Research Design and Methods

2.1 Summary of Research Problem and Premises

Evidence has been collected and presented in the preceding introductory literature review of this thesis that the root of past conflicting outcomes in follow-up growth research has been due to (1) statistical invalidation by using social data and reporting this social outcome as psychological outcome [Zimet et al., 1994, 1997], and (2) assessment by the use of instruments which are less time consuming to administer, but are not sensitive enough to detect psychopathology [Crowne et al., 1990].

In approach, this study will clearly differentiate between social and psychological outcome, and will clearly differentiate between the weak and more powerful psychological assessments. As well as addressing the research problems in past studies (as identified in section 1.6.1), the innovative approach of using the psychological state rather than the biological factor of height as the independent variable is introduced in this thesis. Rather than asking if short men who have been diagnosed as MDSS suffer more psychological distress than tall men, the focus is on the height profile of the psychologically distressed and the question becomes: Are psychologically distressed men significantly shorter in height than the non-psychologically distressed.

2.2 Hypotheses

2.2.1 The main research hypothesis is that adult psychological distress is associated with MDSS. 2.2.2 Null hypothesis: There is no association between psychological distress as measured by the SCL-90-R and MDSS.

2.2.2.1 The research hypothesis is that weak non-comprehensive tests are unable to elicit significant psychological distress. 2.2.2.2 Null hypothesis: The SEI test of self-esteem, being a non-comprehensive test, will not show an association with MDSS.

2.2.3.1 The research hypothesis is that psychological distress is not associated with males who are physically fit and healthy (PPH). 2.2.3.2 Null hypothesis: There is no association between psychological distress as measured by the SCL-90-R and the PPH.

2.2.4.1 The research hypothesis is that PPH men who have a better quality of life (QOL) will be taller than those having a poor QOL. 2.2.4.2 Null hypothesis: There is no association between QOL, as measured by the Chubon LSS, and the measured body height of the PPH.

2.3 Specific Aims for Research Outcome

2.3.1 Maturational Delay Short Stature Males – Outcome
(For the cohort of males who presented at the RAHC/CHW Growth Clinic as children and were diagnosed with MDSS.)

The aims of the studies in this thesis are to:
(1) Examine the adult height outcome;
(2) Determine the incidence of adult psychological distress outcome;
(3) Analyse the relationship of the determined psychological distress state (2) to adult height outcome (1);
(4) Identify the subtypes of psychological states from determined psychological distress state (2);
(5) Analyse the adult QOL outcome as related to adult height;
(6) Examine the adult height effect of administered growth-promoting treatment in childhood, and
(7) Examine the difference in outcome when using different psychological assessment tools short-form (5–10 min) single-state assessment, versus a time consuming (1–2 h) and comprehensive assessment).

2.3.2 Physically and Psychologically Healthy Males – Outcome
(For the cohort of PPH males as determined by assessments during recruitment by the Royal Australian Navy.)

The aims of the secondary studies in this thesis are to:
(1) Examine the adult height profiles;
(2) Determine the incidence of adult psychological distress outcome;

Fig. 3. Relationships between the biological factors of height and treatment and the psychological and sociological outcome studies that are reported in this thesis.
(3) Analyse the relationship of the determined psychological distress state (2) to adult height outcome (1);
(4) Identify the subtypes of psychological states from determined psychological distress state (2);
(5) Analyse the adult QOL outcome as related to adult height, and
(6) Examine the difference in outcome when using psychological assessment tools (short-form, single-state versus a time consuming and comprehensive assessment tool).

### 2.4 Summary of Studies

The relationships between the biological factors of height and treatment and the psychological and socio logical outcome studies that are reported in this thesis are illustrated in figure 3.

Chapter 3: The adult outcome descriptions of the MDSS cohort and the analysis of adult psychological outcome for the MDSS cohort are presented.

Chapter 4: The outcome descriptions of the PPH cohort and the analysis of psychological outcome for the PPH cohort are presented.

Chapter 5: The comparisons between the outcomes of the MDSS and the PPH are summarised.

Chapter 6: The results of the studies are discussed.

Chapter 7: Conclusions are made.

### 2.5 Study Design

The Robert Vines Growth Centre, which functions within the Ray Williams Institute of Endocrinology, RAHC/CHW, receives children for diagnosis and treatment of MDSS growth problems and is an active centre for growth research. Specialist management of growth problems also occurs without the child patient being in contact with the growth centre. Both sources contributed respondents to the main study of this thesis but the majority of MDSS follow-up adult respondents were recruited through the Robert Vines Growth Centre. Patients included those who had not received and those who had received growth-promoting treatment as children: growth-promoting anabolic steroids were given predominantly in two preparations: (1) oral oxandrolone, Lonavar, daily for 6–12 months, or (2) intramuscular injections of testosterone esters, Sustanon, usually 3 injections 1 month apart, but occasionally 6 injections. Other oral preparations may have been used. GH was not given to this group of boys.

FH and psychosocial outcome studies for the longitudinal understanding of the treatment management is important for clinical decision making. Decision making is onerous when direction from conclusions in the outcome growth literature have not been consistent. The studies in this thesis: (1) address the validity problems identified in the previous studies presented in section 1.6.1, which have in the past concluded that there is no detrimental psychological outcome from MDSS; (2) include a replication type study of treatment outcome, and (3) introduce an innovative approach which arises from a psychological rather than a biological perspective.

The difficulty of recruiting a PPH cohort for a secondary study was resolved by identifying a group (in this case from the Navy) who already had had psychological and medical screening performed and were deemed to be in satisfactory health. Although this group has not been treated in the traditional control group manner, the net end result is that of a control group effect and the methodology employed allows for comparison of psychological assessment type outcomes.

### 2.5.1 Sample Size Calculations

The sample size calculations for MDSS psychological distress/non-distress were made using Arcus Quickstat Biomedical software [Buchan and Fellows, undated] which gave for an unpaired t test, a mean difference of 8 cm FH, SD of 9 cm, 85% power – probability of detect-

### Table 5. SPSS sample power table

| Population | Mean | Standard Deviation | n per Group | Standard Error | 95% Lower | 95% Upper |
|------------|------|--------------------|-------------|----------------|-----------|-----------|
| Population 1 | 176  | 10                 | 50          |                |           |           |
| Population 2 | 170  | 10                 | 49          |                |           |           |
| Mean Difference | 6    | 10                 | 99          | 2              | 2         | 10        |

Computational option: variance is estimated (t test). α = 0.05, tails = 2, power = 0.84.
Table 6. Criteria for defining MDSS at presentation at the growth clinic

Height 2 SD or more below the population mean  
Bone age delay > 1.5 years when compared to chronological age  
Pubertal development delayed according to the standards of Tanner – genitalia rating  
Rating < 10th centile for age-matched standards or testes < 4 ml at 14 years  
No clinical evidence of chronic disease, dysmorphic or genetic syndrome  

Cohort: age = 21–30 years.

...ing a significant difference, \( \alpha = 0.05 \) – probability of incorrectly rejecting the null hypothesis, with 1 control per subject, an estimated sample size of 24 subjects and 24 controls required. For the PPH FH vs. MDSS FH, SPSS Sample Power [Borenstein et al., 1997] calculated power of 84%, sample power (table 5).

2.5.2 Approval for This Research

The approval for this research from the Ethics Committee of The Children’s Hospital at Westmead, number 94033, was granted on the 26th August 1994 with amendments granted 26th April 1996.

2.6 Subjects and Methods

2.6.1 Maturational Delay Short Stature – Subjects

The adults who were included in the main MDSS study had previously attended The Robert Vines Growth Centre or who had received specialist endocrinological care for growth failure. All participants had been diagnosed as having idiopathic MDSS (fig. 1, 2). As there had been an approximate lag of a decade since patient respondents were last seen, residential location was established and contact made by recruitment letter to the last-known address, electronic national phone book, address from referring general practitioner if still in practice, national electoral roll address through the State Library or through a parent or relative who had attended with the patient and who was found in the same way as the MDSS respondents. Eligible for inclusion in the study were 106 identified males; identified males with descriptive analysis of the non-attenders and the participants are illustrated in figure 4 (chapter 3). There were 49 respondents in the MDSS group agreeing to participate, with 1 respondent agreeing only to the height measurement and the non-standardised questionnaire; so the results for the standardised questionnaires in the study apply to 48 MDSS respondents. One MDSS person, who had received growth treatment as a child, among those who did not attend for outcome follow-up, phoned in his height to be included in the ‘reported heights list’ and he stated that he considered himself to be of medium height, was married with children and happy in his employment and sporting activities. After reading the information sheet, the MDSS respondents signed an agreement to participate.

The criteria for the diagnosis of MDSS when the cohort members were children and presented for investigation and possible growth-promoting treatment are listed in table 6.

2.6.2 Maturational Delay Short Stature – Method

Details recorded about the respondent’s childhood attendance from the Growth Centre database and from RAHC/CHW medical records included name, date of birth, date of first attendance, sex, treatment type, suburb, postcode and phone number. After reading the information sheet and returning the signed consent form, the adult respondent was enrolled in the study.

After enrolment, appointments were made for assessment either at the hospital or externally. External assessments were carried out for respondents living interstate and in metropolitan and country areas with the most distant intrastate being 300 km to the South and 260 km to the North of Sydney. Anthropometric measurements were taken, which included height measured by the Harpenden Stadiometer [Tanner et al., 1975; Cameron, 1986]. A non-standardised questionnaire specific to MDSS concerns was devised (section 2.7.5 and appendix B) and administered. Standardised psychological assessment was carried out by use of the comprehensive SCL-90-R symptom checklist [Derogatis, 1994], and recorded directly by the respondent onto the computer and calculated by the Microtest Q (MTAQ) (National Computer Systems Inc 1995) software (30 min to 1 h administration time), and the short single-state Test of Self Esteem [Coopersmith, 1987] taking about 5–10 min to complete. QOL was assessed using a standardised instrument [Chubon, 1990]. Intelligence was assessed using the Kaufman Brief Intelligence Test (K-BIT) [Kaufman and Kaufman, 1990].

The SCL-90-R, i.e. the measurement of psychological distress, presents results as standardized (normalised) T
scores using the norm group that is appropriate for the person being examined, and is characterised by a distribution with a mean of 50 and an SD of 10. For the purpose of this study, the MDSS group was assessed in the non-patient (non-psychiatric) norm group. The operational definition of a positive clinical case of psychological distress is defined in the test instruction and scoring procedures by the respondent having a Global Symptom Index (GSI) greater than or equal to a T score of 63 or if any two primary dimension scores are greater than or equal to a T score of 63. Group cohort results using the SCL-90-R are represented either as the proportional number of cohort positive clinical cases or as the overall level of severity of the psychological distress for the cohort.

2.6.3 Physically and Psychologically Healthy – Subjects

Data from military anthropometry are the most common source for estimating secular height and health trends [Kac, 1999] and therefore choosing a cohort from the services is an appropriate strategy. The cohort of 55 PPH males met the criteria for inclusion in the study by being between 21–31 years of age and passing the Royal Australian Navy recruitment process, including psychological assessment, which is advertised by the Defence Force Recruiting Organisation [1998] as ‘Once your application has been submitted, you will then be booked in for a day of testing – this may include a medical examination, a written psychological test, a psychological interview and another chat with a recruiting officer’. The volunteers for this study were recruited by a Navy psychologist and/or by the snowball technique, one volunteer inviting another to participate, by Navy recruits themselves. The PPH respondents signed the same agreement to participate as the MDSS with the omission of references to previous growth clinic attendance.

2.6.4 Physically and Psychologically Healthy – Method

Height of the Navy recruits group was taken as being their height known from their medical examination. The inclusion criteria for health and intelligence were taken as being satisfactory as they had passed the entrance test for the Navy. The two standardised tests, Coopersmith Self-Esteem Inventory (SEI), and the Chubon QOL, were administered as for the MDSS cohort. The SCL-90-R symptom checklist was administered with a 90-page A4 size page book with each page replicating each computer screen as seen by the MDSS group, which allowed for flexibility of location administration, where power supply was uncertain: Later computer entry was performed by the researcher.

2.7 Materials Used in the Assessment of Maturational Delay Short Stature and Physically and Psychologically Healthy Males

The materials to assess the adult outcome of the MDSS males for intelligence, QOL and mental health were selected on the capacity to cover a wide range of ages so that future longitudinal studies might be able to employ the same materials and compare with the results from this study. Also considered was the extensive referencing in previous health studies of these chosen materials.

2.7.1 Kaufman Brief Intelligence Test

The K-BIT is a brief, individually administered measure of the verbal and non-verbal intelligence of a wide range of children, adolescents, and adults, spanning the ages of 4–90 years, taking up to 30 min to administer.

2.7.2 SCL-90-R

This is a self-report measurement modality in the area of psychological distress and psychopathology. It is a means of operationally defining ‘normality’ versus ‘abnormality’ via its implementation in defining psychiatric ‘caseness’ [Derogatis and DellaPietra, 1994]. Using a scale of 0–4 inclusive for each of the 90 questions, the format for the SCL-R-90 response is: ‘Below is a list of problems people sometimes have. Please read each one carefully and blacken the circle that best describes how much that problem has distressed or bothered you during the past seven days including today’. There are nine primary symptom dimensions having clinical significance, which is the primary requisite of a symptom construct. The primary symptom dimensions, which have been clinically verified [Derogatis and Cleary, 1997a, b], and the three global indices of distress are labelled (using precis) as in table 7. The SCL-90-R GSI T score measure response of 63 or over is defined as a clinical case. The T score is characterised by a distribution with a mean of 50 and an SD of 10 points on the T score scale.

2.7.3 Chubon Life Situation Survey

The Life Situation Survey (LSS) is a 20-item Likert type rating scale designed to measure perceived life quality and it is suitable for a broad spectrum of populations [Chubon, 1990]. The rating scale items range from 1 to...
7. The test materials as provided by the author included a bibliography of its extensive use in medical research. For the purpose of the research herein, a score 5 and over was designated as good QOL and a score of less than 5 was designated as poor QOL.

2.7.4 Coopersmith Self-Esteem Inventory

The SEI is designed to measure evaluative attitudes toward the self in social, academic, family, and personal areas of experience. Administration time rarely exceeds 10 min [Coopersmith, 1987]. Interpretation of self-esteem status is given in appendix C.

2.7.5 Non-Standardised Growth Assessment

The Non-Standardised Growth Assessment (NSA) questionnaire (appendix B) devised for growth studies is able to both categorise responses and to give a measure of the depth of the concerns by the use of a Likert [Gelber and Gelber, 1995] type scale. Personal details, demographics, and anthropometric measurement preceded the questionnaire.

2.7.6 Statistical Tests

Preference was given to computer software which was not restricted by annual licences and not restricted to institutional networks thus giving freedom to use computing facilities in different locations.

(1) Arcus Quickstat Biomedical (software) and User Guide [Buchan and Fellows, undated].

(2) Minitab (software) with Student Handbook [Ryan et al., 1976]. This gives a user-friendly option of testing by a Student’s t test for a group mean against a specified mean.

(3) Microsoft Excel V8.0e (software). This is the standard software within Microsoft Office with statistical add-on tools [Microsoft Corporation, 1997].

(4) Microtest Q software [National Computer Systems Inc., 1995]. This is capable of calculating a number of different commonly used psychological assessments, including the SCL-90-R.

(5) Samplepower software, SPSS [Borenstein et al., 1997].

(6) Statistica Release 5.1 software [Statsoft, 1995].

Statistical tests in the study analyses were based on an α of 5% level of significance, 2-tailed, unless otherwise stated. Where n > 30 statistical parametric analyses are applied; where n < 30 and/or the distribution is skewed a non-parametric approach is applied. Student’s t test was also used where n for each group is > 45 as it is ‘robust in the sense that it is approximately valid for quite marked departures from normality’ [Armitage and Berry, 1987].

| Table 7. SCL-90-R primary symptoms and global indices |
|-----------------------------------------------|
| **Primary symptoms**                           |
| 1. Somatization (SOM)                         |
| reflects distress arising from perceptions of bodily dysfunction |
| 2. Obsessive-compulsive (O-C)                 |
| dimension is identified with the syndrome of the same name |
| 3. Interpersonal sensitivity (I-S)            |
| focuses on feelings of inadequacy and inferiority |
| 4. Depression (DEP)                          |
| represents a range of manifestations of clinical depression |
| 5. Anxiety (ANX)                             |
| includes nervousness, tension, trembling, panic attacks, terror |
| 6. Hostility (HOS)                           |
| reflects the negative affect state of anger |
| 7. Phobic anxiety (PHOB)                     |
| is a fear response to a specific person, place, object or situation |
| 8. Paranoid ideation (PAR) disordered        |
| thinking with fear of loss of autonomy and delusions |
| 9. Psychoticism (PSY)                        |
| withdrawn, isolated and living a schizoid lifestyle |

| **Global indices of distress**               |
| 1. Global Severity Index (GSI)               |
| is the best single indicator of the current overall level of distress |
| 2. Positive Symptom Distress Index (PSDI)    |
| functions as a measure of response style |
| 3. Positive symptom total (PST)              |
| is a simple reflection of the number of symptoms endorsed |