunction [15]. Metabolic deficits resulting from skeletal muscle wasting can increase visceral obesity, which elevates risk of cardiovascular disease, the primary cause of death in ESRD [1]. The functional consequences of catabolism
obviously include weakness, fatigue, reduced ability to generate force, reduced exercise tolerance, and impaired performance of activities of daily living (ADL), all of which are highly prevalent amongst hemodialysis patients [16-19]. Overall, muscle catabolism in ESRD is associated with increased morbidity and mortality, and significantly reduced QOL.

The etiology of skeletal muscle wasting in hemodialysis patients has not completely defined. Acidosis, oxidative stress, hyperparathyroidism, neuropathy, protein-restricted diets, anorexia, cytokines, hemodialysis treatment, and other factors appear to be involved [4]. Lifestyle restrictions, including the inactivity imposed by 12-18 hours per week of maintenance HD treatment, may also contribute markedly to this degenerative and debilitating process. Prevalent psychological impairments such as depression and anxiety may negatively impact upon lifestyle choices regarding optimal diet and exercise, which may further compound the catabolic cascade. Hemodialysis patients are significantly less active than healthy, sedentary individuals [20], and low intrinsic motivation has been identified as a major barrier to prescribing exercise in this cohort [21].

To foster exercise adoption in this cohort, several investigators have prescribed exercise during hemodialysis treatment [14, 21-26]. Studies evaluating the efficacy of intradialytic exercise to date have utilized cycle ergometer training as the major [21, 23, 24, 26] or sole component [14, 22, 25] of the exercise regimen. These trials have demonstrated that exercise during dialysis can induce significant physiological, functional, and psychological benefits, is feasible to administer, has important clinical relevance, and results in no serious adverse events [27]. However, although cycle ergometer training appears to be safe and effective when performed during dialysis, aerobic conditioning is not optimal for inducing muscle anabolism.
Progressive resistance training (PRT), by comparison, has become well-established as the modality of choice for inducing skeletal muscle hypertrophy in healthy adults and those with frailty and/or chronic disease [28]. Unfortunately, there has been very little exploration of the myogenic, and overall health-related impact of PRT in hemodialysis patients to date. Kouidi et al [12] in an uncontrolled trial involving 7 hemodialysis patients reported that an exercise program performed on nondialysis days resulted in Type 1 and Type 2 muscle fibre hypertrophy (29%) with a normalization of skeletal muscle morphology at the ultrastructural level. However, the multi-modal intervention implemented in this study, involving both aerobic and low-intensity strength training, precludes assigning the beneficial changes specifically to the use of strengthening exercise. To date, Headley et al [29] have conducted the only trial prescribing PRT in this population. However, this study did not evaluate muscular adaptations. Moreover, similar to Kouidi et al [12] the intervention was also performed on nondialysis days, few patients (N=10) were enrolled, and there was no control group.

The rationale for prescribing PRT to hemodialysis patients is extremely strong given the elevated risk of insidious myopathy in this cohort [30, 31-33]. However, the barriers to exercise adherence in this cohort are many. Access solely to sedentary pursuits such as watching television is typically the only leisure-time activity available to patients in most dialysis units [27]. Twelve to 18 hours per week of this enforced sedentary behavior, coupled with low occupational and recreational activity in this cohort, likely exacerbates muscle catabolism and its associated health-related deficits. Furthermore, it has become evident that there is a lack of widespread rehabilitation programs for hemodialysis patients [27], such as are now commonplace.
in cardiac rehabilitation and pulmonary rehabilitation units, and exercise counseling practices among nephrologists remain low [34].

We postulated that full body PRT could be carried out during routine, outpatient hemodialysis treatment sessions. Such an approach creatively modifies the health care setting and may influence patients to assume greater control over their illness and lives. Intradialytic PRT can be easily supervised, may maximize adherence and progression, requires no additional time commitment by the patients, may relieve boredom and negativity associated with dialysis sessions, and may facilitate behavior change by constant patient role modeling. In our current randomized controlled trial [35, 36], we hypothesized that our PRT regimen would be feasible to administer, safe to perform, and beneficial with respect to inducing muscular hypertrophy and associated health-related adaptations in our patients. Our methodology for applying PRT in this novel setting was is described below in detail to facilitate replication of this intervention in clinical settings.

A METHOD FOR INTRADIALYTIC RESISTANCE TRAINING

Setting and Study Design

The present clinical trial was conducted at outpatient haemodialysis units of the St. George Public Hospital of Sydney, Australia. Ethics approval was obtained from the South Eastern Sydney Area Health Service and the University of Sydney Ethics Committees. The initial phase of the study involved a randomized controlled trial comparing patients receiving usual care HD treatment (wait-list control group), with patients receiving usual care haemodialysis treatment plus PRT (exercise group) for
12 weeks. Following this initial phase of the study, subjects randomly assigned to the control group performed PRT for 12 weeks, while the E group will continue to perform PRT for an additional 12 weeks (24 weeks total). This crossover study design was utilized for ethical reasons, given that all PRT sessions performed by the exercise group were performed in the presence of those subjects randomly assigned to the wait-list control group.

The Medical Screening Process

Patients were approached for participation in the trial if all of the following criteria were met: (1) age ≥ 18, (2) basic comprehension and communication of English, (3) maintenance haemodialysis treatment received for ESRD for ≥ 3 months, (4) adequately dialyzed (Kt/V≥1.2) and stable on haemodialysis, (5) expected to remain on hemodialysis treatment for at least 6 months, (6) ambulatory with or without an assistive device but without direct assistance of a person for at least 50m, (7) no acute or chronic medical conditions which would make PRT potentially hazardous or primary outcomes impossible to assess [37].

Given that patients of various ages, fitness levels, comorbidities, and stability on dialysis were likely to be encountered a staged medical screening process to determine patient eligibility was warranted. The medical screening process involved: (1) Review of the patients medical record and clinical haemodialysis notes by the onsite exercise physiologist, (2) Review of that information by the principal investigator (M.F.S.), (3) Interview of patient by the onsite exercise physiologist, (4) Consent of the nephrologist of the patient via medical screening checklist, (5) Physical examination and interview by a study physician. The purpose of the examination was
to determine patient level of stability during HD, and to detect any signs or symptoms indicate of a possible contraindication to intradialytic PRT.

If there were no potential contraindications and the individual was determined to be stable, the patient was then approached for their consent to participate in the trial. Approximately 18% (23/128) of patients screened were excluded from the training program due to medical contraindications. Primary reasons for medical ineligibility and their relative frequency in our trial over the past 2 years are presented in Table 1. Known cardiac instability, including angina and/or shortness of breath, was the most common contraindication to PRT in our study sample, accounting for 43.5% of the medically ineligible patients.

Approaching Eligible Patients

It was expected that many medically eligible patients approached for participating in the trial would simply not wish to participate, based on previous published data of adherence rates in this cohort [14, 23, 24]. We ensured that every attempt was made to guide patients into the exercise program through overcoming their fears regarding exercise, or reluctance to participate. Upon initial approach, each patient was given a very brief lay description of the study including its purpose. The on-site exercise physiologist addressed any questions, or concerns of the patient accordingly. In our experience, recruiting a patient was commonly a 1 or 2-week long process. This process obviously involved a high degree of rapport and trust building.
The Training Regimen

**PRT Equipment**

All weight training equipment was kept on a trolley (Figure 1) that could be wheeled between patients. The trolley was stored in a spare room in the renal unit when not being used. The PRT regimen was implemented using free-weight dumbbells (Australian Barbell Company, Mordialloc, VIC, Australia) for upper body exercises, and weighted ankle cuffs (Australian Barbell Company, Mordialloc, VIC, Australia) for lower body exercises. Dumbbell loads ranged from 2 to 15 kg. Loading of the weighted ankle cuffs ranged from 0 to 15 kg. Equipment also included Thera-Band™ tubing (Akron, Ohio, USA) for one exercise targeting the hamstrings.

**Specific PRT Exercises**

Upper body exercises included the shoulder press, side shoulder raise, triceps extension, biceps curl, and external shoulder rotation (Figure 2). Lower body exercises included seated knee extension, supine hip flexion, supine hip abduction, supine straight-legged raise, and hamstrings curl (Figure 2). The abdominal musculature was targeted with either bilateral leg raises in a supine position or bilateral leg lifts in a seated position, depending on subject preference and level of ability (Figure 2).

**Method of Delivery**

All PRT exercises were performed in a seated or supine position in a standard hemodialysis chair (LA-Z-BOY Pty Ltd, Moorebank, NSW, Australia). The limb containing the vascular access, forearm arteriovenous fistula (AVF) or forearm Gortex fistula was exercised immediately prior to each treatment session while seated in a firm stationary chair in the waiting area of the unit, unless a vas catheter access precluded upper body training.
Frequency, Intensity, Volume, and Progression

Patients exercised 3 times per week during dialysis under the supervision of an exercise physiologist. During each training session, two sets of 8 repetitions of the 10 specific exercises targeting major muscle groups of the upper and lower extremities, were performed at a rating of perceive exertion of 15-17 ("hard" to "very hard"). The exercise physiologist adjusted training loads accordingly, as the strength of the patient improved.

Timing of the Regimen

Dialysis session times ranged from 4 to 6 hours in our sample population. The average duration of an intradialytic exercise session was approximately 45 minutes. In general, the PRT regimen was delivered before the final hour of treatment, however on occasion subjects not prone to late onset, dialysis-induced hypotension, were exercised up to 10 minutes prior to treatment cessation. In over 2.5 years of experience to date, with 34 subjects performing 12 or 24 weeks of PRT as 79.8% compliance, no adverse, dialysis-related events have resulted from such timing of the PRT regimen. Typically, no adjustment to the dialysis regimen was required, although blood flow rates were reduced by up to 50 ml/min by the renal nursing staff if the dialysis machines were prone to alarming due to elevated arterial and/or venous blood pressures in some patients.
ASSESSMENT OF PROGRAM BY THE DIALYSIS NURSING STAFF

We asked 27 members of the renal nursing staff in the HD unit at St. George Public Hospital to complete an anonymous survey to obtain their assessment of the perceived benefit and/or burden of our PRT exercise program. Questions and results of the survey are presented Figure 3. Overall, 96% (n=26) of the renal nurses 'strongly agreed' or 'agreed' that the PEAK exercise program was of significant benefit to the patients involved (Figure 3). The majority of the nurses also agreed that exercise is safe for this cohort and should be integrated into clinical practice (Figure 3). Sixty-three percent of the nurses indicated that they would be willing to deliver the exercise regimen if it did not interfere with work, while 26% were clearly opposed to this option (Figure). There was disparity noted in answering a question regarding the interference of the exercise regimen with routine clinical care. Thirty-three percent suggested that the exercise program interfered with routine care, while 45% suggested that it did not. In a comments section provided at the end of our survey, 3 nurses mentioned that answering the occasional alarming dialysis machine during intradialytic PRT was a problem.

POTENTIAL MODIFICATIONS OF THE EXERCISE PRESCRIPTION

Despite the limitations encountered while exercising in a standard HD chair (LA-Z-BOY Pty Ltd, Moorebank, NSW, Australia), proper postural control was strongly emphasized. Many patients were capable of moving to the edge of the chair to facilitate technique and utilize a greater range of motion during upper body
exercises, thereby optimizing the opportunity for training induced adaptations. However, it has become evident that if PRT regimens are to be included in the mainstream of medical practice in the long term, certain modifications to the training regimen, chair and equipment specifications will be required.

Large muscle groups of the upper extremity, including the latissimus dorsi and pectorals were not sufficiently targeted with our regimen of resistance exercises. This was due to the fact that all upper body exercises were performed in an upright, seated position using dumbbells. A potential solution to more effectively target the chest and back musculature is to adapt resistance training devices, which optimally recruit these muscles from a seated position, to the hemodialysis setting to optimally target these muscles.

There may also be a strong rationale for simply prescribing all upper body exercises just prior to routine dialysis treatment in the waiting area of the dialysis unit, given that it takes half the time to train the upper body bilaterally (i.e. both extremities simultaneously) versus unilaterally (i.e. one extremity at a time). Training access for the patient remains optimized, as the PRT is still integrated into the dialysis setting, although patients must be willing to arrive early to perform these upper body exercises.

Four lower body exercises in our regimen were performed using weighted ankle cuffs. These exercises primarily targeted the quadriceps and thigh abductors. One additional exercise, a seated leg curl performed using Thera-Band™ tubing (Akron, Ohio, USA) targeted the hamstrings. In our experience, it was difficult to target the gluteal and calf muscle groups while seated in the standard hemodialysis chair. Additionally, while nearly all lower body exercises performed provided continuous overload stimulus throughout the training period for all patients, the knee
extension exercise did not, as the weight cuffs could only be loaded with up 15 kg, which was not challenging for many of the patients by the end of their training period. Thus, it may be of importance to develop training devices, perhaps in concert with an adapted hemodialysis chair, which could more effectively recruit the lower body musculature while the patient is in a fixed seated position.

Supervision of patients needs to be considered, given that financial restrictions in most health care settings would preclude the hiring of full-time exercise physiologists to directly monitor all aspects of the training regimen. According to our survey, 63% of the renal nursing staff would be willing to deliver the PRT regimen to their patients if this did not interfere with their regular nursing duties. In our experience, patients are capable of performing a significant proportion of the training on their own. However, changing of the ankle cuffs, stabilizing the cart while performing hamstring curls, and preventing the chair from rocking were all dealt with by the supervising exercise physiologist in our trial, thus limiting complete independence in the performance of PRT.

SUMMARY

Preliminary evidence from our ongoing randomized controlled trial [35, 36] suggests that intradialytic PRT can creatively modify the health care environment for hemodialysis patients, and enable these individuals to enhance their health status. The method outlined here is feasible within the constraints of typical outpatient hemodialysis clinic and appears to be safe and effective in over 2.5 years of experience to date [35, 36]. However, additional robust clinical trials are needed to
identify optimal modalities and doses of exercise for this cohort, for a broad range of clinical outcomes [38]. Our methodology and future considerations, as presented, may assist in the development of future clinical trials, and the implementation of successful exercise programs within conventional hemodialysis settings throughout the world. Indeed, such efforts are required if the health status and QOL of this special patient population is to be improved.
REFERENCES


Table 1. Medical Exclusions to Intradialytic Resistance Training in PEAK

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Data from 128 patients screened, 23/128 (18%) were excluded for the medical reasons listed.
Figure 1. The weight trolley including dumbbells and weighted ankle cuffs
Figure 2. Specific PRT exercises: (a) shoulder press, (b) side shoulder raise, (c) external shoulder rotation, (d) triceps extension, (e) biceps curls, (f) double leg lifts, (g) seated knee raises, (h) knee extension, (i) straight-legged raise, (j) hip flexion, (k) hip abduction, and (l) hamstrings curl with Theraband™
Figure 3: Results from the survey of renal nurses working in the unit (N=27)

"The PEAK exercise program was of significant benefit to the patients involved" - 40% Agree, 40% Strongly Agree, 11% Neutral, 11% Strongly Disagree, 4% Disagree, 0% Strongly Disagree

"In general, exercise should be integrated into clinical practice for hemodialysis patients" - 30% Strongly Agree, 15% Agree, 15% Neutral, 10% Disagree, 5% Strongly Disagree, 4% Disagree, 0% Strongly Disagree

"I would be willing to implement an exercise program with my patients if it required minimal supervision and did not interfere with my work" - 1% Strongly Disagree, 15% Disagree, 11% Neutral, 41% Agree, 22% Strongly Agree

"The PEAK program interfered with routine care during dialysis" - 22% Strongly Agree, 30% Agree, 15% Neutral, 15% Disagree, 5% Strongly Disagree, 4% Disagree, 0% Strongly Disagree

"Exercise is safe for most hemodialysis patients" - 4% Strongly Disagree, 4% Disagree, 4% Neutral, 22% Strongly Agree, 48% Agree

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CHAPTER 5

Progressive Exercise for Anabolism in Kidney Disease (PEAK): A Randomized Controlled Trial of Resistance Training During Hemodialysis
ABSTRACT

**Background:** Catabolism and skeletal muscle wasting are common and morbid in patients with end-stage renal disease (ESRD). We conducted the first randomized controlled trial of high-intensity, progressive resistance training (PRT) integrated directly into hemodialysis (HD) treatment sessions in an attempt to shift the anabolic/catabolic milieu in patients with ESRD.

**Methods:** Individuals receiving maintenance HD were randomly assigned to: PRT + Usual Care (n=18) or Usual Care Control Only (n=16). The PRT group performed two sets of 10 PRT exercises at high intensity using free-weights targeting upper and lower body musculature 3 times/wk for 12 wks during HD. Outcomes included body composition, strength, functioning, nutritional status and quality of life.

**Results:** Thirty-four patients (64.4yr (31.2-80.5yr), 0.3-16.7yr on HD) were randomized, 29 completed the intervention. Total body strength increased significantly (p<0.01) in the PRT (+24.7±16.6%) versus control group (-2.0±8.9%) as did body weight (p<0.01), thigh (p=0.02) and arm (p=0.01) circumference, and vitality (p=0.05). Inflammatory marker C-reactive protein (CRP) was significantly reduced (p<0.02) in the PRT group. Patients with the lowest estimates of muscle mass and quality and the greatest catabolic milieu at baseline experienced the greatest anabolic shifts in body composition. Energy and protein intake did not change significantly in either group.

**Conclusions:** We have shown for the first time that catabolism and related functional consequences are modifiable by integrating standard anabolic exercise into hemodialysis treatment sessions, without altering dietary intake or usual care.
practices. Enhancement of muscular strength was accompanied by improved body composition and sense of vitality, and reduced inflammation in our cohort.

Keywords: Muscle, End Stage Renal Disease, Quality of Life, Health
INTRODUCTION

According to the United States Renal Data System (USRDS), the incidence and prevalence of end stage renal disease (ESRD) continues to rise each year.\textsuperscript{1} Over 100,000 new cases were reported in the USRDS 2004 report, and nearly 92,000 of these individuals commenced maintenance hemodialysis treatment (HD) as renal replacement therapy.\textsuperscript{1} Over 281,000 patients in the US currently receive HD.\textsuperscript{1} While advances in HD treatment have extended patient lifespan, this treatment alone does not ensure the preservation of quality of life (QOL) in this growing patient population.

One major pathological consequence of ESRD is skeletal muscle wasting or sarcopenia. Many recent empirical reports have documented architectural abnormalities within skeletal muscle in this cohort.\textsuperscript{2-5} Although the catabolic cascade is not completely understood, etiology is multifactorial involving such factors as metabolic acidosis,\textsuperscript{6} protein-energy malnutrition,\textsuperscript{7,8} comorbid illnesses, corticosteroid use,\textsuperscript{9} biological aging, dialysis treatment,\textsuperscript{10} and sedentary behavior exacerbated by 12-18 h/wk of HD treatment. Metabolic impairments associated with the loss of lean body tissue include insulin resistance,\textsuperscript{11} immune system dysfunction,\textsuperscript{12} and reduced peripheral O\textsubscript{2} conductance.\textsuperscript{13} Sarcopenia also negatively impacts mobility, exercise capacity, functional and psychological health status, and QOL.\textsuperscript{12}

Over the past several decades much attention has been directed toward the use of high-intensity progressive resistance training (PRT) as a therapeutic intervention for counteracting catabolism in frail elders and those with certain chronic illnesses.\textsuperscript{14} PRT has become well-recognized as the modality of choice for inducing skeletal muscle hypertrophy and strength adaptations in these diseased cohorts, and is now advocated and prescribed in nursing home residents, cardiac and pulmonary
rehabilitation settings, and community-based falls and frailty programs. The prevalence of malnutrition, disability, and muscle abnormalities in ESRD suggest that PRT may be of significant benefit during HD as well.

The rationale for prescribing PRT to patients with ESRD in an attempt to counteract muscle wasting is extremely strong. However, the barriers to regular participation in robust training regimens are many, and although recent guidelines suggest that exercise is appropriate in this cohort, PRT is not specifically advocated by the *Kidney Disease Outcomes Quality Initiative* (KDOQI) at present. Therefore, we conducted the first RCT to evaluate the efficacy of high-intensity PRT in ESRD with an exercise intervention integrated directly into the dialysis treatment session. We hypothesized that our training regimen would safely elicit anabolic shifts in body composition while improving muscular strength, exercise capacity, psychological health status, and QOL.

**METHODS**

*Setting and Study Design*

The *Progressive Exercise for Anabolism in Kidney disease (PEAK)* trial was conducted at the outpatient HD unit of St. George Public Hospital, Sydney, Australia. The South Eastern Sydney Area Health Service and the University of Sydney Human Research Ethics Committees approved all procedures and written informed consent was obtained from all participants.

Patients were randomized via computer-generated randomly-permuted blocks, stratified by gender in blocks of 4 to: PRT + Usual Care (PRT), or Usual.
Care Control (C) groups. Randomization assignments were generated by an investigator not involved in testing or training, and delivered to patients in opaque sealed envelopes at the completion of all baseline testing.

**Power Calculations**

Sample size estimates were calculated by hypothesized differences between the PRT and C group in thigh muscle cross-sectional area (CSA) on computerized tomography (CT) scan. Based on previous studies, the control group was estimated to have no change while the PRT group was hypothesized to have a +3.5% change in CSA with a SD of ±5.5% after 12 weeks. Setting the alpha at 0.05, and beta at 0.20, a requirement of 40 patients was estimated.

**Patients**

All individuals regularly attending the dialysis unit were evaluated for eligibility. The medical screening process involved a medical record review, a physical examination and interview by a study physician, and clearance from their nephrologist, prior to solicitation of interest and written informed consent. Eligibility criteria included: (1) ≥18 years of age; (2) on HD for >3 mo; (3) without acute or chronic medical conditions precluding PRT or the collection of outcome measures; (4) independent ambulation with or without an assistive device for ≥50m; (5) adequately dialyzed (Kt/V≥1.2) and stable during HD; (6) cognition and English language sufficient to understand research procedures and provide written informed consent, (7) not currently engaged in a PRT regimen, and (8) a willingness to be randomized and to undergo study protocols.
**PRT Intervention**

The PRT group exercised under the direct supervision of an exercise physiologist during routine HD treatment, 3 times per week, for 12 weeks. All PRT exercises were performed in a seated or supine position in a standard HD chair (L-A-Z-BOY Pty Ltd, Moorebank, NSW, Australia). The limb containing the arteriovenous (AVF) or Gortex fistula was exercised immediately prior to the dialysis session. Temporary vas catheter access precluded upper body training. During each PRT session, two sets of 8 repetitions of 10 exercises targeting major muscle groups of the upper and lower extremities, were performed at a rating of perceived exertion of 15-17 (“hard” to “very hard”) on the Borg Scale\(^{20}\) equivalent to approximately 80% of the 1RM. Upper body exercises performed using dumbbells (Australian Barbell Company, Mordialloc, Australia) included the shoulder press, side shoulder raise, triceps extension, biceps curl and external shoulder rotation. Lower body exercises performed unilaterally using weighted ankle cuffs (Australian Barbell Company, Mordialloc, Australia) included seated knee extension, supine hip flexion, supine hip abduction, and supine straight-legged raise. Seated hamstring curls were also performed, using Thera-Band\(^{\text{TM}}\) tubing (Akron, Ohio, USA) attached to a fixed position on the weight trolley. Abdominal musculature was targeted with bilateral leg raises in a supine position or bilateral leg lifts in a seated position, depending on subject preference and level of ability. No changes to usual care or nutritional consultation were made.
Usual Care Control group

Patients randomized to the control group were provided usual care by the clinical staff of the dialysis unit but were given no instructions or access to exercise equipment. Intradialytic exercise was not part of usual care at this dialysis unit.

Outcome Measures

All outcome measures were taken at baseline and after 12 weeks. All body composition, nutritional status and biochemical measures were performed by blinded assessors. Computerized tomography (CT) scans of the non-dominant mid-thigh to determine muscle CSA and attenuation (low muscle density, indicative of intramuscular lipid infiltration\textsuperscript{21}), and total, intramuscular, and subcutaneous fat areas were collected using a General Electric High Speed CTI Scanner (model no. CEE0459). The digitized images were analyzed as previously reported using NIH Image modified by the investigators for CT scan analysis.\textsuperscript{17} CV of triplicate analysis of area and attenuation measures in this cohort is 0.005%.

Peak force (kg) of the knee extensors, hip abductors, and triceps was measured bilaterally in triplicate using an isometric digital dynamometer (Chatillon CSD 200 Dynamometer, AMETEK, Inc. Paoli, PA, USA) fixed to a stand (CV=9.4%). The best measure for each movement was recorded for each patient and total isometric strength summary measures were created for each patient.

The 6-minute walk\textsuperscript{22} was used as an index of overall exercise capacity. CV of this test is reported to be 5-10% in older or clinical cohorts.\textsuperscript{23}

A blinded dietitian collected all nutritional and anthropometric measures, including body weight, height, and waist, mid-arm and calf circumferences, post-dialysis using standard protocols.\textsuperscript{24} Nutritional status was assessed via Mini-
Nutritional Assessment (MNA). Dietary intake over the previous month was evaluated with an Australian Food Frequency Questionnaire (FFQ) analyzed using FoodWorks software (Xyris Software, Version 3, 1998-2000).

All blood samples were drawn pre-dialysis, prior to the mid-week HD session, at least 48 hours after the previous exercise bout. Additionally, urea kinetics evaluation included the collection of blood urea post-dialysis during the mid-week HD session as well as just prior to the following HD session. Samples possibly affected by acute illness or trauma were discarded and repeated. CRP assays were performed using the Dade Behring Dimension RXL (Deerfield, Illinois, USA). This method is based on a particle enhanced turbidimetric immunoassay (PETRIA) technique using the Dade Behring Dimension RCRP calibrator for standardization. The coefficient of variation (CV) for this test was 2.3%. Results less than the detectable range (<1mg/L) were recorded as 1mg/L. Albumin and creatinine were measured using Beckman reagent on a Beckman LX20 analyzer (Fullerton, CA, USA); CV of 1.5%. Prealbumin was measured by nephelometry using Beckman reagent on a Beckman Image analyzer with an inter-run CV of 4.6%. Hemoglobin, hematocrit, WBC and lymphocyte counts were analyzed on a Roche Sysmex XE2100 analyzer (Basel, Switzerland) using reagent supplied by Roche. Urea was measured using the Enzymatic conductivity method, on a Beckman LX20 analyzer, with a CV of 4.8% at a concentration of 4.4mmol/L.

The Medical Outcomes Trust Short Form-36 (SF-36) survey was used to measure health-related quality of life. The Geriatric Depression Scale (GDS) was used to evaluate depressive symptoms. The Physical Activity Scale for the Elderly (PASE), was used to evaluate leisure and daily habitual activity level apart from the
study exercise. All survey items were interviewer-administered privately, during dialysis treatment.

**Compliance and Adverse Events**

Compliance to training (%) was defined as the number of training sessions attempted divided by the number offered x 100. Changes in health status including acute illnesses, new physical, mental and/or emotional symptoms, change in medication usage, dialysis-related complaints (i.e. headaches, hypotension, cramping) and visits to health care professionals were defined *a priori* and documented via weekly interview and clinical HD notes review. Study-related adverse events were defined as any injury, exacerbation of underlying disease, or any other chronic impairment, ≥2 weeks in duration, attributed directly to the PRT regimen.

**Statistical Analyses**

All available patient data were used regardless of compliance, according to intention-to-treat strategy. Statistical analyses were performed using StatView™ statistical software package (Version 5.0 SAS Institute, Cary, NC). Data were inspected visually and statistically for normality (skewness between −1 and +1). Normally distributed data were described using mean±SD, and non-normally distributed data using median and ranges. Groups were compared at baseline using ANOVA for continuous variables and Chi Square tests for categorical variables. Non-normally distributed continuous variables were log-transformed prior to entry into linear models. Changes over time and group by time interactions were analyzed with repeated measures ANOVA models. Potential confounders were identified from baseline comparisons between groups and used as covariates in additional ANCOVA
models with baseline value and diabetes status as covariates. Relationships between variables of interest were analyzed using simple and forward stepwise multiple linear regression models. A p-value of <0.05 was accepted as statistically significant.

RESULTS

Flow of Subjects

Thirty-four eligible patients consented to participate in the PEAK trial, comprising 33% of the entire dialysis cohort (n=104) as presented in Figure 1. Among the 34 patients randomized, 5 were unavailable for follow-up testing (Figure 1). Outcome data are presented on the 29 patients available for both testing periods.

Baseline Characteristics

Patients were comparable at baseline except for a higher proportion of diabetics in the control group (Table 1). There was a high burden of chronic disease and medication use, and 18% of subjects (6/34) had MNA scores <24 (at risk, or undernourished). Total body muscular strength at baseline was significantly associated with many markers of health status at baseline (Table 2). Overall, greater muscular strength was associated with younger age, lower usage of prescription drugs, better nutritional and clinical status, greater muscle mass, and better functional and psychological health status. Eleven potentially etiological factors listed in Table 2 were entered into a forward stepwise multiple linear regression model. Muscle area (standardized coefficient 0.531), self-reported physical function (0.275) and number
of medications (-0.245) remained in the final model (r=0.821, p<0.0001), predicting 67% of the variance in muscle strength at baseline.

**Outcome Measures**

Total body strength (p<0.01), body weight, body mass index (BMI), mid-arm circumference, and mid-thigh circumference improved significantly in the PRT group compared to the controls (Tables 3 and 4). The PRT group also experienced significantly improved perceptions of vitality versus the C group, as evaluated via the SF-36 health survey (p=0.05). Perception of physical functioning (Table 3; p=0.07), depressive symptoms (p=0.08) and exercise capacity (Table 3; p=0.12), evaluated via 6-minute walk test, demonstrated a trend toward improvement in the PRT group compared to the control group. The inflammatory marker CRP decreased in the PRT group and increased in the control group (p=0.02). Mid-thigh muscle area and attenuation detected by CT scan did not change significantly over time, or between groups. Regional fat measures (subcutaneous, intramuscular and total mid-thigh, data not shown) as well as central fat, estimated from waist circumference (Table 4) did not change over time or between groups despite the increase in weight in the PRT group. Dialysis adequacy (Kt/V) did not change significantly between groups (p=0.99). All analyses were repeated using ANCOVA models with diabetic status as a covariate. This did not alter any of the findings (data not shown).

**Baseline Predictors of Body Composition Adaptation**

Patients with the lowest anthropometric estimates of lean mass and muscle quality and the greatest catabolic milieu at baseline experienced greater improvements in certain measures of body composition after 12 weeks: Specifically, baseline mid-
arm circumference was inversely related to change in mid-arm circumference at 12 weeks (r=-0.437, p=0.02); baseline calf circumference was inversely related to change in mid-thigh muscle area (r=-0.386, p=0.05) and directly related to change in mid-thigh muscle attenuation (i.e. lower calf circumference at baseline was associated with a greater improvement in mid-thigh muscle density) (r=0.549, p=0.003) at 12 weeks; and baseline mid-thigh muscle attenuation was inversely related to change in mid-thigh attenuation (i.e. lower mid-thigh density at baseline was associated with greater increase in mid-thigh density at 12 weeks (r=-0.405, p=0.04). Mid-arm circumference improved most in those with a greater catabolic milieu at baseline, as indicated by higher logCRP (r=0.480, p=0.007) and lower hemoglobin (r=-0.373, p=0.04). Mid-thigh muscle attenuation also improved the most in those with higher baseline logCRP (r=-0.481, p=0.011).

The only other measured factor associated with improved mid-thigh muscle attenuation after the intervention was baseline self-reported vitality, with better scores directly associated with decreases in muscle attenuation (i.e. increased muscle density) (r=-0.470, p=0.013). Nutritional intake, physical activity levels, burden of disease, and age were not associated with body composition adaptations to the intervention (data not shown).

**Baseline characteristics predictive of changes in strength**

We identified no baseline characteristics significantly predictive of changes in strength after 12 weeks. However, there was a tendency for those with better scores on vitality (r=0.311, p=0.12), role emotional (r=0.321, p=0.11), depression (r=0.329, p=0.10), and bodily pain (r=0.345, p=0.08) scales to have the greatest improvements in muscle strength.
Relationships Between Changes in Muscle Function and Body Composition and other Outcomes

Significant relationships between the muscle-related and clinical status outcomes are presented in Table 5. Strength improved in association with improvements in body weight, BMI, mid-arm circumference, logCRP, and overall exercise capacity. Reduced logCRP explained 19% of the variance in muscle strength.

Improvements in muscle size, assessed by CT scan of the mid-thigh and mid-arm circumference, were associated with reductions in logCRP and improvements in other indices of nutritional status, including body weight, albumin, prealbumin, hemoglobin, and MNA score (Table 5). Reduced catabolic influence of CRP explained 44% of the variance in thigh muscle area after the intervention.

Change in muscle attenuation (i.e. greater muscle density) was associated with change in protein catabolic rate (PCR) \((r=-0.470; p=0.03)\), but not improved dietary protein intake \((r=0.013, p=0.956)\), suggesting a relationship to protein turnover/retention of available dietary nitrogen sources. As noted for muscle strength, improvements in muscle density were associated with greater 6 min walk distance (Table 5). When muscle strength and muscle density were entered together into a forward stepwise multiple regression model, with change in 6 minute walk distance as the dependent variable, they both contributed independently and significantly to the variance \((r=0.654, p=0.003)\).

Compliance and Adverse Events

Compliance to the training program was 84.6% in the 14 PRT patients who completed both testing periods and 77.7% including 4 patients who were unavailable for follow-up testing (See Figure 1). No statistically significant difference was
observed between the PRT group and C for common dialysis-related complaints including headaches (PRT= 0 (0-2), C= 0 (0-3); p= 0.95), hypotension (PRT= 1 (0-7), C= 0 (0-5); p= 0.15), cramping (PRT= 0 (0-8), C= 0 (0-6); p=0.30), and fistula cannulation difficulties (PRT= 0 (0-2), C= 0 (0-2); p=0.35). No fistula infections were reported in either group. The incidence of falls was low, and did not differ significantly between groups (PRT= 0 (0-1), C= 0 (0-1); p=0.74). There was a trend toward a greater incidence of acute illnesses in PRT versus C (PRT= 2.50±1.65, C= 1.20±1.86; p= 0.06). No difference was noted in medical visits to health care professionals (PRT=3.57±1.34, C=4.53±2.61; p= 0.23). One adverse event was documented. An elderly woman in the PRT group (73.3yr, 3.8yr on HD) suffered partial tearing of the right rotator cuff muscles in week 6 which was managed conservatively, but continued with lower body training for the remainder of the trial.

**DISCUSSION**

The PEAK study is to our knowledge the first randomized controlled trial of isolated high intensity PRT in patients with ESRD. Overall, this trial demonstrates that 12 weeks of intradialytic PRT can significantly improve the anabolic/catabolic milieu in patients with ESRD through the enhancement of total body strength, nutritional indices, body composition (increased weight, BMI, mid-arm and mid-thigh circumference without an increase of visceral or mid-thigh adiposity), and systemic inflammation, as indicated by a reduction in logCRP. Improvements of skeletal muscle functioning, mass and composition were significantly associated with improved markers of nutritional status and exercise capacity (Table 5). Our
intradialytic PRT regimen also significantly improved perceptions of vitality, and tended to improve depressive symptoms, perceptions of physical functioning, and exercise capacity. Importantly, the significant inverse relationships we observed between increased arm circumference, thigh muscle area, and strength gains and decreased logCRP suggest that the exercise-associated reduction in logCRP may be a central mechanism of the adaptive response to PRT in this cohort.

The significant anabolic adaptations experienced by our PRT group occurred despite a trend toward increased dietary protein intake in the control group (p=0.08) and with no significant difference between groups in energy intake or recreational and daily physical activity (PASE score), suggesting that favorable physiological shifts can occur through this intradialytic exercise prescription alone. By contrast, a recent uncontrolled trial involving 9 patients participating in 12-weeks of intradialytic aerobic interval training detected no measurable anabolic shifts as assessed by dual energy X-ray absorptiometry, bioelectrical impedance analysis, and the measurement of growth factors. The patients experiencing the greatest anabolic shifts in body composition in our study were those with the lowest anthropometric estimates of muscle mass and muscle quality, and highest levels of inflammation (CRP) at baseline. These findings demonstrate the importance of involving appropriately screened patients of poorer general health and nutritional status in intradialytic PRT regimens, as these patients may derive the greatest anabolic adaptations. By contrast, older age, gender, depressive symptoms, burden of chronic disease, and length of hemodialysis treatment were not predictive of outcomes, suggesting that these factors are not barriers to a robust physiologic response.

To date, one uncontrolled trial involving 10 HD patients has demonstrated significantly increased lower body strength and exercise capacity (6-minute walk
distance), and reduced CRP after 12-weeks of PRT on nondialysis days.\textsuperscript{31, 32} Five additional trials have elicited strength adaptation in this cohort following 3-6mo exercise regimens involving primarily aerobic training\textsuperscript{2, 30, 33-35} By contrast, one trial involving 6 weeks of intradialytic cycle ergometer training did not improve muscular strength.\textsuperscript{36}

The preservation and enhancement of muscular strength, as we observed, appears to be of clinical importance in this cohort. Those with the greatest muscle strength at baseline were younger, healthier, better nourished, were more physically active, had greater exercise tolerance and muscle mass, and reported less difficulty with physical functioning than their weaker peers (Table 2). Additionally, increased muscular strength over the 12-week intradialytic PRT regimen was associated significantly with increased body weight, BMI, mid-arm circumference, and exercise capacity, and reduced logCRP, all factors linked to morbidity and mortality in this cohort.\textsuperscript{37, 38}

The profusion of catabolic insults chronically assailing patients with ESRD on maintenance HD critically underscores the importance of prescribing anabolic exercise for reversing the catabolic cascade induced by the disease process and disease management,\textsuperscript{7} including HD treatment itself.\textsuperscript{10, 39} Prescribing exercise during dialysis specifically may be of great importance in eliciting an anabolic response. Aerobic exercise during dialysis has been shown to augment the ability of parenteral nutrition to counteract dialysis-induced catabolism by significantly enhancing net protein accretion and post-dialysis growth hormone levels.\textsuperscript{40} PRT, a stronger anabolic stimulus than aerobic exercise, may be even more beneficial in this regard as we have previously demonstrated that the combination of PRT and nutritional supplements improves the hypertrophic response in frail elderly nursing home
residents. Intradialytic high-intensity PRT has not been previously implemented due to perceived difficulty, but our study demonstrates the feasibility of this novel approach to catabolism in ESRD.

There are other reasons to advocate the integration of exercise and dialysis treatment. Exercise during dialysis may enhance the removal of damaging solutes by reducing post-dialysis rebound. Intradialytic exercise may also play an important role in alleviating the boredom and negativity typifying routine dialysis treatment sessions by shifting focus from sedentary pursuits such as watching television toward health promotion and active living. Indeed, the improvements in self-perceptions of vitality (p=0.05) and physical functioning (p=0.07) we noted suggest the potential importance of intradialytic PRT as a QOL intervention in this cohort. Similarly, Painter et al showed that 16 weeks of home-based exercise combined with intradialytic cycling improved various markers of QOL in this cohort, including vitality and physical functioning. Depressive symptoms also tended to improve in the PRT group while worsening in the control group (p=0.08). We have established the efficacy of PRT for treatment of major depression in older adults, but this remains to be investigated with robust intervention trials targeted specifically at clinically depressed patients with ESRD, as only 32% of the patients in our study had GDS scores >9 consistent with at least mild depression.

It is possible that we would have seen significant changes in muscle fiber area using muscle biopsies in addition to CT scans. For example, in our previous RCT comparing 12 weeks of PRT to sham exercise in 26 patients with chronic renal insufficiency, significant type I (p=0.03) and type II (p=0.04) muscle fibre hypertrophy (24% and 22%, respectively) detected via muscle biopsies was
accompanied by a non-significant change in mid-thigh muscle CSA evaluated via CT (p=0.11).

A longer duration of training may have resulted in even greater anabolic adaptations. Metabolic abnormalities may delay the anabolic process in patients with ESRD. Metabolic acidosis induced by chronic uremia activates the ubiquitin-proteasome pathway, which mediates protein degradation through the decarboxylation of branched-chain amino acids. Dysregulation of this catabolic pathway has been recognized as the predominant route by which accelerated skeletal muscle wasting in ESRD occurs. Recent data also suggest that chronic uremia depresses protein synthesis, which may include resistance to anabolic hormones including insulin, hGH, and IGF-1, release of inflammatory cytokines and intrinsic changes in enzymes of major energy-providing pathways. Hemodialysis treatment has also been recognized as a catabolic process as this treatment removes essential amino acids in the dialysate that activates cytokines such as IL-6 which, in turn, activate the ubiquitin-proteasome pathway promoting cellular apoptosis and proteolysis. Given the catabolic milieu induced by ESRD and its chronic management, it is possible that anabolic adaptation to PRT would be delayed in patients with ESRD when compared to other diseased, or healthy cohorts. Currently, this hypothesis remains to be investigated.

Two limitations of our study include the lack of a sham exercise control activity, and the unblinded assessment of physical performance and questionnaire data. Given the shared dialysis unit space, it would not have been possible to blind subjects to the PRT or sham intervention, as only one would involve weights.

In summary, a 12-week PRT regimen delivered during routine HD treatment sessions resulted in significant anabolic adaptations, including improved strength,
body composition, and QOL in patients with ESRD, likely mediated in part by reductions in inflammatory cytokines. Compliance was excellent (84.6%) when delivered in this fully-supervised setting and intradialytic PRT may therefore provide a robust and practical method by which the health status and QOL of this cohort can be improved. Future investigations involving longer duration regimens (>6mo.), portable machine-based PRT equipment allowing for better training of muscle groups such as hamstrings and gluteal muscles with greater overload, as well as more sensitive analysis techniques, including muscle biopsies, should be pursued to define optimal anabolic adaptations and associated reductions in morbidity and mortality.
REFERENCES


Figure 1:

Reviewed (104)

Ineligible (51)
- Died Before Enrolling (14)
- Moved Away from Unit (7)
- Kidney Transplanted (3)
- Medical Exclusion to PRT (20)
- Study-related Exclusion (7)

Eligible (53)

Refused (19)

Consented (34)

Randomized to Intervention (18)
- Unavailable for retesting
  - Moved to home HD training (2)
  - Institutionalized depression (1)
  - Diagnosis of Malignancy (1)
- Completed Protocol and Follow-up Testing (14)

Randomized to Control (16)
- Unavailable for retesting
  - Family reasons (1)
- Completed Protocol and Follow-up Testing (15)
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<th>Characteristic</th>
<th>Total Cohort (n=34)</th>
<th>Experimental (n=18)</th>
<th>Control (n=16)</th>
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<tbody>
<tr>
<td>Age (y)</td>
<td>64.4(13.7)</td>
<td>61.4(16.0)</td>
<td>67.8(16.0)</td>
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<tr>
<td>Men:Women</td>
<td>24:10</td>
<td>12:6</td>
<td>12:4</td>
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<tr>
<td>Hemodialysis Vintage† (y)</td>
<td>2.2, 0.3-16.7</td>
<td>2.4, 0.3-16.7</td>
<td>2.0, 0.6-10.3</td>
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<td>Body weight (kg)</td>
<td>73.9(16.4)</td>
<td>71.7(16.6)</td>
<td>76.3(16.4)</td>
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<tr>
<td>Height (cm)</td>
<td>165.5(10.3)</td>
<td>164.8(8.7)</td>
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<td>BMI (kg/m²)</td>
<td>27.0(5.7)</td>
<td>26.4(5.9)</td>
<td>27.6(5.5)</td>
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<td>Medications/day (n)</td>
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<td>8.3(3.4)</td>
<td>8.1(2.0)</td>
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<td>Tobacco use history (n)</td>
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<td>10</td>
<td>0.29</td>
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<tr>
<td>Chronic Diseases‡ (n)</td>
<td>5.6(1.7)</td>
<td>5.2(1.6)</td>
<td>6.0(1.8)</td>
<td>0.18</td>
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<tr>
<td>• HT (n)</td>
<td>34</td>
<td>18</td>
<td>16</td>
<td>1.00</td>
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<tr>
<td>• Depression§ (n)</td>
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<td>7</td>
<td>4</td>
<td>0.63</td>
</tr>
<tr>
<td>• Diabetes (n)</td>
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<td>7</td>
<td>0.03</td>
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<tr>
<td>• CAD (n)</td>
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<td>4</td>
<td>5</td>
<td>0.55</td>
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<td>• Stroke (n)</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>0.23</td>
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**Etiology of ESRD**

- GN (n) 7 3 4  
- HT (n) 6 2 4  
- Diabetes (n) 4 1 3  
- Ischemia (n) 4 3 1  
- PCKD (n) 4 3 1  
- IgA nephropathy (n) 3 3 0  
- Analgesic use (n) 3 1 2  
- SLE (n) 2 1 1  
- Other (n)  

**BMI**=Body Mass Index; **HT**=hypertension; **CAD**=coronary artery disease; **GN**=glomerulonephritis; **PCKD**=polycystic kidney disease; **SLE**=systemic lupus erythematosus  
Data reported according to mean values with standard deviations presented in parentheses for normally distributed variables  
†Non-normal distribution: median values and range reported  
‡Includes diagnosis of ESRD  
§Mild to severe depression diagnosed according to the Geriatric Depression Scale (GDS)  
Normally distributed variables analyzed with unpaired t-tests  
Non-normally distributed variables analyzed with Mann-Whitney U test, nominal variables with Chi-square test  
p-values correspond to comparisons between the experimental and control group
Table 2: Baseline relationships with total body muscular strength

<table>
<thead>
<tr>
<th>Measure</th>
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<th>p</th>
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<tr>
<td>Age (y)</td>
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<tr>
<td>Medications/day (n)</td>
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<tr>
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<td>Calf Girth (cm)</td>
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<td>Thigh muscle CSA (cm^2)</td>
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<td>Thigh muscle attenuation</td>
<td>-0.453</td>
<td>0.009</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>0.418</td>
<td>0.008</td>
</tr>
<tr>
<td>Creatinine (µmol/L)</td>
<td>0.560</td>
<td>&lt;0.001</td>
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<tr>
<td>Six-minute walk (m)</td>
<td>0.712</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical Function SF-36 (0-100)</td>
<td>0.580</td>
<td>&lt;0.001</td>
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</table>

MNA=Mini-Nutritional Assessment Scale; CSA=cross-sectional area
SF-36=Medical Outcomes Trust Short-Form 36 Version 1

111
<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Experimental Group</th>
<th>Control Group</th>
<th>Time Effect p value</th>
<th>Group x Time p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 0</td>
<td>Week 12</td>
</tr>
<tr>
<td>Total Body Strength (kg)</td>
<td>90.8(31.8)</td>
<td>111.7(38.6)</td>
<td>96.4(31.7)</td>
<td>96.3(36.2)</td>
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<tr>
<td>Six-minute walk (m)</td>
<td>482.9(150.9)</td>
<td>500.3(163.9)</td>
<td>438.1(119.9)</td>
<td>434.3(122.2)</td>
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<tr>
<td>Physical Functioning SF-36 (0-100)</td>
<td>68.9(32.0)</td>
<td>79.3(25.7)</td>
<td>69.7(20.0)</td>
<td>70.0(23.8)</td>
</tr>
<tr>
<td>PASE</td>
<td>82.6(51.7)</td>
<td>104.4(58.6)</td>
<td>75.0(47.6)</td>
<td>79.1(39.8)</td>
</tr>
</tbody>
</table>

SF-36=Medical Outcomes Trust Short Form-36 Heath Survey, higher scores indicate better function
PASE=Physical Activity Scale for the Elderly, higher scores indicate more habitual activity
Data reported according to mean values with standard deviations presented in parentheses
All p-values calculated via repeated measures analysis of variance
†Non-normal distribution, therefore data log transformed for parametric statistical analysis
<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Experimental Group</th>
<th>Control Group</th>
<th>Time Effect</th>
<th>Group x Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 0</td>
<td>Week 12</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>69.9 (15.0)</td>
<td>71.3 (15.1)</td>
<td>77.8 (15.8)</td>
<td>77.4 (15.2)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0 (5.9)</td>
<td>26.5 (5.8)</td>
<td>28.2 (5.2)</td>
<td>28.1 (4.9)</td>
</tr>
<tr>
<td>Mid-thigh circ. (cm)</td>
<td>45.7 (4.0)</td>
<td>46.7 (3.9)</td>
<td>47.6 (5.5)</td>
<td>47.3 (4.3)</td>
</tr>
<tr>
<td>Mid-arm circ. (cm)</td>
<td>29.7 (3.7)</td>
<td>30.2 (3.3)</td>
<td>31.2 (3.3)</td>
<td>30.4 (3.1)</td>
</tr>
<tr>
<td>Mid-calf circ. (cm)</td>
<td>33.9 (3.0)</td>
<td>34.2 (2.8)</td>
<td>35.1 (3.5)</td>
<td>35.3 (3.8)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.2 (18.9)</td>
<td>94.7 (18.9)</td>
<td>98.3 (13.0)</td>
<td>99.4 (13.0)</td>
</tr>
<tr>
<td>Thigh muscle CSA (cm²)</td>
<td>94.6 (23.3)</td>
<td>95.6 (22.0)</td>
<td>96.6 (26.5)</td>
<td>95.8 (25.3)</td>
</tr>
<tr>
<td>Thigh muscle attenuation</td>
<td>86.2 (3.0)</td>
<td>86.1 (2.5)</td>
<td>87.0 (1.9)</td>
<td>87.4 (2.0)</td>
</tr>
<tr>
<td>(Hounsfield units)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy Intake (kcal/kg/d)</td>
<td>34.26 (7.01)</td>
<td>34.70 (6.27)</td>
<td>31.00 (7.86)</td>
<td>32.00 (9.53)</td>
</tr>
<tr>
<td>Protein Intake (g/kg/d)</td>
<td>1.51 (0.27)</td>
<td>1.52 (0.25)</td>
<td>1.27 (0.31)</td>
<td>1.40 (0.41)</td>
</tr>
<tr>
<td>MNA score (0-30)</td>
<td>26.1 (1.7)</td>
<td>26.6 (1.5)</td>
<td>26.1 (1.9)</td>
<td>26.0 (2.5)</td>
</tr>
<tr>
<td>Prealbumin (g/L)</td>
<td>0.37 (0.10)</td>
<td>0.37 (0.08)</td>
<td>0.34 (0.10)</td>
<td>0.32 (0.09)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>33.4 (2.7)</td>
<td>33.5 (2.0)</td>
<td>34.0 (2.9)</td>
<td>34.5 (3.4)</td>
</tr>
<tr>
<td>Lymphocytes (x10⁶/L)</td>
<td>1.498 (0.553)</td>
<td>1.605 (0.657)</td>
<td>1.553 (0.564)</td>
<td>1.733 (0.601)</td>
</tr>
<tr>
<td>PCR (g/kg/d)</td>
<td>1.08 (0.20)</td>
<td>1.07 (0.38)</td>
<td>1.13 (0.13)</td>
<td>1.10 (0.22)</td>
</tr>
</tbody>
</table>
BMI=body mass index; MNA=Mini-Nutritional Assessment Scale, higher scores indicate better nutritional status; PCR=protein catabolic rate
Data reported according to mean values with standard deviations presented in parentheses
All p-values calculated via repeated measures analysis of variance
**Table 5: Variables associated with Changes in Muscle Function, Size, and Attenuation**

<table>
<thead>
<tr>
<th>Primary Skeletal Muscle Outcome</th>
<th>Associated Variables</th>
<th>r</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Body Strength</td>
<td>Body weight</td>
<td>+0.44</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>BMI</td>
<td>+0.43</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>Mid-arm circumference</td>
<td>+0.67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>LogCRP</td>
<td>-0.43</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>6-minute walk</td>
<td>+0.40</td>
<td>0.05</td>
</tr>
<tr>
<td>Mid-Arm Circumference</td>
<td>Albumin</td>
<td>+0.39</td>
<td>0.04</td>
</tr>
<tr>
<td></td>
<td>Prealbumin</td>
<td>+0.44</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>Hemoglobin</td>
<td>+0.56</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>LogCRP</td>
<td>-0.48</td>
<td>0.008</td>
</tr>
<tr>
<td>Thigh Muscle CSA</td>
<td>Body Weight</td>
<td>+0.49</td>
<td>0.01</td>
</tr>
<tr>
<td></td>
<td>Albumin</td>
<td>+0.56</td>
<td>0.003</td>
</tr>
<tr>
<td></td>
<td>Prealbumin</td>
<td>+0.45</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>MNA Score</td>
<td>+0.72</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>LogCRP</td>
<td>-0.66</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Bodily Pain</td>
<td>-0.48</td>
<td>0.01</td>
</tr>
<tr>
<td>Thigh Muscle Attenuation</td>
<td>Protein Catabolic Rate</td>
<td>+0.61</td>
<td>0.001</td>
</tr>
<tr>
<td></td>
<td>6-minute walk</td>
<td>+0.39</td>
<td>0.04</td>
</tr>
</tbody>
</table>

CSA = cross-sectional area; MNA = mini-nutritional assessment. Higher scores equal better nutritional status. Thigh Muscle Attenuation: higher scores indicate lower density (more intramuscular lipid). Simple linear regression models of the absolute changes in each variable (12 wk minus baseline value) are reported.
CHAPTER 6

A Randomized Controlled Trial of Intradialytic Resistance Training to
Counteract Muscle Wasting in End-Stage Renal Disease: The PEAK
Study (Progressive Exercise for Anabolism in Kidney Disease)
ABSTRACT

**Background:** Catabolism is common and morbid in end-stage renal disease (ESRD). We conducted the first randomized controlled prescribing high-intensity, progressive resistance training (PRT) during hemodialysis (HD) treatment to determine the dose of PRT required to induce anabolic adaptations in this cohort.

**Methods:** Individuals receiving maintenance HD were randomly assigned to an experimental group (24WK) who received PRT + Usual Care for 24 weeks, or a wait-list control group (12WK) who received Usual Care only for the first 12 weeks of the trial and then crossed over to PRT + Usual Care for the latter 12 weeks of the trial. The PRT regimen consisted of two sets of 10 PRT exercises at high intensity using free-weights targeting upper and lower body musculature 3 times/wk for 12 wks during HD. Outcome measures included thigh muscle cross-sectional area (CSA), strength, and markers of functional and nutritional health status.

**Results:** Thirty-four patients (64.4yr (31.2-80.5yr), 0.3-16.7yr on HD) were randomized, 28 completed the intervention. The 24WK group significantly improved thigh muscle CSA (p=0.04), albumin (p=0.03), and knee extension strength (p=0.03). Improved thigh muscle CSA in the whole cohort was significantly associated with increased body weight (r=+0.497; p=0.02), BMI (r=+0.427; p=0.04), and role emotional QOL (r=0.618; p=0.001), and negatively associated with logCRP (r=-0.656; p=<0.001), WBC (r=-0.452; p=0.03). Characteristic including age, HD vintage, burden of chronic illness, medication usage, and protein and dietary intake were independent of the anabolic adaptation.

**Conclusions:** We have shown for the first time that extended intradialytic PRT can effectively induce anabolic adaptations in patients with ESRD. The well-documented
morbidity and mortality associated with the catabolic milieu of ESRD may be modifiable by addition of anabolic exercise to routine HD treatment.

Keywords: Exercise, Muscle, End Stage Renal Disease, Quality of Life, Health
INTRODUCTION

According to the United States Renal Data System (USRDS) the incidence of end stage renal disease (ESRD) continues to rise each year. Over 100,000 new cases were reported nationally in the USRDS 2004 report, and nearly 92,000 of these individuals commenced hemodialysis (HD) treatment as renal replacement therapy. Over 281,000 patients in the US currently receive HD. With rapid growth of this patient population expected in years ahead, due in part to the worldwide epidemic of type 2 diabetes, greater efforts must be directed toward addressing risk factors contributing to the grossly elevated morbidity and mortality of this cohort.

One common and significant pathological consequence of ESRD is skeletal muscle wasting or sarcopenia. The loss of muscle mass has been recognized as the most significant predictor of morbidity and mortality in this cohort.\textsuperscript{1} Although the catabolic cascade has not been fully elucidated, the etiology of myopathy in this patient population can be influenced by a multitude of factors resulting from the ESRD process and disease management including metabolic acidosis,\textsuperscript{2} protein-energy malnutrition,\textsuperscript{3,4} co-morbid illnesses, corticosteroid use,\textsuperscript{5} biological aging, dialysis treatment,\textsuperscript{6} and sedentary behavior exacerbated by 12-18 h/wk of HD treatment. Metabolic impairments associated with the loss of lean body tissue include insulin resistance,\textsuperscript{7} immune system dysfunction,\textsuperscript{8} and reduced peripheral O\textsubscript{2} extraction.\textsuperscript{9} The concomitant functional decline, weakness, and deconditioning can negatively impact psychological functioning and perception of quality of life (QOL).\textsuperscript{10}

Progressive resistance training (PRT) has become well-recognized as a therapeutic intervention for counteracting skeletal muscle wasting and inducing strength adaptations in frail elders and those with certain chronic illness.\textsuperscript{11} The prevalence of a catabolic milieu,
malnutrition, disability, and muscle abnormalities in ESRD suggest that PRT may be of significant benefit during HD as well.

Progressive Exercise for Anabolism in Kidney Disease (PEAK) is the first RCT to evaluate the efficacy of isolated high-intensity PRT in ESRD with an intervention delivered within the dialysis treatment session. We have reported the interim results of the first 12 weeks of this trial.\textsuperscript{12} Our training regimen enhanced muscle strength, body composition, nutritional status, and psychological health status compared to usual care.\textsuperscript{12} We hypothesized that an extended duration of training would yield even greater adaptations with respect to anabolic, and other health-related outcomes, including functional, physiological, clinical, and psychological status, and that changes in muscle size and function would be directly related to other clinical benefits observed. Therefore, we now present the full results of the PEAK trial, including the dose-response effect in patients randomized to 12-versus 24 weeks of intradialytic resistance training.

**METHODS**

*Setting and Study Design*

The PEAK trial was conducted at the outpatient HD unit of the St. George Public Hospital, Sydney, Australia. The South Eastern Sydney Area Health Service and the University of Sydney Human Research Ethics Committees approved all research procedures.

Following baseline testing, patients were assigned via computer-generated randomization list\textsuperscript{13} stratified by gender in blocks of 4 to an experimental group (24WK) who received PRT + Usual Care for 24 weeks, or a wait-list control group.
(12WK) who received Usual Care only for the first 12 weeks of the trial and then crossed over to PRT + Usual Care for the latter 12 weeks of the trial. An investigator not involved in screening, testing or training of patients prepared the randomization list, and assignments were handed to the patients to open in opaque sealed envelopes.

The study design provided pre-planned comparisons of both 12 wks of PRT vs. usual care, as well as randomized comparison of the benefits of 12 vs. 24 weeks of PRT, to evaluate the magnitude and time course of changes observed. In addition, it was deemed ethically most appropriate to offer exercise to the usual care group at 12 weeks, given the other known benefits of intradialytic exercise.10,14,15 Outcome measures were collected at baseline, 12, and 24 weeks on all available subjects, regardless of level of compliance with the exercise intervention.

Power Calculations

Sample size estimates were calculated by hypothesized differences between 12 weeks of usual care and 12 weeks of PRT in thigh muscle cross-sectional area (CSA). Based on previous studies,16 usual care was hypothesized to produce no change, while PRT was hypothesized to result in a +3.5% change in CSA over 12 weeks. Given a SD of ±5.5%, alpha of 0.05, and beta of 0.20, a requirement of 40 patients was estimated.17

Patients

All patients receiving chronic hemodialysis at the unit were evaluated for eligibility via medical record review, physical examination and interview by a study physician, and clearance from their nephrologist prior to the solicitation of interest and written informed consent. Eligibility criteria included: (1) ≥18 years of age; (2)
on HD (4-6 hours/d, 3d/wk) for >3 mo; (3) without acute or chronic medical conditions precluding PRT or the collection of outcome measures; (4) independent ambulation with or without an assistive device for ≥50m; (5) adequately dialyzed (Kt/V≥1.2) and stable during HD; (6) cognition of English language sufficient to understand research procedures and provide written informed consent; (7) not currently engaged in a PRT regimen; and (8) willingness to be randomized and to undergo study protocols.

**PRT Intervention**

All PRT sessions were performed under the direct supervision of an exercise physiologist during routine HD treatment, 3 times per week, with the patient in a seated or supine position in a standard HD chair (LA-Z-BOY Pty Ltd, Moorebank, NSW, Australia). The limb containing the arteriovenous (AVF) or Gortex fistula was exercised immediately prior to the dialysis session. Temporary vas catheter access precluded upper body training. During each PRT session, two sets of 8 repetitions of 10 exercises targeting major muscle groups of the upper and lower extremities, were performed at a rating of perceived exertion of 15-17 (“hard” to “very hard”) on the Borg Scale.19 Upper body exercises performed using free-weight dumbbells (Australian Barbell Company, Mordialloc, Australia) included the shoulder press, side shoulder raise, triceps extension, biceps curl and external shoulder rotation. Lower body exercises performed unilaterally using weighted ankle cuffs (Australian Barbell Company, Mordialloc, Australia) included seated knee extension, supine hip flexion, supine hip abduction, and supine straight-legged raise. Seated hamstring curls were also performed, using Thera-Band™ tubing (Akron, Ohio, USA) attached to a fixed position on the weight trolley. Abdominal musculature was targeted with bilateral leg
raises in a supine position or bilateral leg lifts in a seated position, depending on subject preference and level of ability. Patients randomized to the control group were provided usual care by the clinical staff of the dialysis unit but were given no instructions or access to exercise equipment. Intradialytic exercise was not part of the usual care at this dialysis unit.

**Outcome measures**

The primary outcomes of the study were the hypothesized anabolic responses to PRT: muscle size, muscle strength, and nutritional status. Computerized tomography (CT) scans of the non-dominant mid-thigh to determine thigh muscle CSA (cm²), attenuation (Hounsfield units, inversely related to muscle density), and fat area (total, subcutaneous, and intramuscular, cm²) were collected using a General Electric High Speed CTI Scanner (model no. CEE0459). Blinded analyses of the digitized images were performed as previously reported.¹⁶ CV in this cohort is 0.005%.

Peak force (kg) of the knee extensors, hip abductors, and triceps was measured unilaterally in both extremities in triplicate using an isometric digital dynamometer (Chatillon CSD 200 Dynamometer, AMETEK, Inc. Paoli, PA, USA) fixed to a stand (CV=9.4%), with the best trial used for analysis. Total isometric strength summary measures were also created for each subject. Specific tension for the thigh musculature was calculated using knee extension strength of the non-dominant thigh (kg) divided by thigh muscle CSA (cm²) obtained from CT scan.

The 6-minute walk²⁰ was used as a measure of overall exercise capacity. CV of this test is reported to be 5-10% in older cohorts.²¹
A blinded dietitian collected all nutritional and anthropometric measures, including body weight, height, and waist, mid-arm and calf girths, post-dialysis using standard protocols. This dietitian also assessed nutritional status via Mini-Nutritional Assessment (MNA) and dietary intake over the previous month with a validated Australian Food Frequency Questionnaire (FFQ) analyzed using FoodWorks software (Xyris Software, Version 3, 1998-2000).

All blood samples were drawn pre-dialysis, prior to the mid-week HD session, at least 48 hours after the previous exercise bout during follow-up assessments. Additionally, urea kinetics evaluation (protein catabolic rate (PCR) and dialysis adequacy (Kt/V)) included the collection of blood urea post-dialysis during the mid-week HD session as well as just prior to the following HD session. Samples possibly affected by acute illness or trauma were discarded and repeated.

CRP assays were performed using the Dade Behring Dimension RXL (Deerfield, Illinois, USA). This method is based on a particle enhanced turbidimetric immunoassay (PETRIA) technique using the Dade Behring Dimension RCRP calibrator for standardization. The coefficient of variation (CV) for this test was 2.3%. Results less than the detectable range (<1mg/L) were recorded as 1mg/L.

Albumin and creatinine were measured using Beckman reagent on a Beckman LX20 analyzer (Fullerton, CA, USA); CV of 1.5%. Prealbumin was measured by nephelometry using Beckman reagent on a Beckman Image analyzer with an inter-run CV of 4.6%. Hemoglobin, hematocrit, WBC and lymphocyte counts were analyzed on a Roche Sysmex XE2100 analyzer (Basel, Switzerland) using reagent supplied by Roche. Urea was measured using the Enzymatic conductivity method, on a Beckman LX20 analyzer, with a CV of 4.8% at a concentration of 4.4mmol/L.
The Medical Outcomes Trust Short Form-36 (SF-36) survey was used to measure health-related quality of life. The Geriatric Depression Scale (GDS) was used to evaluate depressive symptoms, with scores >9/30 consistent with possible depression. The Physical Activity Scale for the Elderly (PASE), was used to evaluate leisure and daily activity level, with higher scores denoting greater activity.

Compliance and Adverse Events

Compliance to training was defined as the number of training sessions attempted divided by the number offered x 100%. Intensity and progression of training load was assessed by recording the highest weight used for the triceps, hip abduction, and knee extension exercises in each patient during weeks 1, 12, and 24 of training. Changes in health status including acute illnesses, new physical, mental and/or emotional symptoms, change in medication usage, dialysis-related complaints (i.e. headaches, hypotension, cramping) and visits to health care professionals were defined a priori and documented via weekly interview and clinical HD notes review. Adverse events were defined as any injury, exacerbation of underlying disease, or any other chronic impairment, ≥2 weeks in duration, attributed directly to the PRT regimen.

Statistical Analyses

All available data were used in the analyses according to intention-to-treat strategy. Statistical analyses were performed using StatView™ statistical software package (Version 5.0 SAS Institute, Cary, NC). Data distributions were inspected visually and statistically for normality (skewness between −1 and +1). Normally distributed data were described using mean and SD, and non-normally distributed data
using median and ranges. Groups were compared at baseline using paired t-tests for continuous variables and Chi Square tests for categorical variables. Non-normally distributed continuous variables were log-transformed prior to use with parametric statistics. Analysis of covariance (ANCOVA) models of absolute and relative change scores (final -baseline/baseline x 100) were constructed to compare 12 weeks of exercise vs. usual care, 12 vs. 24 weeks of exercise, using the change score as the dependent variable and the baseline score as a covariate. Additional covariates were selected if they were potential confounders and were significantly different between groups at baseline. Only diabetic status was identified as a covariate in this way. Analysis of change over time within the 24WK group was analyzed with repeated measures ANOVA using baseline, 12 wk, and 24 wk data, with Fisher’s least significant difference post hoc t tests performed on all pairwise comparisons whenever the f-ratio was significant. Relationships between continuous variables of interest were analyzed with simple and forward stepwise multiple linear regression models. A p-value of <0.05 was accepted as statistically significant.

RESULTS

Participant Flow

Participant flow through the trial is shown in Figure 1. We screened all available HD outpatients at the unit between November 2002 and January 2005. Fifty-one percent of the patients (53/104) were eligible, 64% of eligible patients (34/53) consented, and 82% of randomized patients (28/34) completed the final 24-week assessment. No withdrawals were study-related.
**Baseline Characteristics**

Participant characteristics at baseline are presented in Table 1. Participants ranged in age from 31.2 to 80.5 yrs, and had a high burden of co-morbid disease, particularly cardiovascular disease, depression, and type 2 diabetes (Table 1). Nutritional risk (BMI< 22 kg/m2 and/or MNA score <24) was present in 26.5% (9/34); whereas 20.6% (7/34) were considered obese (BMI >30kg/m2). No significant differences were observed between the 12WK and 24WK groups at baseline except for the higher prevalence of diabetes in the 24WK group (Table 1).

**Comparisons at 12 weeks: Usual care vs. PRT**

As we have noted in our interim report of this trial, (Cheema et al, unpublished; See Chapter 5 ) patients receiving 12 weeks of PRT + usual care versus usual care control significantly improved total body strength, body composition and regional estimates of muscle mass, inflammation, and vitality. Relative changes in isometric strength at the 12-week time point were +28.8±28.7% vs. −5.6±10.6% for combined knee extensors (p=0.007); +27.0±31.4% vs. +1.0±13.1% for hip abductors (p=0.002); and +15.6±21.2% vs. +4.1±15.0% for triceps (p=0.24) in the PRT group versus usual care controls, respectively. In addition, there was a trend for relative specific tension to improve in the PRT group compared to usual care (29.1±32.5% vs. −1.9±15.8%; see Figure 2a, p=0.07) whereas muscle area was not significantly different between groups, suggesting that neural adaptations predominated as the mechanism of the change in strength at this stage.
Comparisons at 24 weeks: 12WK vs. 24WK of PRT

Comparisons were made at 24 wks between groups randomized to either the 12WK or 24WK of PRT during the 6 months of study. Consistent with our dose-response hypothesis, the 24WK group significantly increased thigh muscle CSA (p=0.04), knee extension strength (p=0.03), and albumin (p=0.03) compared to the 12WK group (Figure 3). There was also a trend toward the improvement of absolute (+30.6±22.4kg vs. +25.5±23.9kg; p=0.16) and relative (+32.8±24.3% vs. 20.7±17.3%; p<0.08) changes in total body strength, and relative gains in knee extension strength (+33.6±46.6% vs. 17.9±20.1%; p<0.07) in the 24WK compared to the 12WK group. Vitality also tended to increase to a greater extent in the 24WK group compared to the 12WK group (+2.7±31.0 points vs. −1.5±17.0 points, p=0.06). Notably, relative increases in specific tension seen after 12 weeks of PRT (p=0.07, Figure 2a) did not increase further in the 24WK group (Figure 2b; p=0.54), suggesting that neural adaptations were an early response to training, and not significantly related to additional significant increases in knee extension strength in the second 12 weeks of the trial. The significant anabolic adaptation (increased thigh muscle CSA) in the 24WK group occurred despite a trend toward significantly increased protein (p=0.13) and energy intake (p=0.06) in the 12WK group versus the 24WK group.

Comparison of Intradialytic and Extradialytic Training Efficacy

This study provided a unique opportunity to assess the relative efficacy of training outside vs. inside the dialysis session, as the fistula arm was trained just prior to starting HD, whereas the non-fistula arm was trained during dialysis. As shown in Figure 4, absolute triceps strength gains made during dialysis were not different to
those achieved outside of the session (p=0.77), supporting the physiologic robustness of this novel approach to PRT prescription.

**Time course of Adaptations to Training**

Additional repeated measures analyses were completed within the 24WK group only, to assess the time course and relative magnitude of changes across 6 months of PRT. The 24WK group significantly increased all measures of strength, specific tension, 6 min walk distance, and self-reported physical function (SF-36) across time, and tended to report more habitual physical activity (p=0.18). There were also trends toward the improvement of total hip abduction strength (p=0.07), and total body strength (p=0.15) between week 12 and 24 (Table 2).

The time course of adaptations can be further appreciated by considering the relative changes in strength and when they occurred. Total body strength increased 32.8% over 24 weeks, with 75% of the adaptation occurring in the first 12 weeks of PRT; total triceps strength increased 25.8% over 24 weeks, with 60.0% of this adaptation occurring in the first 12 weeks of PRT; total hip abduction strength increased 28.7% over 24 weeks, with 94.1% of this adaptation occurring in the first 12 weeks of PRT; total knee extension strength increased 33.6% over 24 weeks, with 85.7% of this adaptation occurring in the first 12 weeks of PRT; specific tension of the thigh musculature increased by 29.1% over the first 12 weeks of the trial and, from this point, decreased 12.5% by 24 weeks of PRT.

Body weight, BMI, and mid-thigh circumference also increased significantly in the 24WK group over time (Table 3). Paralleling the adaptations in strength and self-reported and observed physical functioning, these changes were seen by the 12-
week time point. Notably, the increase in body weight was not accompanied by increases in any measure of fat mass (waist circumference, thigh total, subcutaneous or intramuscular fat areas, suggesting that lean tissue accretion, including thigh muscle CSA, accounted for the increase in body weight. In fact, although not significant, mid-thigh intramuscular fat area decreased by 3.5±23.3% (p=0.39 in an ANCOVA model versus the 12WK group).

Predictors of Anabolic Adaptations

Data from the whole cohort were analyzed to define potential predictors, mechanisms and associated benefits of anabolic adaptations observed. Only baseline creatinine (r=+0.410; p=0.05) predicted the change in knee extension strength. The greatest improvements in albumin were seen in those with higher baseline exercise capacity (6-minute walk) (r=+0.368; p=0.05), PCR (r=+0.382; p=0.04), and lower SF-36 mental health score (r=-0.389; p=0.04). Age, hemodialysis vintage, burden of chronic illness, medication usage, and protein and dietary intake were notably not significant predictors of anabolic adaptation (change in thigh muscle CSA, albumin, and knee extension strength).

Clinical Outcomes Associated with Anabolic Adaptations

The increase in knee extension strength over the 24-week trial was associated with beneficial changes in nutritional status, including decreased waist circumference (r=-0.465; p=0.03) and thigh intramuscular fat (r= -0.544; p<0.02), increased prealbumin (r=+0.422; p=0.04) and albumin (r=+0.422; p=0.04). The increased strength was also directly related to improvements in 6-minute walk distance (r=+0.484; p=0.02), as well as decreased WBC (r=-0.397; p=0.05). Ninety-one
percent of the change in knee extensor strength was explained by increase in specific
tension ($r=+0.956; p<0.001$). Improvement in albumin over the 24-week trial was
significantly associated with a reduction in WBC ($r=-0.388; p=0.04$). Increased thigh
muscle CSA over the 24-week trial was directly associated with increases in body
weight ($r=+0.497; p=0.02$), BMI ($r=+0.427; p=0.04$), and SF-36 role emotional
($r=0.618; p=0.001$), and decreases in logCRP ($r=-0.656; p=<0.001$), and WBC ($r=-
0.452; p=0.03$).

**Compliance**

Total compliance in the 24WK group during the entire trial was 68.2±25.5%
including dropouts and 77.4±16.0% excluding dropouts. In the 24WK group,
compliance was 77.7±18.6 including dropouts and 84.6% excluding dropouts during
the first 12 weeks of PRT. In the 24WK group, compliance was 58.0±34.7 including
dropouts and 69.6±24.3% excluding dropouts during the final 12 weeks of PRT.
Compliance to PRT in the 24WK group was significantly lower in the final 12 versus
initial 12 weeks inclusive of dropouts ($p=0.008$) and tended to be lower exclusive of
dropouts as well ($p=0.06$). Compliance to PRT was not statistically different between
24WK and 12WK exclusive (69.6±24.3 and 71.6±25.2%, respectively) ($p=0.84$) or
inclusive of dropouts (58.0±34.7% and 58.7±35.8%, respectively) ($p=0.96$) during the
final 12 weeks of the trial when both groups were exercising. The number of training
sessions attended was not significantly related to the burden of chronic illnesses or
intercurrent acute illness.

**Adverse events**

Over the entire 24-week trial, no statistically significant differences were
observed between 24WK and 12WK groups in common dialysis-related complaints
including headaches (1(0-4) and 0(0-4), respectively; p=0.43), hypotension (2(0-10) and 0(0-6), respectively; p=0.11), and fistula/cannulation difficulties (0(0-3) and 0(0-2), respectively; p=0.31). The incidence of acute illnesses, including flu/cold symptoms and extreme fatigue/exhaustion over the 24-week trial was significantly higher in 24WK versus 12WK (5.6±2.6 and 3.5±2.5, respectively; p=0.04), as was incidence of cramping during and immediately post-dialysis (1(0-8) and 0(0-6), respectively; p=0.04). There was no significant difference between 24WK and 12WK groups in total visits to health care professionals over 24 weeks (7.4±2.2 visits and 8.3±4.0 visits, respectively; p= 0.45). Incidence of falls was low and did not differ significantly between groups (24WK=0(0-4) and 12WK=0(0-1); p=0.59). One patient in the 12WK group experienced a fistula infection during the usual care portion (initial 12 weeks) of the trial (p=0.73). One elderly patient in the 24WK group (73.3yr female, 3.8yr on HD) suffered a partial tear of the right rotator cuff in week 6 of PRT, but continued lower body training for the remainder of the trial. No cardiovascular symptoms were documented during any exercise testing or training sessions despite the high burden of cardiovascular disease.

DISCUSSION

PEAK is the first randomized controlled trial to evaluate the efficacy of isolated, high-intensity PRT in patients receiving maintenance HD treatment for the management of ESRD. Our previous report (Cheema et al, unpublished; See Chapter 5) demonstrated that 12 weeks of intradialytic PRT could significantly enhance
muscular strength, reduce inflammatory marker C-reactive protein, improve nutritional status and body composition, and enhance QOL versus usual standard of care.

We now report that an extended duration of intradialytic PRT results in significantly greater anabolic adaptation than a shorter duration, as reflected by the significant improvement of knee extension strength (p=0.03), albumin (p=0.03), and thigh muscle CSA (0.04) in the 24WK group versus the 12WK group, and the direct relationship between the number of sessions attended and the relative strength gain in the whole cohort. There was also a trend toward the improvement of vitality with this extended duration of PRT (p=0.06). Overall, six months of PRT was associated with significant and clinically important improvements in strength, nutritional status, body composition, self-reported physical function, and observed exercise capacity.

To date, four uncontrolled trials have evaluated muscle composition outcomes following exercise training in this cohort.29-32 One trial implementing a 6-month aerobic training regimen observed significant muscle fiber hypertrophy,31 while two trials involving 12 weeks of intradialytic cycling did not report significant myogenic adaptation.29,32 Kouidi et al30 reported significant muscle hypertrophy in 7 patients following a 6-month exercise regimen involving aerobic training and low-volume, low-intensity strength training performed on non-dialysis days. None of these studies implemented high-intensity PRT, now recognized as the preferred exercise modality for inducing skeletal muscle hypertrophy in the frail elderly and those with catabolic illness.11 In our previous report of the PEAK trial (Cheema et al, unpublished; See Chapter 5) a holistic anabolic shift was initiated in patients receiving 12 weeks of PRT versus those receiving usual care only. However, the myogenic response of thigh muscle composition, as evaluated via CT scan, was hypothesized to require
extended training, as revealed in our present report. More sensitive analysis techniques, including muscle biopsies, may have revealed skeletal muscle hypertrophy within the first 12 weeks of our training regimen, as has been seen in other cohorts (e.g. predialysis patients) although this hypothesis remains to be investigated.

The increased muscle area observed at 6 months is an important outcome with direct relevance to metabolism, nutritional status, insulin sensitivity, functional status, general health, QOL, and longevity in this cohort. We found that increased thigh muscle CSA was inversely related to logCRP (p=<0.001) and white blood cell count WBC (p=0.03), raising the possibility that a reduction in inflammation accompanying anabolic exercise may partially explain the muscle hypertrophy observed. We have noted this same response pattern to PRT in predialysis ESRD. It is not clear why better emotional health was associated with greater hypertrophy in the current study, but we have also previously reported that fewer depressive symptoms predicted more robust muscle hypertrophy after PRT in frail elders. It is possible that reported associations between inflammatory cytokines and depression may underlie these patterns of response, and this is an extremely important area for further investigation.

Several HD trials have noted improved muscular strength following exercise training interventions. In the only other trial to prescribe high-intensity PRT in this cohort, Headley et al., in an uncontrolled trial, demonstrated an improvement in isokinetic knee extension strength with 12 weeks of high-intensity PRT performed on non-dialysis days. Our present report importantly reveals that similar relative enhancement of muscular strength in this cohort can be elicited by prescribing high-intensity PRT during dialysis, increasingly becoming regarded as the most
appropriate route by which to stimulate exercise adherence in this patient population.\textsuperscript{10,14,15} Lending support to this conclusion is the fact that in our study no difference was observed between strength gains in the fistula arm, which was trained immediately predialysis, versus strength gains in the non-fistula arm, which was trained during dialysis (p=0.77).

The improvement of lower-body muscle strength is functionally important given that patients with ESRD are significantly weaker and have diminished exercise capacity versus healthy, sedentary counterparts. Our findings revealed that the improved knee extension strength was significantly related to improved exercise capacity (6-minute walk; p=0.02), explaining 23.4\% of the variance in distance walked. Moreover, our trial demonstrates that, not only can strength be preserved in the face of a continued catabolic disease state, it can be increased to a clinically meaningful extent in this vulnerable cohort.

Similar to our findings, an improvement of albumin has been observed in an uncontrolled trial prescribing 6-months of intradialytic exercise cycling (p=0.02).\textsuperscript{45} Declining albumin levels and weight loss are consistently and strongly associated with mortality in ESRD.\textsuperscript{46} Notably, improvement in albumin was not related to better dietary intake or improved dialysis adequacy in our study. Others have shown that improved nitrogen retention is improved by PRT in healthy older adults, without altering dietary protein sources.\textsuperscript{47} Given the well-known difficulty of implementing nutritional interventions in dialysis patients due to renal dietary restrictions, anorexia, multiple co-morbid diseases, and concomitant sarcopenia and obesity, the ability to maintain or improve protein nutrition by physical activity rather than diet is of potentially great significance. There is evidence that higher BMI is associated with better health outcomes\textsuperscript{48} and reduced mortality risk\textsuperscript{36} in dialysis patients, with the
protective effect limited to those with greater muscle mass. Thus, the adaptations induced by PRT (increased weight and muscle area with no change in whole body or regional fat mass) would be predicted to yield long-term reduction in morbidity and mortality if they were sustained and/or increased further over time.

The general time course of muscular strength adaptations experienced by our patients are consistent with those observed in studies of untrained older cohorts, which have documented that initial training (e.g. 12 weeks) is associated with greater strength gains, with a reduced rate of adaptation with further training (Table 3). Our findings are also consistent with those of healthy adults in that neuromuscular (i.e. specific tension) adaptations predominated the early phase of adaptation with greater contribution from skeletal muscular hypertrophy as these strength gains progress.

Although completely novel, anabolic exercise was well accepted in the dialysis unit, with a high rate of medical eligibility, consent rate, adherence rate, and low dropout rate. Compliance to training in the 24WK group in the initial 12 weeks in our trial (84.6%) was comparable to that reported in the 12-week trial conducted by Headley et al (87.7%). Although compliance was modestly reduced in the second 12 weeks in our trial, it was unrelated to number of chronic diseases or intercurrent acute illnesses in this cohort, and factors related to long-term compliance remain to be elucidated. Additional long-term trials are needed to identify barriers to intradialytic anabolic exercise participation, and to test behavioral strategies designed to overcome potentially addressable barriers.

Two limitations of our study include the lack of a sham exercise control activity, and the unblinded assessment of physical performance and questionnaire
data. Given the shared dialysis unit space, it would not have been possible to blind subjects to the PRT or sham intervention, as only one would involve weights.

In summary, the PEAK trial supports the clinical utility of a 6-month intradialytic PRT regimen in patients with ESRD undergoing maintenance HD treatment, as a means to induce significant anabolic adaptations, improve nutritional and functional status, and aspects of QOL. Future trials should be undertaken in this unique cohort to explore potential long-term benefits of such adaptations to PRT in terms of morbidity and mortality.

REFERENCES


Figure 1:

Reviewed (104)

Ineligible (51)
- Died Before Enrolling (14)
- Moved Away from Unit (7)
- Kidney Transplanted (3)
- Medical Exclusion to PRT (20)
- Study-related Exclusion (7)

Eligible (53)

Refused (19)

Consented (34)

Randomized to 24WK Group (18)

Unavailable for Week 24 testing (3)
- Moved to Home Dialysis (2)
- Death (1)

Completed Week 24 testing (15)

Randomized to 12WK Group (16)

Unavailable for Week 24 testing (3)
- Family Obligations (1)
- Unstable Cardiac Condition (1)
- Death (1)

Completed Week 24 testing (13)
Figure 2a:

Figure 2b:
Figure 3a:

Figure 3b:

Figure 3c:
Figure 4:

![Triceps Strength Chart](chart.png)

Change in Triceps Strength (Kg) after 12 weeks of PPT

- Fistula Arm
- Non-fistula arm
### Table 1: Baseline characteristics of the total cohort and groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total Cohort (n=34)</th>
<th>24WK Group (n=18)</th>
<th>12WK Group (n=16)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>64.4(13.7)</td>
<td>61.4(16.0)</td>
<td>67.8(16.0)</td>
<td>0.18</td>
</tr>
<tr>
<td>Male:Female</td>
<td>24:10</td>
<td>12:6</td>
<td>12:4</td>
<td>0.60</td>
</tr>
<tr>
<td>Hemodialysis Vintage(^\d) (y)</td>
<td>2.2, 0.3-16.7</td>
<td>2.4, 0.3-16.7</td>
<td>2.0, 0.6-10.3</td>
<td>0.37</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>73.9(16.4)</td>
<td>71.7(16.6)</td>
<td>76.3(16.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>165.5(10.3)</td>
<td>164.8(8.7)</td>
<td>166.2(12.1)</td>
<td>0.69</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>27.0(5.7)</td>
<td>26.4(5.9)</td>
<td>27.6(5.5)</td>
<td>0.54</td>
</tr>
<tr>
<td>Medications/day (n)</td>
<td>8.2(2.8)</td>
<td>8.3(3.4)</td>
<td>8.1(2.0)</td>
<td>0.78</td>
</tr>
<tr>
<td>Tobacco use history (n)</td>
<td>18</td>
<td>8</td>
<td>10</td>
<td>0.29</td>
</tr>
<tr>
<td>Chronic Diseases(^\d) (n)</td>
<td>5.6(1.7)</td>
<td>5.2(1.6)</td>
<td>6.0(1.8)</td>
<td>0.18</td>
</tr>
<tr>
<td>- HT (n)</td>
<td>34</td>
<td>18</td>
<td>16</td>
<td>1.00</td>
</tr>
<tr>
<td>- Depression(^\d) (n)</td>
<td>11</td>
<td>7</td>
<td>4</td>
<td>0.63</td>
</tr>
<tr>
<td>- Diabetes (n)</td>
<td>9</td>
<td>2</td>
<td>7</td>
<td>0.03</td>
</tr>
<tr>
<td>- CAD (n)</td>
<td>9</td>
<td>4</td>
<td>5</td>
<td>0.55</td>
</tr>
<tr>
<td>- Stroke (n)</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>0.23</td>
</tr>
</tbody>
</table>

**Primary Cause of ESRD**

- GN (n)           | 7 | 3 | 4 | -  |
- HT (n)           | 6 | 2 | 4 | -  |
- Diabetes (n)     | 4 | 1 | 3 | -  |
- Ischemia (n)     | 4 | 3 | 1 | -  |
- PCKD (n)         | 4 | 3 | 1 | -  |
- IgA nephropathy (n) | 3 | 3 | 0 | -  |
- Analgesic use (n) | 3 | 1 | 2 | -  |
- SLE (n)          | 1 | 1 | 0 | -  |
- Other (n)        | 2 | 1 | 1 | -  |

BMI=Body Mass Index; HT=hypertension; CAD=coronary artery disease; GN=glomerulonephritis; PCKD=polycystic kidney disease; SLE=systemic lupus erythematosus

Data reported according to mean values with standard deviations presented in parentheses for normally distributed variables

\(^\d\)Non-normal distribution: median values and range reported

\(^\d\)Includes diagnosis of ESRD

\(^\d\)Mild to severe depression diagnosed according to the Geriatric Depression Scale (GDS)

Normally distributed variables analyzed with unpaired t-tests

Non-normally distributed variables analyzed with Mann-Whitney U test, nominal variables with Chi-square test

p-values correspond to comparisons between the experimental and control group

148
### Table 2: Functional Performance, Muscle and Physical Activity

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 24</th>
<th>(p^*)</th>
<th>(p^*)</th>
<th>(p^*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Week 0 vs 12</td>
<td>Week 0 vs 24</td>
<td>Week 12 vs 24</td>
</tr>
<tr>
<td>Total Body Strength (kg)</td>
<td>97.6(30.0)</td>
<td>119.4(37.5)</td>
<td>129.5(42.5)</td>
<td>&lt;0.001</td>
<td>0.005</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Knee Extension Strength (kg)</td>
<td>49.3(22.5)</td>
<td>62.0(27.3)</td>
<td>62.7(27.3)</td>
<td>0.012</td>
<td>0.01</td>
<td>0.008</td>
</tr>
<tr>
<td>Total Hip Abduction Strength (kg)</td>
<td>23.3(9.0)</td>
<td>27.3(8.9)</td>
<td>29.7(10.8)</td>
<td>&lt;0.001</td>
<td>0.007</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Triceps Strength (kg)</td>
<td>26.4(9.1)</td>
<td>30.3(10.0)</td>
<td>33.7(11.3)</td>
<td>&lt;0.001</td>
<td>0.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Six-minute walk (m)</td>
<td>487.3(156.0)</td>
<td>507.4(168.4)</td>
<td>521.6(171.3)</td>
<td>0.01</td>
<td>0.06</td>
<td>0.003</td>
</tr>
<tr>
<td>Physical Functioning</td>
<td>68.9(32.0)</td>
<td>79.3(25.7)</td>
<td>80.7(27.8)</td>
<td>0.003</td>
<td>0.004</td>
<td>0.002</td>
</tr>
<tr>
<td>PASE</td>
<td>82.6(51.7)</td>
<td>104.4(58.6)</td>
<td>105.1(63.5)</td>
<td>0.18</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

SF-36=Medical Outcomes Trust Short Form-36 Heath Survey, higher scores indicate better function
PASE=Physical Activity Scale for the Elderly, higher scores indicate more habitual activity
Data reported according to mean values with standard deviations presented in parentheses
\(p^*\)-values correspond to change over time within the 24Wk experimental group as calculated via repeated measures analysis of variance
\(p^*\)-Fisher least Significant Least significant difference post hoc t-test
Table 3: Body composition indices

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 24</th>
<th>(p^*)</th>
<th>(p^1)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Week 0 vs 12</td>
<td>Week 0 vs 24</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>69.9(15.0)</td>
<td>71.3(15.1)</td>
<td>71.6(15.1)</td>
<td>0.004</td>
<td>0.008</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0(5.9)</td>
<td>26.5(5.8)</td>
<td>26.6(5.7)</td>
<td>0.006</td>
<td>0.01</td>
</tr>
<tr>
<td>Mid-thigh circumference (cm)</td>
<td>46.8(3.9)</td>
<td>47.8(3.7)</td>
<td>48.1(3.3)</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Mid-arm circumference (cm)</td>
<td>29.7(3.7)</td>
<td>30.2(3.3)</td>
<td>30.0(3.3)</td>
<td>0.48</td>
<td>-</td>
</tr>
<tr>
<td>Mid-calf circumference (cm)</td>
<td>33.9(3.0)</td>
<td>34.2(2.8)</td>
<td>34.3(2.9)</td>
<td>0.25</td>
<td>-</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.2(19.5)</td>
<td>94.7(18.9)</td>
<td>95.6(18.1)</td>
<td>0.29</td>
<td>-</td>
</tr>
<tr>
<td>Thigh muscle CSA (cm²)</td>
<td>99.0(22.0)</td>
<td>99.7(20.6)</td>
<td>101.0(22.9)</td>
<td>0.26</td>
<td>-</td>
</tr>
<tr>
<td>Thigh muscle attenuation (Hounsfield units)</td>
<td>85.6(2.8)</td>
<td>85.6(2.2)</td>
<td>86.0(2.2)</td>
<td>0.28</td>
<td>-</td>
</tr>
<tr>
<td>Thigh subcutaneous fat (cm²)</td>
<td>64.1(32.0)</td>
<td>67.3(34.0)</td>
<td>67.8(32.5)</td>
<td>0.25</td>
<td>-</td>
</tr>
<tr>
<td>Thigh intramuscular fat (cm²)</td>
<td>8.22(7.87)</td>
<td>7.85(6.73)</td>
<td>6.85(5.19)</td>
<td>0.34</td>
<td>-</td>
</tr>
<tr>
<td>Thigh total fat (cm²)</td>
<td>82.0(44.1)</td>
<td>85.8(46.0)</td>
<td>85.8(44.4)</td>
<td>0.32</td>
<td>-</td>
</tr>
</tbody>
</table>

BMI=body mass index

Data reported according to mean values with standard deviations presented in parentheses

\(p^*\)=values correspond to change over time within the 24Wk experimental group as calculated via repeated measures analysis of variance

\(p^1\)=Fisher least Significant Least significant difference post hoc t-test
CHAPTER 7

Rotator Cuff Tear During Resistance Training in an Older Woman:

A Case Report and Review of the Literature
ABSTRACT

The purpose of our present report is: (1) To describe the events surrounding a rotator cuff tear in an elderly woman performing progressive resistance training (PRT) in a recent clinical trial, (2) To summarize potential predisposing factors for this injury in this patient, and (3) To perform a literature search to determine if rotator cuff lesions have been documented secondary to PRT in older adults. The patient was a 73-year-old Caucasian woman with end-stage renal disease. Investigation revealed a full-thickness tear of the supraspinatus secondary to performing a shoulder press exercise unilaterally using a 5kg dumbbell. Our literature search yielded one previous report of rotator cuff tear secondary to PRT in the elderly. However, adverse events to PRT in the elderly are often not recorded and reported systematically. Given the medical history, health status, physical condition, and age of our patient it is highly probable that degenerative histological changes predisposed this patient to the tear of the supraspinatus. Maintenance of rotator cuff muscle strength, mobility, and specific exercise throughout life may prevent atrophy, degeneration, and risk of spontaneous rotator cuff tears as well as those occurring during ADL or recreational pursuits. Adequate, thorough reporting of adverse events during clinical trials is necessary to delineate the relative risk of rotator cuff tears among the elderly with all modalities of exercise. Adherence to proper PRT technique is necessary to minimize such events and maintain the favorable risk to benefit ratio suggested by the majority of the literature of PRT in the elderly.

Keywords: Geriatric, exercise, risk, supraspinatus, end-stage renal disease, case study
INTRODUCTION

Over the past several decades, with the prevailing demographic shift, greater attention has been directed toward promoting physical activity and exercise in older adults. In particular, progressive resistance training (PRT) has become widely recognized as an important exercise modality in aging, given its robustness for targeting age-related sarcopenia and associated health-related impairments. To date, research evaluating the efficacy of PRT in diseased and non-diseased adults cohorts has overwhelmingly demonstrated that this modality of training is feasible, beneficial, and safe. However, given its increasing prescription and popularity in this cohort, there is an ongoing need to report on the safety of PRT interventions for the aging population, which includes thorough documentation of adverse events encountered during clinical trials.

The rotator cuff consists of four muscles, the subscapularis, the supraspinatus, the infraspinatus and the teres minor and their musculotendinous attachments, which function in concert to dynamically stabilize the glenohumeral joint. Disorders of the shoulder commonly involve the rotator cuff complex. Rotator cuff tears during exercise are typically the end product of microtrauma incurred by chronic, repetitive movement of the shoulder joint. These injuries have frequently been observed in athletes engaging in a variety of sports involving repetitive overhead arm motion or throwing, including tennis, swimming, baseball, and PRT. Symptoms of rotator cuff lesions may include pain, reduced strength and range of motion, and inability to perform activities of daily living (ADL) involving the affected extremity. Older adults may be more susceptible to rotator cuff lesions during overhead exercise than their younger counterparts due to the degenerative
histological changes that typically accrue with age.\textsuperscript{10} Shoulder pain, involving rotator cuff pathology, is recognized as a significant cause of morbidity and disability in the middle-aged and elderly population.\textsuperscript{8,6,11-15} The incidence of partial and full-thickness rotator cuff tears increases with age,\textsuperscript{16} and such injuries been known to occur spontaneously in older individuals.\textsuperscript{17} At present however, there has been minimal investigation into the susceptibility of elderly individuals to rotator cuff lesions during upper body PRT exercise.

The purpose of our present report is three fold: (1) To describe the events surrounding a rotator cuff tear in an elderly woman performing PRT in a recent clinical trial,\textsuperscript{18,19} (2) To summarize potential predisposing factors for this injury, given the medical history, health status and age of our patient, and (3) To perform a literature search to determine if rotator cuff lesions have been documented secondary to PRT in older adults.

\section*{CASE REPORT OF AN ELDERLY WOMAN}

The \textit{Progressive Exercise for Anabolism in Kidney Disease} (PEAK) trial was initiated to evaluate the efficacy of high-intensity PRT performed during routine hemodialysis treatment for patients with end stage renal disease.\textsuperscript{18,19}

\section*{Medical History of the Patient}

One patient enrolled in PEAK was a 73-year-old Caucasian woman with end-stage renal disease (ESRD) secondary to diabetic nephropathy. She had been receiving hemodialysis treatment 3 times per week, approximately 4.5 hours per
session, for 3.8 years prior to her involvement in the PEAK trial. Past medical history was notable for osteoarthritis of both knees, hypertension, type 2 diabetes, thyroid disease, obesity (BMI=32.3), depression, restless legs syndrome, transient atrial fibrillation related to hyperkalemia, and mitral regurgitation. Past surgical history included a hysterectomy and right nipple removal, negative for malignancy. The patient was prescribed a 4-wheel walker for ambulation and reported poor balance and several falls while walking previously with a cane. Medications included insulin, erythropoietin, amitriptyline hydrochloride, clonazepam, simvastatin, folic acid, vitamin B forte, thyroxine sodium, amiodarone, calcium carbonate, and aspirin. The patient did not drink alcohol or have a history of tobacco use. According to the patient, all ADL were independently performed prior to enrolling in the PEAK trial.

PRT Regimen and the Onset of Shoulder Pain

Resistance training was performed using free-weight dumbbells for upper body exercises and weighted ankle-cuffs for lower body exercises. Supervised exercise was conducted 3 times per week during the first two hours of routine, outpatient hemodialysis treatment. During each PRT session, the patient performed two sets of 8 exercises at a rating of perceived exertion of 15-17 ("hard" to "very hard") according to the Borg Scale, including: (1) shoulder press, (2) external shoulder rotation, (3) side shoulder raise, (4) triceps extension, (5) biceps curl, (6) straight-legged raise, (7) bent knee hip flexion, and (8) straight-legged hip abduction. The patient also completed two sets each of a half-bridge exercise targeting the gluteus maximus, and a double leg raise exercise targeting the upper and lower rectus abdominus. Both of these exercises were performed without resistance being applied.
to momentary neuromuscular fatigue. Our patient preferred receiving hemodialysis while lying in a semi-recumbent position in a hospital bed, while all other patients enrolled in the PEAK trial exercised while seated in a chair.

The patient completed all training sessions (100%), as prescribed, until the second training session of week 4 (session 11). The training load of each resistance exercise was well tolerated and appropriately progressed for a sedentary individual of this age over the first 10 sessions. Maximal training load in all loaded exercises increased linearly up until session 11.

Session 11 began with the shoulder press exercise using a 5kg dumbbell unilaterally. During the few repetitions of the first set, the patient noticed a brief twinge in her right shoulder, but was able to complete the remainder of the set and the remaining upper body exercises (i.e. side shoulder raise, external shoulder rotation, triceps extension, and biceps curl) with appropriate loading without noticing any pain. However, just prior to the next training session the patient mentioned that she had been experiencing pain over the past few days. The pain was localized to the right anterior shoulder, and extended distally along the biceps brachii muscle. The patient mentioned that the pain had not affected her sleep over the previous evenings, but did limit her ability to use here right arm to cook, feed herself, and perform other ADL requiring right arm use.

Upper body training was ceased at this point for the remainder of the trial; however, the patient continued to perform lower body resistance training without incident. Compliance to the training regimen (sessions attempted/sessions offered) in this patient was 79.8 ± 18.6 %. No other adverse events related to exercise training were reported in this patient for the remainder of the study. However, weekly documentation of adverse events revealed that the patient experienced four separate
falling incidents at home during the trial. Bruising of the knees on one occasion was
the only physical consequence communicated by the patient. It should be noted that
the patient was not utilizing her assistive device on any of these occasions.

Medical Examinations and Diagnoses

For the first two weeks following the onset of shoulder pain, the patient self-
medicated with arthritis cream and heat packs. Medical examination two weeks from
the date of injury reported no obvious deformity or swelling, with pain on palpation
of the acromioclavicular joint. Pain was evident between 90 and 180 degrees of
active arm flexion and abduction. Analgesics were prescribed. Radiographic
examination of the shoulder revealed degenerative disease and possible
chondrocalcinosis affecting the acromioclavicular joint and the insertion of the
rotator cuff. No rotator cuff calcification, subacromial spur, fracture or dislocation
was present.

The patient met with a rheumatologist (M.L.) six weeks from the onset of
shoulder pain. Her pain, which was very severe, had improved (rated 3 out of 10,
where 10 is severe pain). The history and examination was consistent with an acute
rotator cuff tear, which was confirmed on ultrasound one week later. A bilateral
ultrasound revealed a large full thickness tear of the right supraspinatus tendon in its
mid and posterior portions (1.3 cm long) associated with a probable tear of the
insertion of the infraspinatus tendon, as well as a large associated subdeltoid bursal
effusion.

As the symptoms were slowly improving the patient refused specific therapy
offered, including physiotherapy and/or cortocosteriod injection into the subacromial
bursa to reduce any associated inflammation.
Eleven weeks post injury, symptoms became worse with increased pain and limitation of shoulder joint range of motion (active abduction reduced to 30 degrees) and a 40 mg cortisone (Depo-Medrol) injection was administered into the subdeltoid bursa. Subsequently, the patient did experience relief of pain symptoms for until week 13, but thereafter the pain returned and became worse. At week 15, the rheumatologist (M.L.) reexamined the patient. Active abduction was limited to just 30 degrees with negligible internal and external rotation. However, on passive movement, the rheumatologist was able to abduct the arm of the patient to between 120 and 140 degrees, with almost full internal and external rotation, suggesting that there was no evidence of frozen shoulder syndrome. Clinically, there was no evidence of biceps pathology. The rheumatologist administered 2ml of Kenacort and a small amount of lignocaine into the subdeltoid bursa, and an orthopedic surgeon was consulted.

MRI at this time revealed degenerative disease of the acromioclavicular joint including lateral downsloping of the acromion and an anteroinferior acromial spur, which would predispose to impingement (Figure 1). Other findings included: (1) a full thickness supraspinatus tendon tear with approximately 3cm of medial retraction of the tendon, (2) minor atrophy affecting the supraspinatus muscle belly, (3) a tear of the supraspinatus insertion to the greater tuberosity, (4) swelling of the subscapular tendon at its insertion in keeping with tendinopathy and a probable partial tear, (5) a fairly extensive anterior labral tear, (6) focal cartilage thinning anteroinferiorly involving the glenoid with some subcortical cysts having formed. The consulting radiologist (R.S.) reported diagnoses according to the images presented in Figure 1.

Approximately 32 weeks following the adverse event, the patient remained
functionally limited. She required the assistance of her husband with all ADL, including cooking and dressing, compensating for her injury by using her left hand as much as possible. She had ongoing pain on active movement of her right arm due to the rotator cuff tear. Use of her walker results in pain that is 6/10 in severity. On examination, she did not have frozen shoulder syndrome and the consulting rheumatologist (M.L.) believed that physiotherapy would not be of any value at this stage.

As surgery is rarely indicated in the management of full-thickness rotator cuff tears in low-functioning elderly patients, such injuries are typically managed conservatively.\(^20\) Surgical repair may be plagued with recurrent tears, peri-operative complications, prolonged recovery periods, and elevated mortality risk. Thus, non-operative management of rotator cuff tears, as described in the literature,\(^21\) has been implemented in this case for over 6 months with minimal success, and referral to an orthopedic surgeon is currently under consideration.

**Potential Predisposing Factors**

The supraspinatus tendon is the most commonly involved tendon in rotator cuff tears.\(^22\) Pathogenesis of this injury in the aged is typically regarded as multifactorial. The supraspinatus is biomechanically prone to impingement,\(^23\) and becomes more hypovascular with age,\(^24\) predisposing this tendon to greater microtrauma and intrinsic degeneration over time versus other rotator cuff tendons. Moreover, it has been suggested that histological degeneration induced by chronic acidosis and hyperparathyroidism may predispose patients with ESRD to tendon rupture.\(^25\)

Given the medical history, health status, physical condition, and age of our
patient it is highly probable that degenerative histological changes predisposed this patient to the full-thickness supraspinatus tear. Diagnosed degenerative changes in our patient included: degeneration of the acromioclavicular joint, development of an anteroinferior acromial spur, and focal cartilage thinning anteroinferiorly involving the glenoid with some subcortical cysts. All of these degenerative changes may all have contributed to the risk of supraspinatus tear in our patient, along with histological intrinsic degeneration of the tendon itself. According to Sano et al\textsuperscript{10} degenerative histological changes of the supraspinatus tendon are negatively correlated with ultimate tensile strength ($r = -0.60$; $p < 0.013$). Thus, in older sedentary individuals even minor straining of the tendon may induce a tear.\textsuperscript{26}

The shoulder press exercise, which the patient was performing when she noted a twinge in her arm, involves the activation of the deltoid, triceps, and all four rotator cuff muscles, either as prime movers in abduction (i.e. supraspinatus) and external rotation of the humerus (i.e. teres minor, infraspinatus) and/or stabilizers of the glenohumeral joint (supraspinatus, teres minor, infraspinatus, subscapularis). It is possible that as the patient extended her arm up upward to complete a repetition of the shoulder press exercise, the supraspinatus became impinged within the coracoacromial arch resulting in the full-thickness tear.

**ROTATOR CUFF TEARS DURING PRT IN THE ELDERLY**

To determine if rotator cuff injuries secondary to PRT in older adults (>$60$ yr) have been reported in the literature, as case studies or as adverse events during randomized controlled trials of PRT, we conducted a literature search in January
2005 from the year 1966 to 2004, limited to the English language, using computerized databases, including Medline, CINAHL, Cochrane Database of Systematic Review, Embase, PEDro, SportDiscus, and Web of Science. The search combined key words related to the rotator cuff complex (i.e. shoulder, rotator cuff, supraspinatus, infraspinatus, supscapularis, teres minor), injury (i.e. rupture, tear, lesion, adverse event), PRT (i.e. exercise, resistance training, weight lifting, strength training), and the elderly (i.e. adult, older adults, geriatric, aged, elderly, seniors). Randomized controlled trials of PRT in the elderly were also hand-searched for evidence of adverse events involving shoulder injuries of any kind.

Results of Search

Evidence of four adverse events involving the shoulder joint were reported in 3 randomized controlled trials of PRT in the elderly (>60yr). In a study by Meulman et al, a subject withdrew from the study due to a “slight shoulder strain”. In a study by Hortobagyi et al, a subject withdrew because of “pain and bruising in the shoulder caused by the shoulder padding on the leg press machine. Neither of these report specifically diagnosed an injury involving the rotator cuff per se however. In a study by Binder et al, two patients from an elderly cohort (83±4 yr) discontinued a 9-month PRT program: one due to a rotator cuff injury sustained during training, and the other due to worsening of an existing shoulder problem during training. No detailed case reports of any of these 4 patients were located.
DISCUSSION

Our report of an older woman sustaining a rotator cuff tear during PRT likely represents a case of underlying risk factors and an acute traumatic event (i.e. a shoulder press exercise). It is likely that chronic inactivity and a greater burden of chronic disease and frailty in this patient predisposed her to this injury. She had 7 chronic diseases, 11 prescribed medications, used a walker for ambulation, had a history of falls, and scored 1.5 to >2 SD below the mean for measures of lower body strength and exercise capacity in our trial.\textsuperscript{18,19} For example, 6-min walk distance was only 158m in this patient compared with to a mean of 470m in our sample cohort (>2 SD difference).

Adverse events to PRT in the elderly are often not recorded and reported systematically.\textsuperscript{30} We were able to document only one rotator cuff tear,\textsuperscript{29} and 3 other musculoskeletal injuries involving the shoulder joint\textsuperscript{27-29} after an extensive search of review articles and randomized controlled trials of PRT in older adults. In a recent meta-analysis, Latham et al\textsuperscript{30} concluded that it is difficult to determine the risks and benefits of PRT in the elderly because adverse events have been poorly reported in the majority of trials to date. Of 66 randomized controlled trials reviewed by Latham et al,\textsuperscript{30} 35 (53\%) made no comments regarding adverse events sustained as a result of the intervention. The authors\textsuperscript{30} commented, however, that even studies suggesting to report on adverse events (31/66; 47\%), are likely to underreport or inaccurately depict these negative outcomes. For example, in 9 trials (13.6\%) greater attrition was observed in the PRT group versus the control group. Reasons for discontinuing training included increasing pain and musculoskeletal injury, however these complaints were not recorded as adverse events.
According to the Latham et al systematic review, only 7 trials (10.6%) provided a priori definition of “adverse event” in their respective methods section. Of these 7 trials however, there was minimal consistency in defining the term, with some studies reporting only serious events that the investigators considered attributable to the training program, while others reported all adverse events in each group. Indeed, many trials have been entirely vague in reporting on adverse events, using indistinct terminology such as “illness”, “soreness”, or “a musculoskeletal complaint” as a primary reason for a subject discontinuing with the prescribed training regimen, with no follow up being reported.

No shoulder injuries were reported secondary to PRT among the 7 trials providing a prior definition, as cited by Latham et al. However, in one of these studies, Pollock et al did note that 5 of 57 subjects (8.8%) incurred an arm/shoulder injury during one-repetition maximum (1RM) bench press strength testing on Nautilus equipment, though not during training as such.

**Rotator Cuff Injuries in Younger Athletes**

Shoulder injuries have been reported to occur in elite level weight lifters and power lifters, occurring at a frequency of 0.31 to 0.71 injuries per 1000 training hours, and affecting 13-17% of the 110 athletes surveyed in one report. The prevalence of rotator cuff involvement among these shoulder injuries was not reported however. Shoulder injuries have also been noted in amateur and recreational weight lifters. Our search yielded one case report of a subscapularis tear in a 49-year-old recreational athlete secondary to unsupervised, home-based resistance training. We found no evidence of a spontaneous rupture of the supraspinatus tendon secondary to resistance training in any cohort.
Prevention of Rotator Cuff Injury

The PEAK trial is has been ongoing for just over two years,\textsuperscript{18,19} with this report describing the only adverse event to date. Maintenance of rotator cuff muscle strength, mobility in general, and specific exercise throughout life may prevent atrophy, degeneration, and risk of tears during ADL, recreational pursuits, or spontaneously.\textsuperscript{24,25} Recommendations to minimize risk of rotator cuff injury during PRT include:

a) Avoid ballistic movements and swinging the weights

b) Use slow, controlled movement speed

c) Avoid extreme external rotation during movements

d) Use load $<90\%$ of 1RM for all exercises

e) Adjust the load progressively with strength adaptation

These recommendations may be considered "best practice" to minimize the risk of rotator cuff injury. The protocol we applied in our study\textsuperscript{18,19} is considered "best practice" by convention, however the injury described occurred nonetheless.

SUMMARY

Rotator cuff tears increase in prevalence with age. Such injuries are mostly attributable to degenerative changes that accrue as a consequence of biological aging and chronic illnesses, including end-stage renal disease. In particular, osteoarthritis, and deterioration of the tendon itself, may predispose older individuals to rotator cuff tears during the performance of ADL or specific exercise. To date, there has been
poor reporting of adverse events in randomized controlled trials of PRT in the elderly. Adequate, thorough reporting of adverse events during clinical trials is necessary to delineate the relative risk of rotator cuff tears among the elderly with all modalities of exercise. Adherence to “best practice” in terms of PRT technique (speed of movement, intensity of resistance, incremental and controlled progression of loading, and vigilance in eliciting new or changing symptoms) is necessary to minimize such events and maintain the favorable risk to benefit ratio suggested by the majority of PRT literature in the elderly.
REFERENCES


http://www.mmhc.com/altc/displayArticle.cfm?articleID=altec69


ACKNOWLEDGEMENTS

We sincerely appreciate the efforts of Ms. Jane Gregory in the preparation of this manuscript.

No conflicts of interest declared.
Figure 1. MRI Images: (1) lateral downsloping of the acromion and an anteroinferior acromial spur, which would predispose to impingement; (2) a full thickness tear of the supraspinatus to the greater tuberosity with approximately 3cm of medial retraction of the tendon, (3) minor atrophy affecting the supraspinatus muscle belly, (4) swelling of the subscapular tendon at its insertion in keeping with tendinopathy and a probable partial tear; (5) a fairly extensive anterior labral tear and focal cartilage thinning anteroinferiorly involving the glenoid with some subcortical cysts having formed.
APPENDIX A

Manual of Procedures
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1. METHODS

a. Screening for Eligibility

The patients of the hemodialysis centers involved in the PEAK study will undergo a multi-stage screening process to determine eligibility prior to recruitment into the study. Each of the steps of this process are done sequentially, as outlined in the sections that follow.

The inclusion criteria for the study are as follows:

- Age > 18 years
- Hemodialysis treatment for End Stage Renal Disease (ESRD) for a minimum of 3 months; expected to remain on hemodialysis for at least 6 months
- No acute or chronic medical conditions which make PRT potentially hazardous or primary outcomes of nutritional status and muscle mass and function impossible to assess (see below)
- Ambulatory, with or without an assistive device, but without the assistance of a person, for at least 50 meters
- Currently adequately dialyzed and stable during dialysis sessions (see below).
- Willingness to undergo study protocols and exercise training 3 days per week during hemodialysis sessions

STEP 1: Determination of Medical Eligibility for Exercise Training

Determination of medical eligibility will be made by a review of medical records, treating nephrologist interview, patient interview, and physical examination. Detailed discussion of the medical screening for progressive resistance training is outlined in Chapter 4- Medical Screening for Progressive Resistance Training in the Elderly (appended to this protocol). Briefly, patients will be evaluated for the presence of specific diagnoses or health conditions which make progressive resistance training potentially unsafe, or make the primary outcomes of the study difficult or impossible to measure. There are 4 separate components to the medical review process:

  a. Medical record review by research assistant
  b. Review of information gathered by Prof. Fiatarone Singh
  c. Patient interview to determine interest in study, and complete medical history details if interested
  d. Interview of treating Nephrologist
  e. In-person targeted history/physical exam by Drs. Fiatarone Singh, Kelly, O'Sullivan or Gillin

STEP 1a: Medical record review/interview

The research assistant will review the medical records on the dialysis unit as well as in the medical record department of the hospital for information required on the two forms:

- Resident Medical Screening Form
- Subject Medical History

(see Questionnaires)
STEP 1b: Review of information gathered by Prof. Fiatarone Singh

Information obtained by medical record review will be discussed with the research assistant following the principles outlined in Chapter 4 (Appendix I). Patients with irreversible conditions which are exclusionary will not be considered further. The remainder of the potential subjects will be classified as temporarily on hold or suitable for further screening immediately.

Step 1c: Solicitation of Patient Interest and Interview

All patients who are not in the permanently excluded category will be approached with a brief description of the study, to see if they are interested in further screening for eligibility. Patient interview will be used to complete portions of the Subject Medical History Form that are not available in the patient’s medical record.

Step 1d: Interview of Treating Nephrologist

A letter will be sent to the patient’s nephrologist in order to determine if there have been any recent events that may exclude the patient from participating in the study (Appendix 3). Attached to this will be a letter of release, signed by the patient, to allow the release of information about their health.

Step 1e: In-Person Targeted History/Physical Exam by Physician

Those patients who are interested in participating in the study will then undergo a physical examination by either Prof. Fiatarone Singh, Prof. Kelly, Dr O’Sullivan or Prof. Gillin (see Physician History and Physical Form in Questionnaires section). The purpose of this examination is to determine the patient’s level of stability on haemodialysis, and to detect any physical signs or symptoms that may be indicative of a possible contraindication to PRT.

If there are no potential contraindications to exercise and the patient is determined to be stable, the patient is then approached to give their consent to participate in the study. If the patient is found to be unstable on haemodialysis or has signs/symptoms of a condition that may be contraindicative to PRT, the physician will categorise the potential subject as either temporarily “On-Hold” or “Ineligible.”
b. Questionnaires

General Guidelines

Administration

All questionnaires are designed to be interviewer-administered in person and based on the self-report of the subjects. In no cases should the instruments be self-administered by subjects, due to problems with misinterpretation of instructions and missing data. Proxy answers for questionnaires are allowed in some cases, where this mode of administration has been validated, and/or it makes sense given the content of the questions. Questionnaires for which proxy answers are allowed are the following:

<table>
<thead>
<tr>
<th>Questionnaires/Record Abstraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject Medical Screening</td>
</tr>
<tr>
<td>Demographics</td>
</tr>
<tr>
<td>Mini-nutritional assessment</td>
</tr>
<tr>
<td>Physical activity scale for the elderly</td>
</tr>
</tbody>
</table>

Whenever a subject is incapable of answering one of the above questionnaires due to illness or other reason, proxy answers should be sought at that time-point. Record on all data sheets whether a given questionnaire was obtained by proxy or by self-report.

Time period covered by questionnaires

Each questionnaire has a unique period of time that is meant to be assessed by the questions it contains. It is critical to understand and adhere to the correct phrasing of the questions so that the subject’s current or previous status is obtained as required. Refer to the table below for the correct time period of each assessment.

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Time Period Covered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject Medical Screening</td>
<td>Life span of subject up to date of assessment</td>
</tr>
<tr>
<td>Physician History and Physical</td>
<td>Time period since last renal clinic visit</td>
</tr>
<tr>
<td>SF-36 Health Status Survey</td>
<td>3 months prior to interview to present day</td>
</tr>
<tr>
<td>Mini-Nutritional Assessment</td>
<td>3 months prior to interview to present day</td>
</tr>
<tr>
<td>Physical Activity Scale for the Elderly</td>
<td>7 days prior to interview to present day</td>
</tr>
<tr>
<td>Demographics</td>
<td>Date of interview</td>
</tr>
<tr>
<td>Geriatric Depression Scale</td>
<td>7 days prior to interview to present day</td>
</tr>
<tr>
<td>Weekly Status Check</td>
<td>7 days prior to interview to present day</td>
</tr>
<tr>
<td>Australian Food Frequency Questionnaire</td>
<td>30 days prior to testing day</td>
</tr>
</tbody>
</table>
Subject Burden

The large number of questionnaires poses a potential burden to the subject which will interfere with the quality of the data gathered and decrease the motivation of the subject to participate in further testing. In order to minimise the burden, adhere to the following principles:

- Ideally, questionnaires should be administered in a quiet, private environment. However, due to time constraints related to the length of the haemodialysis therapy and subject fatigue post-therapy, it is impossible to administer the questionnaires either before or after the haemodialysis session. Accordingly, the questionnaires will be administered during the haemodialysis session. In order to provide as much privacy as possible for the more sensitive questionnaires, a visual scale with “Yes” and “No” will be provided, and the subject will be instructed to point to the answer. Administer all questionnaires when the subject is not distressed and has time to attend to the task. Use visual aids for all multi-part answer formats, regardless of cognitive status of subject.
- Ensure that corrective lenses and hearing aids are in place.
- The questionnaires will take some time to complete. Provide as many breaks as necessary for the comfort of the subject.
- Reserve questionnaires that are likely to provoke emotional distress (GDS) or frustration for last so that the quality of the other questionnaires does not suffer.
- Deliver questionnaires in a pitch and tone that does not indicate to the patient the “correct” or “preferred” answer on your part.
- Avoid administering the questionnaires during mealtimes or medication times as much as possible in order to minimise disruptions and distractions.

Specific Questionnaires

a. Health Status
A tabulation of all medical diagnoses will be obtained via questionnaire of each subject and/or caregiver and review of all available medical records. Both over-the-counter and prescribed medications/ supplements will be recorded from medical records and subject interview. This review will form part of the medical screening of subjects and will be used in order to determine eligibility for a patient to enter the study. The Medical Screening Form, Subject Medical History Form and the Physician History and Physical Form will be completed prior to baseline testing. The health status of the subject will be monitored weekly thereafter by means of the Weekly Status Form.

b. Quality of Life
The Short Form-36 (SF-36) Medical Outcomes survey will be used to measure global health-related quality of life. This instrument has been widely validated in many different healthy and clinical cohorts internationally, and Australian norms are available. The tool provides 8 separate sub-scale rankings normalized on a scale from 0 (worst) to 100 (best). This questionnaire will be administered at baseline, 12 weeks and 24 weeks.
c. **Nutritional Status**

1. **Australian Food Frequency Questionnaire**
   The Australian Food Frequency questionnaire will be analysed using the Foodworks software. Both macronutrient and micronutrient intake will be ascertained using this questionnaire. This questionnaire will be administered at baseline, 12 weeks and 24 weeks.

2. **Mini-Nutritional Assessment**
   The Mini-nutritional assessment (MNA) is used to provide a global index of risk of malnutrition, using a combination of health status, anthropometric, physiological, and dietary intake questions and measurements at a single point in time. It has been found to be valid in comparison with more sophisticated nutritional assessments and correlates with clinical outcomes in older populations in many countries. This questionnaire will be administered at baseline, 12 weeks and 24 weeks.

d. **Habitual Physical Activity Level**
   Leisure, household and occupational activity levels will be estimated by the Physical Activity Scale for the Elderly questionnaire (PASE). The PASE is a brief, reliable and valid instrument for the assessment of physical activity in studies of older people. This questionnaire will be administered at baseline, 12 weeks and 24 weeks.

e. **Depression**
   Depression will be measured by the Geriatric Depression Scale (GDS), a questionnaire containing 30 yes/no questions including a variety of non-somatic symptoms related to depression, which may have been present over the last week. Scores greater than 9 are associated with clinical depression of increasing severity in community-dwelling elderly. This questionnaire will be administered at baseline, 12 weeks and 24 weeks.
B. Performance-based tests

I. General Guidelines

Performance-based testing is a means to quantitatively define or estimate the maximal physiologic capacity in a variety of domains that are thought to be relevant to functional status and mobility in individuals with chronic disease. These tests are valid and reproducible only if the directions are followed meticulously, so as to avoid inter-tester differences, which can otherwise be quite large. *Although each test is simple to perform, small errors in timing, instructions to the subject, or changes in environmental conditions can have large effects on the outcome.* For each test, its purpose, necessary equipment, subject preparation, environmental considerations, and exact protocol and data to be recorded are indicated in the sections that follow.

Because the attempt is to elicit maximal performance in each of these areas, it is essential that the subjects be aware of the requirements of the test, mentally and physically capable of giving a maximal effort, and as unfatigued as possible. The tests are to be performed in the order listed, if possible, in order to reduce the possibility of fatigue interfering with the subsequent test. In general, a 5 minute rest period is given between tests, during which time water may be offered, and additional explanations given. However, if a subject appears to need a longer break, than it should always be given, as this will improve performance.

Before beginning testing, an assessment should be made that the subject is competent to undergo testing, has signed the informed consent papers, and is medically stable. If there is any doubt as to the person's medical condition, or if an acute, previously undiagnosed serious symptom is discovered on questioning, seek advice from study clinical investigators or clinical care team members before continuing with the protocols. Always err on the side of caution in this regard. If a subject refuses all or part of testing in the middle of a session, for any reason, adhere to their wishes and stop at that point.

The most difficult and time-consuming portion of testing is often related to changing the subject’s position, location, and adjustment of the subject’s clothing. Therefore it is essential to group together testing protocols based on where the patient is located, and what condition they must be in.

**Demonstrate all tests** for the subject as well as giving the verbal instructions indicated, as this is usually far easier for most people to grasp. Encouragement to elicit maximal performance is an essential part of these testing procedures and should always be used. Record all data from each test immediately on data sheets (see Section J) so that no information is lost. If multiple trials are part of the test protocol, record all legitimate trials (those done in accordance with protocol requirements). Do not calculate averages or other derived variables from the raw data obtained.
a. Habitual Gait Velocity

Purpose:
This test is meant to record the normal walking speed of the subject, as if he or she was not being observed. Gait velocity is a very good overall indicator of functional status, and it is typically slowed by disease. It has been shown that patients with ESRD have comfortable walking speeds only 66% of normal. In this population, muscle weakness (due to inactivity and uraemic myopathy) and poor balance contribute significantly to abnormal gait velocity.

Equipment:
Ultra-timer (transmitter, receiver, belt)
9 Volt battery (tested prior to procedure) plus spares

Supplier:
Raymar
Unit One, Fairview Estate
Reading Road
Henley on Thames
Oxfordshire, England RG9 1HE
Tel (44) 1491 578446
Fax (44) 1491 410233

Preparing the subject:
Subject should be wearing normal, low-heeled walking shoes, comfortable clothing, eyeglasses and hearing aids, if any. He/she should have been offered to use the restroom prior to starting the test. If an assistive device is normally used for walking, the person should use this during the test, and the device used should be recorded on the worksheet. The same assistive device should be used at all time-points if possible, unless the person has changed to a different device (e.g. walker instead of a cane) due to changing medical condition. If the subject rarely uses a device on questioning, do not use it during the testing.

Environmental Considerations:
The gait speed test should be conducted in an indoor room or hallway that is entirely free of traffic or clutter. An open path of at least 6 meters in length is needed. Preferably, there should be no wall directly in front of the subject as they are walking forward. The path should be well lighted by natural or artificial lighting. A non-slip, non-carpeted surface such as tile or linoleum is best, but if carpeted floor must be used it should be low pile wall-to-wall carpeting, and the same surface must be used at all time-points.

Protocol:
Turn on the Ultra-timer transmitter and make sure that the green light appears on the box. If no light appears, check the battery placement and replace with a new battery if necessary. Place the Ultra-timer transmitter on the belt so that it is positioned in the middle of the subject’s back and is in a direct line with the examiner’s receiver. Fasten belt snugly around waist, and make sure no clothing or belt loops are covering the “eye” of the box. Stand directly behind the subject and tell him/her to walk in a straight line at a normal pace, as though you were not there observing them. Tell the
subject this is **not a test of their fastest walking speed**, which will come later on. The subject is to start walking when you say, "You may begin" and not stop until so instructed.

Turn on the receiver. If no numbers appear on the dial, the battery needs to be replaced before continuing. Hold the transmitter against your body so that it does not move during the test. When the subject has moved approximately 2 meters away from you, press the “Start” button on the receiver you are holding, making sure that it is pointed directly at the transmitter and that you do not change your hand or foot position at all during the test. As soon as the subject has moved an additional 2 meters away from you, the box will automatically stop timing and you can then tell the subject to stop walking at that point.

Record the numbers you see on the dial to the nearest 0.01 sec. This is the number of seconds it took the subject to walk 2 meters. If this number is divided by 2, this is the number of seconds it takes to walk 1 meter. Inverting this will give you gait velocity in **meters/second (m/sec)** which are the required units.

\[\text{e.g.:} \quad 4.00 = \text{Ultra-timer readout} \]
\[2.00 = \text{seconds to walk 1 meter} \]
\[1/2.00 = 0.50 = \text{gait velocity in m/sec} \]

After recording the numbers, press the reset button on the transmitter. Repeat the entire test procedure above and record the numbers you see on the dial. The **average** of the two readings of gait velocity will be the final score that is used ultimately in analyses.

You will only be required to enter the two readings from the Ultra-timer onto the data form and the computer will calculate the average and then convert the score to m/sec.

**Common problems/questions:**
Make sure to let the person walk 2 meters before pressing the start button, so that acceleration is not factored into the speed. Similarly, you do not want deceleration to be part of the measurement, do not mark a finish line or give the subject any indication as to when the walk will end. **The receiver and transmitter cannot be more than 7 meters apart to work.** Therefore, do not let the person “warm-up” for more than 2-3 meters, or you will run out of distance before the measured 2 meter walk is over. The two readings should be almost identical; unless the person has not understood your directions or other errors have been made. If they are not in close agreement, do the test a third time and discard the outlying reading.

Be sure to turn off the transmitter and the receiver after each test or the battery will wear down quickly. Always have a spare battery with you in the Ultra-timer case to avoid delays in testing.
b. Balance Testing

**Purpose:**
These tests are progressively more difficult tests of static balance, which is related to the quality of gait and risk of falling in individuals with ESRD. Balance is a complex phenomenon with many inputs, including vision, proprioception, coordination, muscle strength, reaction time, and others. In static balance testing, by narrowing the base of support over which a person’s center of gravity rests, the task of standing still without moving or falling becomes progressively more difficult.

**Equipment:**
Chair
Stopwatch

**Preparing the subject:**
Subject should be wearing normal, low-heeled walking shoes, comfortable clothing, eyeglasses and hearing aids, if any. He/she should have been offered to use the restroom prior to starting the test. If an assistive device is normally used for walking, the person cannot use this during the static balance tests beyond the first level, as it reduces the difficulty of the tasks greatly, and the purpose is to stress the balance system. If the subject is unable to stand with the use of an assistive device, this should be recorded on the data sheet as the reason the test could not be completed.

**Environmental Considerations:**
A quiet area with vinyl flooring or low pile carpeting with at least a 6 m straight path is needed. The same flooring should be used at all time-points.

**Protocol:**
Be sure to demonstrate all positions to the subject as you explain that you will be testing balance, and the task is to keep the feet in the desired position for 15 seconds while being timed. Arms and trunk may be moved slightly during the test if needed to maintain balance, but the timing ends when the full 15 seconds is reached or when either foot moves, or if the examiner or any object in the environment is touched by the subject, whichever comes first.

Position the subject so that his/her back is about 2 ft in front of a chair, in case they begin to fall. The examiner should be positioned just to either side, close enough to spot them and prevent a fall but not touching them. A wall should be on the non-examiner side of the subject, and a stable object positioned within arm’s reach in front of the subject (e.g., a chair). For each position, demonstrate and then allow the subject to try to assume the correct position while holding onto the object in front of them. If this is not possible, assist the subject in doing so. For the most difficult tests, you may position them and hold onto their hands, letting go just when you begin timing, otherwise the subject may lose his/her balance before the test actually begins.

Do not repeat tests unless it is clear directions were misunderstood, as practice makes the subject learn how to do the task very rapidly, and it is unfair to compare single and multiple attempts among different subjects. All stands should be attempted unless the subject refuses or it is clearly impossible to assume the position based on
the earlier test results. The number of seconds a position is held should not be used to gauge the appropriateness of completing more difficult tasks however.

The series of static balance stands are done in the following order:

1) **Feet apart, no hand support.** Subject's feet are positioned approximately shoulder width apart, or whatever distance represents "normal stance" for them. Hands are positioned within reach of the chair before the subject, but not touching it at all. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.

2) **Feet together, no hand support.** Subject's feet are positioned so that they are touching along the entire length of the foot with the toes aligned. Hands are positioned within reach of the chair, but not touching it at all. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.

3) **Semi-tandem stand, no hand support.** Subject's feet are positioned so that the toes of one foot are at the level of the instep of the other foot, and feet are touching. Either foot may be placed ahead of the other according to the preference/comfort as the position is tried out. Hands are positioned within reach of the chair before them, but not touching it at all. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.

4) **Tandem stand, no hand support:** Subject's feet are positioned so that the toes of one foot are touching the heel of the other foot, and feet are both pointing forward. Either foot may be placed ahead of the other according to preference/comfort as the position is tried out. Hands are positioned within reach of the chair, but not touching it at all. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.

5) **One-legged stand, no hand support:** Subject's feet are positioned so that they are a comfortable distance apart. Either foot may be used as the supporting foot, according to the preference/comfort as the position is tried out. Hands are positioned within reach of the chair, but not touching it at all. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.

6) **One-legged stand, no hand support, eyes closed:** Subject's feet are positioned so that they are a comfortable distance apart. Either foot may be used as the supporting foot, according to the preference/comfort as the position is tried out. Hands are positioned within reach of the chair in before the subject but not touching it at all. The subject is instructed to balance on one foot whilst the eyes are closed. Record the number of seconds to the nearest 0.01 seconds from the stopwatch, up to a maximum of 15 seconds.
c. Six Minute Walk

**Purpose:**
The six minute walk is a proxy for overall cardiovascular endurance capacity (aerobic capacity). In addition to cardiovascular efficiency, however, in the individual with ESRD it may be determined by muscle strength and endurance, balance, neurological abnormalities, and other problems related to co-morbidities. It works best as an estimate of aerobic capacity in individuals who cannot run, so that variations in walking velocity describe most of the possible range of function. Therefore it is very appropriate in patients with ESRD.

**Equipment:**
Measuring wheel (Tajima Road Measure 1000)

**Supplier:**
C.R. Kennedy
108 Miller St.
Pyrmont, NSW 2009

Phone: 9518 9700
Fax: 95189711

Stopwatch

**Preparing the subject:**
Subject should be wearing normal, low-heeled walking shoes, comfortable clothing, eyeglasses and hearing aids, if any. They should have been offered to use the restroom prior to starting the test. If an assistive device is normally used for walking, the person should use this during the test, and the device used should be recorded on the data sheet. The same assistive device should be used at all time-points if possible, unless the person has advanced to a higher level device (e.g. walker instead of a cane) due to changing medical condition. If the subject rarely uses a cane, do not use it during the testing.

**Environmental Considerations:**
This test requires a long open circuit around which the subject can walk continuously for six minutes. Long circular or square corridors around the perimeter of a building without many turns are ideal. All testing should be done indoors rather than outdoors, as there are too many uncontrolled variables in outdoor areas. The path should be free of clutter and all other traffic should be closed off if possible during the testing. No steps, inclines, doors, or other obstacles should be in the path of the subject, and lighting and ventilation should be adequate.

**Protocol:**
The person should be instructed that they are to “cover as much ground as possible in six minutes” by walking as fast as they can the entire time. They must be encouraged and reminded of the task every 30 seconds during the test or they will tend to slow down. Line up the Measuring wheel (with the dial reset to read 0.00) with the subject’s feet on the starting line. Prior to beginning the test, ascertain that the subject’s pulse rate, breathing rate, and blood pressure are in their normal range. Say, “1,2,3, GO!” and begin the stopwatch. Follow closely behind the subject with the Measuring wheel, attempting to follow their path as closely as possible without
getting in their way or influencing their gait speed. The number of meters traveled at the end of 6 minutes is recorded to the nearest cm from the wheel. Use standardised statements such as "Keep Going!", "You’re Doing Well!", "Keep up the Good Work" every 30 seconds during the walk and every 2 minutes provide the subject a time check such as "Only 4 minutes to go!".

If the subject needs to stop to rest during the test, the watch continues to run, and they should be instructed to start back up again as soon as they are able.

If they develop angina during the test, or any other symptoms that seem severe, the test should be terminated immediately and emergency medical help should be contacted. However, shortness of breath, fatigue, and slight muscle or joint pains are not unusual and are not an indication for stopping the test. If claudication occurs, the person may need to stop momentarily, but can go on as soon as they feel able.

Record the assistive device used, the number of stops made during the test, any symptoms that developed during the test, reason for stopping prematurely, if any, and the total distance covered in 6 minutes to the nearest centimeter. This test is only performed once.

Common problems/questions:
The subject should be well rested prior to beginning this test, as it requires physical stamina and mental alertness. The exact wording above should be used to instruct the subject so that consistency is maintained. The subject is not allowed to break into a run; if this happens, stop the test and begin again. If a chair is anticipated to be needed for rest stops, a second examiner can follow closely behind the timer with a wheelchair, which can be positioned behind the subject as needed. If a subject can only ambulate by pushing themselves in a wheelchair, the test can be conducted in this way, but no assistance in moving the wheelchair from anyone else is allowed.
d) Muscle Strength

General preparations:

- Demonstrate each movement to the subject first.
- Indicate the muscles they are using and inform the subject that the joint will not actually move but that the machine registers the force.
- Always have the subject demonstrate the movement they will be trying to do before testing i.e. as a ROM test.
- Be sure that the dynamometer is on; reading in Kg’s and that peak compression force will be recorded (set to C Peak).
- Zero the dynamometer before each test once the subject is in position. For the measurement of triceps strength, zero the dynamometer when the subject’s wrist is resting on the padded bracket with the arm relaxed.
- During testing, observe the subject closely to ensure that they are using only the muscle groups you are testing, i.e. that there are no other body movements.

Equipment:

- Standard height chair with backrest, no armrests;
- Dynamometer
- Dynamometer stand
- Telephone books

Subject set-up:

- Set up the subject so that minimal rearrangement is required and to allow ample rest time.
- Order of strength tests:
  - Right hip abduction
  - Right triceps (alternate between these two measures until all three trials are completed for both muscle groups).
  - Left hip abduction
  - Left triceps (alternate between these two measures until all three trials are completed for both muscle groups).
  - Right Quadriceps
  - Left Quadriceps (alternate between these two measurements until all three trials are completed for both muscle groups).
e. Anthropometry

i.  **Stature:**  *Stature is recorded at baseline only*

- **Equipment:**
  - Stadiometer, accurate to 0.1 cm.
  - The standard method for measuring stature is the *stretch stature technique* defined as the maximum distance from the floor to the vertex of the head.
- **Subject stands barefoot with feet and heels together and their buttocks and upper part of the back touching the scale.**
- **The head is placed in the Frankfort plane: where the orbitale (lower edge of the eye socket) is in the same horizontal plane as the tragion (the notch superior to the tragus of the ear). When aligned thus, the highest point on the skull is the vertex.**
- **The measurer places the hands along the jaw of the subject with the fingers reaching to the mastoid processes.**
- **The subject is instructed to take and hold a deep breath and while keeping the head in the Frankfort plane, the measurer applies a gentle upward lift through the mastoid processes.**
- **The measurer places the headboard firmly down on the vertex, crushing the hair as much as possible.**
- **Ensure that the feet do not come off the floor and the position of the head is maintained in the Frankfort plane.**
- **Measurement is taken at the end of a deep breath inward.**
- **Record measurement upon Anthropometry data sheet.**
- **Repeat the measurement three times and take the average value to be the correct stature. If there is a variance between the repeated measures greater than 2mm, repeat the measurement again until all three values are within 2mm of each other.**
- **Stature is recorded post dialysis**

ii.  **Body Mass:**

- **Equipment:**
  - Electronic Scales (Load Cell), accurate to within 100g

**Calibration of Scales:**

The only scales used for weighing should be the research study scales. These scales should be calibrated once every month using a known weight. A new calibration correction factor should then be calculated for each of the scales and recorded on all data sheets requiring weight.

The calibration procedure is as follows:

- **Person steps onto scales to be calibrated and weight is noted**
- **Four sequential weights are taken, each time the same individual is holding onto a known weight of greater mass.**
- **The absolute difference between the known and measured weight is calculated and recorded.**
• The relative difference is then calculated by dividing the known weight by the measured weight (gives a %). The average relative difference across the range of weights is used as the correction factor. For example, if the measured weights are on average 1% lower than the known weights, then the measured weight of a subject will need to be multiplied by 1.01 and this recorded as the “corrected weight” for use in all subsequent analyses.
• Calculate a new correction factor for each month and use this factor to correct all weights taken during that period.

Procedure for Testing Body Mass

• Body mass is recorded post dialysis, and is taken at all testing time points.
  • Check that scale is weighing zero
  • Advise subject to remove all heavy items of clothing e.g jacket, shoes, jumper etc.
  • If the subject requires the aid of a walker or stick to maintain their balance, weigh the walker prior to taking the subject’s body mass. Zero the scales whilst the walker is in place, then instruct the subject to step onto the scale.
  • Subject stands on the centre of the scales without support and with weight distributed evenly over both feet. Ensure the subject’s head is up and eyes are looking directly ahead.
  • Take measurement and record on Anthropometry Data Sheet
  • Repeat the measurement three times, and take the average value.
  • Record on sheet which scales were used (SGH or RPA) and time of day.

iii. Girth Measurements:

• Equipment:
  o A Lufkin (W606PM) self-retracting metal tape, accurate to the nearest 0.1cm.

• Technique:
  o Circumferences are measured post dialysis
  o The tape is held at right angles to the long axis of the body segment being measured.
  o The cross hand technique is used for measuring all girths.
  o Constant tension is used, making sure there is no indentation on the skin but the tape holds the place at the designated landmark.
  o The tape must be read at eye level to avoid parallax error.
  o Measurements are to be three times. Do each measurement in succession in order to avoid bias. Record each measurement on the Anthropometry Data Sheet.
  o The average of the three measures is taken.
- Record on the Anthropometry Data Sheet which limb was used for measurements (left or right). Measure the dominant side or the non-fistula limb.

- Measurement Sites:
  
  - **Mid-Arm Circumference (Relaxed):**
    
    The perimeter distance of the right arm perpendicular to the long axis of the humerus when the subject is standing erect and the relaxed arm is by the side of the body. The measurement is made at the level of the mid-acromiale radiale line (see Anatomical Landmarks section below for definition).

  - **Waist Circumference:**
    
    This measure is taken at the level of the narrowest point between the lower costal (rib) border and the iliac crest. If there is no obvious narrowing, then the measurement is taken at the midpoint between these two landmarks. The measurer stands in front of the subject to correctly locate the narrowing of the waist. The measurement is taken at the end of a normal expiration with the arms relaxed at the sides.

  - **Calf Circumference:**
    
    This is the maximum girth of the calf. The subject stands facing away from the measurer in an elevated position (for example, on a box or stool) with the weight equally distributed on both feet. The elevated position allows the measurer to align the eyes with the tape more easily. The measurement is taken from the lateral aspect of the leg. Place the tape around the calf in the prescribed manner. The maximal girth is found by using the middle fingers to manipulate the position of the tape in a series of up or down measurements to identify the maximal girth. Record on Anthropometry Data Sheet.
• Anatomical Landmarks:

• Acromiale:
  o Definition:
  The point at the superior and lateral border of the acromion
  process, midway between the anterior and posterior borders of the
  Deltoid muscle when viewed from the side.
  o Location:
  Standing behind and on the right hand side of the subject, palpate
  along the spine of the scapula to the corner of the acromion. This
  represents the start of the lateral border, which usually runs
  anteriorly, slightly superiorly and medially. Apply the straight edge
  of a pencil to the lateral aspect of the acromion to confirm the
  location of the border. The landmark is a point on the most lateral
  and superior part of the border, which is adjudged to be in the mid-
  deltoid position when viewed from the side.

• Radiale:
  o Definition:
  The point at the proximal and lateral border of the head of the
  radius.
  o Location:
  Palpate downward into the lateral dimple of the right elbow. It
  should be possible to feel the space between the capitulum of the
  humerus and the head of the radius. Slight rotation of the forearm
  is felt as rotation of the head of the radius.

• Mid-Acromiale-Radiale:
  o Definition:
  The point equidistant from acromiale and radiale.
  o Location:
  Measure the linear distance between acromiale and radiale with the
  arm relaxed and extended by the side. Place a small horizontal
  mark at the level of the midpoint between these two landmarks.
  Project this mark around to the posterior and anterior surfaces of
  the arm as a horizontal line. This is required for locating the mid-
  arm circumference site.
f. Blood Tests

Bloods are to be taken from subjects at 0, 12 and 24 weeks, and analysed for the following biochemical and haematological markers:

- Haemoglobin
- Haematocrit
- Transferrin
- HbA1c (diabetics)
- Ferritin
- C-reactive protein
- Prealbumin
- Albumin
- Potassium
- Urea
- Creatinine

In addition to this, extra blood will be drawn at each testing time point, centrifuged and saved as plasma and serum.

Urea kinetic modelling will also be performed at 0,12 and 24 weeks in order to assess the adequacy of dialysis. This will be in the form of single pool arterial Kt/V.

Urea Kinetic Modelling:

Numerous studies have demonstrated a correlation between the delivered dose of haemodialysis and patient mortality and morbidity. In order to ensure that the dose of dialysis is sufficient, regular urea kinetic studies are performed. Urea is the substance that is most often monitored in clinical practice as a surrogate for measurement of the clearance of small solutes in general. Reasons for this are that urea is a small, readily dialysed solute that is the bulk catabolite of dietary protein, constitutes 90% of waste nitrogen accumulated in body water between haemodialysis treatments, is easily measured in blood, and that the fractional clearance of urea in body water correlates with patient outcomes, such as mortality and morbidity. Quantification of the prescribed or delivered dose of haemodialysis begins by estimating the difference in pre-dialysis and post-dialysis urea concentration by sampling a patients blood before and after a single dialysis session.

Blood Urea Sampling

- Pre-dialysis blood sampling:
  - Obtain the blood specimen from the arterial needle prior to connecting the arterial tubing or flushing the needle. Be sure that no saline and/or heparin is in the arterial needle and tubing prior to drawing.

- Post-dialysis blood sampling:
  - At the completion of haemodialysis, turn the dialysate flow and TMP off or to the lowest setting.
o Decrease the blood flow to 50 ml/min for 15 seconds. Note: To prevent pump shut off, it may be necessary to adjust the venous pressure limit downwards.

o Draw the blood sample from the arterial sampling port closest to the patient. The blood must be drawn within 15 seconds but no more than 30 seconds after slowing the blood flow rate.

o Alternatively, take the post-dialysis blood sample 30 minutes after dialysis. In this case, the equilibrated Kt/V is used (eKt/V).

**Single pool arterial Kt/V:**

\[
\text{Spa Kt/V} = \text{single pool arterial Kt/V}
\]

\[
\text{Spa Kt/V} = -\ln \left( \frac{C}{Co} - 0.008 \times T \right) + (4 - 3.5 \times \frac{C}{Co}) \times \frac{UF}{W}
\]

Where:

\( Co \) = pre-dialysis urea (mmol/L)

\( C \) = post-dialysis urea (mmol/L)

\( T \) = dialysis time (hours)

0.008 = correction factor for urea generation during dialysis

\( UF \) = ultrafiltration volume (litres)

\( W \) = post-dialysis weight (kg)

Target \( \text{spa Kt/V} \geq 1.3 \)

**Equilibrated Kt/V:**

\[
\text{e Kt/V} = \text{equilibrated Kt/V}
\]

\[
\text{e Kt/V} = \text{spa Kt/V} - 0.6 \left( \frac{K}{V} \right) + 0.03
\]

where:

\( \frac{K}{V} \) = \( \text{spa Kt/V} + T \)

Target \( eKt/V \geq 1.0 \)

**Procedure for Alerting Nursing Staff**

To notify nurses that bloods are to be taken during Haemodialysis:

* **Royal Prince Alfred Hospital:**
When a subject is recruited into the study, a letter to the Nurse Unit Manager will be sent out prior to baseline testing. This letter will detail the dates when blood will need to be drawn over the duration of the study and the blood tests that are required.

- Write the tests needed in the nurses' diary located in nurses staff room/office.
- Write the request for the specific blood tests in the patients' progress notes located within the filing cabinet in nurses staff room/office.
- Write the request detailing the tests needed on the patients' flow charts.
- Attach the collection tubes within a plastic sleeve to the patients' flow charts.

* The St. George Hospital:

- When a subject is recruited into the study, a letter to the Nurse Unit Manager will be sent out prior to baseline testing. This letter will detail the dates when blood will need to be drawn over the duration of the study and the blood tests that are required.
- Fill out the pathology request form detailing the tests required, as well as the stickers attached to the collection tubes.
- Attach along with collection tubes in plastic sleeve to patients' dialysis folder (nurses station).
- Write request in nurses' diary and upon the patients' dialysis notes (pink sheet).
g. CT Scans of Thigh for Soft Tissue Measurements by Digital Analysis

- **Equipment:**
  - GE High Speed CTI Scanner

- **Location:**
  - Royal Prince Alfred Hospital Vic Block X-Ray - CT Department

- **Contact Person for Administrative issues:**
  - CT Section Chief, Kay Cook 9515-7444 or 9515-7163 or 9515 7445

- **Contact Person for Appointment Scheduling:**
  - Leila, Vic Block Radiology, 9515-8947

- **Contact Person for Data Transfer:**
  - Kay Cook, Radiographer, 9515-7444

Note: Procedures typed in **Bold** are done by CT technical staff, the rest is done by the research assistant.

- A **Patient Registration Form** must be filled in prior to a patient attending initial CT scan if patient does not have a **medical record number** and faxed to Maria Barra (Department of Radiology Office Manager – page 80903) so that patients can have a Medical record number generated. **Fax 9515 6155**

- **Initial Scanning Protocol:**

1. Subject is changed into hospital gown, removing all constricting underwear, stockings, belts, etc.

2. Subject lies on scanner bed with non-dominant leg flexed at the hip and knee. Dominant leg is used if there is a metal prosthesis in the non-dominant leg.

3. Measure the thigh length with an anthropometric tape from the inguinal crease to the proximal pole of the patella. Mark the mid-point of this distance with a black marker and then tape a metal ball bearing over the black mark (these are kept in a drawer in the technician desk, but research assistant should have some in hand as well).

4. Return the leg to resting position and separate the legs so that the skin is not touching between the thighs by abducting the leg that is not to be scanned. Keep the scanned leg straight (parallel to the scanner bed)

5. A **scout film is taken thigh region to include the entire knee joint with the ball bearings visualized.**

6. The scanner is set to take a slice at the marker. The ball bearing is then removed from the subject.
The distances and angles from the notch between the femoral condyles and the dotted lines, indicating the position of the slice on the thigh is measured by the CT scanner; and these numbers are recorded on a second scout film and by the RA on the data sheet.

A 1mm slice is taken at the levels of the markers on the thigh using settings:

- kV=100
- mA=170

1 second scanning time.

DFOV= variable depending on size of subject
Field of view is adjusted as needed to include the entire cross-section of the thigh in the slice. A film is taken of the slice. Subject is instructed to hold his or her breath while the scan is being taken.

9. The film that is printed should have 3 pictures: initial scout with ball bearing, scout with measurement lines and angles, cross-section of thigh. Two copies of the film are printed and one is taken by the research assistant when it is printed. The other is left for the radiologist to keep on file.

10. The subject file is transferred to a computer and saved for FTP transfer in original DICOM format. No file transformation is necessary. The file should be saved as the subject’s name/date.dcm

11. The circumference of the thigh at the black marks is measured in triplicate by the research assistant after the scans have been taken, while the subject is still lying supine on the scanner bed.

12. Assist subject off scanner bed.

**Instructions for repeat scans in a previously scanned subject:**

1. Bring the original film with subject to compare measurement lines and reproduce precisely.

2. There is no need to measure the anthropometric sites or tape on a ball bearing.

3. Position legs as in initial scan.

4. Take an initial scout film and compare subject positioning. Adjust if needed.

5. Set scanner to take a cross-section using the distances and angles and DFOV’s noted in the initial scan.

6. Proceed with film printing and file saving as above.
**Instructions for Data transfer by FTP:**

1. The subject file is transferred by the IT staff of the RPAH Department of Radiology to the following FTP site:

   Site IP Number: 129.78.141.154

   Host: EXSS-SERVER.FHS.USYD.EDU.AU (no spaces between dot points)

   Username: ESSUPLOADS

   Password: external

   Folder: /PUBLIC/ESSUPLOADS

   The IP number NOT the host name must be used to access the server from outside the university.

2. Successful transfer of the file is then confirmed by emailing the investigator at: m.singh@fhs.usyd.edu.au
h. Resistance Training

Before each exercise, inform the subjects which muscles are being used to perform the required movement. Demonstrate the movement before each exercise, being sure to alert subjects to incorrect methods of performing each exercise. Show the subject the Exercise Intensity Scale prior to starting the session, indicating which level of intensity the subject should be working at (15 to 18 on Borg scale, which corresponds with 80% of 1RM). Progress to higher weight when perceived exertion falls below 15 on Borg scale. Ankle weights increase in increments of 0.5kg up to a maximum of 10kg for each cuff. If extra weight is required, another weight cuff can be placed on the leg. Dumbbells increase in 1kg increments from 2kg up to a maximum of 10kg.

Prior to commencing exercises, whilst demonstrating the correct form for the lift, indicate to the subject the correct method of breathing (breathe out during the concentric phase of lift), explaining the consequences of holding one's breath during the exercises. Monitor the subject's breathing during the training session and instruct when required. Weights may be rested on lap between repetitions if necessary. If subject has diabetes, ensure that the integrity of their skin is checked before placing the weight cuffs on the legs. Weight cuffs are attached by wrapping the neoprene cuff containing the weights around the subject's ankle, then passing the Velcro strap through the buckle and fastening.

The subjects are to train 3 days per week (Monday, Wednesday and Friday) for either 12 weeks (Group A) or 24 Weeks (Group B). The prescribed volume for each of the exercises is 3 sets of 8 repetitions. In order to allow the muscles to recover, at least three minutes rest is to be given between sets. In order to minimise the time required to perform the exercises and to give sufficient rest between sets, the following sequence of exercises should be used:

**Note: Start with chair in upright position**

a. Overhead Press  
b. Knee Extension  
c. Side Shoulder Raises  
d. Plantar Flexion  
e. Shoulders and Upper Back  
f. Leg Lifts  
g. Triceps Extension  
h. Hip Extension (with Theraband Tubing)  

**Note: Place chair in reclining position**

i. Hip Flexion  
j. Biceps Curls  
k. Hip Abduction
i. **Exercises:**

**Overhead Press**

- *This exercise strengthens the muscles of the shoulder and back of the upper arm, which allow you to reach overhead.*
- Position haemodialysis chair in upright position.
- Subject to sit in chair holding dumbbells at shoulder level with palms facing forward.
- Instruct subject to slowly lift both arms straight overhead until elbows are straight and dumbbells are touching directly over the subject's head.
- Dumbbells are lowered following the same path.
- Repeat.

- Note: Ensure that the subject does not arch back during lift. Weights should be held shoulder-width apart for the duration of lift. Ensure that subject does not turn palms or elbows inward during the lifting or lowering of the weights.
- If the subject has an arm fistula, this arm is to be exercised prior to commencing the HD session. The non-fistula arm can be exercised during the HD session.

**Knee Extension:**

- *This exercise strengthens the quadriceps muscle at the front of the thigh, which straightens the knee.*
- Position haemodialysis chair in upright position.
- Subject to sit in chair with the backs of their knees resting against the chair seat, and the weight cuffs strapped around ankles.
- Instruct subject to slowly raise on foot in front of them until their knee is as straight as possible.
- At the top of each lift, the subject is to pull their toes back towards them (dorsiflex) as far as possible, hold for 5 seconds then point toes.
- Instruct subject to slowly lower leg back to the starting position.
- Repeat, alternating legs.

- Note: Ensure that subject's leg is fully extended, or as high as possible if movement is limited. If needed, insert a towel underneath knees so that the subject's foot clears the ground during the lift. Ensure that the subject extends knee only, and does not flex hip to lift weight, and that they are not slouching or arching their back during the lift.

- If the subject has a leg fistula, exercise that leg prior to the HD session. The non-fistula leg can be exercised during the HD session.

**Side Shoulder Raise:**
• *This exercise strengthens the shoulder muscles, which lift the arm out to the side.*
  Position haemodialysis chair in the upright position. If movement is restricted, place a pillow behind the thoracic region of subject’s back. Ensure that subject will not come into contact with dialysis machine before starting exercises.
• Subject to sit as erect as possible in chair, holding a dumbbell in each hand with arms hanging outside of the armrests of the haemodialysis chair. Ensure that the subject’s palms are facing their body.
• Both arms are to be raised slowly until they are parallel with the ground. Ensure that elbows are kept straight throughout the entire range of motion.
• Slowly lower the arms back to the starting position.
• If one or both of the subject’s shoulders are limited by pain or stiffness, encourage to lift the arm as high as it will go without discomfort.

• Note: Ensure that the subject does not use their back to lift the weight, and that the back is not arched during the lift. Arms are not to be lifted higher than shoulder level, and the palms are not to be turned outward during the lift. Subject not to swing the dumbbells up.

• If the subject has an arm fistula, this arm is to be exercised prior to the HD session. The non-fistula arm can be exercised during the HD session.

**Plantar Flexion:**

• *This exercise will strengthen the ankle and the muscles in the calf.*
  Place haemodialysis chair in the upright position, with a low footstool placed in floor in front of chair if subject’s legs do not reach the ground.
• Subject to sit as erect as possible in HD chair, with feet placed flat upon footstool, and weight cuffs around ankles.
• Instruct subject to slowly rise up as high as possible onto their toes, then slowly lower their feet back down into the starting position.
• When this exercise becomes too easy, instruct the subject to hook one leg behind the other and rise up on one leg instead, alternating left and right legs between sets.

• Note: If subject has a leg fistula, this exercise to be performed prior to the HD session.
Shoulders and Upper Back:

- **Strengthens muscles of the upper torso for good posture and balance.**
- Place haemodialysis chair in the upright position. Place a pillow behind the lumbar region of the subject’s back to allow full range of movement.
- Subject to hold the dumbbells perpendicular to the ground with elbows bent, so that weights are touching a few inches in front of chest.
- Instruct the subject to slowly bring their arms out to the side in an arc while trying to squeeze the shoulder blades together in the back.
- Subjects then to bring weights back to the starting position, trying to return along the same path.
- Repeat.
- Note: Ensure that dumbbells remain perpendicular to the ground throughout the entire range of movement, and that the subject’s elbows are bent at the same angle throughout the lift. Emphasise the importance of squeezing the shoulder blades together.
- If subject has an arm fistula, this arm is to be exercised prior to commencing HD therapy. The non-fistula arm can be exercised during the HD session.

Leg Lifts

- **This exercise strengthens the muscles of the upper and lower abdomen.**
- Place haemodialysis chair in the upright position
- Subject to be wearing leg weights around ankles.
- Instruct subject to slide forward in the chair so that the buttocks are towards the front edge of the seat. Arms are crossed in front of chest.
- Instruct subject to lift both feet approximately 10cm off the ground,
- Subject is to then straighten out the legs, holding them out together in front of them for several seconds, then slowly lowering legs back to the starting position.
- If this is too difficult, instruct the subject to just lift the legs initially, or do the exercise without the leg weights initially until subject is able to progress to using the weight cuffs on both legs.
- If the subject finds this exercise too easy, then use advanced position, where the shoulders and back are lifted from the support of the chair simultaneous to lifting up the legs.
- Note: Ensure that subject’s arms are crossed in front of them, not holding on to the chair.

- If the subject has a leg fistula, this exercise must be performed prior to the HD session.
Triceps Extension

- *This exercise strengthens the muscles at the back of the upper arm which straighten out the elbow*
- Position Haemodialysis chair in upright position. Place 1-2 pillows behind thoracic region of subject’s back, in order to allow full range of movement during exercise. Ask subject to perform the movement and adjust position as necessary.
- Subject to sit as erect as possible in chair with dumbbells in hand.
- Instruct subject to raise arms straight over their head and then bend both elbows so that their wrists are resting behind their neck
- Subject then raises both arms back upwards, ensuring that elbows are kept as close to the ears as possible.
- Repeat.

- Note: Ensure that elbows are kept as close to ears as possible. Subjects may use one dumbbell at a time or progress to two dumbbells. If the subject does not have enough range of motion in the shoulder to reach behind the neck, perform modified triceps extension.
- If the subject has an arm fistula, this arm is to be exercised prior to the HD session. The non-fistula arm can be exercised during dialysis.

Modified Triceps Extension

- Subject sits erect in chair, holding the dumbbells in front of the chest (thumbs pointing towards body), with their elbows pointing directly out to the sides.
- Keeping the weights parallel to the floor, the subject straightens out the elbows fully.
- The subject then bends elbows to slowly return the weights to the starting position.
- Repeat
- Note: Ensure that weights do not travel down towards the floor, and that the elbows are kept up throughout the movement. The upper body and back are not to move except for the forearms.

Hip Extension:

- *This exercise strengthens the muscles in the buttocks and lower back.*
- Place haemodialysis chair in the reclining position, with a length of Grey Theraband tubing tied around the back of the chair. The Theraband should be long enough for the subject to be able to flex their knee and hip towards their body and place their foot against the loop of Theraband. Note the length of the tubing on the Strength Training Data Sheet.
- Ensure that the subject is wearing a shoe with some kind of heel or arch that allows the band to be placed towards the heel of the foot in order to isolate the hip extensors.
• Instruct the subject to slowly extend one leg against the resistance provided by the Theraband, until the leg is fully extended.
• Subject then slowly returns leg to starting position.
• Repeat, alternating legs between sets.

• Note: If subject has a leg fistula, this leg must be exercised prior to the HD session. The non-fistula leg may be exercised during the HD session. Resistance can be increased by decreasing the length of the loop or adding another loop of Theraband tubing when loop length is at a minimum (increase length back to original when another loop is added). The length and number of loops is adjusted according to the subject’s rating of perceived exertion. Note the number of loops and length of each loop in the Strength training Data Sheet. Discard the Theraband tubing when the resistance offered decreases (i.e. when elasticity of the tubing increases).

• Take care to spot this exercise carefully, in order to prevent the Theraband tubing slipping off the subject’s foot or the chair and snapping back onto the subject, or interfering with the dialysis lines or machine.

**Hip Flexion:**

• *This exercise strengthens the muscles which bring the knee towards the chest.*
• Place haemodialysis chair in reclining position
• Subject to sit in chair with weight cuffs around ankles.
• Instruct the subject to slowly bring one knee as close as possible to the chest, then lower back to the starting position and repeat, alternating legs.

• Note: Ensure that subject does not bend forward at the waist

• If the subject has a leg fistula, exercise the fistula leg prior to HD session. The non-fistula leg can be exercised during the HD session.

**Biceps Curl:**

• *This exercise strengthens the upper arm muscles which flex the elbow*
• Position haemodialysis chair in the reclining position in order to achieve largest range of motion
• Patient to sit in chair with arms at sides, resting the dumbbells on the chair
• The weights are to be held initially with the thumb over the top, so that the weights are in the sagittal plane.
• Instruct subject to bend one arm at the elbow to lift the dumbbell towards their shoulder. As the lift is completed, instruct subject to turn the hand so that the fingers face toward the shoulder in order to engage the brachioradialis muscles. Ensure that subject does not move upper arm or shoulder during lift.
• Subject to lower the dumbbell slowly towards starting position
• Repeat with other arm. Alternate arms between each lift.

• Note: Ensure that weight is not lifted by moving the shoulder or upper arm. Elbows are to be fixed at sides, and not to be moved forward during the lift. Ensure that subject's back is not arched whilst lifting.

• If the subject has an arm fistula, exercise the arm with the fistula prior to the HD session. The non-fistula arm can be exercised during the session.

Hip Abduction:

• *This exercise strengthens the muscles at the side of the hips and thighs, which pull the legs out to the side.*
• Place haemodialysis chair in the reclining position, with the foot rest extended.
• Subject to sit in chair with legs extended upon footrest and weight cuffs around ankles.
• Instruct subject to move one leg straight out to the side, without bending the knee or the waist. Ensure that the toes are always pointing up, perpendicular to floor.
• Subject then to return the leg to the starting position and repeat with alternating legs.

• Note: Ensure that toes are not pointing out to the side during the lift, and that leg is kept as straight as possible.

• If subject has a leg fistula, this leg must be exercised outside of the HD session. The non-fistula leg may be exercised during the HD session.
2. Questionnaires and Visual Scales
Subject Medical History

Primary Cause of Renal Failure:
- Glomerulonephritis
- Hypertensive nephrosclerosis
- Analgesic nephropathy
- Polycystic kidney disease
- Diabetic nephropathy
- IgA nephropathy
- Lupus/SLE
- Reflux nephropathy/chronic pyelonephritis
- Aetiology uncertain
- Other: ________________________________________________

Haemodialysis:
- Date commenced HD: ________________________________
- Duration of HD (yr & months): ________________________
- Problems with dialysis over past 6 months:
  Hypotension
  Hypertension
  Arrhythmias (type): _________________________________
  Fistula access problems: ___________________________
  Subjective symptoms during session: _______________

  Laboratory abnormalities: ___________________________
  Other: ___________________________________________

- Kt/V (Date, Value): ________________

Other Diagnoses:
- Active malignancy:
  - Type: __________________________________________
- Gastrointestinal disease:
  - Type: __________________________________________
☐ History of M.I:
   o Date:

☐ History of Cardiac Surgery:
   o Type:
   o Date:

☐ History of Hernia Repair:
   o Date:

☐ Alcohol or Drug Dependency
☐ Amputation of Limb
☐ Inability to use arm or leg (e.g. hemiparesis, stroke, deformity, contracture, neuromuscular disease):
   o Cause:
   o Other:

☐ Number of visits by health care professionals in past 3 months: ____

Medications:

- Prescription Medication

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- Non-Prescription Medication (interview):

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• Supplements (interview):

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Current Level of Physical Activity:
• Aerobic Exercise:
  o Frequency:________________________
  o Intensity:_______________________
  o Modality:_______________________
• Resistance Exercise:
  o Frequency:______________________
  o Intensity/Sets/Reps:_____________
  o Modality:_______________________
• Other:___________________________

History of exercise related Injuries (specify):

___________________________

Comments:__________________________

___________________________
Physician History and Physical

1. Symptoms

Have you had any of the following symptoms since your last visit?

☐ Chest Pain

☐ Shortness of breath

☐ Dizziness or light headedness

☐ Swelling of the legs

2. Signs

☐ Pulse:
  ☐ Supine: __________
  ☐ Sitting: __________
  ☐ Standing: __________

☐ Blood Pressure:
  ☐ Supine: __________
  ☐ Sitting: __________
  ☐ Standing: __________

☐ Is there clinical evidence of pulmonary oedema?

☐ Is there evidence of peripheral oedema?
3. Dialysis Stability:

- 3 months or more of successful dialysis?
  Yes  No

- Problems with fistula / access site?
  Yes  No

- Fluid and electrolyte problems?
  Yes  No

- Hypertension?
  Yes  No

- Hypotension?
  Yes  No

- Arrhythmias?
  Yes  No

- Other? (Specify)

☐ Eligible
☐ On Hold:
  - Reason: ____________________________
  - Follow-up needed: __________________

☐ Excluded:
  - Reason: ____________________________

Physician Signature: ____________________________
Dr......
Level 1, 50 Montgomery Street,
Kogarah, NSW 2217

Dear Dr......,

As part of the medical screening process for the PEAK (Progressive Exercise for Anabolism in Kidney disease) research study, the following patients have had their medical records reviewed for contraindications to exercise, by myself and Dr. Maria Fiatarone Singh, MD, FRACP.

1   LAST NAME, First Name (MRN: XX-XX-XX, DOB: XX-XX-XXXX)

To further the medical screening process please complete the attached checklist for each of your patients and return these forms to me using the pre-paid envelope provided. Your assistance is greatly appreciated.

As you are aware, the purpose of the PEAK study is to evaluate the effects of resistance training during haemodialysis sessions on several indicators of health status in patients with ESRD. Some of the variables to be evaluated include muscle cross-sectional area, muscle function, nutritional status, depression, and quality of life.

I am hopeful that you will recommend participation in this research study to all patients meeting eligibility requirements. Please feel free to contact me if you require further information about the study.

Sincerely,

Bobby Cheema, Doctoral Student
Maria A. Fiatarone Singh, MD, FRACP (Supervisor)
Name of patient:  LAST NAME, First Name (MRN: , DOB: )

Checklist of conditions and events, which would require temporary exclusion from study:

☐ Acute change in mental status or delirium

☐ Cerebral haemorrhage within the past 3 months

☐ Exacerbation of chronic inflammatory joint disease or osteoarthritis

☐ Eye surgery within the past 6 weeks

☐ Fracture in healing stage  

☐ Hernia, symptomatic (abdominal or inguinal)

☐ Myocardial infarction or cardiac surgery within past 3 months

☐ Other acute illnesses or change in symptoms  

☐ Proliferative diabetic retinopathy or severe non-proliferative retinopathy

☐ Pulmonary embolism or deep venous thrombosis within 3 months

☐ Soft tissue injury, healing  

☐ Systemic infection  

☐ Uncontrolled blood pressure (>180/100)

☐ Uncontrolled diabetes mellitus (FBS>14mmol/L)

☐ Uncontrolled malignant cardiac arrhythmia (ventricular tachycardia, complete heart block, atrial flutter, symptomatic bradycardia)

☐ Unstable angina (at rest crescendo pattern, ECG changes)

☐ Other  

Practitioner Name:  

Date:  

A 30
Resident Medical Screening Form

Date ___________________________  Resident Name ___________________________  Resident ID Number ___________________________

Facility ___________________________________  Unit ___________________________________  Evaluator ___________________________________

DIRECTIONS
Check all boxes below that apply to the resident; please note date of evaluation.

I. STOP!  Permanent Exclusion

    ★ any boxes in this column are checked, resident is ineligible for the HEAL/FFYL exercise program.

    a.  ☐ End-stage congestive heart failure
    b.  ☐ Permanent bed-bound status
    c.  ☐ Severe cognitive impairment or behavioral disturbance
    d.  ☐ Unstable abdominal, thoracic or cerebral aneurysm
    e.  ☐ Untreated severe aortic stenosis
    f.  ☐ Other ___________________________

II. WAIT!  Temporary Exclusion

    If any boxes in this column are checked, follow protocols for further evaluation of these concerns with medical staff prior to reevaluating for appropriateness/modification of exercise prescription

    a.  ☐ Acute change in mental status or delirium
    b.  ☐ Cerebral hemorrhage within the past 3 months
    c.  ☐ Exacerbation of chronic inflammatory joint disease or osteoarthritis
    d.  ☐ Eye surgery within the past 6 weeks
    e.  ☐ Fracture in healing stage ___________________________
    f.  ☐ Hernia, symptomatic (abdominal or inguinal)
    g.  ☐ Myocardial infarction or cardiac surgery within past 3 months
    h.  ☐ Other acute illness or change in symptoms ___________________________
    i.  ☐ Proliferative diabetic retinopathy or severe non-proliferative retinopathy
    j.  ☐ Pulmonary embolism or deep venous thrombosis within 3 months
    k.  ☐ Soft tissue injury, healing ___________________________
    l.  ☐ Systemic infection ___________________________
    m.  ☐ Uncontrolled blood pressure (>180/100)
    n.  ☐ Uncontrolled diabetes mellitus (FBS >250mg/dl)
    o.  ☐ Uncontrolled malignant cardiac arrhythmia (ventricular tachycardia, complete heart block, atrial flutter, symptomatic bradycardia)
    p.  ☐ Unstable angina (at rest or crescendo pattern, ECG changes)
    q.  ☐ Other ___________________________

III. GO!  Exercise Recommended

    If only boxes in this column are checked, resident is suitable for exercise program without additional evaluation by medical staff at this time.

    a.  ☐ Arthritis
    b.  ☐ Chronic obstructive pulmonary disease, asthma
    c.  ☐ Congestive heart failure
    d.  ☐ Coronary artery disease
    e.  ☐ Chronic renal failure
    f.  ☐ Cancer (history or current)
    g.  ☐ Chronic liver disease
    h.  ☐ Chronic venous stasis
    i.  ☐ Dementia
    j.  ☐ Depression, anxiety, low morale
    k.  ☐ Diabetes
    l.  ☐ Drugs causing muscle wasting (steroids)
    m.  ☐ Frailty
    n.  ☐ Falls, history of hip fracture
    o.  ☐ Gait and balance disorders, mobility impairment
    p.  ☐ Hypertension
    q.  ☐ HIV infection
    r.  ☐ Hyperlipidemia
    s.  ☐ Malnutrition, poor appetite
    t.  ☐ Neuromuscular disease
    u.  ☐ Obesity
    v.  ☐ Osteoporosis
    w.  ☐ Parkinson’s disease
    x.  ☐ Peripheral vascular disease
    y.  ☐ Stroke

ASSESSMENT OF RESIDENT FUNCTIONAL PERFORMANCE
Check the appropriate boxes below for the resident’s actual performance over the last 7 days in each activity.

1.  INDEPENDENT: received hands-on assistance or supervision/cuing ≤ 2 times in last 7 days;
2.  INDEPENDENT WITH SUPERVISION: used set-up help (cutting food, laying out clothing, locker, wheelchair, etc.);
3.  DEPENDENT

| g. Walking in room | 1 | 2 | 3 |
| h. Transfers | ☐ | ☐ | ☐ |
| i. Dressing | ☐ | ☐ | ☐ |
| j. Eating | ☐ | ☐ | ☐ |
| k. Is wheelchair his/her primary mode of locomotion? | ☐ Yes | ☐ No |
CT SCAN DATA SHEET

Time first supine: ________________________

Image Number: _________

THIGH

Leg used (circle): LEFT RIGHT

Mid point where image taken: _______ cm from inguinal crease

I (Distance) = _________ V (Vector)= _________

Kv = 100 MA = 170 DFOV: _________

Thigh circumference: _______ cm _______ cm

_______ cm Average= _______ cm

Time of girth measurement: ______________________

Scan = 1 mm slice width

Data storage:
- Film Taken
- Data sent by FTP to USYD
- Data burned on CD

Comments:
- protocol completed
- not completed due to death
- not completed due to refusal, drop-out or loss to follow-up
- not completed due to medical illness or incapacity
- not completed due to examiner failure or error
- not completed due to other: ______________________
ANTHROPOMETRY

Comments: _____________________________

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<tr>
<th>Measurement</th>
<th>Side Used</th>
<th>Trial I</th>
<th>Trial II</th>
<th>Trial III</th>
<th>Average</th>
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</thead>
<tbody>
<tr>
<td>Body Weight</td>
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<td>☐ RPA scale</td>
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<td>Mid-arm Circumference</td>
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<tr>
<td>Mid-calf Circumference</td>
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<tr>
<td>Waist Circumference</td>
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Corrected Weight: _____________________________

☐ Protocol completed
☐ Not completed due to death
☐ Not completed due to refusal, drop-out or loss to follow up
☐ Not completed due to medical illness or incapacity
☐ Not completed due to equipment failure or examiner error
☐ Not completed due to other cause (specify)
# Mini-nutritional Assessment

**PEAK**

**Mini-nutritional assessment**

<table>
<thead>
<tr>
<th>I Anthropometric Assessment</th>
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<tbody>
<tr>
<td>1. BMI (weight/(height)^2 in kg/m^2)</td>
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<tr>
<td>0 = BMI&lt;19</td>
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<tr>
<td>1 = 19≤BMI&lt;21</td>
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<tr>
<td>2 = 21≤BMI&lt;23</td>
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<tr>
<td>3 = BMI≥23</td>
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</tbody>
</table>

| 2. Mid arm circumference (MAC in cm) |
| 0.0 = MAC<21                     |
| 0.5 = 21≤MAC<22                  |
| 1.0 = MAC≥22                     |

| 3. Calf circumference |
| 0 = CC<31               |
| 1 = CC≥31               |

| 4. Weight loss during last 3 months |
| 0 = weight loss>3kg            |
| 1 = does not know              |
| 2 = weight loss between 1 and 3 kg |
| 3 = no weight loss             |

<table>
<thead>
<tr>
<th>II. Global Evaluation</th>
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<tbody>
<tr>
<td>5. Does the patient live independently in contrast to a nursing home?</td>
</tr>
<tr>
<td>0 = no 1 = yes</td>
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</tbody>
</table>

| 6. Does the patient take more than 3 prescription drugs (per day)? |
| 0 = yes 1 = no         |

| 7. In the past 3 months, has the patient suffered from psychological stress or acute disease? |
| 0 = yes 1 = no         |

| 8. Mobility |
| 0 = bed or chair bound |
| 1 = able to get out of bed/chair, but does not go out |
| 2 = goes out          |

| 9. Neuropsychological problems |
| 0 = severe dementia or depression |
| 1 = mild dementia |
| 2 = no psychological problems |

| 10. Pressure sores or skin ulcers |
| 0 = yes 1 = no |

<table>
<thead>
<tr>
<th>III. Dietetic assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>11. How many full meals does the patient eat daily?</td>
</tr>
<tr>
<td>0 = 1 meal 1 = 2 meals 2 = 3 meals</td>
</tr>
</tbody>
</table>

| 12. Does he consume: |
| • At least 1 serving of dairy products (milk, cheese, yogurt) per day? |
| 0 = if 0 or 1 yes 1 = yes |

| 13. Does he consume 2 or more servings of fruits or vegetables per day? |
| 0 = no 1 = yes |

| 14. Has the patient food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties? |
| 0 = severe loss of appetite |
| 1 = moderate loss of appetite |
| 2 = no loss of appetite |

| 15. How many cups/glasses of beverages (water, juice, coffee, tea, milk, wine, beer…) does the patient consume per day? |
| 0.0 = less than 3 glasses |
| 0.5 = 3 to 5 glasses |
| 1.0 = more than 5 glasses |

| 16. Mode of feeding? |
| 0 = fed requires assistance |
| 1 = self-fed with some difficulty |
| 2 = self-fed without any problem |

<table>
<thead>
<tr>
<th>IV. Subjective Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>17. Does the patient consider to have any nutritional problems?</td>
</tr>
<tr>
<td>0 = major malnutrition</td>
</tr>
<tr>
<td>1 = does not know or moderate malnutrition</td>
</tr>
<tr>
<td>2 = no nutritional problem</td>
</tr>
</tbody>
</table>

| 18. In comparison with other people of the same age, how would the patient consider his health status? |
| 0.0 = not as good |
| 0.5 = does not know |
| 1.0 = as good |
| 2.0 = better |

**Total (max 30 points)**

**SCORE**

- >24 points: well nourished
- 17 - 23.5 points: at risk of malnutrition
- <17 points: undernutrition
Urea Kinetics

1. Date 1: ______________
   a. Pre Urea _____________
   b. Post Urea _____________
   c. Dialysis Time __________
   d. Ultrafiltrate Removed __________
   e. Post Dialysis Weight __________

2. Interdialytic Time: ____________________

3. Date 2: ______________
   a. Pre Urea _______________

4. Calculations:
   a. R _______________
   b. KT/V _______________
   c. URR _______________
   d. ID Urea ______________
   e. PCR ______________
Blood Test Results

<table>
<thead>
<tr>
<th>Test</th>
<th>Date Drawn</th>
<th>Result</th>
<th>Laboratory</th>
<th>Vial ID No. (Serum and Plasma)</th>
<th>Storage Site (Serum and Plasma)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HbA1c (diabetics)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haematocrit</td>
<td></td>
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</tr>
<tr>
<td>Transferrin</td>
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</tr>
<tr>
<td>Ferritin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C-reactive Protein</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Prealbumin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potassium</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Urea</td>
<td></td>
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</tr>
<tr>
<td>Creatinine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kt/V</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>URR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stored Serum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Stored Plasma</td>
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</tr>
<tr>
<td>RBC count</td>
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</tr>
<tr>
<td>Mean cell volume</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>WBC count (total)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>%lymphocytes</td>
<td></td>
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</tr>
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<td>%neutrophils</td>
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<td>%basophils</td>
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<tr>
<td>%eosinophils</td>
<td></td>
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</tbody>
</table>

Comments:
1= protocol completed
2= not completed due to death
3= not completed due to refusal, drop-out or loss to follow up
4= not completed due to medical illness or incapacity
5= not completed due to equipment failure or examiner error
6= not completed due to other causes (specify cause)
# ISOMETRIC STRENGTH

<table>
<thead>
<tr>
<th>Measurement (kg)</th>
<th>Trial 1</th>
<th>Trial 2</th>
<th>Trial 3</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left Knee Extension</td>
<td></td>
<td></td>
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<tr>
<td>Right Knee Extension</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Left Hip Abduction</td>
<td></td>
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</tr>
<tr>
<td>Right Hip Abduction</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Left Triceps</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right Triceps</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Comments: __________________________________________
____________________________________________________
____________________________________________________

*Code each test in the comments column of table by using the format below:*

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# PERFORMANCE-BASED TESTING

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Trial I</th>
<th>Trial II</th>
<th>Location/Flooring</th>
<th>Assistive Device</th>
<th>Footwear Used</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Habitual Gait Velocity (sec)</td>
<td></td>
<td></td>
<td></td>
<td>None</td>
<td>Barefoot</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Stick</td>
<td>Flat shoe</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Frame</td>
<td>Low heel (2-3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Rollator frame</td>
<td>High heel (&gt;3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td>Other:</td>
<td></td>
</tr>
<tr>
<td>Static Balance (sec)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wide Base</td>
<td>XXX</td>
<td></td>
<td></td>
<td></td>
<td>Barefoot</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flat shoe</td>
<td>Flat shoe</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low heel (2-3cm)</td>
<td>Low heel (2-3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High heel (&gt;3cm)</td>
<td>High heel (&gt;3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td>Other:</td>
<td></td>
</tr>
<tr>
<td>Narrow Base</td>
<td>XXX</td>
<td></td>
<td></td>
<td></td>
<td>Barefoot</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flat shoe</td>
<td>Flat shoe</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low heel (2-3cm)</td>
<td>Low heel (2-3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High heel (&gt;3cm)</td>
<td>High heel (&gt;3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td>Other:</td>
<td></td>
</tr>
<tr>
<td>Half Tandem Stand</td>
<td>XXX</td>
<td></td>
<td></td>
<td></td>
<td>Barefoot</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flat shoe</td>
<td>Flat shoe</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Low heel (2-3cm)</td>
<td>Low heel (2-3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>High heel (&gt;3cm)</td>
<td>High heel (&gt;3cm)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Other</td>
<td>Other:</td>
<td></td>
</tr>
</tbody>
</table>
| Tandem Stand          | XXX | Barefoot □  
|                      |     | Flat shoe □  
|                      |     | Low heel (2-3cm) □  
|                      |     | High heel (>3cm) □  
|                      |     | Other: □  
| One leg (L/R),      | XXX | Barefoot □  
| eyes open            |     | Flat shoe □  
|                      |     | Low heel (2-3cm) □  
|                      |     | High heel (>3cm) □  
|                      |     | Other: □  
| One leg (L/R),      | XXX | Barefoot □  
| eyes closed          |     | Flat shoe □  
|                      |     | Low heel (2-3cm) □  
|                      |     | High heel (>3cm) □  
|                      |     | Other: □  
| 6 minute walk        | XXX | None □  
| (meters)             |     | Stick □  
|                      |     | Frame □  
|                      |     | Rollator frame □  
|                      |     | Other: □  

**Code each test in comments column using format below:**

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2= not completed due to death  
3= not completed due to refusal, drop-out or loss to follow up  
4= not completed due to equipment failure or examiner error  
5= not completed due to other cause (specify)
Name: __________________________
DOB: __________________________ Age: ______
MRN: ___________________________ PEAK ID number: _______________________
Date: __________________________ Interviewer: __________________________

Demographic information

<table>
<thead>
<tr>
<th>Patient details</th>
<th>Person for Notification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td>Relationship</td>
</tr>
<tr>
<td>Address</td>
<td></td>
</tr>
<tr>
<td>Telephone</td>
<td>H:</td>
</tr>
<tr>
<td></td>
<td>W:</td>
</tr>
</tbody>
</table>

Gender

Male
Female

Race / Ethnic background
What is your ethnic background?

Caucasian
Australian
Asian
Aboriginal
European
Middle East
Black
Indian
other __________________________
Marital status
Are you married, widowed, divorced, separated, never married?
married / defacto
widowed
divorced
single/ never married
separated

Residence
In what type of accommodation do you live?
house (own)
house (rented)
unit (own)
unit (rented)
retirement village
hostel
nursing home
board/rooming house

How long have you lived at this address?
Years ______ Months ______

Living Situation
With whom do you live?
alone
spouse / partner
family
paid carer
friend
other residents

Total number of persons in the household
___________ people

Education
What is the highest grade or year of school you completed?
never / kindergarten 0
primary school 1 2 3 4 5 6
high school 7 8 9 10 11 12
tertiary 13 14 15 16
post graduate 17 18 19 20

Work
Do you currently work for pay either for yourself or someone else?
yes
no

How many hours per week do you work for pay?
___________ hours / week

Do you currently work as a volunteer?
yes
no

How many hours volunteer hours / week do you work?
___________ hours / week

Annual income
In what range is your annual income?
< $15,000
$15,000- $30,000
>$30,000

A50
Pension
Do you receive a pension?
Nil
DVA
Age pension
Widows pension
Disability Pension

Hospital admissions
During the past 12 months, how many different times did you stay in hospital over night?
______ number of times
______ number of days in hospital

Smoking
Have you ever smoked cigarettes, cigars or a pipe on a daily basis? yes no
Do you currently smoke at least 1 cigarette, cigar or pipe per day? yes no
If yes, how many cigarettes, cigars or pipes do you smoke on an average day? ________ per day

Alcohol
During the past 30 days, about how many days did you drink any alcoholic beverages (beer, wine, liquor)
almost every day
3-4 times a week
once or twice a week
2-3 times a month
once a month
none

Comments: __________________________________________________________
______________________________________________________________
______________________________________________________________
LEISURE TIME ACTIVITIES

1. Over the past 7 days, how often did you participate in sitting activities such as reading, watching TV or doing handicrafts?

   [0] never  
   [1] seldom (1-2 days)  
   [2] sometimes (3-4 days)  
   [3] often (5-7 days)  

   Go to Q.2

1a. What were these activities?

1b. On average, how many hours per day did you engage in these sitting activities?

   [1] less than 1 hour  
   [2] 1 but less than 2 hours  
   [3] 2 - 4 hours  
   [4] more than 4 hours

2. Over the past 7 days, how often did you take a walk outside your home or yard for any reason? For example for fun or exercise, walking to work, walking the dog etc?

   [0] never  
   [1] seldom (1-2 days)  
   [2] sometimes (3-4 days)  
   [3] often (5-7 days)  

   Go to Q.3

2a. On average, how many hours per day did you spend walking?

   [1] less than 1 hour  
   [2] 1 but less than 2 hours  
   [3] 2 - 4 hours  
   [4] more than 4 hours

b) On average, over the past 7 days, how many kms/miles/blocks have you walked? (1 mile = 12 blocks; 1km = 0.625miles).

Number of blocks _______, or km _______, or miles _______.

   [1] less than 1 mile  
   [2] One but less than 2 miles  
   [3] two to 4 miles  
   [4] more than 4 miles
3. Over the past 7 days, how many flights of stairs have you climbed up? (one flight = 10 steps) Number of steps _________, or flights of steps _________.
   [1] less than 1 flight
   [2] one but less than 2 flights
   [3] two to 4 flights
   [4] more than 4 flights

4. Over the past 7 days, how often did you engage in light sport or recreational activities such as lawn bowls, bowling, water aerobics, golf with a cart, yoga, tai chi, fishing from a boat or pier or other similar activities?
   [0] never
   [1] seldom
   (1-2 days)
   [2] sometimes
   (3-4 days)
   [3] often
   (5-7 days)
   Go to Q.5
   4a. What were these activities?
   4b. On average, how many hours per day did you engage in these light sport or recreational activities?
   [1] less than 1 hour
   [2] 1 but less than 2 hours
   [3] 2 – 4 hours
   [4] more than 4 hours

5. Over the past 7 days, how often did you engage in moderate sport or recreational activities such as doubles tennis, ballroom dancing, golf without a cart, softball or other similar activities?
   [0] never
   [1] seldom
   (1-2 days)
   [2] sometimes
   (3-4 days)
   [3] often
   (5-7 days)
   Go to Q.6
   5a. What were these activities?
   5b. On average, how many hours per day did you engage in these moderate sport or recreational activities?
   [1] less than 1 hour
   [2] 1 but less than 2 hours
   [3] 2 – 4 hours
   [4] more than 4 hours

6. Over the past 7 days, how often did you engage in strenuous sport and recreational activities such as jogging, swimming, cycling, singles tennis, aerobic dance, skiing (downhill or cross country) or other similar activities?
   [0] never
   [1] seldom
   (1-2 days)
   [2] sometimes
   (3-4 days)
   [3] often
   (5-7 days)
   Go to Q.7
   6a. What were these activities?
   6b. On average, how many hours per day did you engage in these strenuous sport or recreational activities?
   [1] less than 1 hour
   [2] 1 but less than 2 hours
   [3] 2 – 4 hours
   [4] more than 4 hours
7. Over the past 7 days, how often did you any exercise specifically to increase muscle strength and endurance such as lifting weights or pushups etc?
   (1-2 days)        (3-4 days)        (5-7 days)
   Go to Q.8

7a. What were these activities?

7b. On average, how many hours per day did you engage in exercise to increase muscle strength and endurance?
   [1] less than 1 hour       [2] 1 but less than 2 hours
   [3] 2 - 4 hours       [4] more than 4 hours

HOUSEHOLD ACTIVITIES

8. During the past 7 days, have you done any light housework such as dusting or washing dishes?

9. During the past 7 days, have you done any heavy housework or chores such as vacuuming, scrubbing floors, washing windows or carrying wood?

10. During the past 7 days, did you engage in any of the following activities?
    Please answer Yes or No and give the total time over the past 7 days spent engaging in the activities.

    No  Yes  Hours/wk
    a. Home repairs like painting, wallpapering, electrical etc  1  2
    b. Lawn work or yard care including snow or leaf removal, wood chopping etc  1  2
    c. Outdoor gardening  1  2
    d. Caring for another person such as a dependent child, dependent spouse or another adult  1  2

WORK-RELATED ACTIVITIES

11. During the past 7 days did you work for pay or as a volunteer?

11a. How many hours per week did you work for pay and/or as a volunteer? ________ hrs/wk

11b. Which of the following categories best describes the amount of physical activity required on your job and/or volunteer work?
    (1) Mainly sitting with light arm movements (eg. Office work, watch maker, seated assembly line worker, bus driver etc)
    (2) Sitting or standing with some walking (eg. Cashier, general office worker, light tool and machinery worker)
    (3) Walking with some handling of materials generally weighing less than 50 pounds (eg. Mailman, waitress, construction worker, heavy tool and machinery worker)
    (4) Walking and heavy manual work often requiring handling of materials weighing over 50 pounds (eg. Lumberjack, stone mason, farm or general labourer).
### PASE Score

<table>
<thead>
<tr>
<th>PASE Activity</th>
<th>Score</th>
<th>PASE weight</th>
<th>PASE score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscle strength/endurance*</td>
<td>h/d</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Strenuous sports*</td>
<td>h/d</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Moderate sports*</td>
<td>h/d</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Light sports*</td>
<td>h/d</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Job involving standing/walking*</td>
<td>h/d</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Walking*</td>
<td>h/d</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td>Lawn work or yard care</td>
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<td>36</td>
<td></td>
</tr>
<tr>
<td>Caring for another person</td>
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<td>35</td>
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</tr>
<tr>
<td>Home repairs</td>
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<td>30</td>
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</tr>
<tr>
<td>Heavy housework</td>
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<td>25</td>
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</tr>
<tr>
<td>Light housework</td>
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<td>25</td>
<td></td>
</tr>
<tr>
<td>Outdoor gardening</td>
<td></td>
<td>20</td>
<td></td>
</tr>
</tbody>
</table>

**PASE Total**

* determine the average number of hours/day (h/d) over a 7-day period

1 = engaged in activity during the previous 7 days

0 = did not engage in activity during the previous 7 days

### Paffenberger Score

<table>
<thead>
<tr>
<th>Activity</th>
<th>Formula</th>
<th>kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blocks walked/wk</td>
<td>X 4 kcal / block = kcal</td>
<td></td>
</tr>
<tr>
<td>Flights climbed/wk</td>
<td>X 8 kcal / flight = kcal</td>
<td></td>
</tr>
<tr>
<td>Minutes light sport/recreation/wk</td>
<td>X 5 kcal / min = kcal</td>
<td></td>
</tr>
<tr>
<td>Minutes moderate sport/recreation or muscle strength/wk</td>
<td>X 7.5 kcal / min = kcal</td>
<td></td>
</tr>
<tr>
<td>Minutes heavy sport/recreation/wk</td>
<td>X 10 kcal / min = kcal</td>
<td></td>
</tr>
</tbody>
</table>

**total kcal / week**

### Comments:
- protocol completed
- not completed due to death
- not completed due to refusal, drop-out or loss to follow-up
- not completed due to medical illness or incapacity
- not completed due to examiner failure or error
- not completed due to other:
SF-36 Health Status Survey

This survey asks you your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

1. In general, would you say your health is:
   1. Excellent
   2. Very Good
   3. Good
   4. Fair
   5. Poor

2. Compared to one year ago, how would you rate your health in general now?
   1. Much better now than 1 year ago
   2. Somewhat better now than 1 year ago
   3. About the same as 1 year ago
   4. Somewhat worse now than 1 year ago
   5. Much worse now than 1 year ago

3. The following items are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

<table>
<thead>
<tr>
<th>Activities</th>
<th>Yes, Limited A Lot</th>
<th>Yes, Limited A Little</th>
<th>No, Not Limited At All</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>b. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>c. Lifting or carrying groceries</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>d. Climbing several flights of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>e. Climbing one flight of stairs</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>f. Bending, kneeling or stooping</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>g. Walking more than a mile</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>h. Walking several blocks</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>i. Walking one block</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>j. Bathing or dressing yourself</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

<table>
<thead>
<tr>
<th>Problems</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>b. Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>c. Were limited in the kind of work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>d. Had difficulty performing the work or other activities (for example, it took extra effort)</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Cut down on the amount of time you spent on work or other activities</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>b. Accomplished less than you would like</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>c. Didn’t do work or other activities as carefully as usual</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

1. Not at all
2. Slightly
3. Moderately
4. Quite a bit
5. Extremely

7. How much bodily pain have you had during the past 4 weeks?

1. None
2. Very mild
3. Mild
4. Moderate
5. Severe
6. Very severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

1. Not at all
2. A little bit
3. Moderately
4. Quite a bit
5. Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks...

<table>
<thead>
<tr>
<th></th>
<th>All of the Time</th>
<th>Most of the Time</th>
<th>A Good Bit of the Time</th>
<th>Some of the Time</th>
<th>A Little Bit of the Time</th>
<th>None of the Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Did you feel full of pep?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>b. Have you been a very nervous person?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>c. Have you felt so down in the dumps that nothing could cheer you up?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>d. Have you felt calm and peaceful?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>e. Did you have a lot of energy?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>f. Have you felt downhearted and blue?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>g. Did you feel worn out?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>h. Have you been a happy person?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>i. Did you feel tired?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

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

1. All of the time
2. Most of the time
3. Some of the time
4. A little of the time
5. None of the time
11. How TRUE or FALSE is each of the following statements for you?

<table>
<thead>
<tr>
<th></th>
<th>Definitely True</th>
<th>Mostly True</th>
<th>Don't Know</th>
<th>Mostly False</th>
<th>Definitely False</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. I seem to get sick a little easier than other people</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>b. I am as healthy as anybody I know</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>c. I expect my health to get worse</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>d. My health is excellent</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
GDS

Choose the best answer for how you have felt in the past week (7 days):

1. Are you basically satisfied with your life?  1. YES  NO
2. Have you dropped many of your activities and interests?  2. YES  NO
3. Do you feel that your life is empty?  3. YES  NO
4. Do you often get bored?  4. YES  NO
5. Are you hopeful about the future?  5. YES  NO
6. Are you bothered by thoughts you can't get out of your head?  6. YES  NO
7. Are you in good spirits most of the time?  7. YES  NO
8. Are you afraid something bad is going to happen to you?  8. YES  NO
9. Do you feel happy most of the time?  9. YES  NO
10. Do you often feel helpless?  10. YES  NO
11. Do you often get restless and fidgety?  11. YES  NO
12. Do you prefer to stay at home, rather than going out and doing new things?  12. YES  NO
13. Do you frequently worry about the future?  13. YES  NO
14. Do you feel you have more problems with memory than most?  14. YES  NO
15. Do you think it is wonderful to be alive now?  15. YES  NO
16. Do you often feel downhearted and blue?  16. YES  NO
17. Do you feel pretty worthless the way you are now?  17. YES  NO
18. Do you worry a lot about the past?  18. YES  NO
19. Do you find life very exciting?  19. YES  NO
20. Is it hard for you to get started on new projects?  20. YES  NO
21. Do you feel full of energy?  21. YES  NO
22. Do you feel that your situation is hopeless?  22. YES  NO
23. Do you think that most people are better off than you are?  23. YES  NO
24. Do you frequently get upset over little things?  24. YES  NO
25. Do you frequently feel like crying?  25. YES  NO
26. Do you have trouble concentrating?  26. YES  NO
27. Do you enjoy getting up in the mornings?  27. YES  NO
28. Do you prefer to avoid social gatherings?  28. YES  NO
29. Is it easy for you to make decisions?  29. YES  NO
30. Is your mind as clear as it used to be?  30. YES  NO

Record number of depressed answers:  

A59
PEAK Study

Your Eating Habits

This questionnaire is to be administered by dietitian,

Glen Pang

Nutrition and Dietetics Department
St George Hospital
Kogarah NSW 2217

Phone: 9350 2752

Questionnaire courtesy of the Nutrition Program
University of Sydney

It should take about 40 minutes of your time
### How To Answer

<table>
<thead>
<tr>
<th></th>
<th>NEVER</th>
<th>RARELY</th>
<th>TIMES A MONTH</th>
<th>TIMES A WEEK</th>
<th>TIMES A DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>R</td>
<td>1M</td>
<td>1W</td>
<td>1D</td>
</tr>
<tr>
<td></td>
<td>2M</td>
<td>2W</td>
<td>AND SO ON</td>
<td>AND SO ON</td>
<td>AND SO ON</td>
</tr>
</tbody>
</table>

### About How Often Do You Usually Eat These Foods?

**Please Give an Answer for Every Food**

<table>
<thead>
<tr>
<th>Cereal Foods, Cakes and Biscuits</th>
<th>How Often</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breakfast cereal</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Bread roll</td>
<td>1 roll</td>
<td></td>
</tr>
<tr>
<td>(NOT hamburger buns)</td>
<td>1 slice</td>
<td></td>
</tr>
<tr>
<td>Bread or toast</td>
<td>1 cup (cooked)</td>
<td></td>
</tr>
<tr>
<td>(remember sandwiches)</td>
<td>1 cup (cooked)</td>
<td></td>
</tr>
<tr>
<td>Fried rice</td>
<td>1 cup (cooked)</td>
<td></td>
</tr>
<tr>
<td>Boiled rice</td>
<td>1 cup (cooked)</td>
<td></td>
</tr>
<tr>
<td>Pasta</td>
<td>1 cup (cooked)</td>
<td></td>
</tr>
<tr>
<td>(spaghetti, noodles, etc)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Sweet bun / Doughnut</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Crispbread / Cracker</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Salted biscuits</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Plain biscuits</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Fancy biscuits</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>(eg Choc coated)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Crumpet / Muffin (English)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Light cake</td>
<td>1 small cake or</td>
<td></td>
</tr>
<tr>
<td>(eg sponge)</td>
<td>1 slice large cake</td>
<td></td>
</tr>
<tr>
<td>Rich cake</td>
<td>1 small cake or</td>
<td></td>
</tr>
<tr>
<td>(eg cheesecake)</td>
<td>1 slice large cake</td>
<td></td>
</tr>
<tr>
<td>Pavlova</td>
<td>2 small or</td>
<td></td>
</tr>
<tr>
<td>(Meringue-type dessert)</td>
<td>1 slice large</td>
<td></td>
</tr>
<tr>
<td>Milk pudding (eg rice, sago)</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td>Steamed sponge-suet</td>
<td>1/4 small pudding</td>
<td></td>
</tr>
</tbody>
</table>

---

*University of Sydney Questionnaire 2002*
**CEREAL FOODS, CAKES AND BISCUITS I CONSUME THAT HAVE NOT BEEN MENTIONED**

If you have any other cereal foods, cakes or biscuits at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. What type of bread do you usually eat? (tick one box)

- [ ] Wholemeal or mixed grain
- [ ] Brown
- [ ] White
- [ ] About half the time wholemeal and half white
- [ ] About half the time wholemeal, half brown
- [ ] About half the time brown, half white
- [ ] Other breads (please specify type)
- [ ] I do not eat bread

2. Which of the following do you usually spread on bread or crackers and, if possible, what brand do you use? (tick one box)

- [ ] Butter
- [ ] Table or cooking margarine
- [ ] Polyunsaturated margarine
- [ ] Light spread
- [ ] Nothing
- [ ] I don't eat bread or crackers
- [ ] Something else: please describe ________________________
  (Canola, Monounsaturated, Plant Sterols)

The brand I usually use is ____________________________________
3. How thickly would you put the spread (eg butter, margarine) on your bread? (tick one box)

☐ Thin
☐ Medium
☐ Thick
☐ I don't use any spread

If you eat breakfast cereal, please answer the next four questions. (If not go to the next page)

4. What type a of breakfast cereals or porridge do you most commonly eat?

Please name ____________________________________________________________
_____________________________________________________________________

5. If you eat muesli, do you usually have toasted or untoasted muesli? (tick one box)

☐ Toasted
☐ Untoasted
☐ I don't have muesli

6. How many cups of milk do you usually add to breakfast cereal?
(Tick the number closest to the amount you have) (Name type of milk)

☐ None
☐ About a half a cup
☐ About one cup
☐ About one and a half cups
☐ About two cups
☐ More than two cups

7. How many teaspoons of sugar or honey do you usually add to breakfast cereal?
(Note: 1 dessertspoon = 2 teaspoons)

Write the number of teaspoons you have here
<table>
<thead>
<tr>
<th>Dairy Foods and Eggs</th>
<th>How Often</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass of plain milk</td>
<td>medium glass</td>
<td></td>
</tr>
<tr>
<td>Glass of flavoured milk</td>
<td>medium glass</td>
<td></td>
</tr>
<tr>
<td>Milk shake</td>
<td>regular size</td>
<td></td>
</tr>
<tr>
<td>Thick shake</td>
<td>regular size</td>
<td></td>
</tr>
<tr>
<td>Cheddar type cheese</td>
<td>30 gr (1 slice)</td>
<td></td>
</tr>
<tr>
<td>Specify &lt;25% or &lt;10% fat</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheddar type cheese- Lite</td>
<td>30 gr (1 slice)</td>
<td></td>
</tr>
<tr>
<td>Brie / Camembert</td>
<td>30 gr (1/4 round cheese)</td>
<td></td>
</tr>
<tr>
<td>Cottage Cheese/ricotta</td>
<td>100 gr (1/2 carton)</td>
<td></td>
</tr>
<tr>
<td>Danish blue type</td>
<td>15 gr (1 tbspn)</td>
<td></td>
</tr>
<tr>
<td>Edam type</td>
<td>30 gr (1 slice)</td>
<td></td>
</tr>
<tr>
<td>Cream cheese/Philly spread</td>
<td>20 gr (1 tbspn)</td>
<td></td>
</tr>
<tr>
<td>Cheese sauce</td>
<td>3 tbspn</td>
<td></td>
</tr>
<tr>
<td>Cream sauce (eg on meat)</td>
<td>1 tbspn</td>
<td></td>
</tr>
<tr>
<td>Yoghurt</td>
<td>200 gr (1 carton)</td>
<td></td>
</tr>
<tr>
<td>Ice-cream</td>
<td>2 scoops (Summer)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Winter)</td>
<td></td>
</tr>
<tr>
<td>Custard</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td>Fried egg</td>
<td>1 egg</td>
<td></td>
</tr>
<tr>
<td>Boiled egg</td>
<td>1 egg</td>
<td></td>
</tr>
<tr>
<td>Omelette/Scrambled eggs</td>
<td>2 eggs</td>
<td></td>
</tr>
</tbody>
</table>

**How to Answer**

<table>
<thead>
<tr>
<th>Never</th>
<th>Rarely</th>
<th>Times a Month</th>
<th>Times a Week</th>
<th>Times a Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>R</td>
<td>1 M</td>
<td>1 W</td>
<td>1 D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 M</td>
<td>2 W</td>
<td>2 D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AND SO ON</td>
<td>AND SO ON</td>
<td>AND SO ON</td>
</tr>
</tbody>
</table>

**About How Often Do You Usually Eat These Foods? Please give an answer for every food.**
DAIRY FOODS AND EGGS THAN YOU CONSUME WHICH HAVE NOT BEEN MENTIONED PREVIOUSLY

If you have any other dairy foods or eggs at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID. 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. When you drink milk or add it to cereal etc, do you mostly / always use: (tick one box)

- [ ] Whole milk
- [ ] Reduced / fat milk (eg shape)
- [ ] Powdered, skimmed milk
- [ ] Something else: Please describe _______________________________
  (Soy milk/Soy fortified)

2. When you eat yoghurt which type is it? (tick one box)

- [ ] Plain (eg not fat reduced)
- [ ] Plain, low fat
- [ ] Fruit flavoured (not fat reduced)
- [ ] Fruit flavoured, low fat
- [ ] I do not eat yoghurt
### HOW TO ANSWER

<table>
<thead>
<tr>
<th>NEVER</th>
<th>RARELY</th>
<th>TIMES A MONTH</th>
<th>TIMES A WEEK</th>
<th>TIMES A DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>R</td>
<td>1 M</td>
<td>1 W</td>
<td>1 D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2 M AND SO ON</td>
<td>2 W AND SO ON</td>
<td>2 D AND SO ON</td>
</tr>
</tbody>
</table>
MEATS (POULTRY NOT INCLUDED) YOU CONSUME WHICH HAVE NOT BEEN MENTIONED PREVIOUSLY

If you have any other meats at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID. 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. If salt is added to the cooking water when boiling foods, is the water? (tick one box)

- [ ] lightly salted
- [ ] Medium salted
- [ ] Heavily salted
- [ ] Salting is highly varied
- [ ] I never add salt to cooking water

2. When you add salt at the table, how much do you usually add? (tick one box)

- [ ] a light sprinkle
- [ ] a medium sprinkle
- [ ] a heavysprinkle
- [ ] Salting is highly varied
- [ ] I never add salt at the table
| HOW TO ANSWER |
|---------|----------|---------|---------|-------|
| NEVER   | RARELY  | TIMES A MONTH | TIMES A WEEK | TIMES A DAY |
| N       | R       | 1M      | 1W      | 1D    |
|         |         | 2M      | 2W      | 2D    |
|         |         | AND SO ON | AND SO ON | AND SO ON |

**ABOUT HOW OFTEN DO YOU USUALLY EAT THESE FOODS?**

**PLEASE GIVE AN ANSWER FOR EVERY FOOD**

<table>
<thead>
<tr>
<th>TAKE AWAYS AND MIXED DISHES</th>
<th>HOW OFTEN</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hamburger with bun (eg Mc Donalds)</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Hamburger patty (WITHOUT bun)</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Cheeseburger with bun</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Pizza</td>
<td>1 small or 4 slices larger pizza</td>
<td></td>
</tr>
<tr>
<td>Chiko roll</td>
<td>1 roll</td>
<td></td>
</tr>
<tr>
<td>Sausage roll</td>
<td>1 large, 2 small</td>
<td></td>
</tr>
<tr>
<td>Meat pie (shop bought)</td>
<td>1 pie</td>
<td></td>
</tr>
<tr>
<td>Meat pie (home made)</td>
<td>1 individual or 1 slice large pie</td>
<td></td>
</tr>
<tr>
<td>Savoury pies/</td>
<td>1 individual or</td>
<td></td>
</tr>
<tr>
<td>Pastries (eg quiche)</td>
<td>1 slice large pie</td>
<td></td>
</tr>
<tr>
<td>Pastie</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Jacket potato with filling (eg fill-a-spud)</td>
<td>1 medium potato</td>
<td></td>
</tr>
<tr>
<td>Crumbed veal (schnitzel)</td>
<td>1 large piece</td>
<td></td>
</tr>
<tr>
<td>Mince meat (eaten as savoury mince)</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Mince Meat dishes (eg shepherds pie)</td>
<td>1 piece (8x8x4 cm)</td>
<td></td>
</tr>
<tr>
<td>Spaghetti sauce or</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td>other spicy mince sauce</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stew / Casserole</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Curry</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Chinese meat &amp; veg dish</td>
<td>1 cup</td>
<td></td>
</tr>
</tbody>
</table>

*University of Sydney Questionnaire 2002*
TAKE AWAYS AND MIXED DISHES YOU CONSUME THAT HAVE NOT BEEN MENTIONED PREVIOUSLY

If you have any other take aways or mixed dishes at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID. 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### HOW TO ANSWER

<table>
<thead>
<tr>
<th>NEVER</th>
<th>RARELY</th>
<th>TIMES A MONTH</th>
<th>TIMES A WEEK</th>
<th>TIMES A DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>R</td>
<td>1M</td>
<td>1W</td>
<td>1D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2M</td>
<td>2W</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AND SO ON</td>
<td>AND SO ON</td>
<td>AND SO ON</td>
</tr>
</tbody>
</table>

### ABOUT HOW OFTEN DO YOU USUALLY EAT THESE FOODS?

**PLEASE GIVE AN ANSWER FOR EVERY FOOD**

#### CHICKEN, FISH AND SEAFOOD

<table>
<thead>
<tr>
<th>Food Description</th>
<th>How Often</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Roast chicken</td>
<td>1 drumstick / 2 wings or 2 slices breast</td>
<td></td>
</tr>
<tr>
<td>Boiled chicken</td>
<td>as above</td>
<td></td>
</tr>
<tr>
<td>Fried or barbecued chicken</td>
<td>as above</td>
<td></td>
</tr>
<tr>
<td>Chicken nuggets</td>
<td>6 nuggets</td>
<td></td>
</tr>
<tr>
<td>Chicken kebab</td>
<td>1 skewer</td>
<td></td>
</tr>
<tr>
<td>Chicken or fish patty</td>
<td>2 patties</td>
<td></td>
</tr>
<tr>
<td>Fried fish</td>
<td>1 piece</td>
<td></td>
</tr>
<tr>
<td>(batter/flour/breadcrumb)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fish without batter</td>
<td>1 piece</td>
<td></td>
</tr>
<tr>
<td>(steamed / grilled)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canned fish</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>(tuna, salmon etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salted fish</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td>(eg herring, sardines)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seafood (eg prawn, crab, lobster etc)</td>
<td>1/2 cup</td>
<td></td>
</tr>
</tbody>
</table>

#### CHICKEN, FISH OR SEAFOOD YOU CONSUME THAT HAVE NOT BEEN MENTIONED

If you have any other chicken fish or seafood at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID, 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

*University of Sydney Questionnaire 2002* 11
1. If you eat fried fish, in which of the following is it usually coated (tick one box)

- ☐ Batter
- ☐ Breadcrumbs
- ☐ Flour
- ☐ Other coating: please describe ________________________________
- ☐ Fried without coating
- ☐ I don't eat fried fish

2. If you eat the following meats how are they usually cooked? (tick one box for each food)

<table>
<thead>
<tr>
<th>Meat</th>
<th>Fried</th>
<th>Grilled</th>
<th>Microwaved</th>
<th>Don’t Eat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steaks</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Lamb chops</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Pork chops</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Sausages</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Bacon</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>Chicken</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

3. If you fry or roast your meat, which of the following do you usually use and, if possible, what brand do you use? (tick one box)

- ☐ Butter
- ☐ Table or cooking margarine
- ☐ Polyunsaturated margarine
- ☐ Dripping or lard
- ☐ Olive oil
- ☐ Sunflower oil
- ☐ Nothing
- ☐ I don't fry or roast my meat
- ☐ Something else: please describe ________________________________

The brand I usually use is ________________________________

4. When you eat meat with fat on it, do you eat: (tick one box)

- ☐ All of the fat
- ☐ Most of the fat
- ☐ About half of the fat
- ☐ Little or none of the fat
- ☐ I do not eat meat
5. When you eat chicken, do you remove the skin? (tick one box)

☐ I usually remove the skin
☐ I remove the skin about half the time
☐ I don't usually remove the skin
☐ I don't have chicken
The following list of foods contains some vegetables that may be eaten much more frequently at some times of the year than others (e.g. in the warmer or cooler weather). Please fill in how often each food is eaten in both the warmer months (SUMMER) and the cooler months (WINTER).

For Example - If you usually have:

A standard serve of peas about twice a week during the warmer months of the year and about every day during the cooler months:

and: Two medium potatoes (baked) a week throughout the year:

You would write:

<table>
<thead>
<tr>
<th>SUMMER</th>
<th>WINTER</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Green Peas</td>
<td>1/3 cup</td>
<td>2W 1D</td>
</tr>
<tr>
<td>Potato - baked</td>
<td>1 medium</td>
<td>2W 2W</td>
</tr>
</tbody>
</table>

ABOUT HOW OFTEN DO YOU USUALLY EAT THESE FOODS?
PLEASE GIVE AN ANSWER FOR EVERY FOOD

FRESH OR FROZEN VEGETABLES

<table>
<thead>
<tr>
<th>HOW OFTEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUMMER</td>
</tr>
<tr>
<td>Potato - fresh &amp; mashed (with milk)</td>
</tr>
<tr>
<td>Potato - jacket, fresh, boiled</td>
</tr>
<tr>
<td>Potato - baked</td>
</tr>
<tr>
<td>Hot chips / French fries</td>
</tr>
<tr>
<td>Sweet potato</td>
</tr>
<tr>
<td>Carrots (fresh/frozen)</td>
</tr>
<tr>
<td>Turnip, Swede (fresh/frozen)</td>
</tr>
</tbody>
</table>

University of Sydney Questionnaire 2002 14
<table>
<thead>
<tr>
<th>Vegetable</th>
<th>Amount</th>
<th>Summer</th>
<th>Winter</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Broad beans (fresh/frozen)</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green beans (fresh/frozen)</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Haricot, Lima beans (fresh/frozen)</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Green peas (fresh/frozen)</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cabbage</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brussel sprouts (fresh/frozen)</td>
<td>5-6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silver beet / Spinach (fresh/frozen)</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Broccoli (fresh/frozen)</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cauliflower (fresh/frozen)</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg plant (each 0.5 cm thick)</td>
<td>2 slices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pumpkin</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sweet corn (fresh/frozen)</td>
<td>1 small cob</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zucchini (fresh/frozen)</td>
<td>2 medium sized</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onion - fried</td>
<td>1/4 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Onion (raw, baked, boiled) (fresh/frozen)</td>
<td>1 medium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Garlic (fresh)</td>
<td>1 clove</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tomato</td>
<td>1 medium</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lettuce</td>
<td>2 small leaves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cucumber (each 0.5 cm thick)</td>
<td>3 slices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Coleslaw</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HOW OFTEN</td>
<td>SUMMER</td>
<td>WINTER</td>
<td>COMMENTS</td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>--------</td>
<td>--------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>Celery (fresh/frozen)</td>
<td>one 15 cm stick</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Capsicum (Green pepper) (fresh/frozen)</td>
<td>2 stripe (each 0.5 cm thick)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mushrooms / fresh</td>
<td>6-7 small ones</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beetroot / fresh</td>
<td>2 slices</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sprouted bean shoots</td>
<td>1/3 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stir fried mixed vegetables</td>
<td>1/2 cup</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**FRESH OR FROZEN VEGETABLES I CONSUME THAT HAVE NOT BEEN MENTIONED**

If you have any other fresh or frozen vegetables at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg 1D, 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
# How To Answer

<table>
<thead>
<tr>
<th></th>
<th>Never</th>
<th>Rarely</th>
<th>Times A Month</th>
<th>Times A Week</th>
<th>Times A Day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>R</td>
<td>1M</td>
<td>1W</td>
<td>1D</td>
</tr>
<tr>
<td></td>
<td>2M</td>
<td></td>
<td></td>
<td>2W</td>
<td>2D</td>
</tr>
<tr>
<td></td>
<td>AND SO ON</td>
<td></td>
<td></td>
<td>AND SO ON</td>
<td>AND SO ON</td>
</tr>
</tbody>
</table>

**About How Often Do You Usually Eat These Foods?**

Please give an answer for every food.

## Canned and Dried Vegetables

<table>
<thead>
<tr>
<th>Food</th>
<th>How Often</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potato - canned</td>
<td>2 - 3 small</td>
<td></td>
</tr>
<tr>
<td>Potato - packet (powdered)</td>
<td>1/3 cup (when cooked)</td>
<td></td>
</tr>
<tr>
<td>Carrots - canned</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Beetroot - canned</td>
<td>2 slices</td>
<td></td>
</tr>
<tr>
<td>Broad beans - canned</td>
<td>1/2 cup</td>
<td></td>
</tr>
<tr>
<td>Green beans - canned</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Haricot, Lima beans - canned/dried</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Baked beans (in tomato sauce)</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Green peas - canned</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Green peas - dried</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Lentils - canned/dried</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Soybeans - canned/dried</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Chick peas - canned/dried</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Zucchini - canned</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Sweetcorn - canned</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Mushrooms - canned</td>
<td>6 - 7 small ones</td>
<td></td>
</tr>
<tr>
<td>Olives</td>
<td>3 medium</td>
<td></td>
</tr>
<tr>
<td>Gherkins / Pickled onions</td>
<td>3 pieces</td>
<td></td>
</tr>
</tbody>
</table>
CANNED AND DRIED VEGETABLES YOU CONSUME THAT HAVE NOT BEEN MENTIONED

If you have any other canned and dried vegetables at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg ID. 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. When your vegetables are cooked, which of the following methods is the one most commonly used? (tick one box)

- Boiled in a little water
- Boiled in a lot of water
- Steamed
- Cooked in a pressure cooker
- Microwaved

2. Do you add fat (eg butter, margarine) to cooked vegetables? (tick one box)

- Usually
- Sometimes
- Never

3. If you fry or bake vegetables, which of the following do you usually use and, if possible, what brand do you use? (tick one box)

- Butter
- Table or cooking margarine
- Polyunsaturated margarine (Canola)
- Dripping or lard
- Olive oil (Monounsaturated oil)
- Sunflower oil/safflower oil/corn/peanut/blended vegetable oil
- Plant sterols
- Nothing
- I don't fry or bake my vegetables
- Something else: please describe ____________________________

University of Sydney Questionnaire  2002  18
The brand I usually use is __________________________
**HOW TO ANSWER**

<table>
<thead>
<tr>
<th>NEVER</th>
<th>RARELY</th>
<th>TIMES A MONTH</th>
<th>TIMES A WEEK</th>
<th>TIMES A DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>R</td>
<td>1M</td>
<td>1W</td>
<td>1D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2M AND SO ON</td>
<td>2W AND SO ON</td>
<td>2D AND SO ON</td>
</tr>
</tbody>
</table>

**ABOUT HOW OFTEN DO YOU USUALLY EAT THESE FOODS? PLEASE GIVE AN ANSWER FOR EVERY FOOD**

<table>
<thead>
<tr>
<th>FRUITS</th>
<th>HOW OFTEN</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orange, Mandarin</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Grapefruit</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Apple, Pear</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Banana</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Mixed fruit salad</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Dried fruit (apple/apricot)</td>
<td>4 - 5 pieces</td>
<td></td>
</tr>
<tr>
<td>Raisins, sultanas or currants</td>
<td>1/3 cup</td>
<td></td>
</tr>
<tr>
<td>Fruit canned in syrup or stewed fruit</td>
<td>100 gr</td>
<td></td>
</tr>
<tr>
<td>Fruit canned in water (eg low calorie fruit)</td>
<td>100 gr</td>
<td></td>
</tr>
<tr>
<td>Fruit pie or pastry or fritters</td>
<td>1 small pie or 1 large slice</td>
<td></td>
</tr>
</tbody>
</table>

The fruits listed below are only available for a short time during the year. Therefore we only want you to record how often you have them when they are IN SEASON.

**HOW OFTEN DO YOU EAT THESE FOODS WHEN THEY ARE IN SEASON**

<table>
<thead>
<tr>
<th>FRUITS</th>
<th>HOW OFTEN</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berries</td>
<td>3/4 cup</td>
<td></td>
</tr>
<tr>
<td>Melon (not watermelon)</td>
<td>1/4 small melon</td>
<td></td>
</tr>
<tr>
<td>Peach</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Plum</td>
<td>3 - 4 plums</td>
<td></td>
</tr>
<tr>
<td>Nectarine</td>
<td>1 medium</td>
<td></td>
</tr>
<tr>
<td>Apricot</td>
<td>3 apricots</td>
<td></td>
</tr>
<tr>
<td>Grapes</td>
<td>about 20</td>
<td></td>
</tr>
<tr>
<td>Avocado</td>
<td>1/2 an avocado</td>
<td></td>
</tr>
</tbody>
</table>

University of Sydney Questionnaire 2002
<table>
<thead>
<tr>
<th>FOOD</th>
<th>HOW OFTEN</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potato crisps, Cornchips,</td>
<td>1 small bag or 14-15 pieces</td>
<td>_________</td>
</tr>
<tr>
<td>Peanuts (fresh)</td>
<td>9-10 nuts</td>
<td>_________</td>
</tr>
<tr>
<td>Nuts - salted &amp; cooked</td>
<td>9-10 nuts</td>
<td>_________</td>
</tr>
<tr>
<td>Other unsalted nuts (eg walnuts/brazils)</td>
<td>5-6 nuts</td>
<td>_________</td>
</tr>
<tr>
<td>Popcorn</td>
<td>1 cup</td>
<td>_________</td>
</tr>
<tr>
<td>Chocolate</td>
<td>1 small bar</td>
<td>_________</td>
</tr>
<tr>
<td>Chocolate covered bar (eg Mars/bounty)</td>
<td>1 bar</td>
<td>_________</td>
</tr>
<tr>
<td>Individually wrapped lollies, Toffees</td>
<td>4-5 lollies</td>
<td>_________</td>
</tr>
<tr>
<td>Packet lollies (eg Lifesavers/Polos)</td>
<td>1 small packet</td>
<td>_________</td>
</tr>
<tr>
<td>Ice blocks or lollies</td>
<td>1 medium</td>
<td>_________</td>
</tr>
<tr>
<td>Muesli bar / Health bar</td>
<td>1 bar</td>
<td>_________</td>
</tr>
<tr>
<td>Honey / Jam / Marmalade</td>
<td>1 tbspn</td>
<td>_________</td>
</tr>
<tr>
<td>Vegemite / Marmite etc</td>
<td>1/2 teaspoon</td>
<td>_________</td>
</tr>
<tr>
<td>Peanut butter</td>
<td>1 tbspn</td>
<td>_________</td>
</tr>
<tr>
<td>Chocolate spread (eg nutella)</td>
<td>1 tbspn</td>
<td>_________</td>
</tr>
<tr>
<td>Thick sauces (tomato/HP etc)</td>
<td>2 tbspn</td>
<td>_________</td>
</tr>
<tr>
<td>Mayonnaise, Salad dressing</td>
<td>1 tbspn</td>
<td>_________</td>
</tr>
</tbody>
</table>
### How to Answer

<table>
<thead>
<tr>
<th>N</th>
<th>R</th>
<th>1M</th>
<th>1W</th>
<th>1D</th>
</tr>
</thead>
<tbody>
<tr>
<td>NEVER</td>
<td>RARELY</td>
<td>TIMES A MONTH</td>
<td>TIMES A WEEK</td>
<td>TIMES A DAY</td>
</tr>
<tr>
<td>2M AND SO ON</td>
<td>2W AND SO ON</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Summer Winter Comments

Soup

1 cup

What kind of soup do you most often eat? (eg homemade pea and ham, canned tomato)

__________________________

**FOODS YOU CONSUME THAT HAVE NOT BEEN MENTIONED**

If you have any other foods at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (eg 1D, 3M).

<table>
<thead>
<tr>
<th>Name of Food</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### How To Answer

<table>
<thead>
<tr>
<th>NEVER</th>
<th>RARELY</th>
<th>TIMES A MONTH</th>
<th>TIMES A WEEK</th>
<th>TIMES A DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>R</td>
<td>1M</td>
<td>1W</td>
<td>1D</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2M</td>
<td>2W</td>
<td>2D</td>
</tr>
<tr>
<td>AND SO ON</td>
<td></td>
<td>AND SO ON</td>
<td>AND SO ON</td>
<td>AND SO ON</td>
</tr>
</tbody>
</table>

### About How Often Do You Usually Have These Drinks?

*Please give an answer for every drink*

<table>
<thead>
<tr>
<th>DRINKS</th>
<th>HOW OFTEN</th>
<th>COMMENTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass of cordial</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>(eg Coca-Cola)</td>
<td>glass</td>
<td></td>
</tr>
<tr>
<td>Glass of fizzy drink</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>(includes mineral water/juice)</td>
<td>glass</td>
<td></td>
</tr>
<tr>
<td>Fruit drink</td>
<td>1 carton</td>
<td></td>
</tr>
<tr>
<td>(eg Fruit Box)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pure fruit juice</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Tea</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Coffee</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Coffee substitute</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>Cocoa / Chocolate</td>
<td>1 cup</td>
<td></td>
</tr>
<tr>
<td>(eg Milo/Ovaltine etc)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Mineral water</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Regular beer (5% alcohol)</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Low alcohol beer (2.2% alcohol eg Tooheys Blue)</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Alcoholic cider</td>
<td>medium</td>
<td></td>
</tr>
<tr>
<td>Wine</td>
<td>1 wine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>glass</td>
<td></td>
</tr>
</tbody>
</table>

---

*University of Sydney Questionnaire*  
*2002*  
*23*
Spirits (whisky, brandy etc) 1 nip

Liqueur 1 small nip

Wine Cooler 1 medium glass

**DRINKS I CONSUME THAT HAVE NOT BEEN MENTIONED**

If you have any other drinks at least once a month that we have not mentioned, please write them down below and tell us how often you have them using the same code as before (e.g. ID. 3M).

<table>
<thead>
<tr>
<th>Name of Drink</th>
<th>Your Usual Serving Size</th>
<th>How Often</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. Do you have milk: (tick one box for each drink)

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Don’t drink it</th>
</tr>
</thead>
<tbody>
<tr>
<td>in your tea?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in your coffee?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>in your coffee substitute?</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

2. Do you make your cocoa or chocolate with: (tick one box)

- [ ] Mostly milk?
- [ ] Mostly water?
- [ ] About half and half?
- [ ] I do not drink cocoa or chocolate

3. How many teaspoons of sugar do you usually have in each cup of: (tick one box for each drink)

<table>
<thead>
<tr>
<th>Tea?</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Don’t drink it</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coffee?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>Don’t drink it</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>Don't drink it</td>
</tr>
<tr>
<td>---------------</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>----------------</td>
</tr>
<tr>
<td>Coffee substitute?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cocoa/chocolate?</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
4. Do you take any vitamin, mineral or other dietary supplements regularly?

☐ Yes
☐ No

5. If you take any type of dietary supplement please fill in the table below. Check the label on the box or bottle if you are unsure of some answers.

<table>
<thead>
<tr>
<th>BRAND</th>
<th>NAME OF PRODUCT</th>
<th>SIZE OF DOSE</th>
<th>NUMBER OF DOSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>(eg Nyal)</td>
<td>(eg vitamin C pills)</td>
<td>(eg 250 mg)</td>
<td>(eg 2 per day)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

😊 THANKS !! 😊

Thank you very much for taking the time to fill in this questionnaire
EXERCISE INTENSITY SCALE

6
7  Very, Very Light
8
9  Very Light
10
11 Fairly Light
12
13 Somewhat Hard
14
15 Hard
16
17 Very Hard
18
19 Very, Very Hard
20
## Training Log

### Exercise Log

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Date:</th>
<th>Set 1L</th>
<th>Set 1R</th>
<th>Date:</th>
<th>Set 1L</th>
<th>Set 1R</th>
<th>Date:</th>
<th>Set 1L</th>
<th>Set 1R</th>
<th>Date:</th>
<th>Set 1L</th>
<th>Set 1R</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shoulder Press</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Leg Extension</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Side Shoulder Raise</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>External Rotation</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Abdominals</td>
<td>N or A</td>
<td>kg</td>
<td>N or A</td>
<td>N or A</td>
<td>kg</td>
<td>N or A</td>
<td>N or A</td>
<td>kg</td>
<td>N or A</td>
<td>N or A</td>
<td>kg</td>
<td>N or A</td>
</tr>
<tr>
<td>Triceps Extension</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Leg Flexion</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Thigh Flexion</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Biceps Curl</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
<tr>
<td>Thigh Abduction</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
<td>reps</td>
<td>kg</td>
<td>RPE</td>
</tr>
</tbody>
</table>

### Comments/Subject Complaints/Adverse Events:


Weekly Status Check

Name: ___________________________ Study ID #: _______________________
Date: ____________________________ Week #: ____________________________
Interviewer: ______________________ Telephone __ In-person __________

During the past week have you had any of the following?  
Yes  No

1. Acute illnesses
   Specify _________________________

2. Change in medication (prescribed, over-the-counter, herbal, nutritional supplement)
   Specify _________________________

3. Visits to a health care professional
   Kind ____________________________
   Indication _______________________
   Treatment ________________________

4. New physical, mental, or emotional symptoms of any kind
   Describe _________________________

5. Falls
   Number __________________________
   Circumstance(s) ____________________
   Injury ____________________________

6. Have you attended all exercise sessions?
   If not, number attended ____________
   Reason for missed session(s) ____________

8. Other Questions or Comments of subject:
   __________________________________
   __________________________________
   __________________________________
   Comments:
   □ protocol completed
   □ not completed due to death
   □ not completed due to refusal, drop-out or loss to follow-up
   □ not completed due to medical illness or incapacity
   □ not completed due to examiner failure or error
   □ not completed due to other: ____________________________________________
APPENDIX B

Consent Form
THE ST. GEORGE HOSPITAL, SOUTH EASTERN AREA HEALTH SERVICE

SUBJECT INFORMATION STATEMENT AND CONSENT FORM

Project Title:
Research Study - "A Randomised Controlled Trial of Progressive Resistance Training During Maintenance Haemodialysis to Counteract Muscle Wasting and Undernutrition"

Introduction:
You are invited to participate in the above study. The following 4 pages provide information about the research. We want to be sure you understand all aspects of the research before you decide whether or not to take part. Please ask any questions if there is still anything you are not clear about.

Study Team:
The study is being conducted by Ms. Maria Chan, Renal Dietitian, Assoc. Professor John Kelly, Staff Nephrologist and Dr. Anthony O'Sullivan, Endocrinologist at the St. George Hospital. The study is also being conducted at The Royal Prince Alfred Hospital (RPAH) Investigators of other institutions: Ms A Patwardhan, Renal Dietitian, RPAH, Assoc. Professor, A Gillin, Staff Nephrologist, RPAH and Professor, M. Fiatarone Singh, Professor of Medicine, The University of Sydney.

Background:
Some people on long-term haemodialysis become weaker over time due to a loss of muscle. This can lead to poor day-to day function and poor nutrition. We hope to learn whether a supervised weight-training program will improve your nutrition, food intake, muscle size, strength and day to day function.

Study design:
The study will last for 24 weeks. Participants will be assigned at random to either 24 weeks of weight lifting exercise, or to exercise during weeks 12-24 only. All participants will be evaluated at the beginning of the study - week 0, 12, and 24 weeks to determine the benefits of the program on health and quality of life.
Research Study - "A Randomised Controlled Trial of Progressive Resistance Training During Maintenance Haemodialysis to Counteract Muscle Wasting and Undernutrition" – cont’d

Procedures:

Exercise training
Before you decide to participate in this study the study investigators will evaluate your health status to make sure you will be able to tolerate the weight lifting exercises. Exercises will be carried out under supervision of the research staff over the 6 month course of the study while you are on haemodialysis (3 times a week). The exercise involves the training of arms, trunk and leg muscles using portable weights (dumbbells and ankle cuffs) which will be increased gradually as your muscle strength improves. Each session will only last for approximately 45 minutes.

Assessments
At the beginning, middle and end of the 24 week study period, you will have assessments of your health status and physical functioning as summarized below:

- Your muscle size will be assessed by CT scan at Royal Prince Alfred Hospital
- You will be asked questions about your medical history, dietary intake, mood, physical activity level, and functioning in daily life.
- Your muscle strength will be tested by asking you to push as hard as you can against a measuring device with several muscle groups
- Your heart rate will be evaluated with a 5-minute resting electrocardiogram (ECG).
- You will have blood tests to check the blood chemistry that reflects how well nourished you are. In most cases these blood tests will be part of the usual monthly tests that are carried out in the dialysis center, so that little or no extra blood will be taken for this study.

Reasons for study termination:
Your participation in this study may be ended prematurely for any of the following reasons:

- you refuse to continue in the study,
- discontinuation is deemed to be in your best interests or in the opinion of your clinical care team or the study investigators, or
- you have a renal transplant, or
- there is an unrelated medical illness or complication that makes study procedures unsafe or unreliable.

Risks:
Other kinds of exercise, such as walking and bike riding have been used safely to improve health and functioning in dialysis patients. Although there have not yet been any studies done on weight training during haemodialysis, this kind of exercise has been proven to be a safe and beneficial way to improve muscle strength & quality of life in other groups. These include very elderly people, people with renal failure not yet on dialysis, and people with other diseases that cause muscle wasting. There are minimal risks associated with participation in this study, as summarized below:

- There may be some changes in blood pressure, pulse and blood flow during dialysis due to the exercise, which will be closely monitored. It is anticipated that the nursing staff at the dialysis unit will be able to manage these quite easily
- Muscle strength testing may cause slight soreness over the next 1-2 days.
Research Study - "A Randomised Controlled Trial of Progressive Resistance Training During Maintenance Haemodialysis to Counteract Muscle Wasting and Undernutrition" - cont’d

- Weight lifting exercises may cause fatigue, muscle soreness, injury to tendons or ligaments, or exacerbation of underlying arthritis or joint pain. Under direct supervision of an experienced trainer, such as will occur in this study, these complications are uncommon, and usually resolve quickly with modifications of the training regimen.
- During the CT scan, you will be exposed to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2-3 millisieverts (mSv) each year. The effective dose from this study is about 0.25mSv. At this dose level, no harmful effects of radiation have been demonstrated and the risk is minimal.

Potential Benefits:
The benefit from participating in this study is that your nutritional status, muscle size and strength, ability to carry out day-to-day tasks, and sense of well being may improve over the course of study.

Cost/Reimbursement:
You will not incur any additional cost if you participate in this study. You will not be charged for any extra doctor’s visits, blood and other tests or procedures and supervised weight training program during this study.

Videotaping:
A video may be made when you perform the exercise. The video will then be used to train other people on Haemodialysis. We will include you only if you agree to be videotaped.

Continuation:
You may wish to continue exercising during hemodialysis sessions beyond the completion of this study. If so, a second consent form will be presented to you at that time.

Confidentiality & Disclosure of Information:
Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission or except as required by law. If you give us your permission by signing this document, we plan to discuss/publish the results in scientific/medical journals. In any publication, information will be provided in such a way that you cannot be identified.

Complaints may be directed to the Ethics Secretariat, South Eastern Sydney Area Health Service Research Ethics Committee (Southern Section):
Miss Doukessa Lerias
Coordinator - South East Health
Human Research Ethics Committee – Southern Section
St. George Hospital
Gray street,
Kogarah 2217
Phone: 9350 2987 or 93502481
Fax: 9350 3968
E-mail: lerissi@sesahs.gov.au

Participation:
Your decision whether or not to participate will not prejudice your future relations with the St. George Hospital. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without prejudice.
If you have any questions at any time during the study, Maria Chan, Renal Dietitian (02-93502752) will be happy to answer them.
You will be given a copy of this form to keep.

THE ST. GEORGE HOSPITAL, SOUTH EASTERN AREA HEALTH SERVICE
SUBJECT INFORMATION STATEMENT AND CONSENT FORM (continued)

(Research Study - "A Randomised Controlled Trial of Progressive Resistance Training During Maintenance Haemodialysis to Counteract Muscle Wasting and Undernutrition")

You are making a decision whether or not to participate. Your signature indicates that you have decided to participate having read the information provided above.

________________________________________  ______________________________________
Signature of subject                      Signature of witness

________________________________________  ______________________________________
Please PRINT name                          Please PRINT name

________________________________________  ______________________________________
Date                                      Nature of Witness

_______________________________________
Signature(s) of investigator(s)

_______________________________________
Please PRINT Name

REVOCATION OF CONSENT

I hereby wish to WITHDRAW my consent to participate in the research proposal described above and understand that such withdrawal WILL NOT jeopardise any treatment or my relationship with The St George Hospital or my medical attendants.

_______________________________________  _________________________________
Signature                                      Date

_______________________________________
Please PRINT Name

The section for Revocation of Consent should be forwarded to Ms Maria Chan, Renal Dietitian, Department of Nutrition & Dietetics, The St. George Hospital, Kogarah, NSW, 2217. Phone: 02-93502752

A93
APPENDIX C

Ethics Approval Forms
SOUTH EAST HEALTH
HUMAN RESEARCH ETHICS COMMITTEE
SOUTHERN SECTION

21st February 2002

Ms M Chan
Dept Nutrition and Dietetics
St George Hospital

Dear Ms Chan,

RE: A randomized controlled trial of progressive resistance training during maintenance haemodialysis (HD) to counteract muscle wasting and undernutrition (02/09 Chan)

Thank you for your letter dated February 2002, stating the required amendments.

As you have now fulfilled all necessary conditions I hereby notify you that, at its meeting held on the 29th January 2002, the South East Health Human Research Ethics Committee - Southern Section agreed to approve:

A randomized controlled trial of progressive resistance training during maintenance haemodialysis (HD) to counteract muscle wasting and undernutrition (02/09 Chan)

The Committee requires a brief six month progress report on research it has approved and yearly reports thereafter. (Estimated duration of the project 2 years).

SER HREC SS
St George Hospital
Gray St.,
KOGARAH 2217

These reports should:

TEL 9350 2461
FAX 9350 3968
Email: lertasd@sesahs.nsw.gov.au

South Eastern Sydney Area Health Service
Be accompanied by abstracts of any articles or publications (if any) arising out of the study.

Confirm security of records.

Confirm compliance with approved consent procedures and documentation.

The investigator should also report immediately to the Ethics Committee anything, which might affect ethical acceptability of the protocol, including:

- Adverse events on subjects.
- Proposed changes in the protocol.
- Unforeseen events that might affect continued ethical acceptability of the project.

I look forward to placing your first report before the Committee and wish you well in this study.

Yours sincerely,

[Blank]

Doukessa Leras
Coordinator
South East Health Human Research Ethics Committee
Southern Section
21 February 2005

Ms A Patwardhan
Department of Nutrition and Dietetics
Level 6, Building 13
Royal Prince Alfred Hospital

Dear Ms Patwardhan,

Re: Protocol No X02-0028 - “A randomised controlled trial of progressive resistance training during maintenance haemodialysis to counteract muscle wasting and undernutrition”

The Ethics Review Committee, at its meeting of 9 February 2005, considered your report on the above study, and it was noted with thanks.

Yours sincerely,

[Redacted]
Lesley Townsend
Secretary
Ethics Review Committee (RPAH Zone)

HERCICOR05-02
The University of Sydney
Room K4.01 Main Quad A14
Sydney 2006

Ms A Patwardhan
Department of Nutrition and Dietetics, RPAH
Camperdown 2050

20/06/2002

Dear Ms Patwardhan

Title: A randomised controlled trial of progressive resistance training during maintenance haemodialysis to counteract muscle wasting and under nutrition

Ref No: 02/05/16

I am pleased to inform you that the Human Ethics Committee at its meeting on 27/05/02 approved your protocol on the above study. Please note that subject to annual monitoring returns, the approved protocol is valid for five years.

In order to comply with the National Statement on Ethical Conduct in Research Involving Humans, and in line with the Human Ethics Committee requirements the Chief Investigator’s responsibility is to ensure that:

(1) The individual researcher’s protocol complies with the final and Committee approved protocol.

(2) Modifications to the protocol cannot proceed until such approval is obtained in writing.

(3) The confidentiality and anonymity of all research subjects is maintained at all times, except as required by law.

(4) All research subjects are provided with a Subject Information Sheet and Consent Form.

(5) The Subject Information Sheet and Consent Form be on University of Sydney letterhead and include the full title of the research project and telephone contacts for the researchers.

(6) The following statement appears on the bottom of the Subject Information Sheet:

Any person with concerns or complaints about the conduct of a research study can contact the Manager of Ethics and Biosafety Administration, University of Sydney, on (02) 9351 4812.

(7) The standard University policy concerning storage of data and tapes should be followed. While temporary storage of data or tapes at the researcher’s home or an off-campus site is acceptable during the active transcription phase of the project, permanent storage should be at a secure, University controlled site for a minimum of five years.

(8) A progress report is provided by the end of each year. Failure to do so will lead to withdrawal of the approval of the research protocol and re-application to the Committee must occur before recommencing.

(9) A report and a copy of the published material is provided at the end of the project.

Yours sincerely,

Associate Professor Stewart Kellee
Chairman
Human Ethics Committee

Professor M Patwardhan, School of Exercise and Sports Science, C41
25 March 2002

Mrs Maria Chan
Department of Nutrition and Dietetics
The St George Hospital

Dear Ms Chan

A randomized controlled trial of progressive resistance training during maintenance haemodialysis (HD) to counteract muscle wasting and undernutrition (HREC 02058) (SESAHS 03/09)

At its meeting held on 19 March 2002, the Executive of the Human Research Ethics Committee (HREC) noted the approval given by the South East Health Human Research Ethics Committee (SS) dated 21 February 2002 for this project to proceed.

Yours sincerely

A/Professor Andrew Lloyd
Presiding Member
HREC
APPENDIX D

Complete Data Summary from Chapter 5 and 6
Table 1: Chapter 5 - Complete Summary of Data Collected

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Experimental Group</th>
<th>Control Group</th>
<th>Time Effect p value</th>
<th>Group x Time p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 0</td>
<td>Week 12</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>69.9 (15.0)</td>
<td>71.3 (15.1)</td>
<td>77.8 (15.8)</td>
<td>77.4 (15.2)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0 (5.9)</td>
<td>26.5 (5.8)</td>
<td>28.2 (5.2)</td>
<td>28.1 (4.9)</td>
</tr>
<tr>
<td>Mid-thigh circ. (cm)</td>
<td>45.7 (4.0)</td>
<td>46.7 (3.9)</td>
<td>47.6 (5.5)</td>
<td>47.3 (4.3)</td>
</tr>
<tr>
<td>Mid-arm circ. (cm)</td>
<td>29.7 (3.7)</td>
<td>30.2 (3.3)</td>
<td>31.2 (3.3)</td>
<td>30.4 (3.1)</td>
</tr>
<tr>
<td>Mid-calf circ. (cm)</td>
<td>33.9 (3.0)</td>
<td>34.2 (2.8)</td>
<td>35.1 (3.5)</td>
<td>35.3 (3.8)</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.2 (18.9)</td>
<td>94.7 (18.9)</td>
<td>98.3 (13.0)</td>
<td>99.4 (13.0)</td>
</tr>
<tr>
<td>Thigh muscle CSA (cm²)</td>
<td>94.6 (23.3)</td>
<td>95.6 (22.0)</td>
<td>96.6 (26.5)</td>
<td>95.8 (25.3)</td>
</tr>
<tr>
<td>Thigh muscle attenuation (HU)</td>
<td>86.2 (3.0)</td>
<td>86.1 (2.5)</td>
<td>87.0 (1.9)</td>
<td>87.4 (2.0)</td>
</tr>
<tr>
<td>Thigh intramuscular fat (HU)</td>
<td>8.4(7.2)</td>
<td>8.0(6.2)</td>
<td>10.8(8.0)</td>
<td>10.6(7.8)</td>
</tr>
<tr>
<td>Thigh subcutaneous fat (HU)</td>
<td>60.8(32.3)</td>
<td>63.7(34.3)</td>
<td>68.2(26.9)</td>
<td>68.1(27.0)</td>
</tr>
<tr>
<td>Total thigh fat (HU)</td>
<td>76.5(42.3)</td>
<td>79.6(44.4)</td>
<td>81.4(32.3)</td>
<td>81.3(32.1)</td>
</tr>
<tr>
<td>Energy Intake (kcal/kg/d)</td>
<td>34.26 (7.01)</td>
<td>34.70 (6.27)</td>
<td>31.00 (7.86)</td>
<td>32.00 (9.53)</td>
</tr>
<tr>
<td>Protein Intake (g/kg/d)</td>
<td>1.51 (0.27)</td>
<td>1.52 (0.25)</td>
<td>1.27 (0.31)</td>
<td>1.40 (0.41)</td>
</tr>
<tr>
<td>MNA score (0-30)</td>
<td>26.1 (1.7)</td>
<td>26.6 (1.5)</td>
<td>26.1 (1.9)</td>
<td>26.0 (2.5)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>33.4 (2.7)</td>
<td>33.5 (2.0)</td>
<td>34.0 (2.9)</td>
<td>34.5 (3.4)</td>
</tr>
<tr>
<td>Outcome Measure</td>
<td>Experimental Group</td>
<td>Control Group</td>
<td>Time Effect p value</td>
<td>Group x Time p value</td>
</tr>
<tr>
<td>-------------------------</td>
<td>--------------------</td>
<td>---------------</td>
<td>---------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 0</td>
<td>Week 12</td>
</tr>
<tr>
<td>Prealbumin (g/L)</td>
<td>0.37(0.10)</td>
<td>0.37(0.08)</td>
<td>0.34(0.10)</td>
<td>0.32(0.09)</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>119.6(10.3)</td>
<td>123.4(14.9)</td>
<td>123.3(14.0)</td>
<td>124.7(10.3)</td>
</tr>
<tr>
<td>Hematocrit (g/L)</td>
<td>.381(.037)</td>
<td>.381(.043)</td>
<td>.388(.037)</td>
<td>.389(.033)</td>
</tr>
<tr>
<td>Phosphate (g/L)</td>
<td>1.69(0.52)</td>
<td>1.74(0.57)</td>
<td>1.67(0.32)</td>
<td>1.61(0.33)</td>
</tr>
<tr>
<td>Potassium (g/L)</td>
<td>4.9(0.8)</td>
<td>4.7(0.7)</td>
<td>4.6(0.4)</td>
<td>4.9(0.6)</td>
</tr>
<tr>
<td>LogCRP$^f$</td>
<td>0.70(0.65)</td>
<td>0.63(0.53)</td>
<td>0.61(0.57)</td>
<td>0.92(0.59)</td>
</tr>
<tr>
<td>Creatinine (g/L)</td>
<td>945.4(157.5)</td>
<td>958.5(177.1)</td>
<td>891.3(169.5)</td>
<td>909.2(149.0)</td>
</tr>
<tr>
<td>Mean Cell Volume (g/L)</td>
<td>96.1(6.1)</td>
<td>95.2(6.3)</td>
<td>88.9(10.4)</td>
<td>88.2(10.4)</td>
</tr>
<tr>
<td>White Blood Cell Count (g/L)</td>
<td>6.62(1.50)</td>
<td>6.96(1.77)</td>
<td>6.89(1.73)</td>
<td>7.23(1.79)</td>
</tr>
<tr>
<td>Lymphocytes ($\times 10^9$L)</td>
<td>1.498(0.553)</td>
<td>1.605(0.657)</td>
<td>1.553(0.564)</td>
<td>1.733(0.601)</td>
</tr>
<tr>
<td>PCR (g/kg/d)</td>
<td>1.08 (0.20)</td>
<td>1.07 (0.38)</td>
<td>1.13 (0.13)</td>
<td>1.10 (0.22)</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.56(0.33)</td>
<td>1.74(0.64)</td>
<td>1.57(0.33)</td>
<td>1.77(0.50)</td>
</tr>
<tr>
<td>URR</td>
<td>72.8(6.9)</td>
<td>73.9(9.8)</td>
<td>73.4(6.3)</td>
<td>76.0(7.3)</td>
</tr>
<tr>
<td>Outcome Measure</td>
<td>Experimental Group</td>
<td>Control Group</td>
<td>Time Effect p value</td>
<td>Group x Time p value</td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>--------------------</td>
<td>---------------</td>
<td>---------------------</td>
<td>----------------------</td>
</tr>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 0</td>
<td>Week 12</td>
</tr>
<tr>
<td>Six-minute walk (m)</td>
<td>482.9(150.9)</td>
<td>500.3(163.9)</td>
<td>438.1(119.9)</td>
<td>434.3(122.2)</td>
</tr>
<tr>
<td>Total Body Strength (kg)</td>
<td>90.8(31.8)</td>
<td>111.7(38.6)</td>
<td>96.4(31.7)</td>
<td>96.3(36.2)</td>
</tr>
<tr>
<td>Total Knee Extension Strength (kg)</td>
<td>46.1(22.3)</td>
<td>57.9(27.2)</td>
<td>48.2(19.2)</td>
<td>46.5(20.1)</td>
</tr>
<tr>
<td>Total Hip Abduction Strength (kg)</td>
<td>21.9(9.2)</td>
<td>26.1(8.7)</td>
<td>21.7(7.7)</td>
<td>22.1(8.6)</td>
</tr>
<tr>
<td>Total Triceps Strength (kg)</td>
<td>25.6(9.2)</td>
<td>29.2(10.3)</td>
<td>26.5(8.9)</td>
<td>27.7(10.0)</td>
</tr>
<tr>
<td>Physical Functioning SF-36 (0-100)</td>
<td>68.9(32.0)</td>
<td>79.3(25.7)</td>
<td>69.7(20.9)</td>
<td>70.0(23.8)</td>
</tr>
<tr>
<td>Role Physical SF-36 (0-100)</td>
<td>73.2(31.7)</td>
<td>66.1(37.5)</td>
<td>73.3(35.9)</td>
<td>65.0(43.1)</td>
</tr>
<tr>
<td>Bodily Pain SF-36 (0-100)</td>
<td>74.9(27.7)</td>
<td>80.8(25.4)</td>
<td>73.9(22.4)</td>
<td>77.1(21.8)</td>
</tr>
<tr>
<td>General Health SF-36 (0-100)</td>
<td>54.6(17.0)</td>
<td>58.9(17.1)</td>
<td>60.0(10.4)</td>
<td>56.3(14.5)</td>
</tr>
<tr>
<td>Vitality SF-36 (0-100)</td>
<td>62.5(21.2)</td>
<td>63.6(19.1)</td>
<td>62.0(24.0)</td>
<td>52.0(28.5)</td>
</tr>
<tr>
<td>Social Functioning SF-36 (0-100)</td>
<td>83.9(23.2)</td>
<td>82.1(31.3)</td>
<td>81.7(29.1)</td>
<td>71.7(33.2)</td>
</tr>
<tr>
<td>Role Emotional SF-36 (0-100)</td>
<td>88.1(28.1)</td>
<td>85.7(36.3)</td>
<td>80.0(32.9)</td>
<td>86.7(30.3)</td>
</tr>
<tr>
<td>Mental Health SF-36 (0-100)</td>
<td>80.9(14.1)</td>
<td>85.7(9.5)</td>
<td>77.3(24.8)</td>
<td>79.8(27.4)</td>
</tr>
<tr>
<td>PASE (0+)</td>
<td>82.6(51.7)</td>
<td>104.4(58.6)</td>
<td>75.0(47.6)</td>
<td>79.1(39.8)</td>
</tr>
<tr>
<td>Geriatric Depression Scale (0-10)</td>
<td>6.9(5.1)</td>
<td>6.5(4.8)</td>
<td>7.1(7.2)</td>
<td>9.1(8.2)</td>
</tr>
</tbody>
</table>
Data reported according to mean values with standard deviations presented in parentheses
All p-values calculated via repeated measures analysis of variance
BMI=body mass index; MNA=Mini-Nutritional Assessment Scale, higher scores indicate better nutritional status;
PCR=protein catabolic rate, Kt/V=dialysis adequacy, URR=urea reduction ratio
SF-36=Medical Outcomes Trust Short Form-36 Health Survey, higher scores indicate better function
Geriatric Depression Scale higher scores indicate more habitual activity
Data reported according to mean values with standard deviations presented in parentheses
†Non-normal distribution, therefore data log transformed for parametric statistical analysis
Table 2: Chapter 6 – Complete summary of 24WK data

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 24</th>
<th>p*</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>69.9(15.0)</td>
<td>71.3(15.1)</td>
<td>71.6(15.1)</td>
<td>0.004</td>
<td>0.008</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.0(5.9)</td>
<td>26.5(5.8)</td>
<td>26.6(5.7)</td>
<td>0.006</td>
<td>0.01</td>
</tr>
<tr>
<td>Mid-thigh circ. (cm)</td>
<td>46.8(3.9)</td>
<td>47.8(3.7)</td>
<td>48.1(3.3)</td>
<td>0.02</td>
<td>0.03</td>
</tr>
<tr>
<td>Mid-arm circ. (cm)</td>
<td>29.7(3.7)</td>
<td>30.2(3.3)</td>
<td>30.0(3.3)</td>
<td>0.48</td>
<td>-</td>
</tr>
<tr>
<td>Mid-calf circ. (cm)</td>
<td>33.9(3.0)</td>
<td>34.2(2.8)</td>
<td>34.3(2.9)</td>
<td>0.25</td>
<td>-</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>94.2(19.5)</td>
<td>94.7(18.9)</td>
<td>95.6(18.1)</td>
<td>0.29</td>
<td>-</td>
</tr>
<tr>
<td>Thigh muscle CSA (cm²)</td>
<td>99.0(22.0)</td>
<td>99.7(20.6)</td>
<td>101.0(22.9)</td>
<td>0.26</td>
<td>-</td>
</tr>
<tr>
<td>Thigh muscle attenuation (HU)</td>
<td>85.6(2.8)</td>
<td>85.6(2.2)</td>
<td>86.0(2.2)</td>
<td>0.28</td>
<td>-</td>
</tr>
<tr>
<td>Thigh intramuscular fat (HU)</td>
<td>8.22(7.87)</td>
<td>7.85(6.73)</td>
<td>6.85(5.19)</td>
<td>0.34</td>
<td>-</td>
</tr>
<tr>
<td>Thigh subcutaneous fat (HU)</td>
<td>64.1(32.0)</td>
<td>67.3(34.0)</td>
<td>67.8(32.5)</td>
<td>0.25</td>
<td>-</td>
</tr>
<tr>
<td>Total thigh fat (HU)</td>
<td>82.0(44.1)</td>
<td>85.8(46.0)</td>
<td>85.8(44.4)</td>
<td>0.32</td>
<td>-</td>
</tr>
<tr>
<td>Energy Intake (kcal/kg/d)</td>
<td>34.3(7.0)</td>
<td>34.7(6.3)</td>
<td>34.2(6.1)</td>
<td>0.92</td>
<td>-</td>
</tr>
<tr>
<td>Protein Intake (g/kg/d)</td>
<td>1.52(0.26)</td>
<td>1.53(0.25)</td>
<td>1.54(0.22)</td>
<td>0.86</td>
<td>-</td>
</tr>
<tr>
<td>MNA score (0-30)</td>
<td>26.1(1.7)</td>
<td>26.6(1.5)</td>
<td>26.8(1.7)</td>
<td>0.42</td>
<td>-</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>33.4(2.7)</td>
<td>33.5(2.0)</td>
<td>33.9(2.9)</td>
<td>0.80</td>
<td>-</td>
</tr>
<tr>
<td>Outcome Measure</td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 24</td>
<td>p*</td>
<td>p*&lt;br&gt;Week 0 vs 12</td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------</td>
<td>------------</td>
<td>------------</td>
<td>----</td>
<td>-------------------</td>
</tr>
<tr>
<td>Prealbumin (g/L)</td>
<td>0.37(0.10)</td>
<td>0.37(0.08)</td>
<td>0.37(0.09)</td>
<td>0.92</td>
<td>-</td>
</tr>
<tr>
<td>Hemoglobin (g/L)</td>
<td>119.6(10.3)</td>
<td>123.4(14.9)</td>
<td>120.8(9.4)</td>
<td>0.46</td>
<td>-</td>
</tr>
<tr>
<td>Hematocrit (g/L)</td>
<td>0.369(0.037)</td>
<td>0.381(0.043)</td>
<td>0.372(0.033)</td>
<td>0.69</td>
<td>-</td>
</tr>
<tr>
<td>Phosphate (g/L)</td>
<td>1.69(0.52)</td>
<td>1.74(0.57)</td>
<td>1.68(0.50)</td>
<td>0.88</td>
<td>-</td>
</tr>
<tr>
<td>Potassium (g/L)</td>
<td>4.9(0.8)</td>
<td>4.7(0.7)</td>
<td>4.6(0.6)</td>
<td>0.62</td>
<td>-</td>
</tr>
<tr>
<td>LogCRP†</td>
<td>0.70(0.65)</td>
<td>0.64(0.53)</td>
<td>0.65(0.75)</td>
<td>0.87</td>
<td>-</td>
</tr>
<tr>
<td>Creatinine (g/L)</td>
<td>945.4(157.5)</td>
<td>958.5(177.1)</td>
<td>933.6(155.2)</td>
<td>0.55</td>
<td>-</td>
</tr>
<tr>
<td>Mean Cell Volume (g/L)</td>
<td>96.1(6.1)</td>
<td>95.2(6.3)</td>
<td>96.4(6.8)</td>
<td>0.18</td>
<td>-</td>
</tr>
<tr>
<td>White Blood Cell Count (g/L)</td>
<td>6.62(1.50)</td>
<td>6.96(1.77)</td>
<td>6.83(1.69)</td>
<td>0.73</td>
<td>-</td>
</tr>
<tr>
<td>Lymphocytes (x10⁹/L)</td>
<td>1.498(0.553)</td>
<td>1.605(0.657)</td>
<td>1.697(0.614)</td>
<td>0.21</td>
<td>-</td>
</tr>
<tr>
<td>PCR (g/kg/d)</td>
<td>1.08(0.20)</td>
<td>1.07(0.38)</td>
<td>1.17(0.27)</td>
<td>0.45</td>
<td>-</td>
</tr>
<tr>
<td>Kt/V</td>
<td>1.54(0.34)</td>
<td>1.73(0.66)</td>
<td>1.95(0.99)</td>
<td>0.17</td>
<td>-</td>
</tr>
<tr>
<td>Outcome Measure</td>
<td>Week 0</td>
<td>Week 12</td>
<td>Week 24</td>
<td>(p^*)</td>
<td>(p^*) Week 0 vs 12</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>---------</td>
<td>---------</td>
<td>---------</td>
<td>----------</td>
<td>----------------------</td>
</tr>
<tr>
<td>Six-minute walk (m)</td>
<td>487.3(156.0)</td>
<td>507.4(168.4)</td>
<td>521.6(171.3)</td>
<td>0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Total Body Strength (kg)</td>
<td>97.6(30.0)</td>
<td>119.4(37.5)</td>
<td>129.5(42.5)</td>
<td>&lt;0.001</td>
<td>0.005</td>
</tr>
<tr>
<td>Total Knee Extension Strength (kg)</td>
<td>49.3(22.5)</td>
<td>62.0(27.3)</td>
<td>62.7(27.3)</td>
<td>0.012</td>
<td>0.01</td>
</tr>
<tr>
<td>Total Hip Abduction Strength (kg)</td>
<td>23.3(9.0)</td>
<td>27.3(8.9)</td>
<td>29.7(10.8)</td>
<td>&lt;0.001</td>
<td>0.007</td>
</tr>
<tr>
<td>Total Triceps Strength (kg)</td>
<td>26.4(9.1)</td>
<td>30.3(10.0)</td>
<td>33.7(11.3)</td>
<td>&lt;0.001</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical Functioning SF-36 (0-100)</td>
<td>68.9(32.0)</td>
<td>79.3(25.7)</td>
<td>80.7(27.8)</td>
<td>0.003</td>
<td>0.004</td>
</tr>
<tr>
<td>Role Physical SF-36 (0-100)</td>
<td>73.2(31.7)</td>
<td>66.1(37.5)</td>
<td>70.3(35.8)</td>
<td>0.79</td>
<td>-</td>
</tr>
<tr>
<td>Bodily Pain SF-36 (0-100)</td>
<td>74.9(27.7)</td>
<td>80.8(25.4)</td>
<td>76.4(23.5)</td>
<td>0.61</td>
<td>-</td>
</tr>
<tr>
<td>General Health SF-36 (0-100)</td>
<td>54.6(17.0)</td>
<td>58.9(17.1)</td>
<td>60.0(15.8)</td>
<td>0.37</td>
<td>-</td>
</tr>
<tr>
<td>Vitality SF-36 (0-100)</td>
<td>62.5(21.2)</td>
<td>63.6(19.1)</td>
<td>64.6(25.7)</td>
<td>0.95</td>
<td>-</td>
</tr>
<tr>
<td>Social Functioning SF-36 (0-100)</td>
<td>83.9(23.2)</td>
<td>82.1(31.3)</td>
<td>93.8(14.5)</td>
<td>0.32</td>
<td>-</td>
</tr>
<tr>
<td>Role Emotional SF-36 (0-100)</td>
<td>88.1(28.1)</td>
<td>85.7(36.3)</td>
<td>95.2(17.8)</td>
<td>0.60</td>
<td>-</td>
</tr>
<tr>
<td>Mental Health SF-36 (0-100)</td>
<td>80.9(14.1)</td>
<td>85.7(9.5)</td>
<td>81.7(18.5)</td>
<td>0.60</td>
<td>-</td>
</tr>
<tr>
<td>PASE (0+)</td>
<td>82.6(51.7)</td>
<td>104.4(58.6)</td>
<td>105.1(63.5)</td>
<td>0.18</td>
<td>-</td>
</tr>
<tr>
<td>Geriatric Depression Scale (0-10)</td>
<td>6.9(5.1)</td>
<td>6.5(4.8)</td>
<td>6.2(4.7)</td>
<td>0.83</td>
<td>-</td>
</tr>
</tbody>
</table>

BMI = body mass index
Data reported according to mean values with standard deviations presented in parentheses.

*p-values correspond to change over time within the 24Wk experimental group as calculated via repeated measures analysis of variance.

Fisher least Significant Least significant difference post hoc t-test.

SF-36=Medical Outcomes Trust Short Form-36 Heath Survey, higher scores indicate better function.

PASE=Physical Activity Scale for the Elderly, higher scores indicate more habitual activity.
15 Mar 2006
The University of Sydney

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