ENDOGENOUS SERUM TESTOSTERONE IN MAN: AGEING, THE METABOLIC SYNDROME, FUNCTIONAL DECLINE AND THE ROLE OF SUPPLEMENTATION

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CHAPTER 1.0 INTRODUCTION

SUMMARY

In men, bioavailable and free testosterone levels decline by about 1.0 and 1.2% per year, respectively after the age of forty. The definition of clinically relevant androgen deficiency in the ageing male remains uncertain. Clinical features common to both ageing and androgen deficiency include decreased muscle mass and strength and increased fatigue, increased fat mass, loss of libido, erectile dysfunction, impaired cognitive function and depression. It is however difficult to separate the effects of ageing per se` as opposed to a range of other concomitant factors including health status on plasma testosterone, as compared to the effects of a decrease in testosterone levels alone. Testosterone supplementation has been shown to be effective in improving many of the clinical features of androgen deficiency in hypogonadal older men and is safe, at least in the short term. However, it remains unclear whether there is any significant benefit in men with testosterone levels in the low-normal range. It is also unclear what the optimal method for measuring testosterone is, which measure is of greatest physiological relevance and what the age-related reference range should be.

ENDOGENOUS SERUM TESTOSTERONE IN MAN: REGULATION, PHYSIOLOGY, EFFECT OF AGEING AND DISEASE, AND THE ROLE OF SUPPLEMENTATION

This chapter outlines the biosynthetic and metabolic pathways of androgens and the negative feedback mechanism by which their secretion is regulated. The chapter then progresses to describe the problems with the currently available methods for measuring testosterone in serum. The focus of the chapter then moves toward a discussion of the current literature on associations between serum testosterone levels and ageing, physiological and psychosexual health. The controversy regarding the clinical definition of androgen deficiency in the ageing male is discussed in terms of serum testosterone concentrations and clinical features. Finally, the efficacy and safety of testosterone supplementation in ageing men is discussed.

ANDROGEN BIOSYNTHESIS AND METABOLISM

Androgens are male sex hormones, synthesised from cholesterol and responsible for the development and maintenance of male secondary sex characteristics. Testosterone, the major androgen, is produced by conversion from pregnenolone and dehydroepiandrosterone (DHEA) and secreted predominantly by the Leydig cells of the testes under the control of hypothalamic gonadotropin releasing hormone (GnRH) and pituitary luteinising hormone (LH). Testosterone can be converted to the more potent androgen dihydrotestosterone (DHT) via the 5α-reductase enzyme or to oestradiol (E2) via the aromatase enzyme. The regulation of these conversions is tissue specific [1]. The effect of ageing on the negative feedback regulation of the hypothalamic-pituitary-gonadal axis is shown in Figure 1.1.

Figure 1 : Effect of Aging on Hypothalamic-Pituitary-Gonadal Axis

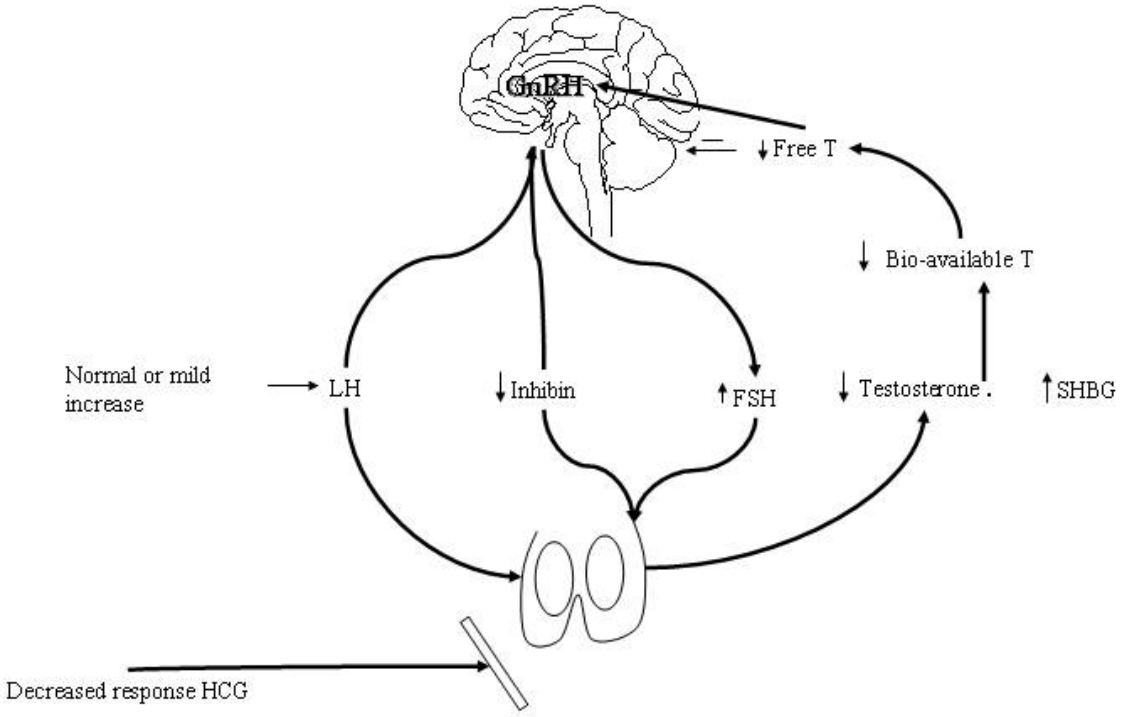

Figure 1.1 The effect of ageing on the negative-feedback regulation of the HPG axis.

(Figure is from Tariq SH, Haren MT, Kim MJ, Morley JE. Andropause: Is the Emperor Wearing Any Clothes? Book chapter, submitted January 2005). HCG = human chorionic gonadotropin, LH = luteinizing hormone, FSH = follicle stimulating hormone, GnRH = gonadotropin releasing hormone.

THE MEASUREMENT OF TESTOSTERONE IN SERUM

Testosterone circulates in the plasma largely bound to the proteins sex hormone binding globulin (SHBG) and albumin; only one to two percent of testosterone is unbound (free)[2]. SHBG is a glycoprotein that is synthesised in the liver and binds testosterone and 5α-dihydrotestosterone (5α-DHT) with high affinity and oestradiol (E_2) with lower affinity [3]. There is some debate as to which portion of plasma testosterone is biologically active [4, 5]. Free testosterone (FT) is generally considered to be the fraction available to tissues but debate continues over the bioavailability of the portion of testosterone bound to albumin. Non-SHBG bound testosterone, often called bioavailable testosterone (BT), refers to both FT and albumin-bound testosterone. A large portion of albumin bound testosterone may be available for use by some androgen responsive tissues [5, 6].

Identification of an SHBG receptor (SHBG-R) in the plasma membrane of some androgen target cells (such as prostate) indicates a role for SHBG beyond the regulation of steroid binding [7, 8]. SHBG-bound testosterone may be able to act on tissues expressing SHBG-R, via the second messenger cyclic adenosine monophosphate (cAMP) [9]. There is some evidence, however, that only unliganded SHBG binds to it's receptor and testosterone may bind to the complex subsequently [8-10]. It is possible that the SHBG/SHBG-R system acts to inhibit or amplify the effects of DHT and oestradiol in cells [11]. The presence of intracellular SHBG has been reported in some steroid target tissues [12] suggesting a complex role for SHBG in the regulation of sex steroid action.

A number of methods are currently being used to estimate the portion of plasma testosterone available to tissues although none have been empirically validated. The equilibrium dialysis method is considered the gold standard for the measurement of FT in serum [13]. Commercial FT assay kits utilising an analogue assay method are unreliable [13] and should not be used. The calculated FT method of

Vermeulen et al. (1999) closely approximates FT values obtained by equilibrium dialysis [14], but both methods may grossly underestimate the concentration of plasma testosterone available to tissues [5] as testosterone bound to albumin is readily dissociated. The free androgen index (FAI, T/SHBG) includes the albumin-bound portion of testosterone in plasma and was initially described as a measure of available circulating testosterone to evaluate hirsutism in females [15]. The FAI calculation assumes that the binding capacity of SHBG greatly exceeds the concentration of testosterone in plasma [16]. This is not the case in adult males, who have markedly lower SHBG and higher testosterone levels than pre-menopausal women. There is a strong relationship between FAI and FT values (measured by centrifugal ultrafiltration) in adult females, but in adult males the relationship is weak [16] and thus the value of the FAI in evaluating available circulating testosterone levels in men is questionable [14, 16]. BT is determined by the precipitation of plasma SHBG-bound T with 50% ammonium sulphate [17] followed by radioimmunoassay of the supernatant. BT includes the free and albumin-bound portions of testosterone in plasma, but is difficult to automate for routine clinical assessment. For this reason, it is of particular interest to develop valid and reliable simple methods for the calculation of this fraction from serum measurements of total T and SHBG. Chapter 3.0 describes the development of such an equation and the age-related reference ranges for both ammonium sulphate precipitation measured and calculated BT.

PHYSIOLOGICAL FUNCTION OF ANDROGENS IN AGEING MEN

This chapter reviews the current literature relating to serum androgen levels and physical and psychosexual function in ageing men. A literature search using PubMed was conducted using the following search strategy: “aging[mh] AND testosterone[mh] AND (male[mh] OR men[mh]) NOT (female[mh] OR women [mh] OR animal [mh] OR child[mh]) AND english[lang].” Medline was also searched via Ovid databases using a similar search strategy. Searches were last conducted on November 8 2004 at which time 408 records matched the search criteria. One hundred and seventy one

articles were deemed not relevant due to not having a major focus on testosterone levels, uncontrolled study design, non-random sampling methods or being pilot studies of which the final full-study data were available. The reference lists of full text versions of included articles were also examined for other relevant articles that were missed in the PubMed search. In total 321 articles were carefully read and reviewed in the context of the aims of this thesis. The review begins by examining the findings of association studies (cohort studies, cross-sectional, case-control studies) and then progresses to examine the effect of testosterone supplementation in ageing men from clinical trials.

The major associations examined were with ageing, body composition, muscle strength, physical function, sexual function (desire and erectile function), mood, metabolic disease risk factors, including: blood pressure, serum lipids, glycaemia, physical activity level, dietary energy and macronutrient intakes, alcohol intake and cigarette smoking. Association with chronic diseases, urogenital surgery and medication use were also examined. Cohort studies and cross-sectional or case-controlled studies that investigated these associations are shown in Tables 1.1 and 1.2 respectively.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Khaw & Barrett-Connor. Ann Epidemiol (1992)[18]	Lower endogenous androgens predict central adiposity in men	511	Men age 30 - 79 years, followed for 12 years	1. Androstenedione, testosterone and SHBG measured at baseline were inversely related to subsequent central adiposity, estimated 12 years later using the waist-hip circumference ratio.
Scopacasa et al. J Gerontol A Biol Sci Med Sci (2002)[19]	Bone density and bone-related biochemical variables in normal men: a longitudinal study	123	Healthy men aged 20 - 83 years	1. Bone loss commenced after 30 years of age and continued with ageing 2. No relationship between rate of change in fat-corrected forearm BMC and serum sex hormones
Barrett-Connor et al. Cancer Res (1990)[20]	A prospective, population-based study of androstenedione, estrogens, and prostatic cancer	1008	Men aged 40 - 79 years, followed for 14 years	1. There were 31 new cases of Pca 2. Total T, estrone, stradiol and SHBG were not associated with Pca 3. Plasma androstenedione was

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				positively asspciated with PCa
Contoreggi et al. J Androl (1990)[21]	Plasma levels of estradiol, testosterone, and DHEAS do not predict risk of coronary artery disease in men	170	46 (Cardiac group) & 124 (Control group), follwed for 9.5 years	1. SBP and cholesterol increased in cardiac group 2. No significant difference in total or free T, E2, E2/T ratio or DHEAS
De Pergola. Metabolism (1997)[22]	Lower androgenicity is associated with higher plasma levels of prothrombotic factors irrespective of age, obesity, body fat distribution, and related metabolic parameters in men	64	Apparently healthy men	1. Men with lower FT serum levels have higher fibrinogen and FVII plasma concentrations and those with lower SHBG serum levels also have higher levels of PAI-1 antigen and activity. 2. Because of the increase in several prothrombotic factors, men with central obesity, particularly those with lower androgenicity, seem to be at

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				greater risk for coronary heart disease (CHD)
Duell & Bierman. Arch Intern Med (1990)[23]	The relationship between sex hormones and high-density lipoprotein cholesterol levels in healthy adult men	55	Healthy men. Consecutively recruited from an ongoing cross-sectional study of cardiovascular disease risk factors. Men taking medications were excluded	1. No correlation with oestradiol level, testosterone level, or the ratio of oestradiol to testosterone levels was apparent.
Feldman et al. J Clin Endocrinol Metab (2002)[24]	Age trends in the level of serum testosterone and other hormones in middle-aged men: longitudinal results from the Massachusetts male aging study	1156	Population-based random-sample cohort of men aged 40-70 yr at baseline. Of 1,709 men enrolled in 1987-1989, 1,156 were followed up 7-10 yr afterward.	1. Longitudinal decline within subjects between baseline and follow-up was 1.6%/yr for total T and 2-3%/yr for bioavailable T 2. DHEA, DHEAS, cortisol, and estrone declined significantly. DHT, pituitary gonadotropins, and PRL rose longitudinally.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				3. Apparent good health (absence of chronic illness, prescription medication, obesity, or excessive drinking) added 10-15% to the level of several androgens and attenuated the cross-sectional trends in T and LH but did not otherwise affect longitudinal or cross-sectional trends.
Goemaere et al. Bone (2001)[25]	Inverse association between bone turnover rate and bone mineral density in community-dwelling men >70 years of age: no major role of sex steroid status	283	Population bases sample of ambulatory men aged 71 - 86 years	1. In univariate analyses: trend toward weak negative associations of bone turnover markers with serum FT, significant only for serum osteocalcin and serum type 1 collagen telopeptide($r = -0.16$ and -0.14, $p < 0.01$). Relationship not maintained in

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				multivariate analysis.
Goodman-Gruen & Barrett-Connor. Diabetes Care (2000)[26]	Sex differences in the association of endogenous sex hormone levels and glucose tolerance status in older men and women	775	Men	1. Men with impaired glucose tolerance had significantly lower total T levels 2. Total T was associated with fasting serum glucose levels
Haffner et al. Int J Obes Relat Metab Disord (1993)[27]	Obesity, body fat distribution and sex hormones in men	178	Men from the San Antonio Heart Study	1. WHR was significantly and inversely associated with DHEAS and free T.
Harris et al. Behav Genet (1998)[28]	The heritability of testosterone: a study of Dutch adolescent twins and their parents			1. SHBG was weakly assoc. with BMI.
Henriksen et al. Epidemiology (1996)[29]	Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand		Vietnam war veterans responsible for arial spraying of agent orange (1962 - 1971) v d.o.b, race and military occupation matched controls	1. No significant effect on serum hormones of exposure to agent orange

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Kalish et al. Urology (2000)[30]	Family history and the risk of prostate cancer	1149	Men from MMAS cohort with an average of 8.7 person-years of follow-up	1. Found an association between prostate cancer incidence and a family history of prostate cancer, independent of environmental factors (smoking, alcohol use, body mass index, physical activity, education, sexually transmitted disease history, diet, and hormone levels). 2. No association with a family history of breast cancer was evident.
Kiratli et al. Urology (2000)[31]	Progressive decrease in bone density over 10 years of androgen deprivation therapy in patients with prostate cancer	36	Prostate cancer patients who had not yet begun planned androgen deprivation therapy (ADT) & age-matched controls	1. Hip BMD was significantly lower in men on ADT 2. Hip BMD decreased with increasing years of ADT

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Kontoleon et al. Int J Cardiol (2003)[32]	Hormonal profile in patients with congestive heart failure	23	Ambulatory men (mean age 51.2 +/- 9.3 years) On standard medical therapy for heart failure due to idiopathic dilated cardiomyopathy.	1. Chronic heart failure due to idiopathic dilated cardiomyopathy is associated with a significant decrease in growth hormone, insulin-like growth factor I, and testosterone concentrations, probably due to chronic disease.
Lima et al. Int J Obes Relat Metab Disord (2000)[33]	Decreased androgen levels in massively obese men may be associated with impaired function of the gonadostat	57	37 obese men & 20 normal weight men	1. 1. Moderately obese men had significantly lower total and free T levels than normal weight men 2. Massively obese men had sig. lower total T, FT and LH levels compared to normal weight men 3. Weight loss resulted in elevated total T, FT ad LH

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Luukkaa et al. J Clin Endocrinol Metab (1998)[34]	Inverse correlation between serum testosterone and leptin in men	269	Elderly men	1. Found that the serum leptin concentration correlated inversely (r = -0.39; P < 0.001) with that of testosterone in elderly men. This inverse correlation was still present when body mass index and plasma insulin were included in the analysis.
Morley et al. Metabolism (1997)[35]	Longitudinal changes in testosterone, luteinizing hormone, and follicle-stimulating hormone in healthy older men	77	Men participating in the New Mexico Aging Process Study who had sera available in 1980 or 1981 and two or more serial samples in 1982, 1984, 1989, and/or 1994. Thirty-nine subjects had samples available from both 1980 and 1994. The age at entry	1. This study demonstrated a longitudinal decline in testosterone and an increase in LH and FSH in older men. The average rate of decrement in testosterone concentration was 110 ng/dL every decade.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			into the study ranged from 61 to 87 years.	
Ng et al. Br J Ind Med (1991)[36]	Male endocrine functions in workers with moderate exposure to lead	171	Current lead workers (N = 122), non-exposed workers (N = 49)	1. Mean current blood lead concentration was 35.2 (range 9.6-77.4) micrograms/dl in the exposed workers, and 8.3 (range 2.6-14.8) micrograms/dl in the non-exposed workers. 2. LH and FSH were both significantly higher in the exposed workers, but testosterone (T) was not significantly different between the two groups. 3. In older exposed workers, however (greater than or equal to 40 years), plasma T concentrations were

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				significantly lower, but LH and FSH concentrations were not significantly different. 4. Compared with non-exposed workers, those exposed for less than 10 years had significantly raised LH and FSH and normal T concentrations whereas those exposed for 10 or more years had significantly lower T, and normal LH and FSH concentrations.
Phillips et al. J Clin Epidemiol (1988)[37]	Serum sex hormone levels and myocardial infarction in the Honolulu Heart Program. Pitfalls in prospective studies on sex hormones	192	Serum oestradiol and testosterone levels were estimated in samples collected prospectively from males aged 52 - 78 years (mean age 60.8 +/- 6.3) who had had a myocardial	1. The only established risk factor that was significantly different was blood pressure, which was higher in the patients 2. Two major pitfalls for prospective

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			6.3) who had had a myocardial infarction (N = 96) and matched control subjects (N = 96) in the Honolulu Heart Program	studies of oestradiol in myocardial infarction, which. might have affected the validity of the results, were observed, namely, deterioration of oestradiol values with prolonged storage (8.5-12 years in this study) and intervention.
Pickles et al. Cancer (2002)[38]	Testosterone recovery following prolonged adjuvant androgen ablation for prostate carcinoma	267	Men treated with between 3 months and 3 years of adjuvant androgen ablation (AA) were followed at 6-month intervals following cessation of their androgen deprivation therapy. A comparative group of 518 men not undergoing AA were also followed.	1. Factors associated on multivariate analysis with delayed testosterone recovery included advanced age (P = 0.008), low pre-therapy testosterone (P = 0.04), and the use of 3 month LHRHa preparations as compared with CPA/DES (P = 0.002) or 1 month LHRHa preparations (P = 0.015).

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			Drugs used included low dose cyproterone/stilboestrol (CPA/DES) in combination (56%) and 1 month depot (18%) and 3 month depot (25%) leutinizing hormone releasing hormone agonist (LHRHa).	
Rosmond et al. J Intern Med (2003)[39]	A 5-year follow-up study of disease incidence in men with an abnormal hormone pattern	141	Population-based cohort study in Swedish men born in 1944. Clinical examination supplemented by medical history aimed to disclose the presence of cardiovascular disease (CVD) (myocardial infarction, angina pectoris, stroke), type 2 diabetes and hypertension were	1. Post follow-up, men with an abnormal hormone secretion pattern (n = 73) had elevated mean arterial pressure (P = 0.003), fasting insulin (P = 0.009) and insulin : glucose ratio (P = 0.005) compared with men with a normal secretion pattern (n = 68). 2. Body mass index, waist

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			and hypertension were performed at baseline and at follow-up in the year 2000. In addition, salivary cortisol levels were measured repeatedly over the day. Serum testosterone concentrations were also determined. Using the baseline data, an algorithm was constructed, which classified the secretion pattern of cortisol and testosterone from each individual as being normal or abnormal.	circumference, and waist : hip ratio were significantly elevated in both groups. 3. 5-year incidence of CVD, type 2 diabetes, and hypertension were significantly higher ($P < 0.001$) in men with an abnormal neuroendocrine secretory pattern compared to men with a normal pattern
Shaneyfelt et al. J Clin Oncol (2000)[40]	Hormonal predictors of prostate cancer: a		Meta-analysis restricted to	1. Men whose total testosterone is in the

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
	meta-analysis		studies that performed mutual adjustment for all measured serum hormones, age, and body mass index.	highest quartile are 2.34 times more likely to develop prostate cancer (95% confidence interval, 1.30 to 4.20). 2. Levels of dihydrotestosterone and oestradiol do not seem to play a role of equal importance. 3. The only study that provides multivariably adjusted SHBG data indicates an inverse relation to prostate cancer risk (odds ratio, 0.46; 95% CI 0.24 to 0.89). 4. Three studies that examined the role of serum IGF-1 have consistently demonstrated a positive and

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				significant association with prostate cancer risk that is similar in magnitude to that of testosterone.
Shores et al. Arch Gen Psychiatry (2004)[41]	Increased incidence of diagnosed depressive illness in hypogonadal older men	278	Historical cohort study using computerized medical records, followed by a manual medical record review. Veterans Affairs Puget Sound Health Care System. Men 45 years and older, without prior diagnosed depressive illness and with consistently normal or low period. testosterone levels (total testosterone level < or =200 ng/dL [< or =6.94 nmol/L]; or free	1. The 2-year incidence of diagnosed depressive illness was 21.7% in hypogonadal men vs 7.1% in others (chi2(1)=6.0, P=.01). 2. A Kaplan-Meier survival analysis showed a significant difference between hypogonadal and eugonadal men in time to diagnosed depression (log-rank test chi2(1)=6.9, P=.008). 3. Controlling for age, race, number of clinic visits, alcohol use disorders, prostate cancer, and overall medical

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			ng/dL [< or =6.94 nmol/L]; or free testosterone level < or =0.9 ng/dL [< or =0.03 nmol/L]) at baseline and during a 2-year follow-up.	comorbidity, hypogonadism remained significantly associated with depression (adjusted hazard ratio, 4.2; 95% confidence interval, 1.5-12.0) (P=.008).
Stellato et al. Diabetes Care (2000)[42]	Testosterone, sex hormone-binding globulin, and the development of type 2 diabetes in middle-aged men: prospective results from the Massachusetts male aging study	1156	Analyses were conducted on the cohort of the Massachusetts Male Aging Study, a population-based random sample of men aged 40-70. Of the 1709 men enrolled in 1987-1989 (T1), 1156 were followed up 7-10 years later (T2). Testosterone and SHBG levels at T1 were used to predict new	1. After controlling for potential confounders, diabetes at follow-up was predicted jointly and independently by lower baseline levels of free testosterone and SHBG. 2. .The odds ratio for future diabetes was 1.58 for a decrease of 1SD in free testosterone (4 ng/dl) and 1.89 for a 1SD decrease in SHBG (16 nmol/l), both significant at P < 0.02.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			cases of diabetes between T1 and T2.	
Tominaga et al. Endocr J (1996)[43]	Effects of surgery on testosterone secretion in male patients with pituitary adenomas	42	Males, N = 20 with GH secreting adenoma, N = 7 with prolactinoma and N = 15 with nonfunctioning (NF) adenoma. Aged 18 to 60 years (mean +/- SEM, 41 +/- 1.9) Gonadal functions were evaluated by measuring total serum testosterone concentrations pre- and postoperatively.	1. The serum testosterone concentration was low at less than 300 ng/dl preoperatively in 14 of 20 patients (70%) with GH producing adenoma, 6 of 7 patients (86%) with prolactinoma, and 7 of 15 patients (47%) with NF adenoma. 2. Postoperatively, the total serum testosterone concentration was normalized in 9 of 14 patients (64%) with GH producing adenoma, one of 6 patients (17%) with prolactinoma, and 5 of 7 patients (71%) with NF

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				adenoma.
Van Den Saffele et al. Clin Endocrinol (Oxf) (1999)[44]	Serum leptin levels in healthy ageing men: are decreased serum testosterone and increased adiposity in elderly men the consequence of leptin deficiency	372	Healthy, ambulatory elderly (N = 271, median age 74 years), middle-aged (N = 61, median 43 years) and young men (N = 40, median 25.5 years). Serum leptin and androgen levels were measured and adiposity was assessed by anthropometrical measurements (body mass index; BMI) and by estimation of fat mass by the bio-impedance method.	1. Multiple linear regression analysis indicated BMI, age and serum insulin, but not serum testosterone, as significant independent correlates of serum leptin. 2. Dehydroepiandrosterone sulphate (DHEAS) and leptin levels emerged as significant independent correlates in a multiple linear regression model for total serum testosterone; BMI and serum insulinbecame highly significant correlates in the same model when leptin was omitted from the independent variables.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Yarnell et al. Arterioscler Thromb (1993)[45]	Endogenous sex hormones and ischemic heart disease in men. The Caerphilly prospective study	2512	45 - 59 year old men from the general population, followed for 5 years	1. 153 new cases of IHD (fatal or non-fatal) during follow-up 2. Plasma testosterone was similar between IHD cases and non-IHD cases at follow-up
Yu et al. J Natl Cancer Inst (2000)[46]	Androgen-receptor gene CAG repeats, plasma testosterone levels, and risk of hepatitis B-related hepatocellular carcinoma	634	285 chronic hepatitis B virus (HBV) carriers with hepatocellular carcinoma (HCC) & 349 HBV carriers without HCC	1. OR for HCC was 1.72 (95% CI 1.03 - 2.89) for HBV carriers with 20 or fewer AR-CAG repeats compared to those with more than 24 repeats 2. HBV carriers in highest tertile of serum T levels had sig. increased risk of HCC (OR 2.06) compared to lowest tertile 3. HBV carriers with 20 or fewer AR-

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				CAG repeats and higher testosterone levels had a 4-fold increase in HCC risk, compared to those with 24 or more repeats and lower T levels
Zmuda et al. J Bone Miner Res (2001)[47]	A common promotor variant in the cytochrome P450c17alpha (CYP17) gene is associated with bioavailability testosterone levels and bone size in men	333	White men aged 51-84 years (mean +/- SD; 66+/-7 years) Determined whether a single base pair (bp) substitution (T-->C) in the promoter region (-34 bp) of CYP17 is associated with sex hormone levels, stature, and femoral mass and size. Femoral neck bone mineral content (BMC), cross-sectional area (CSA), and bone mineral density (BMD) were measured	1. Genotype frequencies did not deviate from Hardy-Weinberg expectations. 2. Serum bioavailable testosterone levels were 20% or 0.5 SDs higher in men with the C/C compared with the T/T genotype, whereas heterozygous men had intermediate hormone levels ($p = 0.019$). 3. Men with the C/C genotype also were nearly 3 cm taller and had 0.6 SD greater femoral neck CSA than men

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			density (BMD) were measured using dual-energy X-ray absorptiometry (DXA).	with the T/T genotype (p < or = 0.01 for both). 4. The association with CSA persisted after adjusting for age, height, and body weight 5. CYP17 genotype was not associated with femoral neck BMC, areal BMD (g/cm2), or estimated volumetric BMD (g/cm3).

Table 1.1 Cohort studies investigating androgens in ageing men.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Nomura et al. Cancer Causes Control (1998)[48]	Serum vitamin D metabolite levels and the subsequent development of prostate cancer (Hawaii, United States)	3737	A nested case-control study in a cohort of 3,737 Japanese-American men examined from 1967 to 1970 was conducted in Hawaii (United States). At the time of examination, a single blood specimen was obtained, and the serum was frozen. After a surveillance period of over 23 years, 136 tissue-confirmed incident cases of prostate cancer were identified. Their stored sera and those of 136 matched controls were measured for the following: 25-hydroxyvitamin D, 1,25-dihydroxyvitamin D, calcium, phosphorus, and parathyroid hormone.	1. There were no notable differences between cases and controls in their median serum levels of the five laboratory measurements. 2. . the findings suggest that there is a lack of a strong association between vitamin D and prostate cancer 3. . the lack of sufficient numbers of study subjects with low vitamin D levels affected the results
Tibblin et al. Diabetes (1996)[49]	The pituitary-gonadal axis and health in elderly men: a study of men born in 1913	659	Total and free testosterone, luteinizing hormone (LH), and sex-hormone binding globulin (SHBG) in a cohort of randomly	1. In multivariate analyses that included BMI, waist-to-hip ratio, total and free testosterone, and SHBG, the remaining independent predictors for the

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
	1913		globulin (SHBG) in a cohort of randomly selected men at 67 years of age.	remaining independent predictors for the development of diabetes were low total testosterone (P = 0.015) and low SHBG (P = 0.053).
Barrett-Connor et al. J Clin Endocrinol Metab (1999)[50]	Bioavailable testosterone and depressed mood in older men: the Rancho Bernardo Study	856	Community-dwelling men, aged 50 - 89 years.	1. Bioavailable testosterone and bioavailable oestradiol decreased with age, but total testosterone, dihydrotestosterone, and total oestradiol did not. 2. BDI scores increased with age. 3. Low bioavailable testosterone levels and high BDI scores were associated with weight loss and lack of physical activity, but not with cigarette smoking or alcohol intake. 4. . By linear regression or quartile analysis the BDI score was sign. and inversely associated with BT (both Ps = 0.007), independent of age, weight

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				change, and physical activity; similar associations were seen for DHT (P = 0.048 and P = 0.09, respectively). 5. .BT levels were 17% lower for the 25 men with categorically defined depression than levels observed in all other men (P = 0.01).
Basaria et al. Clin Endocrinol (Oxf) (2002)[51]	Long-term effects of androgen deprivation therapy in prostate cancer patients	58	Men with PCa who were undergoing medical castration with GnRH agonists for at least 12 months prior to the onset of the study (ADT group, N = 20) Age-matched men with nonmetastatic PCa who were post prostatectomy and/or radiotherapy but had not yet undergone ADT (non-ADT group, N = 18)	1. 1. Men on ADT had castrate levels of serum total T (P < 0.0001), FT (P < 0.0001) and ooestradiol (P < 0.0001), which were sign. lower than in the other groups. 2. Total body (P = 0.03) and lumbar spine (P < 0.0001) BMD was sign. lower in patients on ADT compared to other groups and was associated with higher levels of urinary N-telopeptide (P = 0.02).

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			Age-matched normal healthy and ambulatory men (control group, N = 20). Cross-sectional study at a tertiary care centre to determine the effect of ADT on lean body mass (LBM), muscle strength, bone mineral density (BMD), sexual function,and quality of life (QOL) in men with PCa.	3. The ADT group had higher fat mass compared to the . other groups (P = 0.0001) and significantly reduced upper body strength (P = 0.001) when compared to non-ADT patients. 4. The ADT group had lower overall scores on Watt's Sexual Function Questionnaire comparedto other groups (P = 0.0001), in particular a decrease in desire, arousal and frequency of spontaneous early morning erections. 5. The ADT group had lower overall QOL scores, resulting in significant limitation of physical function (P = 0.001), role limitation (P = 0.02) and perception of physical health (P = 0.004).
Behre et al.	Prostate volume in testosterone-treated	200	Controlled cross-sectional study.	1. 1. Significant positive correlation of prostate volume

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
Clin Endocrinol (Oxf) (1994)[52]	and untreated hypogonadal men in comparison to age-matched normal controls		Prostate volume measured by transrectal ultrasonography, serum levels of prostate-specific antigen (PSA) and sex hormones, and uroflow parameters were determined. Newly diagnosed hypogonadal men before testosterone treatment (N = 47) Hypogonadal men with at least 6 months of effective testosterone therapy (N = 78) Normal men (N = 75)	with age in normal men and testosterone-treated hypogonadal men, whereas no significant correlation was detected in untreated hypogonadal men. 2. Prostate volume was significantly lower in untreated hypogonadal men compared to both other groups. 3. No significant difference in prostate volume was detected between testosterone-treated hypogonadal men and normal men. 4. Similar results were obtained for PSA with comparable values in the testosterone-treated hypogonadal men and normal men, and significantly lower concentrations in the untreated hypogonadal men. 5. . No differences in uroflow parameters were detected

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				between the three study groups. The following were found in women but not in men.
Bonnefoy et al. Age Ageing (1998)[53]	Physical activity and dehydroepiandrosterone sulphate, insulin-like growth factor I and testosterone in healthy active elderly people	60	Independent, community-dwelling elderly subjects (26 men and 34 women) aged 66-84 who volunteered to participate. Physical activity was evaluated by the Questionnaire d'Activite Physique Saint-Etienne and expressed by three indices: mean habitual daily energy expenditure (MHDEE), daily energy expenditure (DEE) [comprising activities with intensities corresponding to at least three metabolic equivalents (MET; 3.5 ml/kg/ min of oxygen consumption)] and sport activity.	1. DHEAS correlated with VO2max, MHDEE, DEE > 3 METs and sport activity 2. IGF-I correlated with MHDEE. 3. DHEAS was correlated with IGF-I (r=0.43; P < 0.02) and with testosterone (r=0.41; P < 0.02).

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			Cardio-respiratory fitness was expressed by VO2max.	
Ferrini & Barrett-Connor. Am J Epidemiol. (1998) [54]	Sex hormones and age: a cross-sectional study of testosterone and estradiol and their bioavailable fractions in community-dwelling men	810	Community-dwelling men aged 24 - 90 years. Analyses of age-hormone associations, adjusting for weight, BMI, alcohol ingestion, smoking, physical activity, caffeine intake, specimen storage time, and disease status, were undertaken.	1. Bioavailable testosterone and bioavailable oestradiol levels decreased significantly with age independently of covariates. 2. Total testosterone and oestradiol levels decreased with age only when analyses were controlled for confounders.
Iannuzzi-Sucich et al. J Gerontol A Biol Sci Med Sci. (2002)[55]	Prevalence of sarcopenia and predictors of skeletal muscle mass in healthy, older men and women	337	Men aged 64 - 92 years (N = 142), women aged 64 - 93 years (N = 195) Appendicular skeletal muscle mass was measured by dual x-ray absorptiometry Body mass index (BMI) was calculated and physical activity and performance	1. The prevalence of sarcopenia in our cohort was 22.6% in women and 26.8% in men. 2. . A subgroup analysis of women and men 80 years or older revealed prevalence rates of 31.0%and 52.9%, respectively.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
			were measured with the Physical Activity Scale for the Elderly, the Short Physical Performance Battery, and the Physical Performance Test. Health-related quality of life by using the SF-36 general health survey. Serum estrone, oestradiol, sex hormone-binding globulin, parathyroid hormone, and 25-hydroxy vitamin D were measured in all participants and bioavailable testosterone was measured in men. Leg press strength and leg press power were determined in men.	3. In women, skeletal muscle mass correlated significantly with BMI and levels of serum estrone, oestradiol, and 25-hydroxy vitamin D. 4. . in men, it correlated significantly with BMI, single leg stance time, leg press strength & power, SF-36 general health score, Physical Performance Test total score, and BT levels. 5. Multiple linear regression analysis showed BMI was the only predictor of appendicular skeletal muscle mass in women, accounting for 47.9% of the variance. 6. In men, BMI accounted for 50.1%, mean strength accounted for 10.3%, mean power accounted for 4.1%, and bioavailable testosterone accounted for

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				2.6% of the variance in appendicular skeletal muscle mass.
Kiel et al. Am J Med (1989)[56]	Sex hormones and lipoproteins in men	148	Men with CAD from among 191 consecutive male patients between the ages of 25 and 75 undergoing coronary angiography (N = 67). Men without angiographic evidence of CAD (N = 26). Men who were clinically free of CAD (N = 55). Sex hormone levels, total cholesterol, and HDL-C were measured.	1. There was a consistently positive correlation between total oestradiol or calculated free oestradiol and both total cholesterol and HDL-C, which persisted after adjustment for potential confounders. 2. Total cholesterol was associated with total testosterone after controlling for age, adiposity, and the presence or absence of CAD, but not with calculated free testosterone. 3. No association was noted between total testosterone or calculated free testosterone and HDL-C. 4. A significant interaction was observed between oestradiol and testosterone with respect to total

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				cholesterol.
Denti et al. J Am Geriatr Soc (2000)[57]	Aging-related decline of gonadal function in healthy men: correlation with body composition and lipoproteins	206	Healthy volunteers aged 18 - 95 years from a University based outpatient centre.	1. A significant age-related decline was found for FT and E2 concentrations, whereas SHBG levels were related positively with age. 2. No significant association was apparent between hormonal changes and the concomitant modifications of body composition and lipoproteins. 3. . Only SHBG showed a significant inverse association between FM% and the waist-to-hip ratio, independent of age. 4. . The comparison between older hypogonadal (with FT levels below the lower limit of the normality range assessed in younger subjects) and eugonadal men did not show any significant differences in body

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				composition or lipid profile.
Duell & Beirman Arch Intern Med (1990)[23]	The relationship between sex hormones and high-density lipoprotein cholesterol levels in healthy adult men	55	Healthy adult males consecutively enrolled from an ongoing x-sectional study of CVD risk factors from a lipid research clinic at University of Washington, Seattle. Men on medication were excluded.	1. Multiple linear regression analysis identified several factors that correlated highly significantly with HDL cholesterol levels, including alcohol intake; frequency of strenuous exercise; age; levels of total cholesterol, low-density lipoprotein cholesterol, and triglyceride; and carbohydrate intake 2. 80% of the heterogeneity in HDL cholesterol levels could be accounted for by these factors. 3. No correlation with oestradiol, testosterone, or the ratio of oestradiol to testosterone.
Field et al. J Clin Endocrinol Metab (1994)[58]	The relation of smoking, age, relative weight, and dietary intake to serum adrenal steroids, sex hormones, and sex hormone-binding globulin in middle-	1241	Randomly sampled middle-aged U.S. men.	1. Compared with nonsmokers and independent of relative weight (body mass index) and age, cigarette smokers had increased serum levels of DHEA, DHEAS, cortisol, androstenedione, testosterone,

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
	sex hormone-binding globulin in middle-aged men			DHEAS, cortisol, androstenedione, testosterone, DHT and SHBG 2. Androstenedione, total plasma testosterone, albumin-bound testosterone, DHT, and SHBG decreased with increasing relative weight. 3. Age was positively associated with serum SHBG and negatively associated with albumin-bound testosterone, DHEA, and DHEAS. 4. An association was found between alcohol intake and DHEA, cortisol and 3-alpha-androstanediol-glucuronide. 5. Cortisol was the only hormone that was associated with carbohydrate intake. 6. The only hormones associated with dietary lipids

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				were DHT (for vegetable fat), cortisol (for total fat), and SHBG (for animal fat). 7. In addition, SHBG was positively associated with dietary and crude fiber.
Gray et al. J Endocrinol Metab (1991)[59]	Age, disease, and changing sex hormone levels in middle-aged men: results of the Massachusetts Male Aging Study	1709	2 large groups of adult males from the Massachusetts Male Aging Study cohort (aged 39 - 70 years).Group 1, N = 415 men free of obesity, alcoholism, prescription medication, chronic illness (cancer, coronary heart disease, hypertension, medication, prostate problems and diabetes and ulcer). Group 2, N = 1294 men who reported one or more of the above.	1. Free testosterone declined by 1.2%/yr, albumin-bound testosterone by 1.0%/yr, SHBG increased by 1.2%/yr, with the net effect that total serum testosterone declined more slowly (0.4%/yr). 2. Androstane-3 alpha,17 beta-diol (androstanediol; 0.8%/yr) and androstanediol glucuronide (0.6%/yr) declined less rapidly than FT, while 5 alpha-DHT remained essentially constant between ages 39-70 yr. 3. Androstenedione declined at 1.3%/yr, a rate

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				comparable to that of FT, while DHEA (3.1%/yr) and DHEAS(2.2%/yr) declined 2-3 times more rapidly. 4. The levels of testosterone, SHBG, and several androgen metabolites followed a parallel course in groups 1 and 2, remaining consistently 10-15% lower in group 2across the age range of the study. 5. Subgroup analyses suggested that obese subjects might be responsible for much of the group difference in androgen level. 6. Serum concentrations of estrogens and cortisol did not change significantly with age or differ between groups. 7. Of the pituitary gonadotropins, FSH increased at 1.9%/yr, LH increased at 1.3%/yr, and PRL declined

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				at 0.4%/yr, with no significant difference between groups.
Baumgartner et al. Obes Res (1999)[60]	Serum leptin in elderly people: associations with sex hormones, insulin, and adipose tissue volumes	56	Non-diabetic elderly Men and Women aged 64 - 94 years	1. Leptin was significantly associated with subcutaneous and visceral fat in men and women 2. Leptin was inversely associated with serum testosterone in men independent of subcutaneous but not visceral fat 3. Leptin was significantly associated with fasting insulin in both sexes, independent of age, sex hormones, SHBG, subcutaneous and visceral fat
Kamischke et al. Eur Respir J (1998)[61]	Testosterone levels in men with chronic obstructive pulmonary disease with or without glucocorticoid therapy	36	Men with COPD (N = 16 were receiving oral glucocorticoids)	1. Seum total T was < 12 nmol/L in 15 of 36 patients 2. Serum FT was low in 25 of 36 patients (including all on glucocorticoids)

Authors/Journal/Year	Article title	N	Recruitment/Methods	Key findings
				3. Serum testosterone levels did not correlate with respiratory function
Yuan et al. Int J Cancer (1995)[62]	A cohort study of serum testosterone and hepatocellular carcinoma in Shanghai, China	18244	Middle aged men in Shanghai, China, follwed for average of 5.3 years	1. 76 incident cases of HCC were observed and 410 control subjects were drawn from the cohort 2. Relative to controls HCC cases had significantly higher serum T at time of recruitment but the difference was attributed to a higher proportion of HBsAg-positive individuals amoung cases

Table 1.2 Cross-sectional and case-controlled studies investigating androgens in ageing men.

THE ASSOCIATIONS BETWEEN AGEING AND THE VARIOUS MEASURES OF PLASMA TESTOSTERONE

In men, plasma testosterone has been shown to progressively decrease beginning around the age of forty in both cross-sectional [2, 54, 63-66] and longitudinal studies [35, 47, 67]. The mechanisms that may be responsible for this include age-related changes to the hypothalamic-pituitary-testicular axis, increased SHBG levels, environmental factors, medication and chronic illness [65]. Plasma LH levels do not increase except in the very old [68], suggesting that there are defects at both a central and testicular level. This decline may contribute to a multitude of physiological, psychosexual and cognitive changes associated with ageing in men. The goal of testosterone replacement therapy might be to prevent osteoporosis, age related frailty and falls, and to maintain optimal physical, sexual, emotional and cognitive health during the ageing process. The consequences of a decrease in testosterone levels from normal (eg 25 nmol/L) at age 20, to low-normal levels (eg 15 or 12 nmol/L) at age 50 or 60 (here termed “androgen deficiency”) and the benefits and risks of testosterone supplementation in this situation remain unclear. In Australia, androgen supplementation for men over the age of forty is provided only for those with a plasma total testosterone level of 8 nmol/l or lower, or 8-15 nmol/L in the presence of an LH level >1.5 times above the upper limit of the reference range for young men (termed “hypogonadism”). The basis for this decision is arbitrary and based on statistically derived cut-offs. There is no well-validated, objective measure of androgen action by which to gauge the effects of gradually declining testosterone levels with age. The optimum method to measure plasma testosterone is also not clear. Furthermore, the factors that influence the extent to which the age related decrease in plasma testosterone levels occurs are unknown.

A number of cross-sectional studies have reported a decline in total T with ageing [54, 58, 59, 66, 69-73]. FT [58, 59, 69, 73] and BT [2, 54, 66, 70, 72] have been shown to decline at a greater rate than total T. Leifke et al. (2000) found that in 572, non-obese healthy German men, aged 20-80, who were sports club members or blood donors, FT and BT decreased to a greater extent than total T (R = -0.56, -0.67 and –0.50 respectively) [74]. The decrease began as early as the third decade and was progressive

throughout life. Plasma levels [58, 59, 69, 75] and the binding capacity [73] of SHBG have been shown to increase with ageing in studies of sufficient sample size. The mechanism of this age-associated increase is unknown, but presumably relates to inhibition of feedback regulating SHBG production in the liver. This inhibition may be a result of the reduction in bioavailable testosterone or an increase in the ratio of plasma oestradiol to testosterone that occurs with ageing. In pools of plasma from males at different stages of genital development, Baker et al. (1976) reported SHBG binding capacities within the adult range and testosterone levels below the “normal range” for men. They interpreted these findings to indicate that the mechanism controlling SHBG binding capacity is sensitive to low plasma testosterone levels [73]. In 138 normal males aged 11-87 years, Maruyama et al. (1984) noted a gradual increase in SHBG levels up to the age of 85 and that average SHBG levels in the mid-eighties were approximately double those observed in the early twenties [75]. The largest of the cross-sectional studies, the Massachusetts Male Aging Study, reported declines of 1.2%, 1.0%, and 0.4% per year for FT, BT and total T respectively and an increase of 1.2% per year for SHBG in 1709 adult males (aged 39-70 years) [59].

To date, only four longitudinal studies have investigated the effect of age on plasma testosterone. Morley and co-workers (1997) [35] found that total T declined at a rate of 110 ng/dl (~3.82 nmol/L) per decade while SHBG increased, but FT and BT were not measured. Harman and co-workers (2001) measured total T and sex hormone-binding globulin (SHBG), by RIA, in stored samples from 890 men in the Baltimore Longitudinal Study on Aging [67]. These investigators demonstrated significant, independent, age-invariant, longitudinal effects of age on both total T and FAI, with an average yearly decrease of -0.124 nmol/L for total T and -0.0049 for FAI. Total T, but not FAI, also decreased with increasing body mass index. Approximately 20% of men over 60, 30% over 70 and 50% over 80 yr of age, had total T levels below the lower level of normal for young adult males (ie: were considered “hypogonadal”); even greater percentages of men fell below the 2 standard deviation cut-off when the FAI was used [67]. Zmuda and co-workers (1997) reported a rate of decline in total T of 0.2% per year

in 66 men aged 41-61 years who were former participants in the Multiple Risk Factor Intervention Trial, and therefore at high risk of coronary heart disease [47]. Feldman et al. (2002) reported a longitudinal decline of 1.6% per year in total T and 2-3% per year in BT [24].

Approximately 50% of male blood donors over the age of 60 have BT levels below the lower end of the normal range for healthy young men aged 19-29 (<3.09 nmol/L) (Wittert et al. unpublished observations), but total T was above 8 nmol/L in all of these men. Therefore, none of these men met the current Australian criteria for "hypogonadism" and androgen supplementation therapy would not be indicated outside of a controlled clinical trial. In elderly men reporting at least two symptoms on the St Louis University androgen deficiency in the ageing male questionnaire [76], 6% had a total T less than 8 nmol/L (Wittert et al. unpublished observations). Tenover (1997) reported that 20% of healthy men aged 55 years and older would be classed as 'hypogonadal' if the lower end of the normal young adult range for total T was used, whereas if BT was used the prevalence would be around 50% [77].

ASSOCIATIONS BETWEEN ANDROGEN LEVELS AND HEALTH IN AGEING MEN

Symptoms of androgen deficiency, mood, psychosexual function and quality of life

An association between decreased libido and BT levels in both healthy ageing men and men with erectile dysfunction has been reported in some but not all studies [78-81]. Hypogonadal men have been shown to be more depressed, angered, fatigued and confused than infertile, treated eugonadal or normal men [82] and positive relationships between androgen levels and mood and wellbeing have been reported [50, 83]. BT has been reported to be 17% lower in categorically defined depressives than in normal healthy men [50]. The cause and effect relationships remain to be defined.

Cognitive function - spatial ability

The relationship between total T and BT and visuospatial ability is quadratic (U-shaped) [84, 85], but it is not known why. Androgens may have a permanent organising effect on some cognitive abilities [86] because men with the idiopathic form of hypogonadism have markedly impaired spatial ability that does not improve with testosterone therapy, whereas visuospatial ability in men with acquired hypogonadism is similar to controls.

Body composition and muscle strength

Muscle mass decreases and fat mass, particularly visceral fat, increases as men age. Obesity, (particularly when visceral) is associated with low plasma testosterone and SHBG [87, 88]. Decreased testosterone levels in men are associated with increased accumulation of visceral fat [89, 90], which is reversible upon testosterone administration [90, 91]. Furthermore, an inverse relationship has been described between testosterone and SHBG at baseline and central adiposity 12 years later as estimated by waist: hip ratio [18]. In contrast, long-term testosterone administration has been shown to increase visceral adiposity in testosterone naïve patients (eg: female to male transsexuals [92]). Much of the data relating to muscle function in the elderly is confounded by wide variability of the measures used [93]. An analysis of the New Mexico Aging Process Study by Baumgartner et. al. (1999) demonstrated that in older males the best predictor of loss of muscle mass and strength was the FAI. Other predictors included age, caloric intake, physical activity, and IGF-1. Unfortunately BT and FT were not measured in this study [94].

Bone mineral density

Studies reporting associations between circulating androgen levels and bone mineral density (BMD) at various skeletal sites have yielded conflicting results. After adjusting for age and body mass index, hip BMD was positively correlated with FAI in 134 elderly men [95] and inversely correlated with SHBG in

12 men with idiopathic osteoporosis and 12 normal men [96]. Kenny et al (1998) reported an absence of relationships between BMD and BT and FT in 35 community dwelling men over the age of 75 and only a weak inverse correlation between total T and spine BMD that lost significance after adjustment for body mass index [97]. Aromatisation of androgens to oestrogens may explain, at least in part, the effects of androgens on skeletal maintenance [98]. Falahati-Nini et al. (2000) lowered testosterone levels in older men and then replaced either oestradiol or testosterone and showed that under these circumstances oestradiol inhibited osteoclast and promoted osteoblast activity, while testosterone affected only osteoblast activity [99]. In a large cross-sectional study of 437 elderly men, low oestradiol and increased SHBG were both independent predictors of low BMD at the lumbar spine and hip, and low FT was an independent predictor of low BMD at the spine but not at the hip [100]. Since osteoporotic fracture is increasingly a problem in men, as it is in women, bone mineral density should be measured in men who have been identified to have hypogonadism. In men with low bone mineral density, plasma testosterone should be measured, since replacement therapy may be of benefit.

Plasma lipids

Positive associations between HDL cholesterol and total and free testosterone [101, 102] and negative associations between HDL cholesterol and SHBG levels have been reported in some but not all studies [101, 103]. Inverse relationships between total serum triglycerides and total T have been found [104, 105]. In a cross-sectional study, Simon et al. (1997) reported that men with lower total plasma T (<10 nmol/L) had significantly higher total and LDL cholesterol and lower HDL cholesterol than men with higher total T, possibly as a result of the increase in visceral adiposity seen in men with low testosterone levels [105].

In a longitudinal analysis of 66 male, former Multiple Risk Factor Intervention Trial participants aged 41-61 years, the decline in testosterone levels at the 13 year follow-up, after controlling for obesity and

other lifestyle covariates, was associated with both increased triglycerides and decreased HDL, but not with changes in total or LDL cholesterol [47].

Apart from its effects on surrogate markers, the relationship between testosterone and cardiovascular disease is not clearly established. The incidence of coronary artery disease does not increase in female to male transsexuals receiving testosterone treatment [106].

Prostate

A prospective study in 222 men matched for age, smoking status and length of follow up showed that when SHBG, oestradiol and DHT were adjusted simultaneously, there was a strong increase in the risk of developing prostate cancer with increasing levels of testosterone [107]. In contrast, a quantitative review of eight prospective epidemiological studies revealed no differences in average total T, BT, DHT, SHBG or oestradiol concentrations between 644 men diagnosed with prostate cancer and 1048 controls [108].

THE PROBLEM OF DEFINING RELATIVE (OR PARTIAL) ANDROGEN DEFICIENCY

The definition of relative androgen deficiency in ageing men remains unresolved. The clinical relevance of reduced androgen levels in ageing men as compared to those who maintain levels within the normal range for young adult men is also unknown. Vastly different prevalence's are observed depending upon the method of testosterone measurement and the cut-off used [77]. In the absence of a well-defined and reproducible empirical measure of "androgenicity" the validity of cut-offs based on statistical differences between groups are uncertain. Men with two or more symptoms on the St Louis University androgen deficiency in the ageing male questionnaire have lower mean BT and increase SHBG levels but similar total T levels to healthy age matched blood donors [109]. Therefore the measurement of total T may not be adequate to define the partial androgen deficiency seen in some ageing men as opposed to the profoundly decreased levels seen in frank hypogonadism, as total T declines at a slower rate that FT or

BT [2, 66, 70, 72]. In clinical settings where the concentration of SHBG is altered (eg: in ageing), falsely high values for total T may underestimate the age associated decline in testosterone availability. Furthermore the cause and effect relationships between the reported symptoms and change in testosterone are unclear.

Should the definition of relative androgen deficiency be based on age specific normal ranges or on the deviation from the levels seen in young adults? The answer may ultimately depend on determining under what circumstances the optimum response to treatment occurs.

SCREENING FOR RELATIVE (OR PARTIAL) ANDROGEN DEFICIENCY

The plethora of non-specific symptoms associated with ageing and other disease processes in men makes screening for partial androgen deficiency problematic and explains the low specificity of currently available screening questionnaires. Morley and co-workers developed a ten-symptom questionnaire to screen for the presence of androgen deficiency in ageing men (ADAM) Figure 1.2. This questionnaire was validated against BT levels in 316 Canadian physicians, for the screening of androgen deficiency in men over 40 years of age [76]. A positive response to questions 1 or 7, or any combination of 3 positive responses had a sensitivity of 88% and specificity of 60% in identifying males with BT levels below 71 ng/dL (2.46 nmol/L). This cut-off was used as it represents a concentration not seen in healthy eugonadal older men. Smith and co-workers constructed a screening questionnaire based on risk factors for low testosterone from the Massachusetts Male Aging Study [110]. This was validated in 304 men aged 40-79 years presenting for routine check-up for minor medical problems. Using a questionnaire cut-off score of 5, the sensitivity and specificity of identifying men with plasma total T below 12.1 nmol/L (cut-off based on the recommendations of 53 respondents to a mail survey of The USA Endocrine Society) were 71% and 53% respectively.

Chapters 5.1 – 5.5 describe cross-sectional associations of the different measures of serum testosterone and SHBG with age, demographics, behavioural and lifestyle risk factors, chronic disease and medication use, body composition and physical function, sexual function, lower urinary tract symptoms and maximal urinanry flow rates, neuropsychological function and mood in a randomly recruited cohort of men aged 35 – 80 years.

Figure 1.2. The Saint Louis University (ADAM) Questionnaire.

A positive response is a yes answer to 1 and 7, or any three other questions.

BENEFITS AND RISKS OF ANDROGEN SUPPLEMENTATION IN AGEING MEN.

The direct comparison of data from the currently available testosterone supplementation trials is confounded by the different baseline plasma testosterone levels used as entry criteria and the variety of doses and modes of therapy studied. Randomised controlled trials of testosterone replacement in older men are shown in Table 1.3.

Of the studies cited below that stated a minimal plasma testosterone level required for enrolment [2, 3, 111-118], only five [111, 112, 114, 115, 117] stated the rational for the cut-off specified. Morley et al. (1993) and Hajjar et al. (1997) used a cut-off of BT< 70 ng/dL(2.43 nmol/L) [115] and <72 ng/dL (2.5 nmol/L) [112] respectively, because it is a value not seen in eugonadal younger males. Arver et al. (1997) enrolled only men with a total T < 8.7 nmol/L or 10.3 nmol/L if they had Klinefelters syndrome [114]. The rationale given for the use of these particular criteria was “historical”. Snyder et al. (1999) enrolled men with total T levels below 475 ng/dL (16.5 nmol/L); this value was 1 SD below the mean for normal young men [111, 117]. Other studies cited below have been performed in hypogonadal men already being treated with testosterone [52, 119-122] and one in anabolic steroid abusers and male to female transsexuals [123]. One study investigated newly diagnosed “hypogonadal” men [52] and another, older men with “borderline-low” total T and FT levels [124], but neither specified the testosterone level required for entry.

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
Clague et al. Int J Androl (1999)[93]	Difficulties in measuring the effect of testosterone replacement therapy on muscle function in older men	14	Men aged 60 and older Total T < 14 nmol/L N = 7 T.E. 200 mg i.m. every 2 weeks N = 7 placebo	12 wks	1. Total body mass, Hct and PCV increased with testosterone treatment 2. . No improvements in grip, knee flexor or extensor strength or leg extensor power
Lambert et al. JCEM (2002)[125]	Effects of testosterone replacement and/or resistance exercise on the composition of megestrol acetate stimulated weight gain in elderly men: a randomized controlled trial	30	Men (Mean age 67 +/- 5.8) All subjects received MA & were randomized to following groups: (P) Placebo (P+RT) P + resitance training (T) testosterone (100 mg/wk i.m.) (T + RT) T + resistance training	12 wks	1. Weight increase (mean 3.8 kg) did not differ between groups 2. . Thigh x-sectional area decreased in P, which was not prevented in T 3. RT prevented this decline 4. Muscle x-sectional area increased in T+RT 5. MA has anti-anabolic effect on muscle even when combined with T RT attenuated the reduction in muscle mass and had anabolic effect when combined

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					with T
Snyder et al. Am J Med (2001)[126]	Effect of transdermal testosterone treatment on serum lipid and apolipoprotein levels in men more than 65 years of age	108	Men aged 65 and older Serum T > 1SD below mean for young men Transdermal T (6mg/day) N = 54 PLB N = 54	36 mo	1. No significant difference in total & LDL-c decrease between groups 2. .HDL-c, triglycerides, apolipoproteins A-1 and B did not change 3. .Lipoprotein A levels increased similarly in both groups
Kenny et al. J Gerontol A Biol Sci Med Sci (2002)[127]	Effects of transdermal testosterone on lipids and vascular reactivity in older men with low bioavailable testosterone levels	67	Men aged 65 - 87 years BT < 4.44 nmol/L Randomised to receive Transdermal T (2-2.5 mg patches/day) PLB	12 mo	1. 23 men (34%) withdrew from the study prior to completion of protocol 2. Total cholesterol, trigycerides & LDL did not change with tretment 3. . HDL (particularly HDL-2) decreased with T

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					treatment 4. Endothelium dependent bracial artery reactivity did not change in either group
Steidle et al. JCEM (2003)[128]	AA2500 testosterone gel normalizes androgen levels in aging males with improvements in body composition and sexual function	406	Hypogonadal men Randomised to receive: 50 mg/day T gel 100 mg/day T gel T patch PLB gel	90 days	1. T gel treatments resulted in dose-dependent improvements in all pharmacokinetic parameters: Average T concentrations at day 90 were 13.8, 17.1, 11.9 & 7.3 nmol/L in 50 mg T gel, 100 mg T gel, T patch and PLB respectively 2. At day 90, 100 mg T gel resulted in significantly greater increases in lean body mass (1.7 kg) and decreases in body fat % (1.2%) compared to control treatments 3. Significant improvement in spontaneous erections,

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					sexual desire & sexual motivation occurred in the 100 mg T gel group compared to PLB
Seidman et al. J Clin Psychiatry (2001)[129]	Testosterone replacement therapy for hypogonadal men with major depressive disorder: a randomized, placebo-controlled clinical trial	32	Men with DSM-IV MDD & tota T <= 350 ng/dL Mean age 52 +/- 10 years Randomised to receive: T.E. (200 mg/wk i.m.) N = 13 PLB N = 17	6 wks	1. HAM-D scores declined similarly in both groups 2. Sexual function improved significantly in the T group
Morley et al. Clin Geriatr Med (1997)[130]	Testosterone and frailty: Testosterone replacement in older hypogonadal men: a 12-month randomized controlled trial	32	Men (mean age 66.5 +/- 6.5 yrs) BT < 60 ng/dL Randomised to receive: T.C (200 mg i.m. bi-weekly) PLB	12 mo	1. Testosterone improved bilateral grip strength and increased Hb 2. Testosterone treatment decreased serum leptin levels 3. No significant effects of testosterone on PSA levels or memory

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					4. 3 men from PLB group and 7 from the T group withdrew prior to protocol completion; 3 of the 7 withdrew because of significantly elevated Hct's
Marin et al. Int J Obes Relat Metab Disord (1992)[131]	The effects of testosterone treatment on body composition and metabolism in middle-aged obese men	23	Middle-aged, obdominally obese men Randomised to receive: Testosterone or placebo	8 mo	1. T treatment resulted in significantly reduced visceral adiposity 2. Insulin resistance improved and blood glucose, DBP and serum cholesterol decreased with T treatment 3. A small increase in prostate volume was noted in the T group but PSA levels were unchanged 4. Insulin sensitivity improved more in men with lower baseline T levels
Tenover	Effects of testosterone supplementation in	13	Healthy men aged 57 - 76 years	3 mo	1. T treatment resulted in a significant increase in lean

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
JCEM (1992)[132]	the aging male		Serum total T <= 13.9 nmol/L Randomised to receive: T.E. (100 mg/wk i.m.) PLB		body mass 2. . Urinary hydroxyproline excretion was significantly depressed in the T group 3. T treatment also resulted in a significant increase in Hct and PSA and a decline in total and LDL cholesterol
Schiavi et al. Arch Sex Behav (1997)[78]	Effect of testosterone administration on sexual behaviour and mood in men with erectile dysfunction	12	Men aged 45 - 74 with ED or low sexual desire Randomised to receive: T.E. (200 mg i.m. bi-weekly) PLB followed by 4 wk washout and 6 wks on cross- over treatment	6 wks 4 wk washout 6 wks	1. Ejaculatory frequency was statistically greater during T treatment 2. Marked but non-significant increases in sexual desire, masturbation, sexual experiences with a partner and sleep erections were observed during T treatment 3. There were no treatment effects on penile rigidity, sexual satisfaction mood or psychological symptoms

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
			wks on cross- over treatment		
Bakhshi et al. J Am Geriatr Soc (2000)[133]	Testosterone improves rehabilitation outcomes in ill older men	15	Men aged 65 - 90 years admitted to a Geriatric Evaluation Management unit for rehabilitation Randomised to receive: T.E. (100 mg/wk i.m.) PLB	variable	1. At discharge, T treated patients had improved functional independence scores and grip strength compared to baseline 2. There were no such improvements in the PLB group
Snyder et al. JCEM (1999)[111]	Effect of testosterone treatment on body composition and muscle strength in men over 65 years of age	108	Men over 65 years Randomised to receive: T patch or PLB	36 mo	1. 12 men withdrew prior to completion of the protocol 2. T treatment resulted in a significant reduction in fat mass and increase in lean mass, compared toPLB 3. The decrease in fat was principally in the arms and

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					legs and increase in lean mass was mainly in the trunk 4. There was no significant treatment effect on knee extensor strength
Snyder et al. JCEM (1999)[117]	Effect of testosterone treatment on bone mineral density in men over 65 years of age	108	Men over 65 years Randomised to receive: T patch or PLB	36 mo	1. 12 men withdrew prior to completion of the protocol 2. There was no significant treatment effect on lumbar spine BMD 3. Post-hoc linear regression showed that greates improvements in lumbar spine BMD occurred in men with the lowest baseline T levels
Ferrando et al. Am J Physiol Endocrinol Metab (2002)[134]	Testosterone administration to older men improves muscle function: molecular and physiological mechanisms	12	Men aged 60 and over Serum total T < 17 nmol/L Randomised to receive:	6 mo	1. T treatment significantly increased total and leg LBM, muscle volume and leg and arm muscle strength after 6 months, compared to PLB

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
			T.E. (N = 7) PLB (N = 5) T.E. dose (initially administered weekly, then bi-weekly) was adjusted to maintain nadir T b/w 17 - 28 nmol/L		2. LBM accretion was due to reduced muscle protien breakdown, leading to a positive protein net balance 3. T treatment increased AR protein expression at 1 month, but expression returned to baseline levels after 6 months 4. IGF-1 protein expression increased at 1 month in the T treated group and remained elevated at 6 months
Kenny et al. J Gerontol A Biol Sci Med Sci (2001)[135]	Effects of transdermal testosterone on bone and muscle in older men with low bioavailable testosterone levels	67	Men aged 65 - 87 years BT < 4.44 nmol/L Randomised to receive Transdermal T (2-2.5 mg patches/day) PLB	12 mo	1. 23 men (34%) withdrew from the study prior to completion of protocol 2. . BT levels increased from 3.2 =/- 1.2 nmol/L at baseline to 5.6 +/- 3.5 nmol/L at 12 months with T treatment, with no change in the PLB group

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
					3. Estrone levels significantly increased in the T treated group 4. .There was a significant positive effect of T on femoral neck BMD 5. No significant effects on markers of bone turnover were observed 6. Improvements in strength occurred in both groups with no significant effect of treatment 7. T treatement resulted in significant increases in LBM and decreases in fat mass No significant T effects were observed on Hb, Hct, BPH symptoms or PSA levels

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
Park et al. Aging Male (2003)[136]	Oral testosterone undecanoate (Andriol) supplement therapy improves the quality of life of men with testosterone deficiency	39	10 men with primary hypogonadism 29 men with "andropause" with sexual dysfunction as the most common problem Single blind administration of: TU (160 mg/day) (N = 33) PLB (N = 6)	3 mo	1. T treatment significantly improved sexual dysfunction and symptom scores of metabolic, cardiopulmonary, musculoskeletal and GI functions compared to PLB 2. St Louis University ADAM questionnaire scores were significantly improved after 3 months of TU treatment 3. No significant effects of testosterone on DRE or laboratory safety measures
Crawford et al. JCEM (2003)[137]	Randomized placebo-controlled trial of androgen effects on muscle and bone in men requiring long-term systemic glucocorticoid treatment	51	Men on mean prednisolone dose (12.6 +/- 2.2 mg/d) Randomized to receive: T (200 mg mixed esters i.m. bi-	12 mo	1. Both androgens resulted in increased muscle mass and strength 2. Lumbar spine BMD was significantly increased with T treatment

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
			weekly) Nandrolone decanoate (200 mg i.m bi-weekly) PLB		3. No significant changes in hip or total body BMD 4. . T treatment but not nandrolone or PLB improved quality of life
English et al. Circulation (2000)[138]	Low-dose transdermal testosterone therapy improves angina threshold in men with chronic stable angina: A randomized, double-blind, placebo-controlled study	46	Men with stable angina 2 wk, single-blind placebo run-in followed by Randomisation to either of the following: Testosterone patch (5 mg) PLB	12 wks	1. T treatment increased androgen levels 2-fold and resulted in a significant increase in time to 1 mm ST-segment depression 2. The magintude of response was greater in those with lower baseline levels of BT 3. No treatment effect was observed on PSA, Hb, lipids or coagulation profiles
Aversa et a. Clin	Androgens improve cavernous	20	Men with arteriogenic ED, normal	1 mo	1. T treatment resulted in significant increases in serum

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
Endocrinol (Oxf) (2003)[139]	vasodilation and response to sildenafil in patients with erectile dysfunction		sexual desire and total and free T in the lower quartile of then normal range and who were non-responders to sildenafil treatment (100 mg) on six consecutive attempts All subjects received sildenafil on demand and were randomised to receive: Transdermal T (5 mg/day), PLB		total and free T and increased arterial inflow to cavernous arteries 2. T treatment also resulted in significant improvement in erectile function scores on the IIEF and on a global assessment questionnaire
Gluud et al. Gastroenterology (1988)[140]	No effect of oral testosterone treatment on sexual dysfunction in alcoholic cirrhotic men	221	Alcohol men with liver cirrhosis Randomised to receive: Testosterone or placebo	Variable 1 - 48 mo	1. There was significant treatment effect on libido, erectile or ejaculatory function
Cherrier et al. Neurology	Testosterone supplementation improves	25	Healthy community-dwelling men	6 wks	1. Total T increased 130% at week 3 and 116% at wk 6

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
(2001)[141]	spatial and verbal memory in healthy older men		aged 50 - 80 years Randomised to receive: T.E. (100 mg/wk i.m.) PLB		2. E2 increased 77% at week 3 and 73% at wk 6 3. . Significant improvements in spatial memory, spatial ability and verbal memory were observed in the T group compared to PLB
O'Carroll & Bancroft Br J Psychiatry (1984)[142]	Testosterone therapy for low sexual interest and erectile dysfunction in men: a controlled study	20	Men complaining principally of loss of sexual interest (N = 10) or erectile failure (N = 10) with normal serum T levels Double-blind, cross-over randomisation to: Testosterone and placebo injection		1. Testosterone therapy improved sexual interest but not erectile function
Holmang et al. Prostate (1993)[143]	Effect of long-term oral testosterone undecanoate treatment on prostate volume and prostate-specific antigen concentration	23	Middle-aged men without urinary tract symptoms Randomised to receive:	8 mo	1. T.U. treatment increased prostate volume by 12% 2. T.U. suppressed SHBG and FSH

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
	and prostate-specific antigen concentration in eugonadal middle-aged men		receive: T.U. (160 mg/day) PLB		3. . Serum PSA did not change with T.U. treatment 4. No treatement effect on micurition habits or urine flow charts
Uyanik et al. Jpn Heart J (1997)[144]	Beneficial effects of testosterone undecanoate on the lipoprotein profiles in healthy elderly men: a placebo controlled study	37	Men aged 53 - 89 years Randomised to receive: T.U. (120 mg/day) PLB	2 mo	1. T.U. treatment reduced serum total and LDL cholesterol and E2 2. . There was no significant treatment effect on triglycerides, HDL apolipoprotein A-1 or B 3. . Total cholesterol/HDL and LDL/HDL ratios decreased significantly after T.U. treatment but not after PLB
Wu & Weng Chin Med J (Engl) (1993)[145]	Therapeutic effects of an androgenic prepartation on myocardial ischemia and	62	Elderly men with CHD Randomised to receive: T.U. (160	2.5 mo	1. 1.T.U. treatement increased serum T and decreased E2/T ratio, with no change in E2

Authors/Journal/Year	Article title	N	Recruitment/Methods	Study duration	Key findings
	cardiac function in 62 elderly male coronary heart disease patients		mg/day), PLB		2. T.U. improved angina pectoris and myocardial ischemia in ECG and Holter recordeings 3. .There was no treatment effect on Doppler echocardiography

Table 1.3 Randomised controlled trials of testosterone replacement in ageing men.

All studies included in this table are placebo-controlled and either double- or single-blinded.

The possible risks and benefits of testosterone supplementation in ageing men are shown in Figure 1.3. Testosterone supplementation in both young and older men has been shown to improve libido in placebo controlled [2, 3, 142] and uncontrolled [112, 113, 116] treatment studies. The effects of testosterone treatment on erectile function are less clear. Placebo controlled replacement studies in eugonadal men show no benefit of treatment [142, 146]. However, in uncontrolled testosterone treatment studies in men with lower plasma testosterone levels (<10.4 nmol/L [113] and <8.7 nmol/L or <10.3 nmo/L in men with Klinefelter's syndrome [116]) improvements in strength and frequency of erections have been reported. While testosterone replacement may improve erectile function in the presence of low plasma testosterone levels [147] there is no evidence of benefit for treating impotence in eugonadal men.

In healthy elderly men with low plasma testosterone levels relative to younger men, replacement therapy has been reported to increase muscle strength in non-controlled preliminary [3, 115, 116], but not in placebo controlled studies [111]. Specifically, improvements in grip strength in men with serum BT <70 ng/dl (2.43 nmol/L) [3, 115] and leg strength in men with serum total T <480 ng/dl (16.66 nmol/L) [116] have been reported after testosterone supplementation, but these trials were small and not placebo controlled. In contrast, Snyder et al. (1999) reported no improvements in leg strength in men aged 65 or over (mean serum total T 16.48 nmol/L) after 36 months of treatment using a testosterone patch as compared to men on placebo [111].

Benefits	Risks
Increase bone mineral density.	Increased haematocrit
Increase muscle mass and strength.	Fluid retention
Decrease fat mass.	Worsen sleep apnoea
Decrease cardiovascular risk.	Gynaecomastia
Improve sexual function.	Promote the development of pre-exisiting Prostate cancer.
Better mood and general being.	
Improved cognitive function.	

Figure 1.3. The potential risks and benefits of testosterone treatment in ageing men.

In ageing men with serum testosterone levels within or just below the normal young adult range, testosterone supplementation has been shown to increase lean body mass [111, 132] and decrease fat mass [111] above that of a placebo. In men with primary and secondary hypogonadism, uncontrolled studies of testosterone treatment demonstrate an increase in lean body mass [118-120], accompanied by a decrease in fat mass, in some [118, 120, 148] but not all [119] studies.

Snyder et al. (1999) showed no benefit of testosterone patch treatment over placebo on BMD of the lumbar spine, femoral neck, Ward's triangle or trochanter in men aged 65 or over with serum total T at least 1 SD below the mean for normal young men (<475 ng/dl ≅16.5 nmol/L) [117]. In this study BMD of the lumbar spine increased in both the placebo and testosterone treated groups, but the increase was not significantly different between the two groups. There was however, an inverse relationship between pre-treatment total T levels and the effect of testosterone treatment on BMD at the lumbar spine, suggesting that the lower the pre-treatment testosterone level the greater the increase in lumbar spine BMD after testosterone treatment.

Testosterone treatment has been reported to be without effects on mood in either placebo controlled [85] or uncontrolled [115] studies in elderly men. Similarly, little or no benefit on mood has been reported in younger hypogonadal men in uncontrolled [114] or placebo controlled studies [146]. However, improvements in specific mood parameters including anger, irritability, sadness, tiredness and sense of wellbeing have been reported after testosterone replacement in men aged 22-60 years with serum total T <8.7 nmol/L [121] and men aged 19-68 years with serum total T <10.4 nmol/L [113]. Whether testosterone has a similar effect on depressed mood in older men with slightly reduced testosterone levels remains to be determined. Morley et al (2000) reported the improvement in ratings of fatigue, mood and well-being, following testosterone supplementation in men with a mean age of 58 years and plasma total and bioavailable T levels of 10.93 nmol/L and 2.05 nmol/L respectively [76].

These data suggest that the benefits of testosterone in alleviating such symptoms in ageing males may be confined to those with total T and BT levels below the normal range for healthy young men.

The cognitive domains most affected by declining testosterone levels remain to be determined. Visuospatial ability may be unchanged [149] or improved [85] following testosterone supplementation. Janowsky et al. (1994) reported improved performance on the block design test in men aged 60-75 years of age treated with testosterone in comparison to placebo treated men [85].

Prostate size is dependent on both androgens and oestrogens. Although a 12% increase in prostate volume following eight months of testosterone undecanoate therapy in eugonadal older men has been reported [143], total prostate volume and PSA have been found to be normal in anabolic steroid abusers [123]. Prostate volume and PSA of treated hypogonadal men are similar to those in normal men, but significantly lower in untreated hypogonadal men [52]. PSA expression by Western blot analysis was not dependent on plasma total T concentration in ten treated hypogonadal men [122]. Plasma PSA has been reported to be unchanged in non-placebo controlled studies [3], studies with a non-treatment control group [115] and in placebo controlled studies [131, 143]. However, in a placebo-controlled cross-over study, Tenover et al. (1992) reported a 21% increase in PSA after 3 months of testosterone supplementation compared to no change after 3 months of placebo [132]. In a non-placebo controlled study comparing the effects of testosterone gel to transdermal patch, Wang et al. (2000) reported increases in serum PSA levels (that remained within the normal range) with testosterone treatment that were related to the plasma level of testosterone achieved [113]. These studies were all of relatively short duration ($\leq$12 months). The effect of longer duration testosterone replacement therapy on the prostate and PSA levels in ageing men requires further evaluation.

Dose related increases in haemoglobin and haematocrit occur with testosterone treatment [112, 115, 132]. Increases of up to 7% have been reported in haematocrit after 3 months of testosterone supplementation with a 200mg/2 week, intra-muscular dosing regimen [115]. In comparison, there was

no change in haematocrit after 24 months of low dose treatment (25-50 mg/2 week intra-muscularly) [124].

In the majority of studies, testosterone treatment leads to a decrease in total [115, 124, 131, 132] and in particular LDL cholesterol levels [124, 132] the magnitude of which is proportional to the baseline cholesterol level, but there is little, if any, effect on HDL cholesterol [115, 124, 131, 132]. Although there is a relationship between relative androgen deficiency and a number of surrogate markers of cardiovascular risk, and testosterone supplementation may favourably modify these risk factors, there is no data at the current time to suggest that there will be an overall beneficial effect on cardiovascular disease.

Chapters 6.1 – 6.3 report the effects of testosterone undecanoate supplementation in men aged 60 years and over with low-normal gonadal status in a double-blind, placebo-controlled study. Effect on body composition, muscle strength and safety parameters are reported in Chapter 6.1; effect on androgen deficiency symptoms are reported in Chapter 6.2 and the effect on visuospatial cognition, mood, wellbeing and quality of life is reported in Chapter 6.3.

From the available data it appears that supplementation with testosterone is safe and of benefit for hypogonadal elderly men as for young men, at least in the short term. The efficacy and safety of supplemental testosterone in older men with low testosterone levels relative to young eugonadal men is not as clear. At this time it can be stated that the maximum benefit from testosterone treatment is obtained in the men with the lowest testosterone levels. The efficacy and short term safety of oral testosterone undecanoate (160 mg/day) in men aged 60 years and over is reported in Chapters 6.1 – 6.3.

The precise measure of testosterone and cut-off below which testosterone treatment should be offered is unknown, and will be difficult to determine in the absence of a well-validated empirical measure of androgen action. An attempt to define appropriate cut-off's that predict the presence of androgen deficiency signs and symptoms, from the different measures of testosterone, have been made from data in a non-random, clincal sample in Chapter 3.0 and from a random population-based sample in Chapter 5.1. Moreover, Chapter 7.0 reports preliminary feasibility data for the development of an empirical bioassay of testosterone action.

The optimal dose and safety of long-term testosterone treatment also remains to be determined. At the current time, testosterone supplementation therapy in older men with reduced plasma testosterone levels relative to young eugonadal men is not indicated outside of controlled clinical trials. The baseline testosterone cut-off, defined in the inclusion criteria is currently a major problem in clinical trial protocol design and is most likely a major source of conflicting results. BT rather than total T should be used to select men for supplementation therapy. The precise cut-off below which treatment should be offered remains unclear, but 2 standard deviations below the young adult mean seems appropriate in the absence of a clear biological marker. Lastly, it is unknown which symptoms most closely relate to plasma testosterone levels, well-designed longitudinal and cross-sectional data is required to clarify this issue. Chapter 5.1 – 5.5 report such cross-sectional associations.

GENERAL HYPOTHESIS

BT will be the most physiologically relevant measure of serum testosterone as determined by stronger independent associations with markers of testosterone action such as lean body mass, abdominal fat mass, muscle strength, sexual and cognitive function and mood, than other measures of testosterone. Supplementation in older men with low-normal serum testosterone will raise BT levels and improve associated markers of androgen deficiency indicated above.

SPECIFIC HYPOTHESES

Higher levels of serum testosterone will be independently associated with greater lean body mass, lower abdominal fat mass, greater maximal handgrip strength and better physical function and these associations will be strongest for BT.

Higher levels of serum testosterone will be independently associated with higher levels of sexual desire and better erectile function and these associations will be strongest for BT.

Higher levels of serum testosterone will be independently associated with lower obstructive and irritative lower urinary tract symptoms and these associations will be strongest for BT. No measure of serum testosteone will be associated with maximal urinary flow rate.

Higher levels of serum testosterone will be independently associated with better visuospatial function, better memory and higher mood scores and these associations will be strongest for BT.

Testosterone supplementation will increase lean mass, decrease fat mass and improve muscle strength in men aged 60 and over with low-normal testosterone levels.

Testosterone supplementation will improve symptoms of androgen deficiency in men aged 60 and over with low-normal testosterone levels.

Testosterone supplementation will improve visuospatial cognition, mood, wellbeing and quality of life in men aged 60 and over with low-normal testosterone levels.

Bioactivity of plasma testosterone can be measured validly and reliably using a cell-culture based bioassay utilising a transfected androgen responsive promoter, luciferase reporter gene.

SIGNIFICANCE OF PROJECT

This project will determine, cross-sectionally, the major predictors of the different measures of serum testosterone. The cross-sectional associations of each measure of testosterone with markers of androgen deficiency such as lean body mass, abdominal fat mass, muscle strength, sexual and cognitive function and mood, will be determined in a random population-based sample. These markers of androgen deficiency will the be assessed for treatment effects in a randomised, double-blind, placebo-controlled trial of standard dose oral testosterone undecanoate in men aged 60 and over with low-normal testosterone levels. The potential for a cell-culture based assay of plasma testosterone bioactivity will be studied. This will provide high-quality cross-sectional, treatment efficacy and testosterone measurement data to improve the ability to diagnose and effectively treat ageing men with low-normal serum testosterone levels and clinical signs and symptoms indicating testosterone deficiency.

PROPOSED STUDIES

This thesis first reports the establishment of the ammonium sulphate precipitation assay for the measurement of BT in the Institute of Medical and Veterinanry Science (IMVS), Endocrine Laboratory, with age-related reference ranges and associations with clinical signs of testosterone deficiency (Chapter 3.0). Secondly, in a randomly recruited cohort of men aged 35 – 80 years, cross-sectional associations were assessed between the different measures of serum testosterone and: age, demographics, behavioural and lifestyle risk factors, chronic disease and medication use (Chapter 5.1);

body composition and physical function (Chapter 5.2); sexual function (Chapter 5.3); lower urinary tract symptoms and maximal urinary flow rates (Chapter 5.4); and neuropsychological function and mood (Chapter 5.5). In a double-blind, placebo-controlled trial, the effect of 160 mg/day of oral testosterone undecanoate was assessed on: body composition, muscle strength and safety parameters (Chapter 6.1); androgen deficiency symptoms (Chapter 6.2); and visuospatial cognition, mood, wellbeing and quality of life (Chapter 6.3). Finally, preliminary feasibility studies for the development of a cell-culture based assay of plasma testosterone bioactivity were conducted (Chapter 7.0).

CHAPTER 2.0 COMMON METHODOLOGIES

SUMMARY

This chapter details the methodologies common to the two major studies that form this thesis; The Florey Adelaide Male Ageing Study (Chapters 4.0 – 5.5) and the randomised controlled trial of testosterone supplementation in ageing men (Chapters 6.1 – 6.3).

INTRODUCTION

The methods presented in this chapter detail the measurements and techniques common to the two major studies that give rise to this thesis (The Florey Adelaide Male Ageing Study (FAMAS) and the randomised controlled trial of Andriol® in ageing males. Two methodological studies are also reported in subsequent chapters These include: (1) the establishment of a bioavailable testosterone assay and the development of an equation for the calculation of the bioavailable fraction of testosterone in plasma (Chapter 3.0) and (2) preliminary experiments toward the development of an in-vitro transactivation assay for the measurement of testosterone in plasma samples (Chapter 7.0).

ETHICAL APPROVALS AND SAFETY CONSIDERATIONS

All protocols were approved by the Royal Adelaide Hospital Research Ethics committee, and where appropriate the Royal Adelaide Hospital Investigational Drug Sub-committee (Chapters 6.1 – 6.3) and the Aboriginal Health Research Ethics Committee of South Australia (Chapters 4.0 – 5.5).

Each participant received an information sheet and signed, informed consent was obtained. The studies were completed without incident, apart from one episode of a vasovagal reaction following venesection.

All abnormal findings were communicated to the participant and their General Practitioner for follow-up investigation, unless consent was withheld.

STUDY ENVIRONMENT

The studies conducted in this work took place in the Department of Medicine and Endocrine Unit at the Royal Adelaide Hospital (RAH), the Endocrine Bone and Menopause Centre (Norwood, South Australia), the Department of Medicine and the Osteoporosis Centre at the Queen Elizabeth Hospital (TQEH), and the Outpatients Unit at the Lyell McEwin Health Service (LMHS). Laboratory assays were done at The Institute of Medical and Veterinary Science (IMVS, Adelaide, South Australia).

PHYSICAL MEASUREMENTS

BLOOD PRESSURE

Resting systolic (SBP) and diastolic (DBP) blood pressures were measured by mercury sphygmomanometer (Accoson, London, England) after 10 minutes of seated rest. Systolic pressure was recorded at the appearance of the first and diastolic pressure at the fourth Korotkov sound. Two measurements were obtained and the mean values were used in analyses.

ANTHROPOMETRY

Anthropometry was performed in accordance with the methodology outlined by Norton & Olds (1996) [150]. Height was measured using a wall-mounted stadiometer and the stretch stature method. Participants stood with the feet together and the heels, buttocks and upper back touching the wall. The head was positioned in the Frankfort plane (lower edge of the eye socket in the same horizontal plane as the notch superior to the tragus of the ear). The measurement was taken at the end of a deep inhalation, with the measurer applying gentle upward lift through the mastoid processes.

Body weight was obtained using portable electronic scales incorporating a load cell (accurate to 100g). Scales were regularly checked for accuracy by engineering services at each of the hospitals involved. Measurements were obtained in the morning, prior to breaking an overnight fast with participant's barefoot and wearing only light clothing.

Waist circumference was measured three times, taken at the level of the narrowest point (or midway) between the lower costal border and the top of the iliac crest and read in the midaxillary line. The mean of the three measurements was used in analyses.

Hip circumference was measured three times at the level of the greatest posterior protuberance of the buttocks with the tape maintained in a horizontal plane. The mean of the three measurements was used in analyses.

UROLOGICAL ASSESSMENT

The International Prostate Symptom Scale (IPSS) [151] was used to determine the degree of both obstructive and irritative lower urinary tract symptoms (LUTS). The symptom assessment consists of seven questions covering frequency, nocturia, weak urinary stream, hesitancy, intermittence, incomplete emptying and urgency (see Appendix II). Internal consistency was demonstrated by a Cronbach's alpha of 0.86, the questionnaire has excellent test-retest reliability (R = 0.92) and it is strongly discriminative of benign prostatic hyperplasia (BPH) from control subjects (ROC area 0.85) [151].

NEUROPSYCHOLOGICAL ASSESSMENT

The trail-making test is a test of visuomotor tracking and attention and discriminates between levels of dementia classified as mild, moderate or severe, based on the Halstead-Reitan neuropsycholgical battery [152]. The part B/part A ratio of performance provides an index of executive function [153]. Crowe et al. (1998) demonstrated that performance on Part A of the trail making test was uniquely

determined by visual search and motor speed and that performance on part B was determined by lowered reading level, poor skill in visual search, poor ability to maintain two simultaneous sequences and decreased attention and working memory functions [154].

Part A of the test consisted of circled numbers 1-15 on a page. Participants were first given a sample trail to ensure they understood the task. They traced a line beginning at circle 1 and ending at circle 15 in as little time as possible. If errors were made they were immediately asked to restart from the last correct move. Part B of the test consisted of numbers 1-13 and letters A-L on a page. Participants were required to draw a specific trail between these circles alternating sequentially between numbers and letters in as little time as possible.

MUSCLE FUNCTION

Bilateral handgrip peak force was measured during maximal isometric contraction using a grip dynamometer (Smedley, Chicago, Illinois, USA) and the maximal voluntary contraction protocol (ACHPER, 1987). Participants were instructed to complete either 3 (FAMAS protocol) or 15 (Andriol® protocol) repetitions on each hand. Prior to the actual test, subjects completed a minimum of three repetitions at 50% of maximum followed by three at 75% and one at maximum. The subjects were then rested for two minutes before starting the test. During the test, subjects were verbally motivated by the tester in order to maintain maximal contraction throughout the repetitions. This protocol with the same dynamometer has been shown to have excellent test-retest reliability (ICC 0.999) [155].

BODY COMPOSITION

Whole body and lumbar spine bone mineral density (BMD) and whole body and regional body fat and lean mass were measured by dual energy x-ray absorptiometry (DEXA). This was performed at TQEH in the FAMAS study using the LUNAR DPX+ pencil beam Densitometer (GE Lunar Corporation, Madison, Wisconsin USA, and software version 4.7e) and at the Endocrine Bone and Menopause

Centre (Norwood, South Australia) in the Andriol® study using the Norland XR36 Densitometer (Norland Medical Systems, Fort Atkinson, Wisconsin USA). The within-subject coefficients of variation for fat and lean body mass are 1.6% and 1.2% respectively for both densitometers [156]. A whole body DEXA is associated with exposure to minor doses of radiation (~0.18 μSv per scan).

LABORATORY ASSAYS

PLASMA TOTAL TESTOSTERONE (TOTAL T)

Total T was determined by chemiluminescent immunoassay using Elecsys (ROCHE, Indianapolis, USA). The coefficient of variation (CV) for this assay is 9.3% at a concentration of 10.7 nmol.L^{-1}.

SEX HORMONE-BINDING GLOBULIN (SHBG)

SHBG was determined in subject serum diluted to 1:21 by adding SHBG sample dilutent. DPC IMMULITE SHBG (Diagnostic Products Corporation, Los Angeles, CA), a solid-phase, two-site chemiluminescent, immunometric assay was used (CV 4.0% at 32.3 nmol.L^{-1}). The free androgen index (FAI) was calculated as Total T/SHBG.

BIOAVAILABLE TESTOSTERONE (BT)

The ammonium sulphate precipitation method for the measurement of BT was established in our lab using previously established methodology (O'Connor et al. 1973) as described in Chapter 3.0. The inter-assay CV's for the measurement of serum BT in this laboratory are 6.15% at 4.99 nmol/L and 14.17% at 0.18 nmol/L and intra-assay CVs are 3.02% at 8.13 nmol/L and 3.32% at 1.38 nmol/L.

CALCULATED BIOAVAILABLE (CBT) AND FREE TESTOSTERONE (CFT)

BT was calculated using an equation devised by us from male Red Cross blood donors between 19 and 65 years of age [109](Chapter 3.0). FT was calculated from total testosterone and SHBG measurements using the method of Vermeulen et al. (1999) [14].

FOLLICLE STIMULATING HORMONE (FSH), LUTENISING HORMONE (LH), OESTRADIOL (E_2)

FSH, LH and E2 were measured by an automated enzyme immunometric assay (CV's: 3.1% at 7.0 IU/L for FSH; 4.0% at 7.7 IU/L for LH; 14.0% at 155 pmol/L for E_2). The male reference ranges are: 0-10 IU/L for both FSH and LH and 0-200 pmol/L for E_2.

LIPID AND GLUCOSE METABOLISM

Blood was drawn into 8 mL heparinised gel tubes. Fasting plasma glucose, insulin and lipids (triglyceride, total cholesterol, HDL, LDL) were measured on autoanalysers in the Diagnostic Services laboratory (IMVS) on a 24-hour basis. Determination of serum lipids was done enzymatically using a Hitachi 911 (Boehringer, Germany). The inter-assay CV's for the measurement of serum lipids are as follows; triglyceride 3%, total cholesterol 2.3%, HDL 6.7% and LDL 3.7%. Glucose was determined using an automated chemistry analyser system (Olympus AU5400, Olympus Optical Co Ltd. Japan). The inter-assay CV's for this assay are 2.5% at 3.5 mmol/L and 3.0% at 19.6 mmol/L. Insulin was measured on an Abbott Architect, immunoassay analyser (Abbott Pk, IL). The inter-assay CV's for this assay are 5.5% at 9.5 mU/L, 4.3% at 72 mU/L and 6.5% at 135 mU/L.

GLYCLATED HAEMOGLOBIN (HBA1C)

HbA1c was measured by high-pressure liquid chromatography (HPLC) using a sperical cation exchange gel (CV 2% at 6% of total haemoglobin). The reference range is 4% - 6% of total haemoglobin.

PROSTATE SPECIFIC ANTIGEN (PSA)

Total PSA was measured by automated enzyme immunometric assay (CV 5.2% at 4.1 ng/ml). The reference ranges for total PSA are: men aged <60 years, 0-4 ng/ml; 60-70 years, 0-5 ng/ml; and >70 years, 0-6 ng/ml.

CHAPTER 3.0 THE MEASUREMENT AND CALCULATION OF BIOAVAILABLE TESTOSTERONE IN PLASMA

SUMMARY

There is no clearly defined empirical measure of testosterone action in humans. Testosterone circulates in blood either bound to SHBG with high affinity, albumin with low affinity or in free form, not bound to any plasma proteins. The physiologically important fraction of serum testosterone may include the fraction loosely bound to albumin as well as the free fraction. The ammonium sulphate precipitation assay for the measurement of BT was established in our laboratory using plasma from male Australian Red Cross blood donors aged 19 – 65 years. SHBG and total T were measured in the same plasma. Assay quality control data and inter- and intra-assay coefficients of variation and age-specific male references ranges for BT were determined. BT was demonstrated to decline with increasing age.

The BT assay however, is difficult to automate for routine use and it was therefore of interest to establish a simple method for the calculation of BT in plasma. The dissociation constant (Kd) of the testosterone-SHBG complex was calculated using the law of mass action. Subsequently, an equation was derived which permits the calculation of BT (cBT) from the measurement of TOTAL T and SHBG. The age-specific male reference ranges, based on a range of ± 2 standard deviations from the mean, for cBT were similar to those for BT.

Cross-validation of the equation was performed in an independent population of 131 men aged over 60 with two or more symptoms of androgen deficiency on the St Louis University ADAM questionnaire. In this group, cBT was strongly reflective of assayed BT values, inversely related to age and positively related to grip strength and quality of life.

INTRODUCTION

Testosterone circulates in blood predominantly bound to plasma proteins, the majority is bound with high affinity to SHBG and low affinity binding to albumin also occurs [5]. Minimal testosterone circulates bound to cortisol binding globulin and non-specifically bound to other plasma proteins. One to two percent of testosterone circulates unbound and this is referred to as the free fraction [14].

Plasma testosterone levels have been demonstrated to decrease with ageing in some, but not all men. Testosterone treatment for a low plasma total T (<8 nmol/L), in ageing men is of benefit. However, relative androgen-deficiency in ageing males is not well defined in either biochemical or clinical terms, and the benefits of treatment remain uncertain [132]. Furthermore, the prevalence of the condition depends on the method used to measure the plasma testosterone concentration as well as the defined cut-off value [13].

Plasma free (FT) and BT concentrations decrease by approximately 1.2% per year in adult men, whereas the age-related decline in total T is slower (approx 0.4% per year) [35]. Whilst the free fraction of circulating hormones is considered to be biologically active, some evidence suggests that a large portion of albumin-bound testosterone may also be available to some androgen target tissues. In rats for example, free and albumin-bound testosterone is readily transported across the blood-brain barrier (BBB) whereas SHBG-bound testosterone is not [5, 157, 158]. Therefore the measurement of tissue available testosterone (FT or BT) may be of greater clinical significance than that of total T.

There is no clearly defined empirical measure of testosterone action in humans. Associations between androgen levels and body fat, muscle strength, bone mineral density, sexual function, cognitive ability and mood in ageing men are inconsistent and vary according to the method used to measure plasma T [13]. BT has been shown to relate to mood [50], visuomotor tracking and attention [159] and libido [79].

We hypothesise that BT may be a better measure of tissue available testosterone than either total T or FT.

This study aimed to establish the routine use of the ammonium sulphate precipitation method [17] for the measurement of BT in our laboratory. The BT assay is labour intensive and cannot be automated therefore we further aimed to: (1) derive a simple equation for the calculation of BT (cBT) from measured total T and SHBG and (2) to validate cBT by relating it to grip strength and quality of life (QOL) self-ratings in men over 60, screened for the Andriol® trial.

MATERIALS AND METHODS

AMMONIUM SULPHATE PRECIPITATION PROCEDURE

This technique measures the fraction of non-SHBG bound testosterone in human plasma. It involves the overnight incubation of plasma with a tritium labelled testosterone tracer and the removal of SHBG heterodimers and the testosterone that is bound to them by way of precipitation with saturated ammonium sulphate [17].

Blood products for assay development

Whole blood was obtained from the Australian Red Cross Blood Service (ARCBS) by way of a standard request for supply of blood samples for non-clinical use. In total, 143 individual male samples and 99 individual female samples between the ages of 19 and 65 years were obtained over a six-week period. Daily batches of samples were delivered on water ice by courier to the Institute of Medical and Veterinary Science (IMVS, Adelaide, South Australia). On arrival at IMVS, plasma was obtained by centrifugation and stored at –20^{o}C.

Standard plasma

A pool of equal amounts of the male and female plasma obtained from the ARCBS was used as the reference from which test samples were compared. This pooled plasma was heated to 60^{o}C for 30 minutes to denature the SHBG so that all testosterone in the plasma was free or "bioavailable". It was then stored frozen in 1 ml aliquots at –20^{o}C or lower, and run in quadruplicate as 'standards' in all BT assays.

Quality control plasma

A pool of male and a pool of female plasma obtained from the ARCBS were used as quality control (QC) samples. They were stored frozen in 500 ul aliquots at –20^{o}C and were run in duplicate in all assays.

Testosterone tracer

The tracer used in these studies was [1,2,6,7-^{3}H] Testosterone (Amersham, Buckinghamshire, England), which has a specific activity of 97 Ci/mmol. A stock solution of 0.25ml of ^{3}H-T tracer plus 1.7ml of 100% ethanol was made and stored at –20^{o}C. On the first day of every assay, a fresh working ^{3}H-T tracer solution was made up using 20 ul of stock tracer solution to every 6 mL of 0.85% sodium chloride (NaCl).

Saturated ammonium sulphate

Saturated ammonium sulphate was made by mixing 85 g of ammonium sulphate in 100 mL of distilled water for at least 30 minutes. The solution was stored at room temperature.

Assay protocol

Assays were set up by adding 100 ul of standard plasma, in quadruplicate, 100 ul of male and female QC plasma, each in duplicate and 100 ul of test serum in duplicate, to plastic micro tubes. Fresh working ^{3}H-T solution was made as specified above and 50 ul was added to each tube, shaken and left to incubate overnight at 4 ^{o}C.

Following incubation, 150 ul of 0.85% NaCl (normal saline) was added to standard tubes and 150 ul of saturated ammonium sulphate was added to QC and test sample tubes. Tubes were then shaken and left to incubate at room temperature for 15 minutes. Tubes were then centrifuged at 15000 g (3500rpm for 20 mins) at room temp. 150 ul of resulting supernatant was removed from all tubes by careful pipetting and transferred into marked scintillation vials. 5ml of scintillation fluid was added to each vial, shaken and counted on a liquid scintillation counter for 5 mins per sample.

Counts and total T values were then entered into a formulated MS Excel spreadsheet to generate BT values. Average counts for the four standard plasma tubes, the QC's and the duplicate test sample tubes were calculated. Percent (%) BT = average test counts/average standard counts. BT (nmol/L) = %BT x total T (nmol/L)

DEVELOPMENT OF AN EQUATION FOR CALCULATING BT (CBT)

Subjects

Serum samples from men (aged 60-88 years, N = 131) with two or more symptoms on the St Louis University ADAM questionnaire [76] and male ARCBS blood donors (aged 19-65 years, N = 143) were used in this study.

Measurements

Serum was assayed for total T, SHBG as specified in Chapter 2.0 and BT as detailed previously in this chapter. The dissociation constant (Kd) of the testosterone-SHBG complex was calculated in these two groups using the law of mass action: [S][BT]/[ST] = Kd

where [S] = free SHBG = SHBG - (total T-BT)

[BT] = measured bioavailable testosterone and

[ST] = SHBG-bound testosterone = total T - BT

To establish age-related reference ranges cBT was calculated in a further 214 ARCBS male blood donor samples which had been assayed for total T and SHBG in the previous year, giving a total of 357 data points.

Of the 131 symptomatic men, 84 (aged 60-88 years) with at least 2 symptoms on the ADAM questionnaire [76] and a free androgen index (FAI, T/SHBG) less than 0.50 were enrolled in the 12-month Andriol® trial. BT, cBT and FT, handgrip strength as described in Chapter 2.0 and the 10-point VAS QoL rating as described in Chapter 6.1 were obtained at baseline and relationships between these variables were determined.

Statistical Analysis

Descriptive data are presented as mean ± SD. Reference ranges are defined as ± 2SD from the mean. Calculated BT data were logarithmically transformed to achieve normality for the calculation of references ranges. Pearson's correlation coefficient was used to determine relationships between testosterone concentrations and other measured variables. Partial correlations were used to control for multiple variables. All analyses were performed using SPSS 10.0 for Windows.

RESULTS

QUALITY CONTROL

Pooled male and pooled female sera from the ARCBS donors were used for quality control in all assays. Mean BT for the male and female QC's, determined from the first 21 assays were 4.99 ± 0.31 (range 4.38 – 5.61 nmol/L) and 0.18 ± 0.03 (0.13 – 0.23 nmol/L) respectively. Subsequent assays with QC's outside these ranges were rejected and re-run.

VARIATION AND REPRODUCIBILITY

The inter-assay coefficients of variation (mean/SD*100) determined from 21 assays were 6.15% at 4.99 nmol/L and 14.17% at 0.18 nmol/L. The intra-assay CV's determined by running a high and low concentration sample 10 times within the single assay were 3.02% at 8.13 nmol/L and 3.32% at 1.38 nmol/L.

AGE-SPECIFIC REFERENCES RANGES FOR ASSAYED BT

Australian Red Cross Blood Service donors ranged in age from 19 – 65 years, 26-31 samples per age decade were obtained. One male, aged 29 was clearly hypogonadal (Total T = 6.53 nmol/L) and removed from all analyses. Both total T and BT declined significantly with age (R = -0.23 and -0.59, respectively).

To establish age-specific reference ranges for the assay, data was stratified by age into the following groups: 19 – 29 years; 30 – 39 years; 40 – 49 years; 50 –59 years and 60 – 65 years. Total T data were normally distributed but BT data required logarithmic transformation ($\log_{10}$) to achieve normality. The age-specific normal range for BT and total T was defined as the range 2 standard deviations from the mean of the age group. Logarithmic values for BT were transformed back to standard assay values by taking the inverse logarithm ($10^{BT\log10}$) in order to give a meaningful range. Age-specific normal ranges are shown in Table 3.1.

Age group	19-29	30-39	40-49	50-59	60+
Total T (nmol/L)	8.20 - 30.60	6.40 - 28.56	4.12 - 26.52	6.91 - 25.07	8.01 - 25.09
cBT (nmol/L)	3.09 - 13.50	2.63 - 10.47	1.82 - 8.71	2.09 - 6.31	1.70 - 6.76
BT (nmol/L)*	3.09 - 13.87	2.89 - 11.62	1.71 - 11.52	1.93 - 6.63	1.57 - 6.38

Table 3.1 Age-related reference ranges for total T and cBT from 357 male Red Cross blood donors and for BT in 143 blood donors.

Reference ranges are defined as ±2SD from the mean of the age group. *Previously reported data [160].

KD OF THE TESTOSTERONE-SHBG COMPLEX

The Kd of the testosterone-SHBG complex was 10.34 ± 2.76 x 10^{-9} M and 5.88 ± 1.54 x 10^{-9} M in symptomatic men and in blood donors, respectively (P<0.0001). The distribution of Kd was skewed towards lower values in symptomatic elderly men (skewness 1.95±0.21) and normally distributed in blood donors (skewness 0.48±0.20) (Figure 3.1).

CALCULATION OF BT

Since the Kd and the total concentrations of testosterone and SHBG are known;

$$[S] + [ST] = C_S \qquad (1)$$ and

$$[T] + [ST] = C_T \qquad (2)$$

Where C_S = total SHBG and C_T = total testosterone.

Then, from (1) $[ST] = C_S - [S]$

Subtracting (1) from (3) gives:

$$[T] = [S] + C_T - C_S \qquad (3)$$

Substituting these values into the mass action equation yields

$$\frac{}{([S] + C_T - C_S)\,[S]} = Kd,$$

$$C_S - [S]$$

Which when rearranged becomes a quadratic of the form:

$$[S]^2 + [S]\,(C_T - C_S + Kd) - KdC_S = 0$$

Only the positive solution is applicable so from (3) we can now calculate BT as:

$$[T] = ½ [C_T – C_S – Kd + \sqrt{} (C_S – C_T – Kd)^2 + 4KdC_S]$$

Using the Kd of the testosterone-SHBG complex calculated here (5.88nM), the equation becomes:

$$cBT= ½ [C_T – C_S – 5.88+\sqrt{} (C_S – C_T – 5.88)^2+ 4 \times 5.88 \times C_S].$$

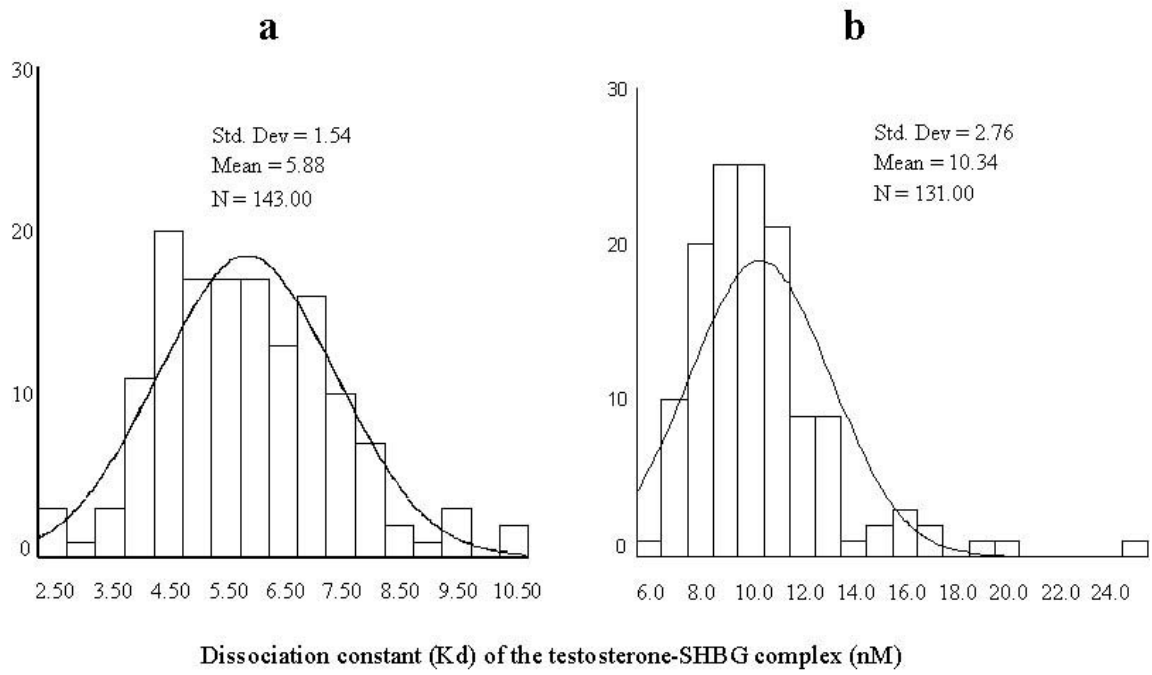

Figure 3.1 The frequency distribution of dissociation constant (Kd) values for the testosterone-SHBG complex in (a) male Red Cross blood donors aged 19-65 years and (b) men aged 60-88 with symptoms of androgen deficiency.

Kd values are normally distributed in the blood donor group (skewness 0.48, kurtosis 0.40) but are positively skewed in the symptomatic group (skewness 1.95, kurtosis 6.16).

Mean values for BT and cBT were 3.67 ± 1.11 and 3.14 ± 1.14 nmol/L respectively in symptomatic men and 4.91 ± 2.36 and 4.97 ± 2.36 nmol/L respectively, in blood donors (Table 3.2). These measures were strongly related to each other in both groups (symptomatic men R = 0.79, P < 0.001; blood donors R = 0.96, P < 0.001) (Figure 3.2). cBT was significantly lower (P < 0.0001) and age and SHBG were significantly greater (P < 0.0001) in the symptomatic group of men (N = 131) compared to the blood donors (N = 357), but there was little difference in total T.

AGE-SPECIFIC REFERENCE RANGES FOR CBT

BT was calculated using the derived equation in 357 male Red Cross blood donors (19-85 years). Mean concentrations of total T, SHBG, and cBT are shown in table 1. cBT was inversely related to age (R = -0.54, P < 0.01) and to SHBG independent of age (R = -0.16, P = 0.002). The age-specific reference ranges for cBT are shown in Table 3.1.

RELATIONSHIPS OF CBT, BT, FT AND TOTAL T WITH MUSCLE STRENGTH AND QOL

The characteristics of the cohort screened for the Andriol® trial (N = 84) are described in Chapter 6.1 (Table 6.1.1). This study investigated the efficacy of oral testosterone undecanoate (Andriol) in men aged over 60 with symptoms of androgen deficiency and low-normal testosterone levels. In this group the mean calculated FT concentration was 0.283 ± 0.007 nmol/L and was strongly related to cBT (R = 0.92, P < 0.001) (Figure 3.2). Data are corrected for age where appropriate. cBT was positively related to QoL (R = 0.22, P = 0.045) and grip strength (R = 0.23, P = 0.04), but not fatigue index of either hand, whereas BT was inversely related to grip fatigue index in both hands (R = -0.30, P = 0.008 and R = -0.23, P = 0.04, right and left respectively), but not to QoL. Both total T and FT were positively related to QoL (R = 0.22, P = 0.045 and R = 0.25, P = 0.02, respectively) but neither measure related to grip strength or fatigue index.

	Mean	SD	Mean	SD	Mean	SD
	Blood donors (N=357)		Symptomatic men (N=131)		Trial patients (N=84)	
Age	42.11	13.35	68.46	6.18	68.79	5.78
Total T (nmol/L)	16.94	5.45	16.48	5.77	15.61	5.28
cBT (nmol/L)	4.95	2.23	3.14	1.14	2.82	0.81
BT (nmol/L)	4.91*	2.36*	3.67	1.11	3.52	0.94
SHBG (nmol/L)	28.33	11.23	40.3	16.27	40.27	14.06

Table 3.2 Descriptive data from blood donor, screened symptomatic men and Andriol® trial patients.

*BT in this population was measured in a cohort of 143 men.

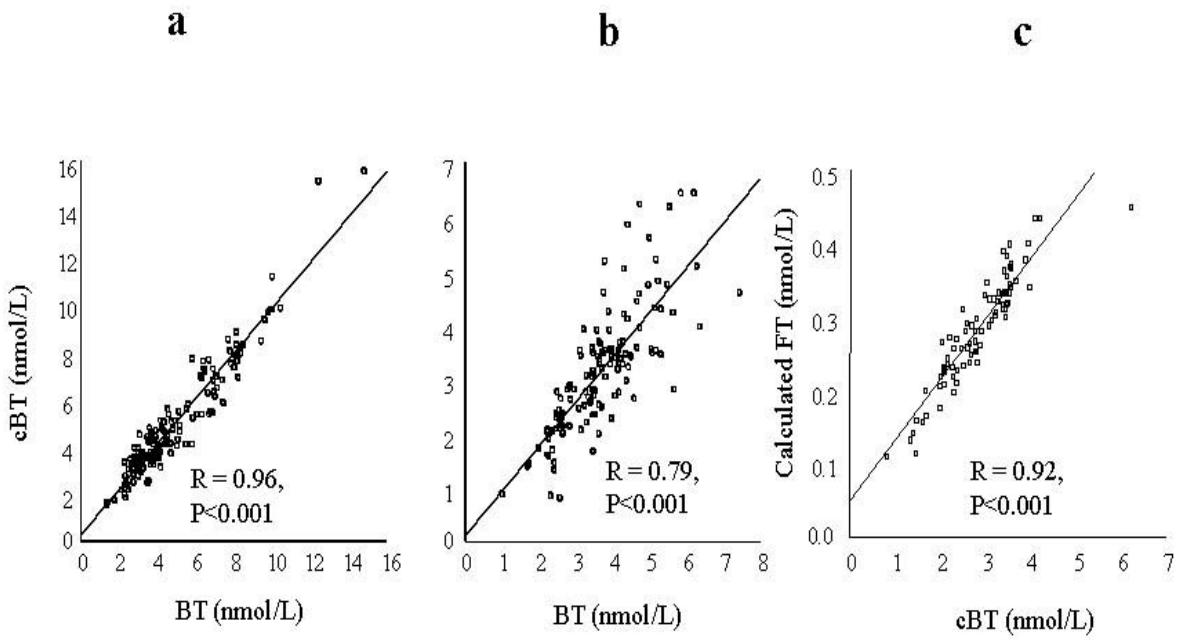

Figure 3.2 The relationship between BT and cBT in (a) male Red Cross blood donors aged 19-65 years (N = 143) and (b) men aged 60-88 years with symptoms of androgen deficiency (N=131) and (c) the relationship between cBT and calculated FT in men aged 60-88 years enrolled in a clinical trial of testosterone supplementation (N=84).

The relationships between BT and cBT are described by the equations (a) y = 0.957x + 0.2697 and (b) y = 0.817x + 0.147. (c) The relationship between cBT and calculated FT is described by the equation y = 0.0827x + 0.049.

DISCUSSION

Over the first 21 runs of the ammonium sulphate precipitation assay for BT, the assay performed well with QC's and CV's similar to those observed in the laboratory of Professor Morley, with whom we collaborated in setting up this assay. The reference ranges determined from these data were based on the assumption that values falling outside 2 standard deviations either side of the mean were abnormal. In the absence of an empirical measure of testosterone action by which to gauge an inappropriate level, this was deemed to be a reasonable approach, at least in the first instance.

As expected, plasma BT concentration declined with increasing age as has been widely demonstrated both cross-sectionally and longitudinally [24, 35, 59, 67, 70, 72].

The Kd calculated from measured BT, total T and SHBG was reasonably consistent between blood donors but greater variability was observed in the group with at least 2 ADAM symptoms. Moreover, the Kd calculated in the group with symptoms was almost twice that of the blood donors (ie: twice the concentration of total T is required to dissociate testosterone from half of the binding sites on the SHBG dimer). This was due to the fact that both groups had similar total T levels but the older group with symptoms had significantly higher SHBG and lower BT levels than the younger blood donors. The assumption when using the law of mass action, as was done here, is that the body system regulates itself to maintain a constant pool of bioavailable hormone. Accordingly, it would be expected that in an intact system, an increase in SHBG would be offset by a proportional increase in total T in order to maintain an appropriate level of BT. If this occurred, a similar Kd would have be observed between the two groups. It is of interest that the older population with significant symptoms attributed to relative testosterone deficiency, as a group, did not appear to display this feedback mechanism. This suggests a deficit in the production or secretion of testosterone.

The use of the blood donor Kd for the T-SHBG complex in the equation for cBT resulted in values that were highly correlated with measured BT values in the blood donor group. This was to be expected as the Kd was derived partly from measured BT in this group. This relationship was of similar magnitude to the relationship between calculated and assayed FT reported by Vermeulen et al. (1999) [14]. The strength of the correlation was slightly weaker in the independent group of older men with symptoms. This is likely to be due predominantly to the fact that the Kd value was not derived from the hormone concentrations and binding characteristics of this particular group. Moreover, the variation between cBT and BT may be due in part to the technical aspects of the assay and the level of intercurrent illnesses in this population. For example, it has been observed in our laboratory that highly fatty serum prevents the precipitation and centrifugation of the SHBG-T complexes resulting in falsely high BT levels, this could account for some of the scatter below the regression line in Figure 3.2 (panel b). Other serum components could potentially affect the performance of the assay.

Nevertheless, in the group enrolled in the Andriol® trial, relationships were observed between both BT and cBT levels and purported markers of relative testosterone deficiency. In the present study, cBT, total T and FT were positively related to QoL independent of age, but BT was not. Both cBT and BT, but not total T or FT, were related to aspects of grip strength and fatigue independent of age. Reported cross-sectional relationships between these variables in older men are generally weak and the effect of ageing is confounding. However, some studies have reported improvements in QoL and grip strength with testosterone supplementation in older men with low BT levels [136, 161]. The interpretation of the present cross-sectional data is limited as the population is highly selected for plasma testosterone levels in the low-normal range.

In conclusion, the ammonium sulphate precipitation assay was successfully established and has satisfactory precision and repeatability. References ranges were derived from a normal population of blood donors, based on standard deviation from the mean. The SHBG levels and the Kd for the T-SHBG

complex were significantly higher in the group of older men with symptoms of androgen deficiency than in the blood donors, suggesting a deficiency of the homeostatic mechanism to maintain adequate bioavailable testosterone levels. Overall, there was excellent agreement between calculated and measured BT values. Notwithstanding the limitations of this highly selected group, there were subtle differences in the relationships between quality of life and each estimate of testosterone and both BT and cBT but not total T or FT related to muscle strength.

CHAPTER 4.0 THE FLOREY ADELAIDE MALE AGEING STUDY (FAMAS): PROTOCOL AND CHARACTERISATION OF THE COHORT

SUMMARY

This chapter describes the protocol and methods specific to the Florey Adelaide Ageing Male Study and describes the socio-demographic and basic health characteristics of the cohort. Socio-demographics of the cohort are, where possible, compared to equivalent parameters in the wider community of the same region, age and gender using available Census 2001 data. Basic health characteristics of the cohort are compared, where possible, to those of other population based studies. There appeared to be an under-representation of single men in all but the oldest age-group and an under-representation of smokers and men with known high cholesterol and high blood pressure. Within the cohort, laboratory and clinical tests revealed a high prevalence of high cholesterol and high blood pressure in men who did not know they had the diseases, bringing the prevalence in the cohort in-line with that of negative responders. The current cohort appears to be more overweight and obese than previously reported Australian and international cohorts. These comparisons provide a contextual framework through which to view and interpret the findings presented subsequently in Chapters 5.1 – 5.5.

INTRODUCTION

Australian men of all ages have lower life expectancy and poorer health outcomes when compared to women [162-165]. The difference in health status largely reflects the prevalence of preventable factors. In 1995, the Australian Institute of Health and Welfare (AIHW) cited evidence at the National Men's Health Conference suggesting that significant health differentials; using standard markers of health status, mortality, risk factors and health service utilisation, still existed between Australian men and women [166]. Men experience higher prevalence of and mortality rates from chronic conditions such as obesity, cancer, diabetes and cardiovascular disease than women. Prostate cancer accounts for 15.3% of all cancers and 27.6% of male cancers in Australia, and benign prostatic hyperplasia (BPH) is the most commonly occurring benign, proliferative abnormality found in any internal organ. In an era when the proportion of older people in the Australian population (and most significantly, the South Australian population) is increasing, it is imperative to identify why men have poorer health outcomes and what measures can be taken to promote a healthy and active lifestyle, prevent disease, and guide the development of appropriate health services and policy. The South Australian Generational Health Review (GHR), the first review of the South Australian Health Care system since the Bright Committee Enquiry in January 1973, seeks to promote greater linkages between research, policy and practice (http://www.dh.sa.gov.au/generational-health-review).

Recently, much of the focus on ageing and men's health research has been centred on the phenomenon of the age associated decline in serum androgen levels. This physiological change has been, although not comprehensively, linked to the presence of numerous chronic disease risk factors and disease states observed in elderly men such as obesity and the metabolic syndrome, sarcopenia and frailty, memory and cognitive impairment and changes in psychosexual function. These changes

may be mediated, in part, by many and varied socio-demographic (income, education, work status, marital and family status and sense of role in society) and modifiable lifestyle factors (smoking, alcohol intake, diet and physical activity level). This study aims to identify and develop a sound working hypothesis for the complex interplay between declining serum androgen levels, socio-demographic and lifestyle factors and the development of risk factors and chronic disease.

In men, T levels decline with age from around the 3rd decade while SHBG concentrations increase and therefore serum FT and BT decline more markedly than total T [59]. Dependent on the definition used to define hypogonadism (for review see [13]), 10-20% of men over the age of 60 have low total T levels and over 50% have low BT levels [109]. The physiological and clinical significance of these changes are unclear since in many men T levels may remain in the normal young male range. There is also no clearly defined symptom complex associated with an age-related decline in plasma T levels. Reduced libido, erectile dysfunction, depressed mood, cognitive decline in the domains of memory and visuospatial function, increased body fat and a decline in muscle mass and strength may result from reduced plasma T levels [167], or may be concomitant changes associated with ageing, other lifestyle, behavioural, clinical or psychological factors. Knowledge of lifestyle determinants of reproductive hormones is limited. In cross-sectional studies, T levels are positively related to carbohydrate intake [168],[169] and cigarette smoking [58], and inversely related to obesity, malnutrition and alcohol intake [167]. Health status affects T levels [24, 59] which are 10-15% lower in men with obesity, coronary heart disease or diabetes.

Cross-sectionally, the FAMAS aimed to determine the associations between serum testosterone levels, erectile function, sexual desire, lower urinary tract symptoms, depressive symptoms, indicators of cognitive impairment and body composition and physical function. The inter-relationships of socio-demographic factors, chronic disease and lifestyle factors such as physical activity, diet and smoking were also investigated.

This chapter describes the cohort in terms of standard socio-demographic and health indicators and compares the enrolled cohort to Census 2001 data for the same geographical area and to other relevant Australian population based health studies. The purpose of this chapter is to provide a context in which to view and interpret the findings discussed in the proceeding 5 chapters (Chapters 5.1 – 5.5).

METHODS

RECRUITMENT OF PARTICIPANTS

All households in the northern and western suburbs of Adelaide (see Figure 4.1 for catchment area) with a telephone connected and the number listed in the Electronic White Pages (EWP) were eligible for selection in this study. The sample was stratified into the two health regions: Western Adelaide and Northern Adelaide. Within each household, the male person aged between 35 and 80 years to last have his birthday was selected for interview and invited to attend the clinic.

A letter introducing the study, along with an information brochure, was sent to the household of each selected telephone number. The letter and brochure informed potential participants of the purpose of the study and indicated that they could expect to be contacted by telephone.

The telephone recruitment interview included questions relating to self-reported health conditions, mental health, smoking status, reasons for not wanting to participate in the study and demographic questions (Appendix I).

Recruitment was undertaken from August 2002 to July 2003. Telephone calls were made in the evening between 1600h and 2000h on Mondays, Tuesdays and Wednesdays and between 1100h and 1500h on Saturdays. On some occasions calls were made on other days at other times when specifically requested by potential participants. Professional interviewers conducted the interviews and were

supervised by Population Research and Outcome Studies (PROS) personnel (South Australian Department of Human Services, Adelaide, South Australia).

On contacting the household, the interviewer first identified themselves and the purpose of the study. The interviews were conducted in English. When required for non- or poor-English speaking interviewees, a friend or family member of the interviewee was arranged to join the telephone interview as an interpreter.

The Questionnaire Programming Language (QPL) system was used to conduct the interviews. This is a "freeware" package that provides a way of efficiently and reliably automating survey data by allowing immediate entry of data from the interviewer's questionnaire screen to the computer database. The advantage of this system is that it correctly sequences questions as specific answers are given. In addition, it enforces a range of checks on each response with most questions having a set of pre-determined response categories. The QPL programme allows open-ended responses to be transcribed exactly by the interviewer.

Figure 4.1 The sampling region for the Florey Adelaide Male Ageing Study (FAMAS).

Shaded areas indicate regions not sampled. The total geographical area of the sampling region is approximately 831.7 sq kilometers; the northern region (672.2 sq kilometers) is almost 4.25 times larger than the Western region (159.5 sq kilometers). The total population of the sampling region was 540,228 at the time of the 2001 Australian Census (Northern region 337,580; Western region 202,648).

Selection and exclusion criteria

To be enrolled in the study subjects had to be males, aged 35 to 80 years, living in the defined catchment area of north and west Adelaide (Figure 4.1), willing and able to comply with the protocol and to give written informed consent. Exclusion criteria were limited to living outside the catchment area and to telephone numbers that belonged to non-residential properties (i.e. businesses, institutions and residential-care facilities). No other exclusion criteria were specified as the study aimed to represent a true cross-section of the male community dwelling population of Adelaide's northern and western suburbs.

STUDY PLAN AND DESIGN

This study was designed as a cohort study with follow-up assessment planned at two and 5-year intervals. Cross-sectional data from the initial intake of participants was analysed and forms the basis of the following 5 chapters of this thesis.

Study procedures took place at the Queen Elizabeth (TQEH) and Lyell McEwin Hospitals (LMHS) between 0700 hours and 1130 hours after signed informed consent from volunteers. The study involved attending the clinic on two separate occasions. The first clinic took place at either TQEH or LMHS (participant's convenience). Approximately 40 ml (4 tubes) of blood were drawn from a forearm vein by venipuncture after an overnight fast from 9pm. Blood was transported to the Institute of Medical and Veterinary Science (Royal Adelaide Hospital) for processing and analysis. A questionnaire pack (see Appendix II) including Questionnaire A and the dietary questionnaire were completed at home by participants and brought with them to the clinic. Questionnaires were carefully reviewed for completeness, clarity and consistency. Anthropometry (height, weight, waist and hip measurements), blood pressure, a brief neuropsychological assessment (Fuld Object Memory Evaluation, Trail Making

Test, Finger tapping and handgrip strength), uroflowmetry and questionnaire B (Appendix III) were completed. Finally, an appointment for a body composition scan was made at TQEH.

The second visit was conducted at the Osteoporosis Centre at TQEH. Whole body bone density and body composition was measured by dual energy x-ray absorptiometry (DEXA) as described in Chapter 2.0. Additionally, abdominal fat was analysed using the method described by Campbell et al. (1996)[170], that uses a standard size RO1 spanning the top of second lumbar vertebra (L2) to the bottom of fourth (L4).

QUESTIONNAIRES

A comprehensive questionnaire (Questionnaire A) was mailed to volunteers after the telephone interview, along with the dietary questionnaire, a participant information sheet and clinic appointment details. Questionnaire A included standard demographic questions taken from Australian Census 2001 regarding ethnicity, income, education and work status, and health information regarding medical conditions, prior surgery, medication use and cigarette smoking. Also included in this questionnaire were the 36-item short-form health survey (SF-36), the Beck Depression Inventory (BDI), the frequency of symptoms of obstructive sleep apnoea (OSA), physical activity level and the IPSS as described in Chapter 2.0.

Physical and mental health

The SF-36, developed by the Medical Outcomes Study in the United States [171, 172], was used to assess physical and mental function. It was developed as a generic indicator of health status for use in population surveys and has been applied to assess the outcomes of various health conditions in the general population. The instrument has been assessed for validity and reliability in Australia [173-175], the USA [176] and the UK [177]. The instrument comprises of 36 questions that are summarised to eight domains: physical function (PF), general health (GH), vitality (VT), mental health (MH), role limitations due to physical health problem (RP), role limitations due to emotional health problems (RE), social function (SF) and bodily pain (BP). Responses to the 36 questions were recorded, summed and transformed to provide the eight dimensions with scores between 0 and 100, with higher scores indicating better health.

The BDI was used to assess the presence of depression and dysphoria [178]. The total score for this instrument was obtained by adding the highest score circled for each of the 21 items. Item 19 (which asks about weight loss) was designed to assess anorexic symptoms. If the participant answered affirmatively to the supplementary question “Are you trying to lose weight by eating less?” the score on that item was not added to the total score. Studies show good test-retest reliability of 0.9 [179], Spearman-Brown reliability of 0.93 and internal consistency for test items of 0.86 [180]. Other authors have reported coefficient alpha’s of 0.88 [181], 0.91 for elderly patients and 0.71 for elderly patients with depression [182]. There are no set guidelines all purpose classification of degrees of depression, however the interpretive guidelines suggested by Marsella et al. (1974) [183] and Beck et al. (1987) [184] were used in this study (Table 4.1).

BDI score	
0 - 9	Normal range
10 - 15	Mild depression
16 - 19	Mild-moderate depression
20 - 29	Moderate-severe depression
30 +	Severe depression

Table 4.1 Interpretive guidelines for the BDI.

From Marsella et al. (1974) and Beck et al. (1987).

Physical activity

Physical activity level was assessed using questions from the 1999 National physical activity survey (Australian Institute of Health and Welfare, Canberra)[185]. The questions determined the volume of walking, moderate exercise and vigorous exercise in both number of sessions and total minutes in the last two weeks. The agreement between exercise volumes over "the last week" reported by the questionnaire and over a "usual week" determined as the average weekly physical activity over the previous six months was strong (ICC = 0.76, 95% CI = 0.75 – 0.78) [185].

Nutrient intake

The Australian Cancer Council of Victoria's (ACCV) electronically scored dietary questionnaire was used to assess the composition of participant's diets. The Spearman correlation coefficients for reproducibility over 12 months were 0.73 for energy and 0.71 for protein in Australian men. This questionnaire has been extensively used in population surveys of dietary intake and has been validated against biomarkers of nutrient intake in Australian men. The estimated mean energy intake (9761 kJ) was appropriate for middle-aged, relatively sedentary men and the ratio of this to basal metabolic rate (BMR) was 1.37 for males. The estimated mean daily intake of protein (119.2 g) was comparable to an estimate imputed from urinary nitrogen excretion (105.7 g). The estimated mean daily intakes of potassium (110.8 mmol) were higher than the estimate imputed from urinary potassium excretion (75.7 mmol). The relative validity of the ACCV dietary questionnaire for energy, protein and potassium were 0.27, 0.35 and 0.32 respectively. The low Pearson correlation coefficients are typical of nutritional questionnaires [186]

Sexual function

A separate questionnaire assessing sexual desire and erectile function (Questionnaire B) was completed during the first clinic visit and comprised the Sexual Desire Inventory 2 (SDI-2), the International Index of Erectile Function (IIEF) and a Global Impotence Rating (GIR). The SDI-2 was used to assess participant's levels of sexual desire [187]. The inventory measures two aspects of sexual desire: dyadic, meaning an interest in or wish to engage in sexual activity with another person, or a desire for intimacy and sharing with another; and solitary sexual desire, meaning an interest in engaging in sexual behaviour with oneself and may involve a wish to refrain from intimacy and sharing with others. Internal consistency of the inventory was high with Chronbach's alpha values of 0.86 for dyadic and 0.96 for solitary sexual desire [187]. The IIEF [188] was used to measure 4 of the 5 domains of sexual function covered by the index: erectile function (EF), sexual desire (SD), intercourse satisfaction (IS) and overall satisfaction (OS). The orgasmic function domain of the IIEF was omitted. A high degree of internal consistency has been demonstrated for each of the five domains and for the total index (Chronbach's alpha values of 0.73 and higher and 0.91 and higher, respectively) and each domain has a high degree of sensitivity and specificity to effects of treatment [188]. Moreover, test-retest reliability correlation coefficients for the five domain scores were highly significant (EF = 0.84, SD = 0.71, IS = 0.81, OS = 0.77) [188]. The GIR [189] was used to categorise participants as having: no, mild, moderate or severe ED. This single question rating correlated well with the IIEF and the Brief Male Sexual Function Inventory ($r = 0.71 – 0.78$, $P < 0.001$) [189]. Moreover, the prevalence of ED detected by the GIR was similar to that predicted by the IIEF and agreement was moderate (kappa = 0.56 – 0.58) [189].

Obstructive sleep apnoea

Three questions were included as Section I of Questionnaire A (Appendix II) to assess the frequency of symptoms of OSA. The sum of the mean of non-missing values for the 3 symptoms: snorting/gasping; loud snoring; breathing stops/chokes, together with age and body mass index (BMI) were used, as determined by Maislin et al. (1995), to calculated the probability of having OSA [190]. This prediction formula has been shown to have good sensitivity (approximately 85%) but poor specificity (approximately 55%), indicating that the majority of men with sleep apnoea were detected, but many without sleep apnoea were also detected [190].

DIRECT MEASUREMENTS

Clinical investigation of blood pressure, anthropometry and handgrip dynamometry (3 reps), as described in Chapter 2.0 were conducted at the first clinic visit. Urinary flow rate and voided volume were measured directly using UROCAP-II, a portable uroflowmetry analyser (Laborie Medical Technologies, Mississauga, Ontario, Canada) with serial printer for providing output. The unit was calibrated according to manufacturers instructions prior to the beginning of the study and then again after six months. The accuracy of the UROCAP-II system is ± 1% for voided volume and ± 2% for flow rate (UROCAP-II User Manual, Document number 230; version 1.0, 2 Nov. 2000, Quality Assurance, Laborie Medical Technologies).

Neuropsychology

A brief neuropsychological test battery including the Fuld object memory evaluation (FOME), trail-making tests part A and B (TMT's: TMT-A, TMT-B) as described in Chapter 2.0 and a finger tapping test (FTT) was administered to assess various domains of cognitive function. Reliable sensitivity and

specificity data for these tests in terms of cut-off values signifying the likelihood of cognitive impairment are not available or are not agreed upon in the contemporary literature [191, 192]. In this study, test scores were treated as either continuous or as categorical based on scores at the 10th and 90th percentiles rather than at any specific cut-off defining impairment.

The FOME was used to assess learning, error feedback and memory [193]. Participants used one hand, then the other alternately to identify objects from a bag by touch alone, removing each item in turn to say its name out loud. The bag contained 10 everyday items such as a playing card, a key, a coin, a button, scissors, cup, ball, etc. Each revealed object was then hidden from sight until all 10 emerged from the bag. The participant then verbally repeated the objects, and was reminded of those forgotten. A distraction task (the TMT's) was then given, and the participant was again asked to recall the 10 objects. Four more selective reminding trials were given without distraction. After a 30 minute delay the participant was again asked to recall the 10 items. Each recalled item was recorded along with each item forgotten at each trial. Scoring of the test involved calculating the number of repeated retrievals (RR's) and ineffective reminders (IR's) between each successive trial. RR's referred to items that were recalled in two consecutive trials; IR's referred to items that were forgotten in two consecutive trials. Data for RR's and IR's were analysed as the difference between recall trials 1 and 2, trials 1 and 3, trials 2 and 3 and the difference between trials 1, 2 and 3 and the 4th (delayed) trial. The greater RR scores between trials reflect greater improvement in ability to recall items. The lower IR scores between trials reflect less forgetting of items or an improvement in ability to recall items after being reminded of them.

The finger-tapping test is a measure of rapid alternating muscle movements and was used to assess subtle motor and other cognitive impairment. The test is very sensitive to the presence and laterality of brain lesions [194], [195, 196]. There is evidence that tapping frequency is reduced in a number of conditions including chronic alcoholism [197], closed-head injury [198] and the mild stages of degenerative dementias [199, 200]. Better performance on this test has been shown to be associated

with male gender [201, 202], younger age [201], preferred hand [203], increasing IQ [197] and more years of education [201]. The finger-tapping device comprised of a counter with a lever that was purchased from Psychological Assessment Resources Inc. (Odessa, FL USA). Participants began the test with their preferred hand palm down and fingers extended with the index finger placed on the lever. Participants were instructed to depress and release the lever, as quickly as they could over a 10-second period moving the index finger alone, not the whole hand or the arm. Participants were given two familiarity trials on each hand before beginning the first recorded trial. The test was timed over 5 trials of 10 seconds each with the preferred hand then the other. The finger tapping score was calculated for each hand separately as the mean of the 5 consecutive 10-second trials, within a range of 5 taps.

Laboratory measurements

All laboratory tests specified in Chapter 2.0 were used in this study. In addition free PSA was measured by Chemiluminescent Microparticle Immunoassay (Abbott Laboratories, Abbott Park IL) on the Abbott ARCHITECT® system (CV 5.9% at 0.129 ug/L and 2.78% at 3.569 ug/L). The analytical sensitivity of the assay was 0.008 ng/mL and the specificity was less than or equal to 10% when bilirubin (20 mg/dL), haemoglobin (500 mg/dL), total protein (2 g/dL and 12 g/dL) and prostatic acid phosphatase (1000 ng/mL), triglycerides (3000 mg/dL), Proscar® (25 ug/mL) and Flomax® (1 ug/mL) were tested for interference. Furthermore, an aliquot of each participant's plasma was frozen and stored at –70^{o}C for future studies. Whole blood was transferred to Guthrie Cards and stored at –70^{o}C for future DNA and gene polymorphism studies.

COMMUNICATION OF PERSONAL RESULTS

Each participant received a summary of their test results after review and interpretation by the investigators. Testosterone results were withheld unless requested specifically by the participant. The implications of abnormal findings were communicated to the participant and their choice of medical

practitioner. In some cases this resulted in further evaluation of the problem by a member of the study team, or referral to appropriate specialists. In the event an of abnormally high PSA, the implications were discussed with the participant and follow-up was recommended with their general practitioner.

DATA MANAGEMENT, CLEANING AND CODING PROCEDURES

All clinic data were entered into a custom database with in-built data quality checks, designed in Microsoft Access 2000 by Mr Andrew Ly, Mr Brian McDermott and Ms Elizabeth Griffith at the Adelaide Data Management Centre, Department of General Practice, University of Adelaide. The database was maintained on a secure server at the University of Adelaide. Two data entry personnel entered all data, using specific criteria for dealing with data queries. In the event of unclear questionnaire data, participants were contacted by telephone to clarify their answers. If clinic data were unclear or out of range according to the preset system checks, the clinic attendant who attended to that particular participant was contacted and asked to verify the data. Medications were coded at data entry according to the EPAZDEX system for coding of medications. Health conditions, cancers and surgical procedures that were not specifically detailed in Questionnaire A, but that were recorded by participants under the "other" options and also indications for medication use were coded, post-entry, by the Adelaide Data Management Centre, Department of General Practice, University of Adelaide according to ICPC coding procedures for medical conditions. Overall, there were a total of 10 coding anomalies identified during the coding process and these are detailed in Table 4.2. Microsoft Access 2000 data tables were converted, using Stat Transfer 6.0 for Windows (STATA Corporation, College Station, TX USA), to STATA 7.0 for Windows (STATA Corporation, College Station, TX USA) data files for higher level data cleaning and statistical analyses.

Post-entry data cleaning followed the general principle of the first stage being graphical and statistical univariate analyses and assessment of frequency distributions. Anomalous and outlying data were checked against source notes and any corrections were made in the original database and the updated

data table was re-converted to a new STATA data file for second stage cleaning. All individual data files were merged using the study identification number, a unique identifier as the common variable, to create a single master data file. Bivariate cross-tabulations were performed to ensure that correct horizontal alignment of data had been accomplished.

Medications (Questionnaire A_E)

Medication	*Reason for taking*	*QstA_ICPC*	*Comment*
ENDEP10	bladder	N/A	this is a drug to treat depression, coded as N/A
HYGROTON	Balance (inner ear)	K86-005	this is a drug to treat hypertension - was the imbalance a side effect of the medication? - coded for hypertension
CARTIA	mild eye irregularity	K49-003	this drug is an anticoagulant, coded "On anti-coagulants"
CAPTOPRIL	unknown	K86-005	coded as hypertension
DEPTRAN	Skin condition	P01-003	this is a drug to treat depression, patient indicates anxiety and skin cancer - coded for anxiety
SAMBUCUM	mucus	N/A	queried: no further information

Other health conditions (Questionnaire A_F15)

Other health conditions	*F15_ICPC*	*Comment*
Minor brain damage at birth	N/A	queried: no further information
right ear broken	N/A	queried: no further information
right eye	N/A	queried: no further information

Other pelvic surgery (Questionnaire A_G8)

Other pelvic surgery	*G8_ICPC*	*Comment*
base of spine (ingrowing hair)	S85-003	presume this was excised - but no specific code, coded as pilonidal sinus

Table 4.2. A log of the queries and solutions to coding anomalies

generated by the Adelaide Data Management Centre (Department of General Practice, University of Adelaide) for reasons for taking medications, other health conditions and other pelvic surgery.

STATISTICAL ANALYSES

POWER CALCULATIONS FOR TESTOSTERONE EFFECT

In the following, two-sided testing at a significance of 5% is assumed. An a priori target of recruiting 1000 participants to FAMAS meant that correlations, as weak in magnitude as 0.09, could have been detected with a power of 80% in cross-sectional analysis. The assumed distribution of the 1000 participants was four equal age groups: 35 – 44, 45 – 54, 55 – 64 and 65 – 80, i.e. 250 participants per age group. Table 2.3 shows the smallest differences in testosterone (assuming a SD of 6.2 nmol/L) and SHBG (assuming a SD of 13.4) that could be detected with a power 80%, between disease states within an age group. The data contained in this chapter and Chapters 5 .1 – 5.5 relate to the first 568 men recruited under this protocol thus, the above power calculations are likely to overestimate the statistical power of the analyses reported in these chapters.

STATA 7.0 for Windows (STATA Corporation, College Station, TX USA) was used for all data analyses. Data was analysed as survey data to account for sampling procedures and probable biases to allow for information to be generalised to the North West Adelaide male population. Probability weights (based on age and residential region (Northern or Western)) were calculated and the sample was stratified by Northern and Western residential regions. Using STATA's survey specific commands resulted in more accurate point estimates and truer standard errors and confidence intervals. Where non-weighted data or non-survey analyses were used, it was clearly stated. In this chapter, univariate analysis was used to describe the cohort in terms of demographic and basic health information and subsequently, health information was described and post estimation analysis of mean and proportion difference was determined between demographic strata using accumulated t-tests. These data where framed against and, where possible, quantitatively compared to equivalent data from the 2001 Australian Census and other population-based data of interest. Quantitative comparison's where sample number, group means

and standard deviations were available were made using student's t-tests. $P < 0.05$ was considered significant.

Disease prevalence within age group	2%	5%	10%	20%	50%
Number with disease	5	12	25	50	125
Number without disease	245	238	225	200	125
Testosterone difference (nmol/L)	7.9	5.2	3.7	2.8	2.2
SHBG difference (nmol/L)	17.0	11.2	7.9	6.0	4.8

Table 4.3 Power calculations for testosterone effect within an age group.

A total of 250 participants per age group were assumed. The smallest differences in testosterone and SHBG that could be detected with a power of 80% between disease and no disease are shown.

RESULTS

PARTICIPATION AND RESPONSE RATES

Five hundred and eighty six men were enrolled in the study. Figure 4.2 shows the participant disposition from initial random sampling through to participation in study clinics. The overall response rate for the study (percentage of sample eligible for recruitment) was 46%, the overall participation rate (percentage of eligible sample who agreed to be interviewed) was 58% and the final response rate of the eligible sample that finally attended the clinic was 52%. The reasons for sample members refusing to participate in the study are shown in Table 4.4.

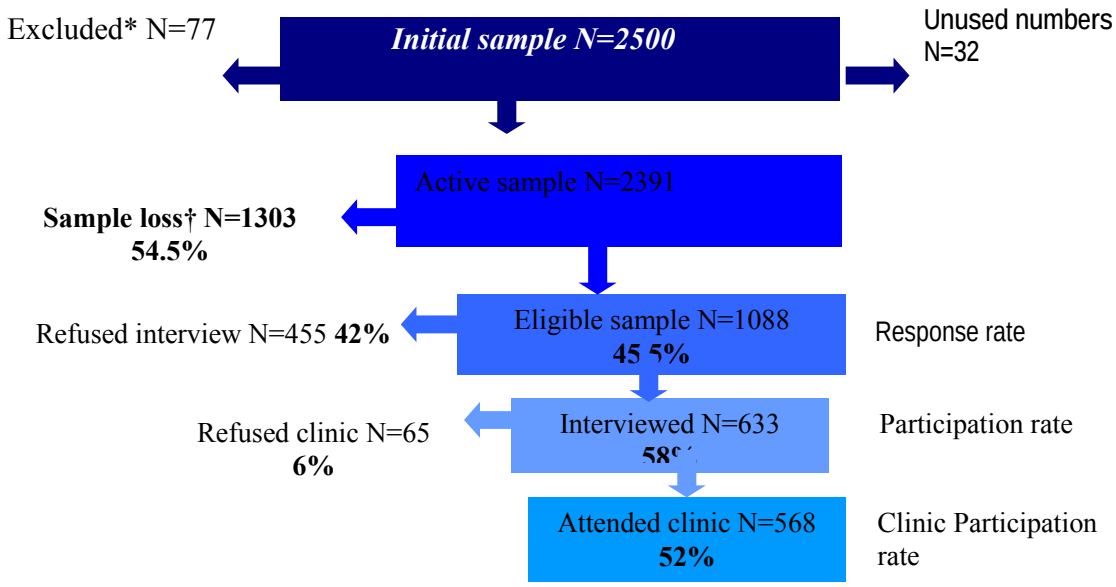

Figure 4.2 Participant disposition.

*Excluded because they were already involved in or randomly selected for the North West Adelaide Health Study. †Unable to be contacted after 10 attempts, ineligible due to no male aged 35-80 in the household, non-connected numbers, non-residential numbers, fax/modem connections.

	Number	Frequency
Too old	0	0
Too sick	13	0.55
No health problem	1	0.04
Too busy	60	2.52
Don't want to participate	106	4.45
Other	28	1.17
Refused to answer	1	0.04
Total	209	8.77

Table 4.4 Reasons for not participating in the study.

DEMOGRAPHICS AND HEALTH OF NEGATIVE RESPONDERS COMPARED TO STUDY PARTICIPANTS

A comparison of age and household size between the 455 negative responders and the 633 study participants is shown in Table 4.5. There were no differences between negative responders and study participants in the mean number of adults or the mean total number of people living in the household. However, households that agreed to participate in the study had a significantly greater number of members aged less than 18 years ($P < 0.0001$). There was no obvious difference in the type of work that men had done for most of their lives between negative responders and study participants (data not shown).

Comparisons of body mass index (BMI) and prevalence of diabetes, asthma, bronchitis, emphysema, heart attack, stroke, angina, high cholesterol, high blood pressure, anxiety, depression, stress problems, any other mental health problems and past and present cigarette smoking between negative responders and study participants are shown in Table 4.6. There was no difference in BMI between negative responders and participants. With the exception of stroke and mental health problems other than anxiety, depression and stress problems, participants had a greater prevalence of chronic diseases and also a greater prevalence of men without any known chronic disease. Study participants had a lower prevalence of past and present high cholesterol and high blood pressure measurements. The prevalence of current smoking was lower and past smoking higher in participants when compared to negative responders.

Number of persons	455	633
Age		
35 - 39	18	75
40 - 44	27	80
45 - 49	25	99
50 - 54	25	90
55 - 59	28	96
60 - 64	24	64
65 - 69	18	50
70 - 74	16	44
75 +	14	33
Other	1	0
Not answered	259	2
Adults in household		
Mean ± SD	2.14 ± 1.07	2.14 ± 0.75
Range	1 - 12	1 - 5
Not answered	256	15

Persons under 18 years in household		
Mean ± SD	0.237 ± 0.74	0.55 ± 0.97*
Range	0 - 5	0 - 7
Not answered	6	8
Total persons in household		
Mean ± SD	2.71 ± 1.59	2.70 ± 1.27
Range	1 - 14	1 - 9
Not answered	260	16

Table 4.5 Comparison between negative responders and study participants for age and household demographics.

*P < 0.0001.

	Negative responders	Study participants
Number of persons	455	633
BMI from self-reported height and weight, mean (kg/m^2)	28.77	28.94
Diabetes	17 (4%)	53 (9%)
Asthma	15 (3%)	54 (8.5%)
Bronchitis	22 (5%)	77 (12%)
Emphysema	2 (<0.5%)	19 (3%)
Heart attack	6 (1%)	34 (5%)
Stroke	3 (0.5%)	11 (<0.5%)
Angina	9 (2%)	35 (5.5%)
Ever had high cholesterol	390 (86%)	209 (33%)
Currently have high cholesterol	371 (81.5%)	126 (20%)
Ever had high blood pressure	405 (89%)	179 (28%)
Currently have high blood pressure	393 (86%)	130 (20.5%)
Anxiety	9 (2%)	24 (4%)
Depression	6 (1%)	33 (5%)
Stress problem	8 (2%)	39 (6%)

	Negative responders	Study participants
Number of persons	455	633
Other mental health problem	3 (0.5%)	4 (0.5%)
Currently smoke	387 (85%)	127 (20%)
Current non-smoker's who used to smoked at least once per day	79 (17%)	289 (46%)
No health condition	143 (31%)	425 (67%)

Table 4.6 A comparison of BMI, chronic disease status and smoking between negative responders and study participants.

Data presented are counts (proportions) with the exception of BMI, which are presented as group means.

DEMOGRAPHICS OF RECRUITED COHORT

Age

Figure 4.3 shows the age distribution of the cohort. The mean age of study participants was 54.31 ± 11.17 (min 35 – max 79).

Regional distribution

The proportion of men who visited the western region clinic at TQEH compared to those who visited the northern region clinic at LMHS is compared in Figure 4.4 (Panel A). Fifty-three percent (N = 299) of men attended the clinic at TQEH and the remainder (N = 269) attended the LMHS clinic. The number and proportion of men who lived in the northern and western region of Adelaide at the time of the 2001 Australian Census is also shown in Figure 4.4 (Panel B). There was a difference between the north/west distribution in terms of men aged 35 to 79 years, residing in the geographical sampling area when compared to the LMHS/TQEH clinic attendance distribution; more men in the age-range in the general population of the north-west region of Adelaide, resided in northern suburbs in 2001 but most men in the current cohort attended the TQEH study clinics in the western suburbs in 2002-2003.

Marital status

Figure 4.5 shows the marital status of men in the cohort. Eighty-two percent (N = 467) of men were married or living with a partner. The distribution of marital status in the current cohort is compared, by 5-year age group, to Australian Census 2001 data from the same geographical region in Figure 4.6. Overall, most strikingly, there was an over-representation of men who were married or living with a partner and an under-representation of men who had never married.

Gross annual household income

The distribution of gross annual household income for the cohort is shown in Figure 4.7 (Panel A). Four participants refused to disclose details about their household's annual income. Six percent (N = 35) of men had gross household incomes in the lowest bracket (up to $12,000 p.a) and 15% (N = 88) were in the highest bracket (more than $80,000 p.a). Overall, the distribution of gross annual household income in the cohort was considerably even from the $12,001 - $20,000 bracket through to the highest income bracket and reflected a similar distribution to that described for the wider northern and western population of Adelaide in the 2001 Australian Census (Figure 4.7, panel B).

Aboriginality

Ninety-eight percent (N = 557) of the cohort was of non-Aboriginal or non-Torres Strait Islander origin. One man was of Aboriginal and one was of Torres Strait Islander descent; 9 men chose not to specify whether or not they were of Aboriginal or Torres Strait Islander origin. In the overall, all-ages, population of northern and western Adelaide, 1.3% were Aboriginal, 0.055% was Torres Strait Islander and 0.045 were both Aboriginal and Torres Strait Islander at the time of the 2001 Australian Census.

Country of birth and immigration year

The distribution of countries of birth in the cohort, are shown in Figure 4.8 (panel A). Sixty-seven percent (N = 381) of participants were born in Australia. The most significant country of birth, outside of Australia, was the United Kingdom including Ireland, Scotland and Wales with 101 participants (18%) being born there. These figures matched very closely with the data of males in the same geographical area, from the 2001 Australian Census (Figure 4.8, panel B). Of the men born outside Australia, 65% (122 / 187) arrived in Australia between 1949 and 1969 (Table 4.7).

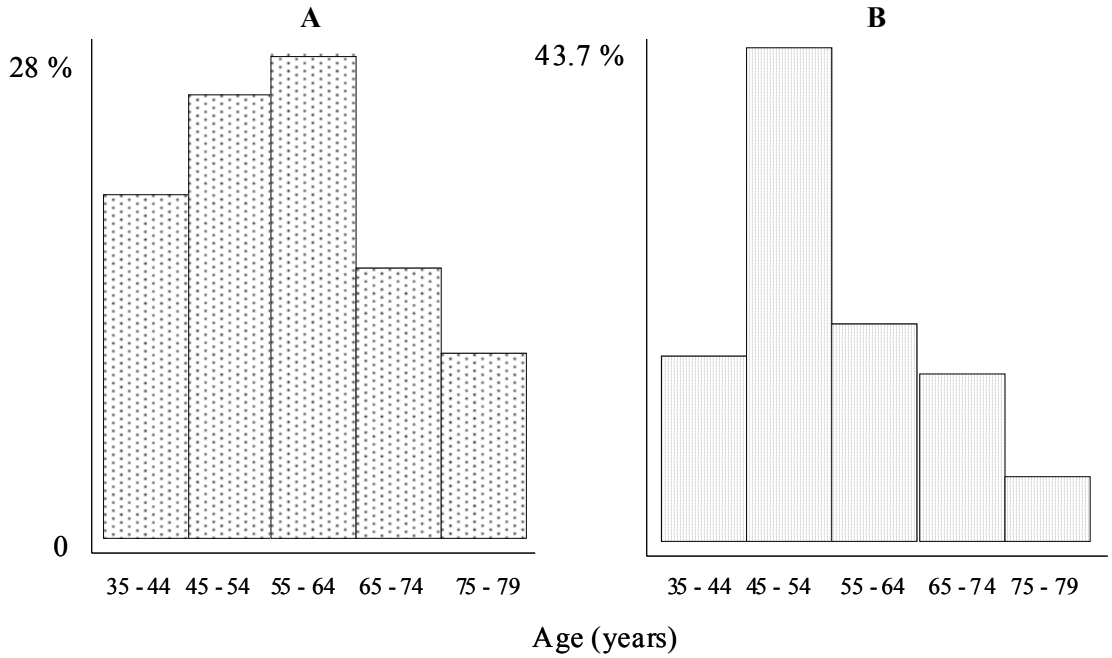

Figure 4.3 The age distributions of the FAMAS cohort (A) and of northern and western Adelaide males between the ages of 35 and 79 years (B).

The mean age of the cohort was 54.31 ± 11.17 years in 568 men randomly recruited from the north and west suburbs of Adelaide (A). Data in panel B are from the 2001Australian Census taken in the same region of Adelaide from which the FAMAS cohort was sampled.

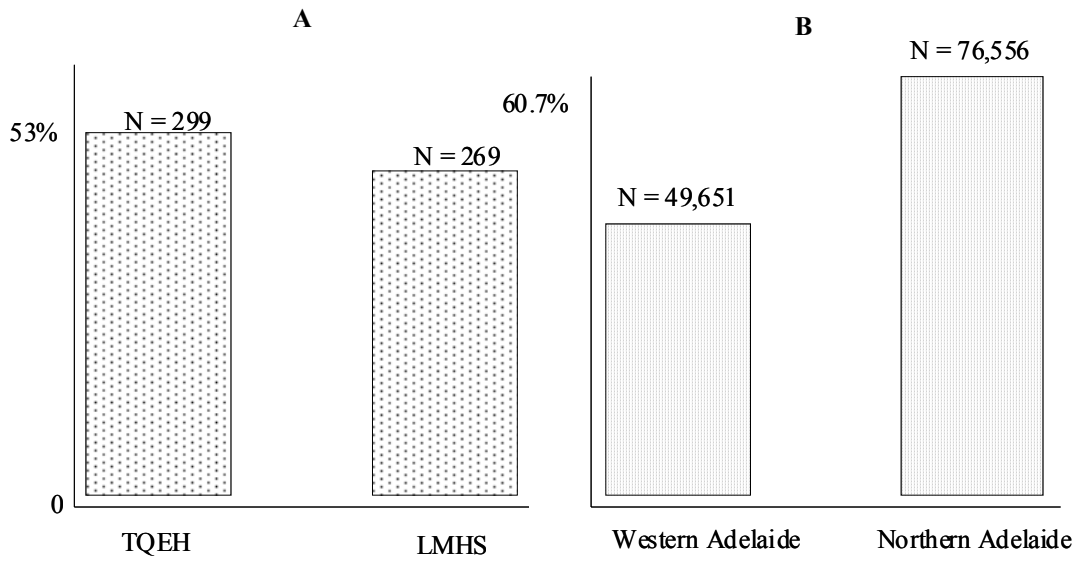

Figure 4.4 Number of participants by clinic (A) and the number of men aged between 35 and 79 by residential region, from Census 2001 (B).

Fifty-three percent of participants attended the western region clinic at TQEH and the remainder attended the northern region clinic at LMHS. TQEH = The Queen Elizabeth Hospital, LMHS = Lyell McEwin Health Service.

Figure 4.5 Marital status of the cohort.

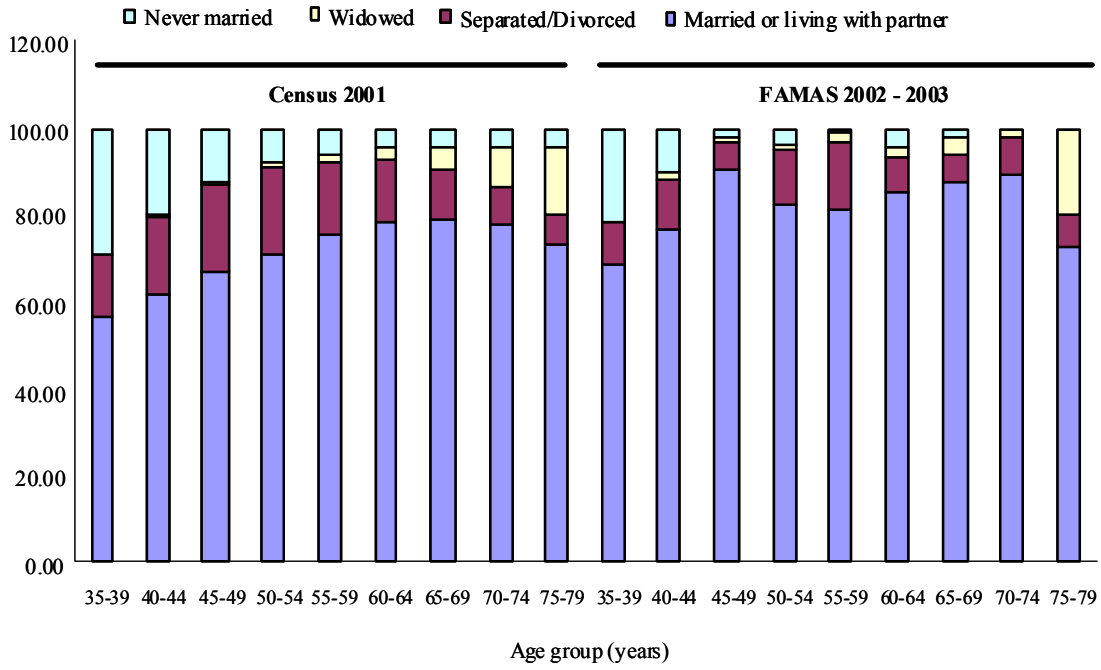

Figure 4.6 A comparison of the distribution of marital status, by 5-year age group between the FAMAS cohort and 2001 Australian Census data from northern and western Adelaide.

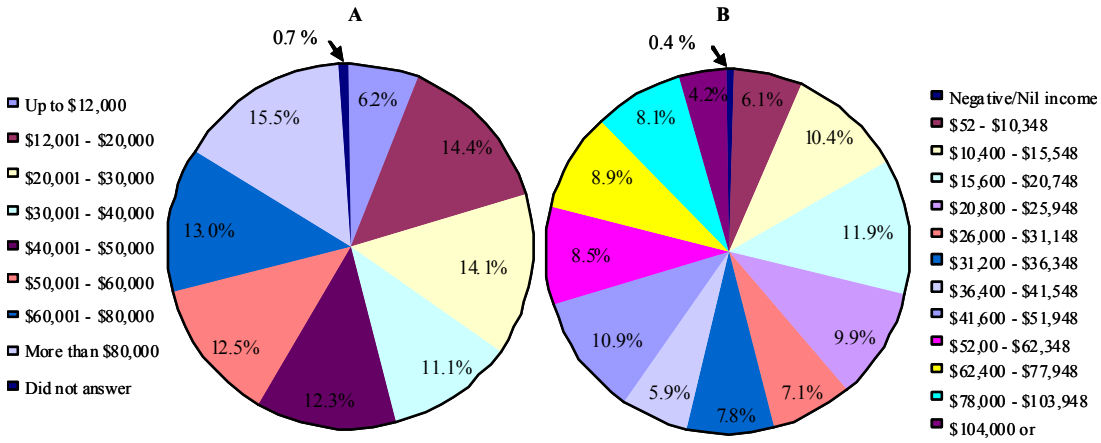

Figure 4.7 The distribution of gross annual income in the households of men aged 35 – 79 years enrolled in the FAMAS, randomly recruited from the north and west suburbs of Adelaide (panel A) and in 2001 Australian Census data from northern and western Adelaide households (panel B).

Four participants in the FAMAS cohort refused to disclose their gross annual household incomes. Panel B figures have been converted to annual from weekly income by multiplying each end of the income range by 52. This resulted in jumps of $52 between each income category and is simply a guide by which to loosely compare between cohort and Census data.

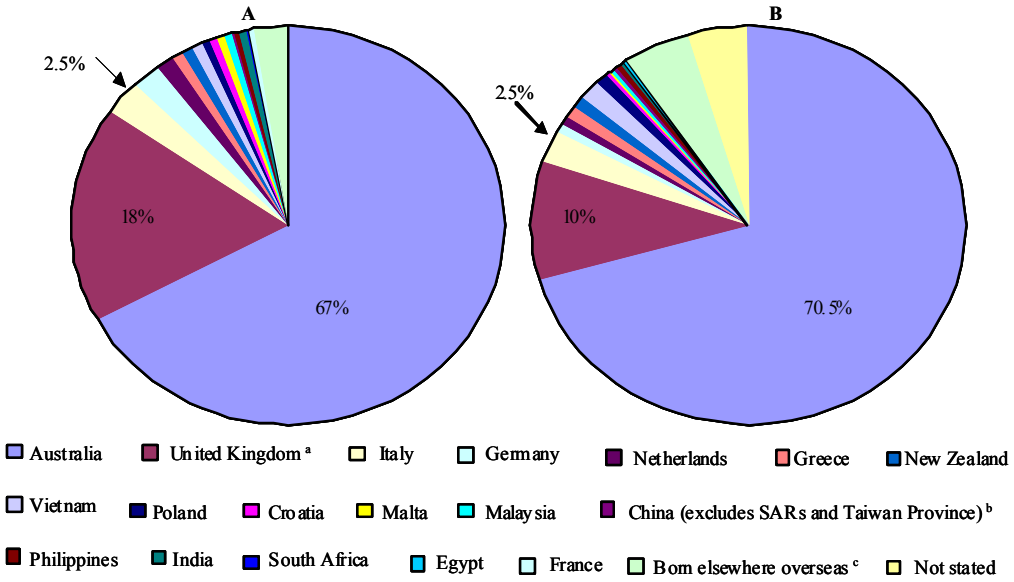

Figure 4.8 A comparison of the distribution of countries of birth in the FAMAS cohort (A) and in the northern and western Adelaide male population (B).

Data in panel B are from the 2001 Australian Census taken in the same region of Adelaide from which the FAMAS cohort was sampled and include all males from age 15 years.

[a]Includes 'England', 'Ireland', 'Scotland', 'Wales', 'Isle of Man', 'Channel Islands' and 'United Kingdom, not further defined'. [b]SAR is an abbreviation for "Special Administrative Region". SARs comprise Hong Kong (SAR of China) and Macau (SAR of China). [c]For panel A includes: the Czech Republic, El Salvador, Cambodia, Argentina, Ukraine, Syria, Russia, Malawi and Romania. For panel B it includes: Federal Republic of Yugoslavia, the USA, Lebanon, Hong Kong (SAR of China), Indonesia, Canada, Former Yugoslav Republic of Macedonia, Sri Lanka, Singapore, Fiji, Republic of South Korea, Turkey 'inadequately described', 'at sea' and 'not elsewhere classified'.

Year of arrival in Australia	FAMAS 2002-2003		Census 2001	
	N	%	N	%
Before 1986	164	87.7	99418	73.5
1986 - 1990	15	8.0	10473	7.7
1991 - 1995	6	3.2	8520	6.3
1996	1	0.5	1884	1.4
1997	0	0.0	1550	1.1
1998	0	0.0	2001	1.5
1999	1	0.5	2120	1.6
2000	0	0.0	2167	1.6
2001	0	0.0	1269	0.9
Not stated	0	0.0	5805	4.3
Total immigrants	187		135207	
Total population	568		540228	
Immigrants as % of total population	32.9		25.0	

Table 4.7 The number and proportion of immigrant arrivals in Australia pre-1986 through to 2001

from the FAMAS cohort of men between the ages of 35 and 79 years, randomly recruited from the north and west suburbs of Adelaide and from 2001 Australian Census data of males and females of all ages.

Education level

Figure 4.9 shows the variation in education levels of participants in the cohort. One participant did not answer whether he had obtained a qualification since leaving school and one other reported that he did not know. This participant subsequently reported that his highest qualification was “year 3”. Seventy-two percent (N = 407) of men had obtained some form of qualification since leaving school. Forty-nine percent (199 / 407) had obtained a trade qualification or apprenticeship; 31% (128 / 407) had a certificate or diploma; 14% (59 / 407) had a bachelor degree of higher; 5% (21 /407) reported having some other qualification (Table 4.8) and 1 man did not know his highest qualification.

Work status

Figure 4.10 shows the variation in work status of participants in the cohort. Fifty-two percent (N = 296) of men were in full-time employment; 28% (N = 159) were retired and 10% (N = 55) were in part-time or casual employment. Six percent (N = 35) of men reported having some other work status (Table 4.9), the majority of which were men on disability pensions (12 / 35) or who were self-employed (10 / 35).

DSS pension

Figure 4.11 shows the proportion of men receiving a Department of Social Security (DSS) pension. One man responded that he didn’t know whether or not he received a DSS pension. Thirty-percent (N = 170) of men in the cohort were receiving a pension from the DSS. No comparison data was available at the time this thesis was produced, for the overall male population, of the same age, in northern and western Adelaide from the 2001 Australian Census.

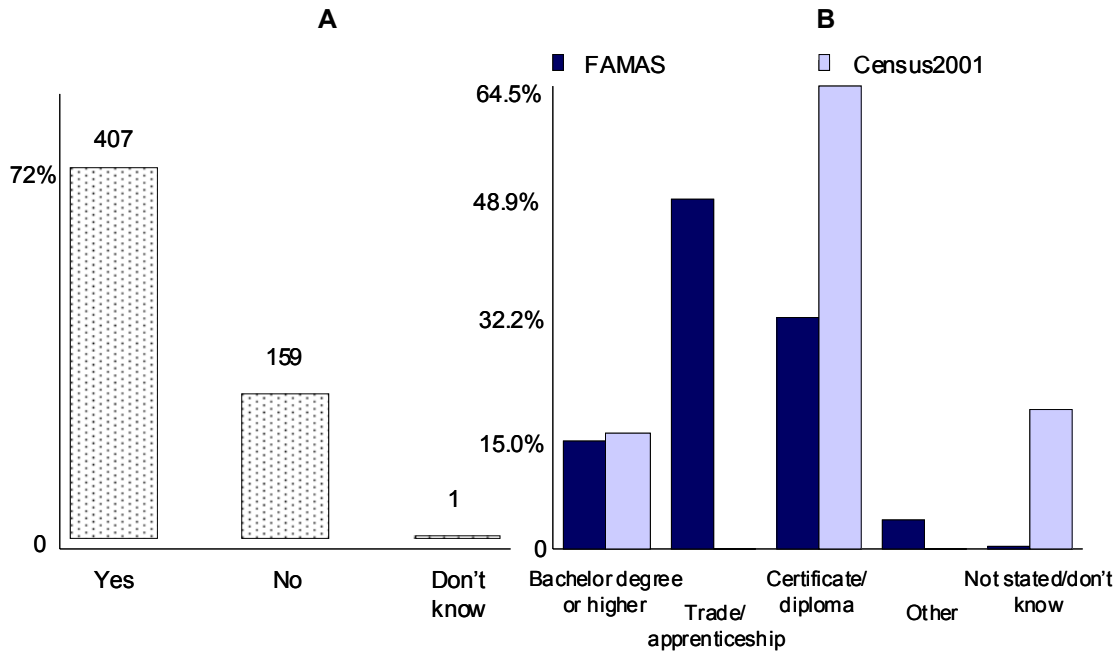

Figure 4.9 The proportions of men with and without post high-school qualifications (Panel A) in the FAMAS cohort and the distribution in the levels of highest post-high school qualification achieved (Panel B)

in the FAMAS cohort and in men with post high-school qualifications who were residing in the northern and western regions of Adelaide at the time of the 2001 Australian Census. Census data were not available for 'trade/apprenticeship' or 'other' classifications of highest qualification since leaving school

Highest qualification since leaving school (other)	Frequency
Accredited driving instructor	1
Builder	1
Cinematography	1
Communications operator	1
Fire Fighting	1
First Aid	1
Security and Investigation	1
Trade course	1
Bricklayer ticket	1
Job specific training	1
Land agent certificate	1
Master plumbers ticket	1
Photographer	1
Post Office certificates	1
Private pilot licence	1
Total	16

Table 4.8 Highest qualifications reported in the cohort since leaving school outside of Bachelor degrees or higher, trades/apprenticeships and certificates/diplomas.

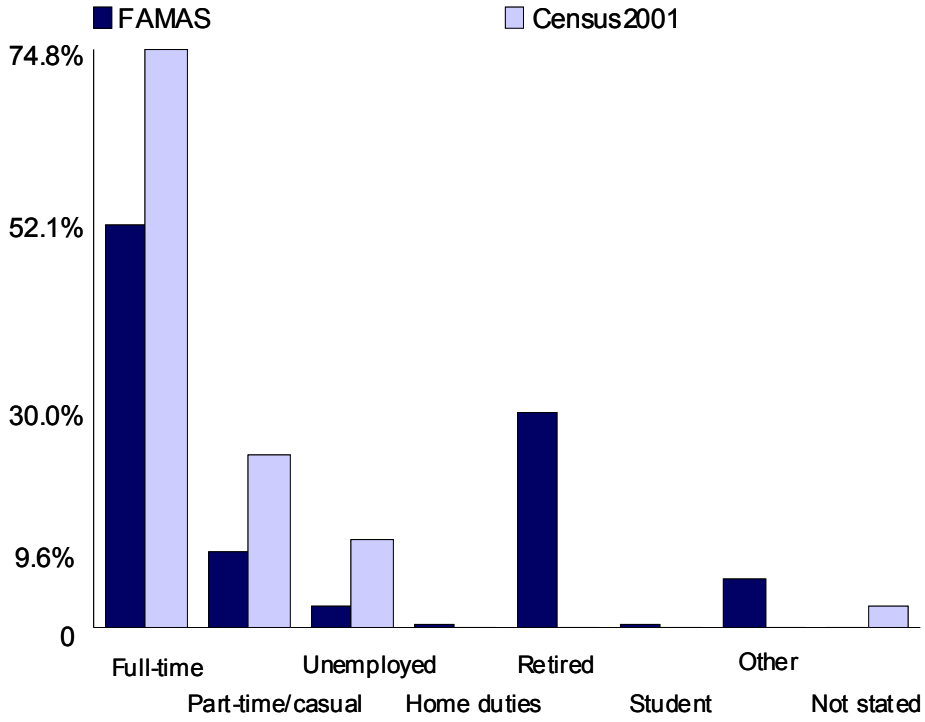

Figure 4.10 The variation in work status amongst FAMAS cohort

men aged 35 - 79 years, randomly recruited from the north and west suburbs of Adelaide and in the overall population of the northern and western regions of Adelaide. Overall population data is taken from the 2001 Australian Census for northern and western Adelaide. Census data were not available for 'home duties', 'retired', 'student', or 'other' classifications.

Work status (other)	Frequency
Disability pension	12
Self employed	10
TPI DVA pension	3
Pensioner	3
Carer	2
Contractor	1
Disability support pension	1
Sole parent	1
Recent redundancy (anticipate return to work)	1
Work injury (public liability pension)	1
Total	35

Table 4.9 The frequency of responses given for work status other than full-time, part-time/casual, unemployed, home-duties, retired and student.

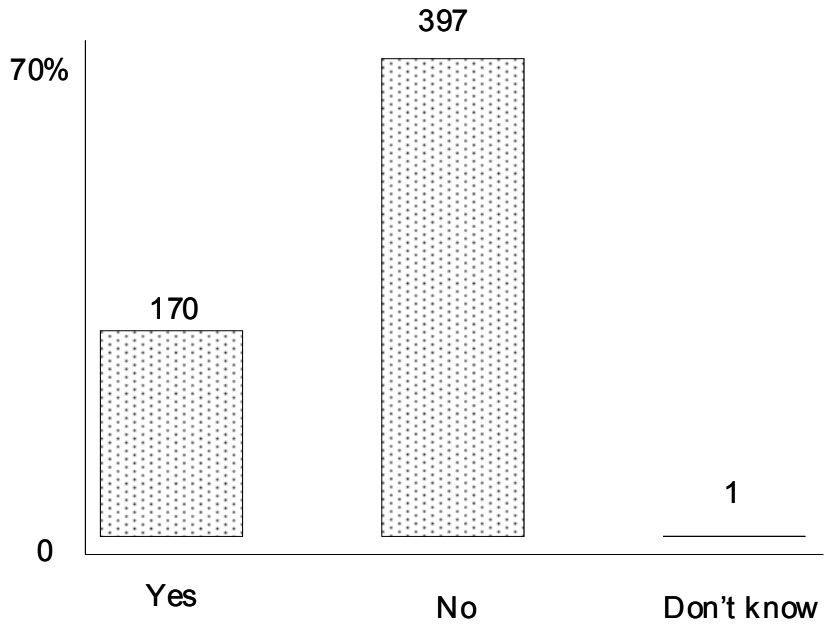

Figure 4.11 The proportions of men aged 35 – 79, randomly recruited from the north and west suburbs of Adelaide, who were receiving pensions from the Department of Social Security.

HEALTH INDICATORS

BLOOD PRESSURE

The mean SBP and DBP of the cohort by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth is described in Table 4.10. Both systolic and diastolic blood pressures increased with increasing age. Systolic but not diastolic pressure decreased as school-leaving age increased. Neither pressure was related to the level of post-school qualification achieved, but systolic and not diastolic pressure was lower in men from households with higher gross annual incomes, in men who worked, did not receive a DSS pension and who had never married.

Twenty-eight percent (N = 159) of men self reported having high blood pressure. Thirty-three percent (N = 189) of men had SBP > 140 mmHg and 30%(N = 168) had DBP > 90 mmHg; 20% (N = 114) had both pressures above the recommended level. Twenty-nine percent (N = 164) of men reported taking medication for high blood pressure. Figure 4.13 shows the proportion of diagnosed and undiagnosed hypertensive men with elevated blood pressure at the clinic visit, the proportion that were taking anti-hypertensive medication and the proportion that had taken their medication in the 24 hours prior to their visit.

	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	131.7	0.8	130.2	133.2	84.2	0.4	83.4	85.0
Age group: 35 - 44 years	121.9	1.1	119.7	124.0	81.7	0.7	80.4	83.1
45 - 54 years	131.0	1.1	128.9	133.2	86.2	0.7	84.7	87.6
55 - 64 years	136.0	1.2	133.6	138.4	86.0	0.6	84.8	87.3
65 - 74 years	143.8	2.0	139.8	147.8	84.3	1.1	82.1	86.6
75 - 79 years	144.3[a]	4.0	136.5	152.1	82.9[b]	1.8	79.4	86.5
School leaving age: 13 years or younger	138.6	3.4	131.9	145.3	83.3	1.9	79.5	87.0
14 years or younger	138.7	2.4	134.0	143.4	83.4	1.2	81.1	85.8

	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)			
15 years	131.7	1.7	128.4	135.1	84.4	0.9	82.7	86.1
16 years	132.9	1.6	129.9	136.0	85.3	0.8	83.6	87.0
17 years	127.6	1.3	125.1	130.1	83.5	0.8	82.1	85.0
18 years or older	128.8[c]	1.9	125.2	132.4	83.9[d]	1.0	81.9	85.8
Post school qualifications: None	132.5	1.4	129.7	135.4	84.4	0.7	83.0	85.8
Non bachelor qualification	132.1	1.0	130.2	134.1	84.2	0.5	83.1	85.2
Bachelor degree or higher	127.7[e]	1.9	124.0	131.3	83.9[f]	1.0	81.8	85.9
Annual gross household income: Up to $20,000	137.9	2.0	134.0	141.9	83.8	0.9	82.1	85.5
$20,001 - $40,000	133.8	1.4	131.0	136.6	84.3	0.8	82.7	85.9

	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)			
$40,001 - $60,000	128.4	1.3	125.8	131.1	84.6	0.8	83.1	86.1
$60,001 - $80,000	127.9	2.0	124.0	131.9	83.7	1.2	81.4	86.0
More than $80,000	129.2[g]	1.7	126.0	132.5	84.2[h]	0.9	82.4	86.0
Work status: Full time/part time/casual employment	127.5	0.8	125.9	129.1	83.8	0.5	82.8	84.8
Retired	142.7	1.5	139.8	145.7	84.8	0.8	83.2	86.4
Other(1)	128.8[i]	1.8	125.3	132.3	85.1[j]	1.0	83.2	87.0
DSS pension: Yes	139.1	1.6	136.0	142.1	83.9	0.8	82.3	85.4
No	128.6[k]	0.8	127.1	130.2	84.3[l]	0.5	83.5	85.2
Marital status: Married/living with a partner	131.6	0.8	130.0	133.2	84.1	0.4	83.3	85.0

	Systolic blood pressure (mmHg)				Diastolic blood pressure (mmHg)			
Separated/divorced	135.4	2.6	130.3	140.5	86.3	1.2	83.8	88.7
Widowed	138.1	5.8	126.8	149.4	82.6	2.4	77.8	87.4
Never married	125.6[m]	2.8	120.1	131.1	82.7[n]	1.6	79.6	85.8
Country of birth: Australia	131.5	0.9	129.8	133.3	84.3	0.5	83.4	85.2
United Kingdom(2)	131.2	2.0	127.3	135.0	83.8	0.9	82.0	85.7
Other	133.4[o]	2.1	129.3	137.4	84.3[p]	1.1	82.0	86.5

Table 4.10 Mean systolic and diastolic blood pressures in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a F(4,563) = 34.49, P < 0.0001; b F(4,563) = 7.01, P < 0.0001; c F(5,551) = 5.08, P = 0.0001; d F(5,551) = 0.64, P = 0.67; e F(2,565) = 2.54, P = 0.08; f F(2,565) = 0.09, P = 0.91; g F(5,588) = 5.72, P = 0.0002; h F(5,558) = 0.16, P = 0.957; i F(2,565) = 39.86, P < 0.0001; j F(2,565) = 1.01, P = 0.365; k F(1,566) = 35.86, P < 0.0001; l F(1,566) = 0.3, P = 0.584; m F(3,564) = 2.67, P = 0.047; n F(3,564) = 1.37, P = 0.252; o F(2,565) = 0.38, P = 0.682; p F(2,565) = 0.09, P = 0.915.

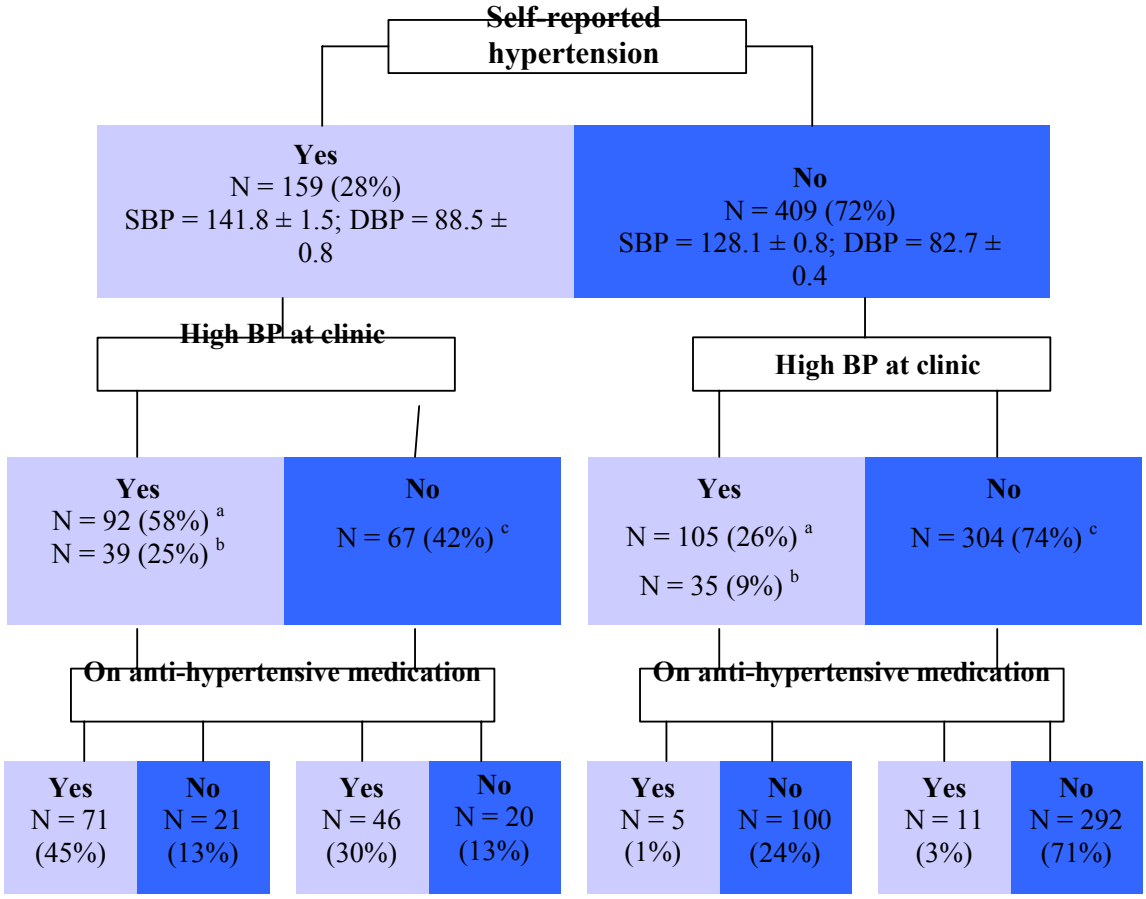

Figure 4.12 The proportions of self-reported hypertensive and non-hypertensive men with high blood pressure measured at clinic and the proportion that took anti-hypertensive medication.

aSBP > 140 or DBP > 90, bSBP > 140 & DBP > 90, cSBP ≤ 140 & DBP ≤ 90.

BODY MASS INDEX AND WAIST CIRCUMFERENCE

The mean BMI and waist circumference of the cohort by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth is described in Table 4.11. Thirty-five percent (N = 196) of men had a BMI of 30% or greater and another 47% (N = 268) had a BMI between 25% and 30%. Forty-eight percent (N = 270) of men had a waist circumference of 100 cm or greater. Both BMI and waist circumference were influenced by age and school-leaving age, post-school qualifications and work status influenced waist circumference but not BMI. Gross annual household income, marital status and country of birth did not influence either BMI or waist circumference but BMI and not waist circumference was greater in men not receiving a DSS pension.

	Body mass index (kg/m2)				Waist circumference (cm)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	28.70	0.19	28.32	29.08	99.87	0.53	98.82	100.92
Age group: 35 - 44 years	28.20	0.39	27.44	28.96	97.08	1.09	94.95	99.21
45 - 54 years	29.60	0.37	28.88	30.32	101.28	1.01	99.31	103.26
55 - 64 years	28.95	0.35	28.25	29.64	101.54	1.00	99.58	103.51
65 - 74 years	28.30	0.47	27.37	29.22	100.89	1.20	98.53	103.25
75 - 79 years	27.63[a]	0.56	26.52	28.74	100.86[b]	1.80	97.32	104.40
School leaving age: 13 years or younger	28.67	0.60	27.49	29.86	100.58	1.98	96.69	104.47
14 years or younger	28.03	0.46	27.11	28.94	100.47	1.34	97.83	103.11

	Body mass index (kg/m2)				Waist circumference (cm)			
	Mean	SE	95% CI		Mean	SE	95% CI	
15 years	29.70	0.45	28.80	30.59	102.40	1.15	100.13	104.67
16 years	28.78	0.38	28.04	29.52	100.37	1.01	98.38	102.36
17 years	27.97	0.39	27.20	28.74	97.06	1.05	94.99	99.13
18 years or older	28.77[c]	0.55	27.69	29.85	99.25[d]	1.74	95.83	102.68
Post school qualifications: None	29.14	0.37	28.40	29.87	101.38	1.02	99.38	103.38
Non bachelor qualification	28.62	0.24	28.14	29.10	99.74	0.69	98.39	101.09
Bachelor degree or higher	28.00[e]	0.56	26.90	29.10	96.73[f]	1.44	93.89	99.56
Annual gross household income: Up to $20,000	28.19	0.42	27.36	29.02	100.68	1.22	98.28	103.08

	Body mass index (kg/m2)				Waist circumference (cm)			
	Mean	SE	95% CI		Mean	SE	95% CI	
$20,001 - $40,000	28.35	0.39	27.59	29.11	99.39	1.10	97.23	101.54
$40,001 - $60,000	28.59	0.36	27.88	29.30	98.98	0.97	97.07	100.88
$60,001 - $80,000	29.78	0.65	28.50	31.06	101.19	1.82	97.61	104.77
More than $80,000	29.12[g]	0.39	28.36	29.88	99.71[h]	1.06	97.62	101.80
Work status: Full time/part time/casual employment	28.74	0.25	28.26	29.23	98.83	0.69	97.49	100.18
Retired	28.37	0.34	27.70	29.04	101.46	0.92	99.66	103.27
Other(1)	29.33[i]	0.64	28.07	30.59	102.24[j]	1.86	98.58	105.90
DSS pension: Yes	28.09	0.34	27.41	28.76	100.17	1.00	98.20	102.13

	Body mass index (kg/m2)				Waist circumference (cm)			
	Mean	SE	95% CI		Mean	SE	95% CI	
No	28.95[k]	0.23	28.49	29.41	99.76[l]	0.64	98.51	101.01
Marital status: Married/living with a partner	28.83	0.21	28.42	29.24	100.11	0.57	99.00	101.22
Separated/divorced	27.67	0.62	26.45	28.89	98.02	1.86	94.37	101.68
Widowed	28.28	0.86	26.58	29.98	101.74	3.60	94.66	108.82
Never married	28.87[m]	0.94	27.03	30.71	99.17[n]	2.74	93.79	104.55
Country of birth: Australia	28.97	0.24	28.50	29.44	100.71	0.65	99.43	101.98
United Kingdom(2)	27.83	0.43	26.99	28.67	97.65	1.18	95.34	99.97
Other	28.48[o]	0.47	27.56	29.41	98.68[p]	1.43	95.88	101.48

Table 4.11 Mean body mass index and waist circumference in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a F(4,563) = 3.11, P = 0.015; b F(4, 563) = 2.88, P = 0.022; c F(5,551) = 2.05, P = 0.071; d F(5,551) = 2.49, P = 0.03; e F(2,565) = 1.51, P = 0.22; f F(2,565) = 3.46, P = 0.032; g F(4,558) = 1.55, P = 0.187; h F(4,558) = 0.48, P = 0.749; i F(2,565) = 0.94, P = 0.39; j F(2,565) = 3.42, P = 0.033; k F(2,566) = 4.33, P = 0.038; l F(1,566) = 0.12, P = 0.731; m F(3,564) = 1.13, P = 0.337; n F(3,564) = 0.49, P = 0.689; o F(2,565) = 2.81, P = 0.061; p F(2,565) = 2.91, P = 0.055.

CIGARETTE SMOKING

The proportion of current, former and non-smokers in the cohort is described by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth in Table 4.12. Current and former smokers reported taking up daily smoking at average age of 17.1 ± 4.3 years and last quitting smoking at an average age of 38.9 ± 12.78 years. All demographic variables except post-school qualifications and country of birth had an influence on whether men were current, former or non-smokers.

PHYSICAL ACTIVITY

Participation

Sixty-one percent (341/568) of all men walked for sport, physical activity or recreation in the two weeks prior to their clinic visit, 49% participated in moderate intensity exercise and 23% in vigorous intensity exercise.

Time spent in physical activity

The mean time spent in physical activity per week (as number of sessions and minutes) of the physically active cohort, is summarised in Table 4.13 and Table 4.14, respectively by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth. As age increased, the mean number of weekly sessions of walking and moderate exercise, but not vigorous exercise, increased. School-leaving age influenced the number of weekly session of walking but not of moderate or vigorous exercise. Gross annual household income influenced the number of weekly walking and moderate but not vigorous exercise sessions and work status and receiving a DSS pension influenced only the number of walking sessions per week.

Post-school qualifications, marital status and country of birth had no effect on the number of sessions of walking, moderate or vigorous exercise sessions per week.

There was no effect of age on mean time per week spent walking or doing moderate exercise, however age did effect the time spent doing vigorous exercise. School-leaving age and post-school qualifications had no effect on the weekly time spent in any of the three intensities of exercise. Gross annual household income and work status had an effect on the weekly time spent walking but not doing moderate or vigorous exercise. Marital status influenced the weekly time spent walking and doing vigorous, but not moderate intensity exercise. Receiving a DSS pension and being born outside of Australia did not influence the weekly time spent in any of the three intensities of exercise.

Sufficient physical activity to confer a health benefit

The percentage of sedentary, insufficiently and sufficient active men is shown by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth in Table 4.15. Overall, 39% of men did a sufficient amount of physical activity per week to confer a health benefit. The proportion of men doing sufficient physical activity in the present cohort was between 26% and 33% lower than in men of the same age in the 1999 National Physical Activity Survey [185] and 13% lower than men and women aged 18 and over living in the same regions of Adelaide [204]. Post-school qualification, but not any of the other demographic variables had a significant effect on whether men were classified as sedentary, insufficiently or sufficiently active enough to confer a health benefit.

	Current smokers	Former smokers	Non-smokers	Design-based F	P
Overall	0.203	0.450	0.347		
Age group: 35 - 44 years	0.097	0.112	0.118		
45 - 54 years	0.053	0.116	0.100		
55 - 64 years	0.031	0.100	0.058		
65 - 74 years	0.017	0.084	0.054		
75 - 79 years	0.005	0.038	0.017	F(7.63, 4316.37) = 3.027	0.0026
School leaving age: 13 years or younger	0.002	0.018	0.012		
14 years or younger	0.025	0.068	0.027		
15 years	0.047	0.121	0.055		

	Current smokers	Former smokers	Non-smokers	Design-based F	P
16 years	0.052	0.109	0.094		
17 years	0.052	0.092	0.088		
18 years or older	0.028	0.043	0.069	F(9.77, 5431.43) = 2.12	0.021
Post school qualifications: None	0.071	0.135	0.081		
Non bachelor qualification	0.116	0.276	0.211		
Bachelor degree or higher	0.016	0.040	0.055	F(3.99, 2259.59) = 2.19	0.0682
Annual gross household income: Up to $20,000	0.058	0.101	0.045		
$20,001 - $40,000	0.031	0.134	0.083		
$40,001 - $60,000	0.068	0.103	0.083		

		Current smokers	Former smokers	Non-smokers	Design-based F	P
	$60,001 - $80,000	0.018	0.049	0.073		
	More than $80,000	0.025	0.063	0.065	F(7.97, 4471.39) = 3.68	0.0003
Work status:	Full time/part time/casual employment	0.130	0.269	0.234		
	Retired	0.028	0.151	0.029		
	Other(1)	0.045	0.031	0.021	F(3.99, 2259.91) = 8.22	< 0.0001
DSS pension:	Yes	0.065	0.155	0.074		
	No	0.138	0.295	0.273	F(2.00, 1128.01) = 4.24	0.0147
Marital status:	Married/living with a partner	0.131	0.387	0.288		
	Separated/divorced	0.042	0.036	0.024		

	Current smokers	Former smokers	Non-smokers	Design-based F	P
Widowed	0.008	0.010	0.007		
Never married	0.022	0.018	0.028	F(5.88, 3328.21) = 3.83	0.0009
Country of birth: Australia	0.145	0.290	0.244		
United Kingdom(2)	0.034	0.090	0.053		
Other(3)	0.024	0.070	0.049	F(3.99, 2259.65) = 0.65	0.626

Table 4.12 The proportion of current, former and non-smokers in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands.

	Number of walking sessions per week				Number of moderate intensity exercise				Number of vigorous intensity exercise			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall	3.2	0.1	3.0	3.5	2.9	0.2	2.6	3.2	2.0	0.2	1.7	2.4
Age group: 35 - 44 years	2.5	0.2	2.1	3.0	2.4	0.2	1.9	2.8	1.9	0.3	1.4	2.5
45 - 54 years	3.2	0.3	2.7	3.8	2.8	0.4	2.1	3.5	2.5	0.4	1.7	3.3
55 - 64 years	3.4	0.2	3.0	3.9	3.2	0.3	2.7	3.7	1.7	0.3	1.0	2.3
65 - 74 years	4.0	0.4	3.3	4.8	3.5	0.4	2.7	4.3	2.0	0.6	0.8	3.3
75 - 79 years	4.1[a]	0.6	2.8	5.3	3.5[b]	0.8	1.8	5.1	1.4[c]	0.3	0.9	1.9
School leaving age: 13 years or younger	5.0	0.9	3.3	6.8	3.5	0.7	2.1	4.9	2.1	0.3	1.5	2.7
14 years or younger	4.6	0.4	3.8	5.4	3.9	0.6	2.7	5.2	3.3	1.1	1.0	5.6
15 years	3.3	0.2	2.8	3.7	2.8	0.4	2.1	3.6	2.0	0.5	1.0	3.0
16 years	2.8	0.3	2.3	3.3	3.0	0.4	2.2	3.7	1.9	0.4	1.2	2.7
17 years	2.8	0.3	2.2	3.4	2.5	0.2	2.1	3.0	2.0	0.2	1.6	2.5
18 years or older	3.3[d]	0.4	2.5	4.1	2.5[e]	0.3	1.9	3.1	1.7[f]	0.2	1.3	2.2

	Number of walking sessions per week				Number of moderate intensity exercise				Number of vigorous intensity exercise			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Post school qualifications: None	3.8	0.3	3.2	4.5	2.8	0.3	2.2	3.4	2.4	0.5	1.4	3.3
Non bachelor qualification	3.1	0.2	2.7	3.4	3.0	0.2	2.5	3.4	2.1	0.2	1.6	2.5
Bachelor degree or higher	3.0[g]	0.3	2.4	3.6	2.6[h]	0.3	2.0	3.2	1.6[i]	0.3	1.0	2.3
Annual gross household income: Up to $20,000	4.5	0.3	3.8	5.1	3.5	0.4	2.8	4.2	2.2	0.6	1.0	3.4
$20,001 - $40,000	3.1	0.2	2.6	3.6	3.4	0.3	2.7	4.0	2.2	0.4	1.3	3.1
$40,001 - $60,000	2.8	0.2	2.3	3.3	2.8	0.4	2.0	3.6	2.3	0.4	1.5	3.1
$60,001 - $80,000	3.1	0.5	2.1	4.1	1.9	0.2	1.4	2.3	1.8	0.2	1.3	2.3
More than $80,000	2.8[j]	0.2	2.3	3.2	2.6[k]	0.2	2.1	3.0	1.6[l]	0.2	1.2	2.1
Work status: Full time/part time/casual employment	2.9	0.2	2.6	3.2	2.6	0.2	2.3	3.0	2.1	0.2	1.6	2.5
Retired	4.1	0.3	3.6	4.6	3.4	0.3	2.8	4.0	1.8	0.3	1.1	2.4
Other(1)	2.8[m]	0.5	1.8	3.7	2.7[n]	0.4	2.0	3.5	2.2[o]	0.6	0.9	3.4
DSS pension: Yes	4.0	0.3	3.4	4.5	3.3	0.3	2.7	3.9	1.7	0.4	1.0	2.5

	Number of walking sessions per week				Number of moderate intensity exercise				Number of vigorous intensity exercise			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
No	2.9[p]	0.2	2.6	3.2	2.7[q]	0.2	2.3	3.1	2.1[r]	0.2	1.7	2.5
Marital status: Married/living with a partner	3.1	0.1	2.8	3.4	2.9	0.2	2.5	3.2	2.0	0.2	1.6	2.4
Separated/divorced	4.1	0.8	2.5	5.7	2.5	0.3	1.9	3.1	1.6	0.4	0.9	2.4
Widowed	3.5	1.1	1.4	5.5	4.7	2.4	0.1	9.3	5.6	3.2	-0.6	11.9
Never married	3.9[s]	0.6	2.6	5.1	2.5[t]	0.6	1.4	3.7	1.9[u]	0.4	1.1	2.8
Country of birth: Australia	3.1	0.2	2.8	3.5	2.9	0.2	2.5	3.3	2.2	0.2	1.7	2.6
United Kingdom(2)	3.1	0.3	2.5	3.7	2.7	0.3	2.1	3.3	1.6	0.4	0.8	2.4
Other(3)	4.0[v]	0.5	3.0	5.0	2.7[w]	0.4	2.0	3.4	1.8[x]	0.4	0.9	2.6

Table 4.13 Mean number of weekly walking, moderate intensity exercise and vigorous intensity exercise sessions in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a F(4,325) = 4.28, P = 0.002; b F(4,246) = 2.42, P = 0.049; c F(4,108) = 1.41, P = 0.234; d F(5,319) = 4.06, P = 0.0014; e F(5,242) = 1.34, P = 0.247; f F(5,105) = 0.49, P = 0.78; g F(2,327) = 2.77, P = 0.064; h F(2,248) = 0.62, P = 0.54; i F(2,110) = 1.01, P = 0.368; j F(4,323) = 5.03, P = 0.0006; k F(4,245) = 5.88, P = 0.0003; l F(4,108) = 0.72, P = 0.582; m F(2,327) = 8.26, P = 0.0003; n F(2,248) = 2.28, P = 0.104; o F(2,110) = 0.3, P = 0.742; p F(1,328) = 11.03, P = 0.001; q F(1,249) = 2.81, P = 0.095; r F(1,111) = 0.66, P = 0.417; s F(3,326) = 0.88, P = 0.454; t F(3,247) = 0.61, P = 0.61; u F(3,109) = 0.76, P = 0.519; v F(2,327) = 1.41, P = 0.245; w F(2,248) = 0.28, P = 0.753; x F(2,110) = 0.85, P = 0.432.

	Minutes of walking per week				Minutes of moderate intensity				Minutes of vigorous intensity			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall	203.7	15.8	172.5	234.9	201.4	21.5	159.1	243.7	133.5	25.6	82.5	184.5
Age group: 35 - 44 years	171.7	34.0	104.9	238.6	231.2	56.6	119.6	342.7	126.8	44.2	39.0	214.6
45 - 54 years	212.2	24.9	163.2	261.2	159.7	23.5	113.3	206.2	148.2	40.1	68.6	227.9
55 - 64 years	214.4	33.8	147.8	281.0	202.6	29.7	144.1	261.0	150.5	47.2	56.5	244.4
65 - 74 years	232.1	33.1	166.8	297.3	211.4	33.0	146.4	276.3	118.7	21.4	76.2	161.1
75 - 79 years	232.4[a]	50.0	134.0	330.9	195.4[b]	34.9	126.7	264.2	15.0[c]	0.0	15.0	15.0
School leaving age: 13 years or younger	362.5	117.2	131.7	593.2	272.5	113.6	48.4	496.7	144.1	5.8	132.5	155.8
14 years or younger	237.0	35.9	166.2	307.7	231.2	45.1	142.1	320.2	346.3	160.2	27.5	665.0
15 years	209.1	23.7	162.4	255.8	232.4	74.7	85.0	379.8	186.7	114.8	-41.8	415.2
16 years	167.7	22.3	123.7	211.6	183.7	27.4	129.5	237.8	91.5	20.9	50.0	133.1
17 years	168.1	20.3	128.1	208.1	176.0	29.6	117.7	234.3	111.6	32.7	46.6	176.6
18 years or older	230.1[d]	75.5	81.4	378.8	202.4[e]	84.5	35.7	369.1	124.2[f]	53.3	18.3	230.2

	Minutes of walking per week				Minutes of moderate intensity				Minutes of vigorous intensity			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Post school qualifications: None	220.5	22.7	175.9	265.1	233.6	61.1	113.2	354.0	204.8	109.3	-12.7	422.2
Non bachelor qualification	209.4	24.1	162.0	256.8	191.7	24.7	143.0	240.3	133.1	27.6	78.2	188.0
Bachelor degree or higher	152.1[g]	19.9	113.0	191.2	200.2[h]	46.5	108.6	291.8	85.0[i]	17.3	50.6	119.5
Annual gross household income: Up to $20,000	229.2	26.0	178.0	280.4	193.0	27.4	138.9	247.1	190.6	83.3	25.0	356.2
$20,001 - $40,000	205.2	32.7	140.8	269.6	232.6	40.4	153.0	312.3	107.1	29.0	49.5	164.7
$40,001 - $60,000	149.1	15.0	119.6	178.5	205.5	59.5	88.1	322.9	152.8	67.7	18.1	287.5
$60,001 - $80,000	176.7	27.0	123.6	229.8	132.3	21.0	90.8	173.7	81.9	13.2	55.7	108.1
More than $80,000	267.5[j]	65.4	138.8	396.2	219.9[k]	64.2	93.3	346.4	125.8[l]	42.8	40.7	210.9
Work status: Full time/part time/casual employment	203.9	22.7	159.2	248.5	199.1	31.2	137.6	260.6	120.8	31.1	59.0	182.7
Retired	227.2	22.6	182.8	271.7	191.9	21.2	150.1	233.7	154.8	60.1	35.3	274.4
Other(1)	139.4[m]	23.3	93.6	185.2	243.9[n]	71.1	103.6	384.2	186.6[o]	69.2	48.9	324.4
DSS pension: Yes	222.0	21.2	180.1	263.8	191.9	20.5	151.5	232.3	179.4	66.7	46.6	312.1

	Minutes of walking per week				Minutes of moderate intensity				Minutes of vigorous intensity			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
No	195.7[p]	20.7	154.8	236.5	205.4[q]	29.2	147.9	263.0	124.2[r]	28.0	68.4	179.9
Marital status: Married/living with a partner	203.6	18.3	167.5	239.7	203.7	24.6	155.2	252.2	149.2	31.4	86.8	211.6
Separated/divorced	227.2	29.4	169.4	285.0	135.6	19.6	96.9	174.2	62.0	15.3	31.5	92.4
Widowed	106.6	33.7	40.1	173.0	209.9	44.2	122.9	297.0	60.0	0.0	60.0	60.0
Never married	206.5[s]	43.9	120.0	293.0	297.6[t]	144.1	13.4	581.7	71.8[u]	21.3	29.3	114.2
Country of birth: Australia	198.4	20.2	158.6	238.2	209.8	28.6	153.4	266.2	145.4	35.1	75.5	215.2
United Kingdom(2)	210.7	32.5	146.8	274.6	199.1	38.8	122.6	275.7	88.3	26.8	34.9	141.7
Other	221.0[v]	38.7	144.8	297.2	160.8[w]	32.9	95.8	225.7	150.7[x]	71.3	8.9	292.6

Table 4.14 Mean number of weekly minutes of walking, moderate intensity exercise and vigorous intensity exercise in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a F(4,254) = 0.48, P = 0.749; b F(4,196) = 0.69, P = 0.598; c F(4,80) = 11.98, P < 0.0001; d F(5,249) = 1.36, P = 0.239; e F(5,192) = 0.38, P = 0.862; f F(5,77) = 1.61, P = 0.167; g F(2,256) = 3.03, P = 0.05; h F(2,198) = 0.2, P = 0.817; i F(2,82) = 1.58, P = 0.213; j F(4,253) = 2.52, P = 0.042; k F(4,195) = 1.79, P = 0.132; l F(4,80) = 0.8, P = 0.48; m F(2,256) = 3.90, = 0.0215; n F(2,198) = 0.25, P = 0.781; o F(2,82) = 0.43, P = 0.653; p F(1,257) = 0.78, P = 0.377; q F(1,199) = 0.14, P = 0.704; r F(1,83) = 0.57, P = 0.451; s F(3,255) = 2.76, P = 0.043; t F(3,197) = 2.17, P = 0.093; u F(3,81) = 2.74, P = 0.049; v F(2,256) = 0.15, P = 0.857; w F(2,198) = 0.66, P = 0.52; x F(2,82) = 0.98, P = 0.381.

	Sedentary	Insufficient PA	Sufficient† PA	Design-based F	P
Overall	0.442	0.169	0.389		
Age group: 35 - 44 years	0.148	0.055	0.124		
45 - 54 years	0.115	0.050	0.105		
55 - 64 years	0.081	0.030	0.078		
65 - 74 years	0.062	0.023	0.070		
75 - 79 years	0.033	0.005	0.022	F(7.63, 4319.86) = 0.50	0.5
School leaving age: 13 years or younger	0.011	0.002	0.018		
14 years or younger	0.054	0.008	0.057		
15 years	0.112	0.034	0.076		
16 years	0.099	0.054	0.101		
17 years	0.094	0.045	0.094		
18 years or older	0.068	0.020	0.053	F(9.77, 5422.15) = 1.35	0.2
Post school qualifications: None	0.147	0.040	0.100		

	Sedentary	Insufficient PA	Sufficient† PA	Design-based F	P
Non bachelor qualification	0.255	0.113	0.234		
Bachelor degree or higher	0.037	0.010	0.065	F(3.99, 2446.49) = 3.32	0.01*
Annual gross household income: Up to $20,000	0.083	0.026	0.094		
$20,001 - $40,000	0.118	0.032	0.099		
$40,001 - $60,000	0.112	0.057	0.086		
$60,001 - $80,000	0.066	0.019	0.055		
More than $80,000	0.058	0.029	0.066	F(7.97, 4470.17) = 1.12	0.35
Work status: Full time/part time/casual employment	0.277	0.120	0.236		
Retired	0.117	0.027	0.126		
Other(1)	0.044	0.016	0.037	F(3.97, 2244.20) = 1.80	0.13
DSS pension: Yes	0.122	0.038	0.134		
No	0.316	0.124	0.265	F(3.82, 2162.19) = 1.16	0.32
Marital status: Married/living with a partner	0.346	0.137	0.323		

	Sedentary	Insufficient PA	Sufficient† PA	Design-based F	P
Separated/divorced	0.048	0.012	0.041		
Widowed	0.009	0.006	0.010		
Never married	0.036	0.007	0.025	F(5.91, 3345.94) = 0.46	0.84
Country of birth: Australia	0.303	0.105	0.271		
United Kingdom(2)	0.072	0.028	0.077		
Other	0.064	0.029	0.051	F(3.99, 2256.42) = 0.40	0.81

Table 4.15 The proportion of men classified as sedentary, insufficiently active and sufficiently active enough to confer a health benefit in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth.

†Sufficient physical activity is 150 minutes of activity per week calculated as the sum of walking, moderate and vigorous physical activity (weighted by two). (1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands.

NUTRIENT INTAKE

The mean daily intakes of energy, fat and protein are shown in Table 4.16 and , carbohydrate, alcohol and calcium intakes of the cohort in Table 4.17 by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth are summarised in Table 4.16. Energy, fat, protein, carbohydrate and calcium intakes were influenced by age, work status and receiving a DSS pension. Energy, fat, carbohydrate and calcium intake were influenced by country of birth. Alcohol intake was influenced by work status and receiving a DSS pension.

Distribution of total energy intake

The contribution of the macronutrients to total daily energy intake, by age, is shown in Figure 4.13. Overall, in terms of energy intake, dietary fat equated to approximately 37% of the total daily energy intake. Saturated, polyunsaturated and monounsaturated fats, on average, constituted 40%, 16% and 36% of total dietary fat intake, respectively. The remaining 8% of dietary fat intake was from non-classified fat sources. Protein contributed to approximately 20% and carbohydrate to 42% of total daily energy intake. Of all participants, less than 1% (40 / 568) was a non-drinker. The mean daily intake of alcohol approximated 2 standard drinks per day. In terms of energy intake, on average, alcohol constituted approximately 6% of the total daily energy intake.

	Energy (KJ/day)				Fat (g/day)				Protein (g/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall	9138.99	140.08	8863.84	9414.13	91.69	1.65	88.46	94.93	105.20	1.79	101.68	108.72
Age group: 35 - 44 years	10007.54	286.37	9445.06	10570.02	102.09	3.39	95.43	108.75	114.25	3.59	107.20	121.30
45 - 54 years	9244.79	242.45	8768.57	9721.00	93.70	2.81	88.18	99.22	109.04	3.48	102.20	115.88
55 - 64 years	8845.49	275.87	8303.63	9387.35	88.41	3.36	81.81	95.01	102.45	3.47	95.62	109.27
65 - 74 years	7872.61	262.64	7356.74	8388.48	76.23	2.96	70.42	82.04	88.69	2.90	82.99	94.38
75 - 79 years	8116.80[a]	442.17	7248.29	8985.30	76.18[b]	4.85	66.66	85.70	89.80[c]	5.26	79.47	100.12
School leaving age: 13 years or younger	8069.81	708.11	6678.92	9460.71	74.56	7.67	59.49	89.62	93.15	8.14	77.16	109.14
14 years or younger	8690.44	361.69	7979.99	9400.89	88.46	4.43	79.75	97.16	101.18	4.79	91.78	110.59
15 years	9161.91	253.64	8663.69	9660.13	92.77	2.90	87.08	98.47	105.19	3.61	98.09	112.28
16 years	9297.88	316.51	8676.18	9919.58	93.39	3.64	86.24	100.55	105.31	3.82	97.80	112.81
17 years	9082.05	286.91	8518.49	9645.61	90.22	3.36	83.63	96.81	103.90	3.60	96.83	110.96
18 years or older	9576.48[d]	410.18	8770.78	10382.19	97.44[e]	4.86	87.89	106.99	114.07[f]	5.30	103.66	124.49

	Energy (KJ/day)				Fat (g/day)				Protein (g/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Post school qualifications: None	9332.86	270.23	8802.08	9863.64	94.77	3.20	88.48	101.06	107.51	3.64	100.36	114.67
Non bachelor qualification	9043.56	179.57	8690.85	9396.26	90.73	2.11	86.58	94.88	104.00	2.22	99.63	108.37
Bachelor degree or higher	9157.21[g]	403.50	8364.67	9949.75	88.98[h]	4.58	79.97	97.98	105.73[i]	5.22	95.47	116.00
Annual gross household income: Up to $20,000	8710.81	294.66	8132.05	9289.57	86.52	3.40	79.86	93.19	100.71	3.86	93.12	108.30
$20,001 - $40,000	8930.92	278.62	8383.65	9478.18	87.77	3.30	81.28	94.26	100.96	3.63	93.83	108.08
$40,001 - $60,000	9246.61	287.31	8682.27	9810.95	94.16	3.43	87.41	100.90	104.93	3.40	98.26	111.60
$60,001 - $80,000	9793.27	428.95	8950.72	10635.82	98.95	4.89	89.34	108.56	114.24	5.65	103.15	125.34
More than $80,000	9133.06[j]	300.12	8543.57	9722.56	93.19[k]	3.58	86.16	100.22	108.50[l]	3.95	100.75	116.26
Work status: Full time/part time/casual employment	9500.17	185.70	9135.43	9864.91	96.18	2.19	91.89	100.47	109.51	2.36	104.87	114.15
Retired	7984.89	204.92	7582.38	8387.39	77.12	2.36	72.48	81.76	91.89	2.65	86.68	97.10
Other(1)	9998.49[m]	399.00	9214.79	10782.19	103.05[n]	4.59	94.03	112.07	114.16[o]	5.53	103.29	125.02
DSS pension: Yes	8420.60	231.30	7966.29	8874.90	84.08	2.76	78.65	89.51	95.65	2.91	89.94	101.36

	Energy (KJ/day)				Fat (g/day)				Protein (g/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
No	9439.32[p]	170.61	9104.21	9774.43	94.89[q]	2.01	90.94	98.83	109.20[r]	2.19	104.90	113.51
Marital status: Married/living with a partner	9261.53	158.54	8950.14	9572.93	92.73	1.86	89.07	96.39	106.50	2.02	102.53	110.46
Separated/divorced	8597.08	379.38	7851.90	9342.25	83.83	4.38	75.23	92.43	99.56	5.38	88.99	110.13
Widowed	8245.02	743.33	6785.00	9705.03	85.47	8.64	68.51	102.43	95.90	7.88	80.41	111.39
Never married	8813.86[s]	519.36	7793.76	9833.96	93.40[t]	6.43	80.78	106.03	101.54[u]	6.52	88.73	114.35
Country of birth: Australia	9239.60	173.97	8897.89	9581.31	93.75	2.08	89.67	97.82	106.14	2.23	101.77	110.51
United Kingdom(2)	9410.87	305.30	8811.22	10010.53	93.01	3.29	86.55	99.46	106.28	4.13	98.16	114.40
Other	8330.46[v]	339.08	7664.45	8996.47	80.41[w]	3.99	72.58	88.24	99.43[x]	4.14	91.29	107.56

Table 4.16 Daily intakes of energy, fat and protein in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,563) = 8.76$, $P < 0.0001$; b $F(4,563) = 10.69$, $P < 0.0001$; c $F(4,563) = 10.32$, $P < 0.0001$; d $F(5,551) = 1.03$, $P = 0.399$; e $F(5,551) = 1.48$, $P = 0.195$; f $F(5,551) = 1.15$, $P = 0.334$; g $F(2,565) = 0.4$, $P = 0.673$; h $F(2,565) = 0.73$, $P = 0.48$; i $F(2,565) = 0.35$, $P = 0.707$; j $F(4,558) = 1.23$, $P = 0.297$; k $F(4,558) = 1.62$, $P = 0.168$; l $F(4,558) = 1.46$, $P = 0.212$; m $F(2,565) = 18.81$, $P < 0.0001$; n $F(2,565) = 22.57$, $P < 0.0001$; o $F(2,565) = 14.49$, $P < 0.0001$; p $F(1,566) = 12.46$, $P = 0.0004$; q $F(1,566) = 9.94$, $P = 0.0017$; r $F(1,566) = 13.78$, $P = 0.0002$; s $F(3,564) = 1.47$, $P = 0.223$; t $F(3,564) = 1.35$, $P = 0.259$; u $F(3,564) = 1.06$, $P = 0.368$; v $F(2,565) = 3.41$, $P = 0.034$; w $F(2,565) = 4.57$, $P = 0.011$; x $F(2,565) = 1.09$, $P = 0.338$.

	Carbohydrate (g/day)				Alcohol (g/day)				Calcium (mg/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall	237.18	3.73	229.87	244.50	20.39	0.99	18.45	22.33	947.59	16.76	914.67	980.51
Age group: 35 - 44 years	256.89	7.76	241.65	272.13	22.80	2.13	18.61	26.99	1041.67	37.61	967.80	1115.54
45 - 54 years	235.16	6.22	222.95	247.38	21.92	1.80	18.38	25.46	933.99	26.88	881.18	986.79
55 - 64 years	229.61	7.05	215.77	243.45	19.22	1.72	15.84	22.61	866.23	25.65	815.85	916.61
65 - 74 years	212.67	7.79	197.36	227.97	15.21	2.10	11.09	19.33	883.81	32.36	820.26	947.36
75 - 79 years	225.97[a]	13.70	199.05	252.88	17.37[b]	3.28	10.92	23.82	917.73[c]	57.63	804.53	1030.93
School leaving age: 13 years or younger	223.46	21.66	180.92	266.01	19.90	5.39	9.31	30.48	809.03	79.41	653.06	965.00
14 years or younger	221.89	9.46	203.32	240.47	16.03	2.09	11.94	20.13	874.07	35.37	804.59	943.56
15 years	236.36	7.22	222.17	250.55	16.77	1.77	13.29	20.25	945.89	36.58	874.05	1017.74
16 years	242.88	8.34	226.50	259.26	24.22	2.31	19.68	28.76	993.01	42.27	909.97	1076.04
17 years	238.23	7.69	223.12	253.34	21.48	2.15	17.25	25.72	949.21	27.17	895.85	1002.58
18 years or older	241.17[d]	10.40	220.73	261.60	22.36[e]	2.75	16.96	27.75	969.59[f]	44.25	882.66	1056.52

	Carbohydrate (g/day)				Alcohol (g/day)				Calcium (mg/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Post school qualifications: None	239.74	6.89	226.22	253.27	20.04	2.12	15.87	24.21	955.18	32.18	891.98	1018.38
Non bachelor qualification	234.86	4.85	225.34	244.38	20.85	1.23	18.44	23.27	938.10	22.24	894.41	981.78
Bachelor degree or higher	243.18[g]	11.03	221.52	264.84	18.77[h]	2.30	14.26	23.29	979.47[i]	38.22	904.40	1054.54
Annual gross household income: Up to	227.65	7.93	212.07	243.23	16.43	2.06	12.38	20.48	909.15	39.82	830.93	987.37
$20,001 - $40,000	237.87	7.48	223.17	252.57	19.91	2.27	15.46	24.36	938.44	29.96	879.58	997.30
$40,001 - $60,000	238.46	7.70	223.33	253.59	21.69	2.08	17.61	25.77	950.77	33.70	884.58	1016.95
$60,001 - $80,000	250.86	10.83	229.60	272.13	19.14	2.12	14.97	23.30	1046.49	57.28	933.99	1159.00
More than $80,000	229.97[j]	8.25	213.76	246.18	25.42[k]	2.29	20.92	29.92	917.60[l]	29.73	859.20	976.00
Work status: Full time/part time/casual	244.42	4.91	234.77	254.06	21.37	1.22	18.96	23.78	970.10	22.69	925.54	1014.67
Retired	213.99	6.07	202.07	225.90	16.40	1.59	13.29	19.52	865.70	24.51	817.57	913.83
Other(1)	254.64[m]	10.45	234.12	275.16	25.11[n]	4.37	16.52	33.69	1028.88[o]	50.06	930.54	1127.21
DSS pension: Yes	220.93	6.09	208.98	232.89	16.73	1.73	13.34	20.12	886.14	25.74	835.59	936.69

	Carbohydrate (g/day)				Alcohol (g/day)				Calcium (mg/day)			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
No	243.94[p]	4.56	234.97	252.91	21.94[q]	1.20	19.58	24.30	973.46[r]	20.95	932.31	1014.61
Marital status: Married/living with a partner	240.92	4.20	232.67	249.16	19.31	1.06	17.23	21.39	948.68	19.09	911.18	986.18
Separated/divorced	228.07	9.75	208.92	247.22	21.72	3.52	14.81	28.63	949.39	51.18	848.86	1049.93
Widowed	206.89	21.16	165.34	248.45	24.43	5.69	13.26	35.60	904.09	86.23	734.72	1073.46
Never married	217.31[s]	14.20	189.41	245.21	29.74[t]	4.70	20.50	38.98	947.56[u]	52.15	845.13	1049.98
Country of birth: Australia	237.69	4.53	228.79	246.59	21.65	1.22	19.25	24.06	959.52	20.49	919.28	999.76
United Kingdom(2)	249.84	9.02	232.13	267.56	17.58	2.47	12.72	22.44	1004.39	41.43	923.02	1085.76
Other(3)	219.24[v]	8.84	201.88	236.60	17.88[w]	2.18	13.60	22.16	821.53[x]	34.89	753.01	890.05

Table 4.17 Daily intakes of carbohydrate, alcohol and calcium in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a F(4,563) = 4.17, P = 0.0025; b F(4,563) = 2.18, P = 0.070; c F(4,563) = 4.06, P = 0.003; d F(5,551) = 0.71, P = 0.619; e F(5,551) = 2.22, P = 0.051; f F(5,551) = 1.65, P = 0.146; g F(2,565) = 0.33, P = 0.719; h F(2,565) = 0.33, P = 0.721; i F(2,565) = 0.45, P = 0.637; j F(4,558) = 0.91, P = 0.455; k F(4,558) = 2.30, P = 0.057; l F(4,558) = 1.17, P = 0.322; m F(2,565 = 9.57, P = 0.0001; n F(2,565) = 3.83, P = 0.022; o F(2,565) = 6.92, P = 0.0011; p F(1,566) =9.08, P = 0.0027; q F(1,566) = 6.11, P = 0.0137; r F(1,566) = 6.88, P = 0.009; s F(3,564) = 1.88, P = 0.133; t F(3,564) = 1.84, P = 0.139; u F(3,564) = 0.09, P = 0.968; v F(2,565) = 3.03, P = 0.049; w F(2,565) = 1.82, P = 0.163; x F(2,565) = 7.39, P = 0.0007.

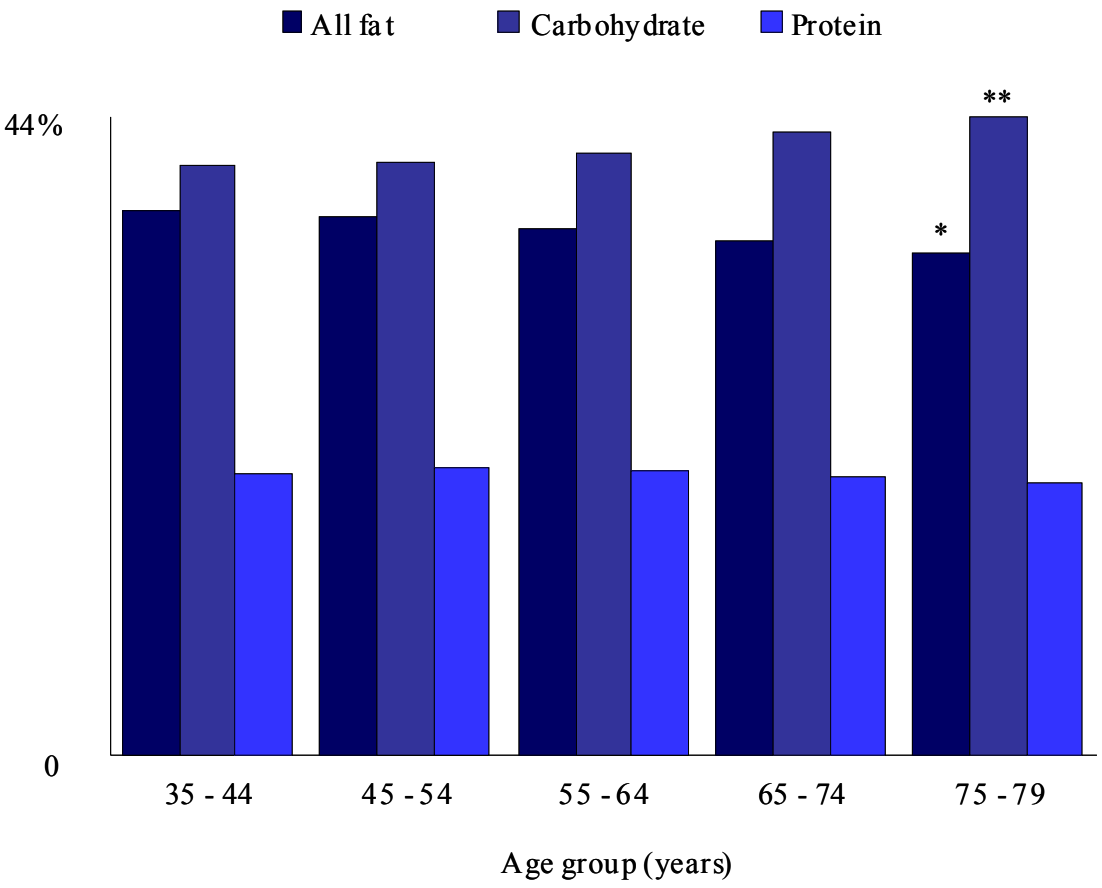

Figure 4.13 The contribution of fat, carbohydrate and protein to total daily energy intake, by age group.

As age increased the proportion of daily energy intake from fat declined (*F(4,563) = 2.65, P = 0.032) and that from carbohydrate increased (**F(4,563) = 3.92, P = 0.004), whilst the contribution of protein remained stable (F(4,563) = 0.99, P = 0.42).

PHYSICAL AND MENTAL HEALTH

The mean SF-36 domain scores of the cohort by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth are summarised in Tables 4.17 – 4.19. Age-specific normative values for the male South Australian population, determined by the South Australian Health Omnibus Survey [205] are included in these tables.

Physical functioning (PF)

Except for men aged between 75 and 79 years, scores on the PF domain were significantly lower in each of the 10-year age groups in the current cohort than in the Health Omnibus Survey (P = 0.02 or lower). PF was influenced by all demographic variables except for country of birth.

Role physical (RP)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly higher mean RP score in 55 – 64 year olds (P = 0.035). RP was influenced by all demographic variables except for country of birth.

Bodily pain (BP)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly lower mean score on the BP domain in men aged 65 – 74 (P = 0.009). All demographic variables, except marital status and country of birth, influenced BP domain scores.

General health (GH)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly lower mean GH domain score in the 45 – 54 year age group (P = 0.013). Scores on this domain were affected by school-leaving age, gross annual household income, work status, marital status and receiving a DSS pension.

Vitality (VT)

VT scores in the 45 – 54 year age group were lower in the current cohort than in South Australian men included in the Health Omnibus Survey (P = 0.0495). VT scores were affected by school-leaving age, gross annual household income, work status and receiving a DSS pension.

Role emotional (RE)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly higher mean RE score (P = 0.026). RE scores were affected by school-leaving age, work status, receiving a DSS pension and country of birth.

Mental health (MH)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly lower MH score (P = 0.025) in the 35 – 44 year age group and a significantly higher score in the 65 – 74 year age group (P = 0.011). MH scores were affected by work status, marital status and country of birth.

Social functioning (SF)

Compared to men of the same age group in the Health Omnibus Survey, the current cohort had a significantly higher mean SF score (P = 0.021) in the 45 – 54 year age group. SF domain scores were affected by all demographic variables except for age and country of birth.

		Physical function				General health				Vitality			
		Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall		78.99	0.90	77.23	80.74	67.38	0.85	65.70	69.06	63.19	0.87	61.49	64.89
Age group:	35 - 44 years	87.66	1.41	84.90	90.42	69.28	1.65	66.04	72.51	64.51	1.68	61.21	67.81
Norms		90.6		89.4	91.9	74.9		73.2	76.5	63.1		61.5	64.8
	45 - 54 years	80.78	1.51	77.81	83.75	68.32	1.57	65.24	71.40	61.92	1.55	58.88	64.96
Norms		84.9		83.1	86.7	72.5		70.6	74.5	62.5		60.6	64.4
	55 - 64 years	76.17	1.69	72.85	79.48	68.17	1.54	65.15	71.20	65.05	1.54	62.03	68.06
Norms		79.5		77.2	81.8	69.1		66.7	71.5	62.4		59.9	64.8
	65 - 74 years	66.24	2.39	61.54	70.93	63.91	2.22	59.56	68.27	61.89	2.35	57.28	66.50
Norms		72.7		69.6	75.8	65.8		63.0	68.6	61.9		59.0	64.9
	75 - 79 years	65.37a	3.60	58.30	72.43	59.13b	3.72	51.82	66.43	59.19c	3.88	51.57	66.80
Norms		56.4		52.9	59.9	62.5		59.7	65.2	56.2		53.4	59.9

	Physical function				General health				Vitality			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
School leaving age: 13 years or younger	75.25	3.84	67.70	82.80	72.06	3.44	65.31	78.82	74.38	4.02	66.48	82.29
14 years or younger	63.62	2.63	58.45	68.80	59.90	2.56	54.88	64.93	59.47	2.22	55.11	63.83
15 years	75.99	1.85	72.37	79.62	66.59	1.75	63.15	70.03	61.35	2.10	57.22	65.48
16 years	82.13	1.48	79.23	85.04	68.92	1.58	65.82	72.01	63.44	1.66	60.19	66.70
17 years	85.05	1.66	81.79	88.31	69.78	1.85	66.15	73.42	64.55	1.66	61.29	67.81
18 years or older	81.51[d]	2.73	76.14	86.88	66.81[e]	2.57	61.76	71.87	63.11[f]	2.46	58.27	67.95
Post school qualifications: None	77.46	1.58	74.37	80.55	67.65	1.54	64.63	70.67	64.95	1.54	61.93	67.97
Non bachelor qualification	78.15	1.21	75.77	80.52	66.76	1.12	64.55	68.96	62.31	1.16	60.03	64.58
Bachelor degree or higher	87.45[g]	1.99	83.53	91.36	70.02[h]	2.58	64.95	75.09	63.45[i]	2.40	58.74	68.16
Annual gross household income: Up to $20,000	65.90	2.27	61.45	70.36	58.80	2.02	54.83	62.77	58.93	2.20	54.60	63.26
$20,001 - $40,000	76.45	1.75	73.02	79.89	68.35	1.71	64.99	71.71	62.23	1.83	58.64	65.82
$40,001 - $60,000	83.84	1.67	80.56	87.12	68.44	1.60	65.30	71.59	65.05	1.62	61.87	68.22

	Physical function				General health				Vitality			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
$60,001 - $80,000	85.71	1.67	82.44	88.99	70.30	1.84	66.68	73.91	66.12	1.87	62.44	69.80
More than $80,000	86.72[j]	1.69	83.39	90.05	72.55[k]	2.26	68.12	76.98	64.60[l]	2.05	60.58	68.62
Work status: Full time/part time/casual employment	86.08	0.87	84.38	87.78	71.41	0.97	69.51	73.32	66.09	1.00	64.12	68.06
Retired	67.26	1.72	63.88	70.64	61.45	1.67	58.17	64.73	60.72	1.76	57.27	64.18
Other(1)	65.43[m]	3.70	58.15	72.71	57.58[n]	3.34	51.02	64.14	51.20[o]	2.84	45.63	56.77
DSS pension: Yes	65.28	1.83	61.68	68.87	59.86	1.68	56.55	63.17	58.74	1.74	55.33	62.16
No	84.70[p]	0.86	83.02	86.38	70.52[q]	0.94	68.68	72.37	65.02[r]	0.97	63.11	66.92
Marital status: Married/living with a partner	79.99	0.93	78.16	81.83	68.42	0.88	66.68	70.15	64.18	0.88	62.45	65.92
Separated/divorced	73.44	3.49	66.59	80.29	63.40	3.56	56.41	70.40	57.71	3.36	51.10	64.32
Widowed	61.50	6.72	48.30	74.69	54.72	5.40	44.11	65.33	57.52	5.19	47.32	67.73
Never married	81.58[s]	3.51	74.68	88.49	65.51[t]	3.74	58.17	72.85	61.62[u]	4.66	52.46	70.77
Country of birth: Australia	78.23	1.10	76.06	80.39	67.65	1.02	65.64	69.65	62.22	1.07	60.12	64.32

	Physical function				General health				Vitality			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
United Kingdom(2)	83.10	1.87	79.43	86.78	68.29	2.01	64.34	72.24	64.99	1.89	61.28	68.70
Other	77.49[v]	2.39	72.80	82.19	64.98[w]	2.40	60.27	69.70	65.56[x]	2.23	61.17	69.95

Table 4.18 A summary of physical function, general health and vitality SF-36 domain scores in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

*Normative data is from the 2002 South Australian Health Omnibus Survey (Dal Grande & Taylor, 2004). (1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,563) = 21.08$, $P < 0.0001$; b $F(4,563) = 2.31$, $P = 0.056$; c $F(4,563) = 1.02$, $P = 0.398$; d $F(5,551) = 11.16$, $P < 0.0001$; e $F(5,551) = 2.64$, $P = 0.023$; f $F(5,551) = 2.38$, $P = 0.037$; g $F(2,565) = 9.39$, $P < 0.0001$; h $F(2,565) = 0.69$, $P = 0.502$; i $F(2,565) = 0.94$, $P = 0.39$; j $F(4,558) = 18.21$, $P < 0.0001$; k $F(4,558) = 6.55$, $P < 0.0001$; l $F(4,558) = 1.96$, $P = 0.01$; m $F(2,565) = 57.4$, $P < 0.0001$; n $F(2,565) = 18.6$, $P < 0.0001$; o $F(2,565) = 13.93$, $P < 0.0001$; p $F(1,566) = 92.21$, $P < 0.0001$; q $F(1,566) = 30.48$, $P < 0.0001$; r $F(1,566) = 9.91$, $P = 0.0017$; s $F(3,564) = 3.59$, $P = 0.014$; t $F(3,564) = 2.73$, $P = 0.043$; u $F(3,564) = 1.68$, $P = 0.171$; v $F(2,565) = 2.81$, $P = 0.061$; w $F(2,565) = 0.63$, $P = 0.531$; x $F(2,565) = 1.42$, $P = 0.241$.

	Mental health				Role physical				Role emotional			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Overall	77.01	0.71	75.62	78.40	77.43	1.61	74.27	80.59	91.97	1.01	89.99	93.95
Age group: 35 - 44 years	76.27	1.34	73.63	78.91	87.30	2.55	82.29	92.30	94.93	1.44	92.10	97.77
Norms	79.1		77.7	80.5	80.7		77.8	83.6	86.2		83.7	88.7
45 - 54 years	75.87	1.37	73.18	78.55	79.68	2.73	74.33	85.03	90.01	2.11	85.86	94.16
Norms	77.2		75.5	78.9	77.0		73.8	80.3	84.1		81.3	86.9
55 - 64 years	78.95	1.24	76.51	81.39	78.92	2.95	73.13	84.71	92.10	1.93	88.31	95.89
Norms	81.4		79.5	83.3	70.8		66.7	74.9	87.9		84.9	91.0
65 - 74 years	77.63	1.81	74.07	81.19	60.65	4.86	51.10	70.20	91.00	2.85	85.41	96.59
Norms	81.9		79.9	83.9	66.4		61.7	71.0	87.7		84.2	91.2
75 - 79 years	78.45[a]	3.14	72.27	84.62	51.91[b]	8.11	35.97	67.85	86.68[c]	5.99	74.91	98.44
Norms	81.3		79.2	83.4	55.4		50.3	60.6	85.6		81.8	89.5
School leaving age: 13 years or younger	84.25	3.24	77.88	90.61	81.10	7.56	66.25	95.95	100.00	0.00	100.00	100.00
14 years or younger	77.73	1.76	74.27	81.19	51.81	5.25	41.51	62.12	88.97	3.58	81.93	96.01
15 years	77.20	1.48	74.29	80.11	76.40	3.39	69.73	83.06	90.80	2.24	86.40	95.20
16 years	77.59	1.37	74.90	80.29	81.71	2.99	75.83	87.59	94.57	1.68	91.27	97.87
17 years	76.03	1.57	72.95	79.10	82.29	3.15	76.10	88.49	89.56	2.34	84.97	94.14

	Mental health				Role physical				Role emotional			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
18 years or older	74.48[d]	2.12	70.31	78.65	83.22[e]	3.92	75.52	90.92	92.60[f]	2.64	87.41	97.79
Post school qualifications: None	78.44	1.15	76.18	80.69	77.17	3.07	71.13	83.20	93.14	1.72	89.77	96.52
Non bachelor qualification	76.77	0.94	74.93	78.61	75.64	2.10	71.53	79.76	91.98	1.32	89.39	94.57
Bachelor degree or higher	74.63[g]	2.43	69.86	79.39	87.76[h]	4.14	79.62	95.89	88.88[i]	3.36	82.28	95.48
Annual gross household income: Up to $20,000	76.07	1.68	72.78	79.37	59.58	4.15	51.43	67.72	86.20	3.11	80.09	92.31
$20,001 - $40,000	75.81	1.51	72.84	78.78	72.45	3.60	65.37	79.53	92.63	1.91	88.89	96.38
$40,001 - $60,000	77.95	1.33	75.34	80.56	83.56	2.58	78.49	88.63	94.20	1.65	90.96	97.44
$60,001 - $80,000	78.69	1.71	75.32	82.06	91.62	3.14	85.46	97.78	93.66	2.25	89.25	98.08
More than $80,000	77.38[j]	1.78	73.89	80.87	85.88[k]	3.35	79.31	92.46	92.97[l]	2.19	88.68	97.27
Work status: Full time/part time/casual employment	78.28	0.83	76.64	79.91	88.40	1.52	85.41	91.39	94.99	0.93	93.15	96.82
Retired	77.01	1.45	74.16	79.86	60.59	3.56	53.60	67.58	89.25	2.34	84.66	93.84
Other(1)	68.76[m]	2.46	63.92	73.59	52.84[n]	6.06	40.94	64.74	79.74[o]	5.07	69.78	89.69
DSS pension: Yes	75.76	1.34	73.14	78.39	57.00	3.53	50.07	63.93	86.20	2.51	81.26	91.14
No	77.50[p]	0.83	75.86	79.14	85.91[q]	1.54	82.88	88.93	94.36[r]	0.94	92.51	96.22
Marital status: Married/living with a partner	78.01	0.75	76.54	79.47	80.38	1.65	77.13	83.63	92.94	1.05	90.88	95.01
Separated/divorced	69.84	2.74	64.46	75.22	63.92	6.14	51.86	75.99	85.28	4.41	76.61	93.95

	Mental health				Role physical				Role emotional			
	Mean	SE	95% CI		Mean	SE	95% CI		Mean	SE	95% CI	
Widowed	77.91	3.76	70.53	85.29	43.82	10.27	23.64	63.99	84.77	7.37	70.30	99.25
Never married	75.57[s]	2.75	70.18	80.97	74.61[t]	7.16	60.54	88.68	93.01[o]	3.41	86.31	99.71
Country of birth: Australia	77.25	0.86	75.57	78.93	76.15	1.96	72.29	80.01	91.15	1.27	88.64	93.65
United Kingdom(2)	79.57	1.47	76.68	82.47	83.60	3.41	76.90	90.30	96.14	1.56	93.07	99.20
Other(3)	72.71[v]	2.00	68.78	76.65	75.86[w]	4.42	67.17	84.55	90.75[x]	2.97	84.92	96.58

Table 4.19 A summary of mental health, role physical and role emotional SF-36 domain scores in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

*Normative data is from the 2002 South Australian Health Omnibus Survey (Dal Grande & Taylor, 2004). (1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,563) = 0.90$, $P = 0.464$; b $F(4,563) = 8.95$, $P < 0.0001$; c $F(4,562) = 1.36$, $P = 0.246$; d $F(5,551) = 1.41$, $P = 0.218$; e $F(5,551) = 6.04$, $P < 0.0001$; f $F(5,550) = 12.81$, $P < 0.0001$; g $F(2,565) = 1.25$, $P = 0.288$; h $F(2,565) = 3.43$, $P = 0.033$; i $F(2,564) = 0.65$, $P = 0.524$; j $F(4,558) = 0.59$, $P = 0.669$; k $F(4,558) = 11.67$, $P < 0.0001$; l $F(4,558) = 1.34$, $P = 0.254$; m $F(2,565) = 6.71$, $P = 0.0013$; n $F(2,565) = 38.32$, $P < 0.0001$; o $F(2,565) = 6.54$, $P = 0.0016$; p $F(1,566) = 1.22$, $P = 0.271$; q $F(1,566) = 56.35$, $P < 0.0001$; r $F(1,566) = 9.25$, $P = 0.0025$; s $F(3,564) = 2.90$, $P = 0.034$; t $F(3,564) = 6.18$, $P = 0.0004$; u $F(3,563) = 1.32$, $P = 0.268$; v $F(2,565) = 3.80$, $P = 0.023$; w $F(2,565) = 1.90$, $P = 0.15$; x $F(2,564) = 3.36$, $P = 0.036$.

	Social function				Bodily pain			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	90.52	0.78	88.99	92.05	73.48	1.06	71.39	75.57
Age group: 35 - 44 years	92.17	1.42	89.37	94.96	79.93	1.98	76.05	83.82
Norms	87.9		86.1	89.6	77.6		75.6	79.6
45 - 54 years	90.56	1.30	88.01	93.11	73.38	1.87	69.71	77.05
Norms	84.1		81.3	86.9	74.1		71.9	76.3
55 - 64 years	91.02	1.52	88.04	94.01	69.78	1.88	66.09	73.47
Norms	87.8		85.5	90.2	71.1		68.3	73.9
65 - 74 years	86.56	2.38	81.88	91.24	67.31	2.63	62.15	72.48
Norms	85.1		82.1	88.2	70.8		67.4	74.1
75 - 79 years	89.97a	3.23	83.64	96.31	66.29b	5.67	55.16	77.42
Norms	81.0		77.7	84.4	66.9		63.4	70.4
School leaving age: 13 years or younger	96.87	1.67	93.59	100.15	75.48	5.03	65.60	85.36
14 years or younger	86.12	2.30	81.60	90.65	60.59	3.18	54.35	66.84
15 years	89.39	1.82	85.81	92.96	69.23	2.25	64.82	73.65
16 years	92.67	1.29	90.13	95.21	78.00	1.82	74.44	81.57
17 years	91.36	1.52	88.37	94.36	78.79	2.05	74.77	82.81

	Social function				Bodily pain			
	Mean	SE	95% CI		Mean	SE	95% CI	
18 years or older	88.40[c]	2.64	83.20	93.59	72.62[d]	3.35	66.05	79.19
Post school qualifications: None	93.12	1.22	90.71	95.52	74.60	1.80	71.06	78.14
Non bachelor qualification	88.80	1.10	86.64	90.97	71.35	1.46	68.48	74.22
Bachelor degree or higher	93.15[e]	1.70	89.81	96.49	82.12[f]	2.55	77.11	87.12
Annual gross household income: Up to $20,000	86.19	2.16	81.94	90.43	64.80	2.53	59.83	69.77
$20,001 - $40,000	88.63	1.86	84.97	92.29	71.18	2.27	66.73	75.63
$40,001 - $60,000	92.78	1.22	90.39	95.18	74.81	2.12	70.65	78.97
$60,001 - $80,000	93.82	1.44	91.00	96.64	81.85	2.22	77.49	86.21
More than $80,000	93.20[g]	1.35	90.54	95.85	79.04[h]	2.33	74.46	83.62
Work status: Full time/part time/casual employment	93.35	0.81	91.76	94.93	78.55	1.23	76.13	80.96
Retired	88.21	1.66	84.95	91.47	66.66	2.09	62.55	70.77
Other(1)	78.56[i]	3.51	71.68	85.45	59.46[j]	3.68	52.24	66.69
DSS pension: Yes	85.29	1.75	81.84	88.73	64.33	2.13	60.15	68.50
No	92.69[k]	0.80	91.12	94.25	77.31[l]	1.16	75.03	79.59
Marital status: Married/living with a partner	91.76	0.74	90.29	93.22	74.33	1.12	72.13	76.53
Separated/divorced	80.64	4.02	72.74	88.53	68.26	3.82	60.76	75.77

	Social function				Bodily pain			
	Mean	SE	95% CI		Mean	SE	95% CI	
Widowed	85.68	5.37	75.13	96.24	59.35	8.24	43.17	75.53
Never married	92.38[m]	2.74	86.99	97.77	76.21[n]	4.95	66.49	85.93
Country of birth: Australia	89.98	0.98	88.06	91.90	73.09	1.29	70.56	75.61
United Kingdom(2)	93.60	1.49	90.68	96.52	77.57	2.34	72.97	82.17
Other	89.31[o]	2.09	85.21	93.40	70.29[p]	2.96	64.46	76.11

Table 4.20 A summary of social function and bodily pain SF-36 domain scores in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

*Normative data is from the 2002 South Australian Health Omnibus Survey (Dal Grande & Taylor, 2004). (1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,563) = 1.04$, $P = 0.386$; b $F(4,563) = 5.30$, $P = 0.0003$; c $F(5,551) = 3.82$, $P = 0.0021$; d $F(5,551) = 6.52$, $P < 0.0001$; e $F(2,565) = 4.23$, $P = 0.015$; f $F(2,565) = 6.73$, $P = 0.0013$; g $F(4,558) = 3.32$, $P = 0.011$; h $F(4,558) = 7.86$, $P < 0.0001$; i $F(2,565) = 11.28$, $P < 0.0001$; j $F(2,565) = 20.76$, $P < 0.0001$; k $F(1,566) = 14.75$, $P = 0.0001$; l $F(1,566) = 28.76$, $P < 0.0001$; m $F(3,564) = 2.87$, $P = 0.036$; n $F(3,564) = 1.87$, $P = 0.133$; o $F(2,565) = 2.38$, $P = 0.093$; p $F(2,565) = 2.13$, $P = 0.119$.

LABORATORY

Fasting serum lipids

Complete serum lipids were not obtained in 2 participants due to coding errors made by Diagnostic Services at the IMVS. Serum LDL was not calculated in 28 participants due to extremely high serum triglyceride levels. Triglyceride, total cholesterol, LDL and HDL cholesterol of the cohort by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth are summarised in Tables 4.20 and 4.21. Age had an effect on triglyceride, total cholesterol and LDL but not HDL cholesterol levels. School-leaving age and gross annual household income affected LDL but not HDL or total cholesterol or triglycerides. Work status, had no effect on triglyceride levels but did affect total, LDL and HDL cholesterol levels and receiving a DSS pension had an effect on both total and LDL cholesterol but not HDL cholesterol or triglyceride levels. Post-school qualifications, marital status and country of birth had no effect on any of the measures of serum lipid.

Thirty-two percent (N = 179) of men reported having high cholesterol levels and 19% (N = 110) reported taking lipid-lowering medication. Figure 4.14 shows the proportion of self-reported normal and hypercholesterolaemic men with total cholesterol levels greater than 5.5 mmol/L at the clinic visit, the proportion that were taking lipid-lowering medication and the proportion that had taken their medication in the 24 hours prior to their visit.

Fasting serum glucose and HbA1c

Fasting glucose and HbA1c levels of the cohort by age, school-leaving age, highest post-secondary qualification, annual gross household income and work status, receipt of a DSS pension, marital status and country of birth are summarised in Table 4.23. Age, school-leaving age, gross annual household income, work status and receiving a DSS pension all had significant effects on both fasting glucose and

HbA1c levels. Post-school qualifications had an effect on fasting serum glucose levels but not on HbA1c and marital status had an effect on HbA1c but not on fasting serum glucose levels.

Nine percent (N = 50) of men reported having diabetes and 11% (N = 64) had an HbA1c of 6.2% or greater. Thirteen percent (N = 74) of men had fasting plasma glucose levels of 5.5 mmol/L or greater and 35% (N = 198) had fasting insulin levels of 12 mU/L or greater. The proportion of men with and without self-reported diabetes that had HbA1c greater than 6.2% is shown in Figure 4.15. Eleven percent (N = 62) of men reported taking medication for diabetes.

	Triglycerides (mmol/L)				Total cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	1.70	0.06	1.58	1.82	5.41	0.05	5.32	5.51
Age group: 35 - 44 years	1.76	0.14	1.49	2.03	5.62	0.08	5.46	5.79
45 - 54 years	1.65	0.08	1.49	1.80	5.54	0.09	5.36	5.71
55 - 64 years	1.97	0.14	1.70	2.23	5.43	0.09	5.26	5.60
65 - 74 years	1.42	0.09	1.24	1.60	4.90	0.11	4.69	5.11
75 - 79 years	1.47[a]	0.17	1.14	1.81	5.02[b]	0.21	4.62	5.43
School leaving age: 13 years or younger	1.93	0.39	1.17	2.69	5.01	0.23	4.57	5.46
14 years or younger	1.83	0.20	1.45	2.21	5.11	0.14	4.84	5.38
15 years	1.74	0.08	1.57	1.91	5.36	0.10	5.16	5.56
16 years	1.75	0.14	1.47	2.03	5.49	0.10	5.29	5.69
17 years	1.59	0.12	1.37	1.82	5.50	0.09	5.33	5.68
18 years or older	1.62[c]	0.15	1.33	1.90	5.51[d]	0.11	5.29	5.74
Post school qualifications: None	1.85	0.13	1.58	2.11	5.45	0.09	5.27	5.63

	Triglycerides (mmol/L)				Total cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Bachelor degree or higher	1.61[e]	0.20	1.23	2.00	5.36[f]	0.12	5.13	5.58
Annual gross household income: Up to $20,000	1.92	0.14	1.65	2.20	5.23	0.11	5.03	5.44
$20,001 - $40,000	1.60	0.13	1.34	1.85	5.28	0.10	5.08	5.48
$40,001 - $60,000	1.72	0.12	1.49	1.96	5.54	0.09	5.36	5.73
$60,001 - $80,000	1.69	0.13	1.43	1.95	5.58	0.12	5.35	5.82
More than $80,000	1.56[g]	0.13	1.30	1.82	5.51[h]	0.10	5.31	5.71
Work status: Full time/part time/casual employment	1.65	0.07	1.52	1.78	5.59	0.06	5.48	5.71
Retired	1.60	0.09	1.41	1.78	5.06	0.09	4.88	5.23
Other(1)	2.30[i]	0.31	1.69	2.90	5.25[j]	0.14	4.96	5.53
DSS pension: Yes	1.72	0.09	1.54	1.91	5.10	0.08	4.93	5.26
No	1.69[k]	0.07	1.54	1.84	5.55[l]	0.06	5.44	5.66
Marital status: Married/living with a partner	1.69	0.06	1.56	1.81	5.42	0.05	5.32	5.52
Separated/divorced	1.85	0.24	1.39	2.32	5.28	0.16	4.97	5.59

	Triglycerides (mmol/L)				Total cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Never married	1.60[m]	0.17	1.26	1.94	5.64[n]	0.20	5.25	6.03
Country of birth: Australia	1.69	0.07	1.55	1.83	5.44	0.06	5.33	5.55
United Kingdom(2)	1.73	0.16	1.42	2.05	5.38	0.11	5.17	5.60
Other	1.70[o]	0.15	1.42	1.99	5.34[p]	0.13	5.09	5.60

Table 4.21 Mean serum triglyceride and total cholesterol levels in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,561) = 3.33$, $P = 0.01$; b $F(4,561) = 8.54$, $P < 0.0001$; c $F(5,549) = 0.45$, $P = 0.814$; d $F(5,549) = 2.07$, $P = 0.067$; e $F(2,563) = 0.97$, $P = 0.38$; f $F(2,563) = 0.21$, $P = 0.814$; g $F(4,556) = 1.09$, $P = 0.363$; h $F(4,556) = 2.35$, $P = 0.053$; i $F(2,563) = 2.35$, $P = 0.097$; j $F(2,563) = 13.82$, $P < 0.0001$; k $F(1,564) = 0.07$, $P = 0.786$; l $F(1,564) = 20.40$, $P < 0.0001$; m $F(3,562) = 0.34$, $P = 0.796$; n $F(3,562) = 0.93$, $P = 0.426$; o $F(2,563) = 0.03$, $P = 0.967$; p $F(2,563) = 0.27$, $P = 0.761$.

	LDL cholesterol (mmol/L)				HDL cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	3.50	0.04	3.41	3.58	1.18	0.01	1.15	1.20
Age group: 35 - 44 years	3.73	0.08	3.58	3.88	1.16	0.02	1.11	1.20
45 - 54 years	3.63	0.08	3.47	3.79	1.16	0.02	1.11	1.21
55 - 64 years	3.43	0.08	3.28	3.58	1.19	0.02	1.15	1.24
65 - 74 years	3.04	0.10	2.84	3.24	1.21	0.04	1.14	1.28
75 - 79 years	3.11[a]	0.18	2.75	3.47	1.26[b]	0.06	1.14	1.39
School leaving age: 13 years or younger	3.05	0.21	2.64	3.46	1.22	0.08	1.06	1.38
14 years or younger	3.14	0.13	2.89	3.40	1.20	0.04	1.12	1.27
15 years	3.46	0.09	3.28	3.64	1.13	0.03	1.08	1.18
16 years	3.56	0.09	3.39	3.73	1.16	0.02	1.11	1.20
17 years	3.61	0.09	3.44	3.79	1.20	0.03	1.15	1.25
18 years or older	3.59[c]	0.10	3.39	3.79	1.21[d]	0.04	1.14	1.28
Post school qualifications: None	3.49	0.08	3.32	3.65	1.18	0.02	1.14	1.23

	LDL cholesterol (mmol/L)				HDL cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Bachelor degree or higher	3.51[e]	0.11	3.29	3.73	1.18[f]	0.04	1.11	1.25
Annual gross household income: Up to $20,000	3.23	0.10	3.04	3.42	1.19	0.03	1.13	1.25
$20,001 - $40,000	3.37	0.09	3.19	3.55	1.21	0.03	1.15	1.26
$40,001 - $60,000	3.63	0.08	3.47	3.79	1.14	0.02	1.10	1.19
$60,001 - $80,000	3.73	0.11	3.51	3.95	1.13	0.03	1.07	1.19
More than $80,000	3.62[g]	0.10	3.44	3.81	1.23[h]	0.03	1.16	1.29
Work status: Full time/part time/casual employment	3.70	0.05	3.60	3.80	1.17	0.01	1.15	1.20
Retired	3.13	0.08	2.97	3.29	1.22	0.03	1.17	1.27
Other(1)	3.19[i]	0.13	2.93	3.45	1.10[j]	0.04	1.01	1.18
DSS pension: Yes	3.15	0.08	2.99	3.30	1.19	0.03	1.14	1.24
No	3.65[k]	0.05	3.55	3.75	1.17[l]	0.01	1.15	1.20
Marital status: Married/living with a partner	3.52	0.05	3.43	3.61	1.18	0.01	1.15	1.21
Separated/divorced	3.28	0.13	3.03	3.54	1.18	0.04	1.09	1.26

	LDL cholesterol (mmol/L)				HDL cholesterol (mmol/L)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Never married	3.72[m]	0.20	3.33	4.10	1.19[n]	0.05	1.09	1.28
Country of birth: Australia	3.51	0.05	3.41	3.62	1.18	0.02	1.15	1.21
United Kingdom(2)	3.49	0.09	3.31	3.68	1.17	0.03	1.11	1.23
Other	3.43[o]	0.11	3.22	3.65	1.21[p]	0.03	1.14	1.27

Table 4.22 Mean serum LDL and HDL cholesterol levels in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,533) = 9.43$, $P < 0.0001$; b $F(4,561) = 1.19$, $P = 0.313$; c $F(5,521) = 3.08$, $P = 0.0096$; d $F(5,549) = 1.11$, $P = 0.352$; e $F(2,535) = 0.02$, $P = 0.981$; f $F(2,563) = 0.03$, $P = 0.973$; g $F(4,528) = 4.49$, $P = 0.0014$; h $F(4,556) = 2.10$, $P = 0.079$; i $F(2,535) = 21.33$, $P < 0.0001$; j $F(2,563) = 3.09$, $P = 0.046$; k $F(1,536) = 30.38$, $P < 0.0001$; l $F(1,564) = 0.29$, $P = 0.593$; m $F(3,534) = 1.98$, $P = 0.117$; n $F(3,562) = 0.02$, $P = 0.996$; o $F(2,535) = 0.22$, $P = 0.803$; p $F(2,563) = 0.46$, $P = 0.633$.

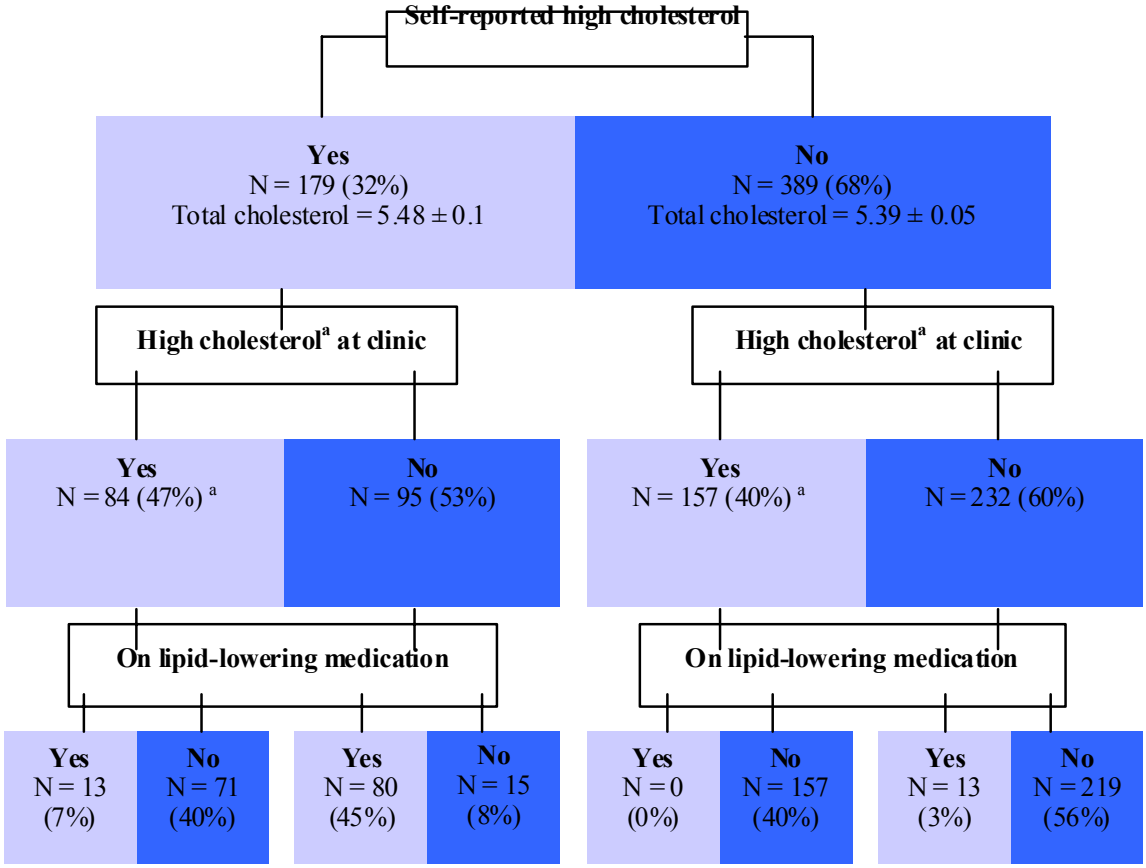

Figure 4.14 The proportions of self-reported hypercholesterolaemic and non-hypercholesterolaemic men with high total cholesterol levels measured at clinic and the proportion that took lipid-lowering medication.

[a]Total cholesterol > 5.5 nmol/L.

	Fasting glucose (mmol/L)				Glycated haemoglobin (%)			
	Mean	SE	95% CI		Mean	SE	95% CI	
Overall	4.67	0.05	4.58	4.76	5.67	0.03	5.60	5.74
Age group: 35 - 44 years	4.29	0.05	4.20	4.39	5.43	0.04	5.35	5.51
45 - 54 years	4.60	0.09	4.43	4.77	5.62	0.06	5.51	5.73
55 - 64 years	5.02	0.13	4.76	5.28	5.84	0.08	5.67	6.00
65 - 74 years	4.98	0.11	4.76	5.20	5.93	0.09	5.74	6.11
75 - 79 years	5.09[a]	0.26	4.59	5.59	6.02[b]	0.20	5.62	6.41
School leaving age: 13 years or younger	5.20	0.34	4.53	5.88	5.88	0.15	5.58	6.17
14 years or younger	4.83	0.11	4.61	5.05	5.89	0.10	5.70	6.08
15 years	4.76	0.12	4.53	4.99	5.79	0.07	5.64	5.93
16 years	4.71	0.10	4.50	4.91	5.70	0.07	5.56	5.84
17 years	4.42	0.07	4.28	4.57	5.46	0.05	5.35	5.57
18 years or older	4.61[c]	0.10	4.41	4.82	5.57[d]	0.10	5.38	5.76
Post school qualifications: None	4.81	0.10	4.61	5.01	5.69	0.07	5.56	5.81
Non bachelor qualification	4.64	0.06	4.53	4.75	5.69	0.04	5.60	5.77
Bachelor degree or higher	4.44[e]	0.11	4.22	4.66	5.55[f]	0.08	5.38	5.71
Annual gross household income: Up to $20,000	5.05	0.12	4.80	5.29	5.94	0.08	5.79	6.10

	Fasting glucose (mmol/L)				Glycated haemoglobin (%)			
	Mean	SE	95% CI		Mean	SE	95% CI	
$20,001 - $40,000	4.78	0.10	4.57	4.98	5.71	0.08	5.56	5.87
$40,001 - $60,000	4.41	0.07	4.27	4.55	5.54	0.05	5.45	5.64
$60,001 - $80,000	4.48	0.08	4.31	4.65	5.53	0.09	5.35	5.70
More than $80,000	4.58[g]	0.12	4.35	4.81	5.58[h]	0.08	5.43	5.73
Work status: Full time/part time/casual employment	4.47	0.05	4.38	4.56	5.53	0.04	5.46	5.59
Retired	5.03	0.10	4.84	5.22	5.97	0.08	5.82	6.12
Other(1)	4.93[i]	0.22	4.50	5.36	5.78[j]	0.11	5.56	6.00
DSS pension: Yes	4.97	0.10	4.78	5.16	5.88	0.06	5.75	6.01
No	4.54[k]	0.05	4.44	4.64	5.58[l]	0.04	5.51	5.66
Marital status: Married/living with a partner	4.65	0.05	4.55	4.74	5.65	0.03	5.59	5.72
Separated/divorced	4.60	0.17	4.28	4.93	5.67	0.12	5.43	5.90
Widowed	5.49	0.54	4.43	6.56	6.80	0.45	5.92	7.69
Never married	4.68[m]	0.19	4.31	5.06	5.50[n]	0.09	5.32	5.68
Country of birth: Australia	4.62	0.05	4.52	4.72	5.63	0.04	5.56	5.70
United Kingdom(2)	4.65	0.13	4.39	4.92	5.71	0.09	5.52	5.89
Other	4.91[o]	0.14	4.64	5.17	5.81[p]	0.09	5.63	5.99

Table 4.23 Mean serum fasting glucose and glycated haemoglobin levels in the overall cohort and by age group, school-leaving age, post-school qualification and annual gross household income, work status, DSS pension, marital status and country of birth in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

(1) Includes unemployed, invalid pensioners and work-cover recipients. (2) Included England, Ireland, Scotland, Wales, Isle of Man and Channel Islands. a $F(4,561) = 14.55$, $P < 0.0001$; b $F(4,563) = 10.31$, $P < 0.0001$; c $F(5,549) = 3.11$, $P = 0.0089$; d $F(5,551) = 4.95$, $P = 0.0002$; e $F(2,563) = 3.12$, $P = 0.045$; f $F(2,565) = 1.18$, $P = 0.309$; g $F(4,556) = 6.27$, $P = 0.0001$; h $F(4,558) = 5.42$, $P = 0.0003$; i $F(2,563) = 14.65$, $P < 0.0001$; j $F(2,565) = 15.37$, $P < 0.0001$; k $F(1,564) = 15.57$, $P = 0.0001$; l $F(1,566) = 15.48$, $P = 0.0001$; m $F(3,562) = 0.84$, $P = 0.472$; n $F(3,564) = 3.02$, $P = 0.029$; o $F(2,563) = 1.97$, $P = 0.14$; p $F(2,565) = 1.76$, $P = 0.173$.

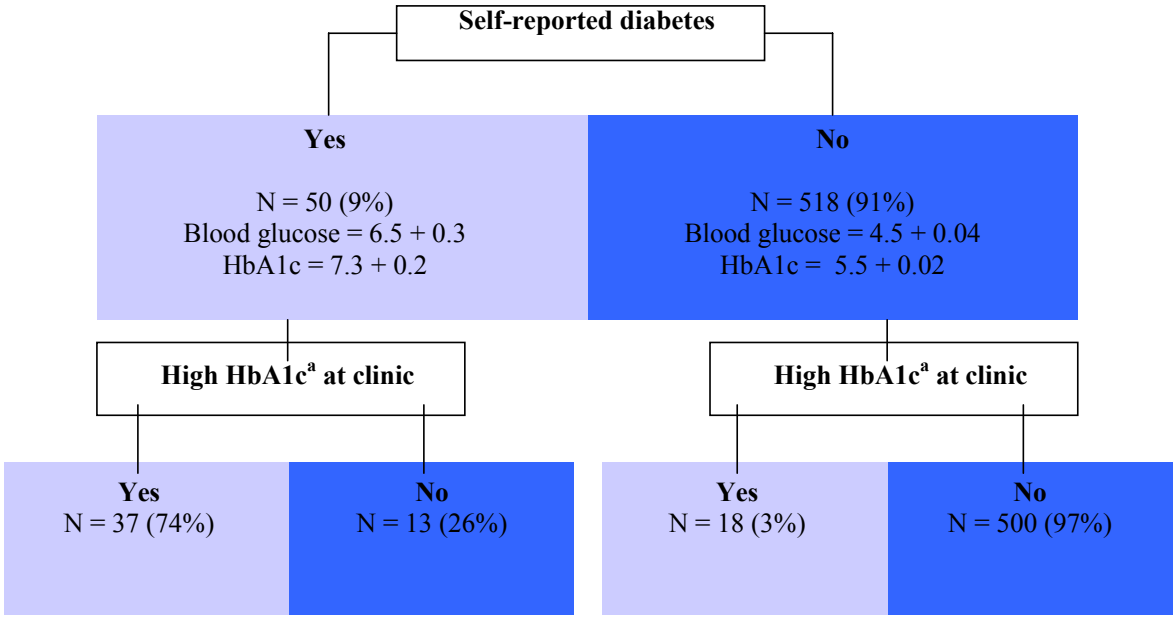

Figure 4.15 The proportions of self-reported diabetic and non-diabetic men with high HbA1c levels measured at clinic.

[a]HbA1c > 6.2%.

SELF-REPORTED HEALTH CONDITIONS

Table 4.24 shows the frequency of self-reported health conditions in the cohort. The frequency of "other health conditions" and "other cancers" that were not prompted by the questionnaire are shown in Tables 4.24 and 4.25 respectively.

Psychological illness

Overall, 12% (N = 68) of men reported suffering depression, 9% (N = 52) anxiety and 10% (N = 58) insomnia. In total, medication for psychological illness constituted 5% of all medications used by the cohort.

Benign prostate disease, prostate cancer & urogenital surgery

Eight percent (N = 46) of men reported having an enlarged prostate and 2% (N = 10) reported having prostate cancer; 5 men reported having both. Four percent (N = 20) of men reported taking medication for prophylaxis against or treatment of current prostate or lower urinary tract problems. In total, medications for problems of the urinary and male genital systems constituted 3% of all medications used by the cohort. Table 4.27 shows the frequency of urogenital surgical procedures experienced in the cohort. Table 4.28 shows the frequency of "other pelvic surgery" by ICPC coded body system.

Sleep Apnoea

Overall, 4% (N = 24) of men reported that they had been diagnosed with sleep apnoea. The mean probability of having sleep apnoea, based on questionnaire scores, age and BMI was 58.35 ± 23.05%. Twenty-four percent (N = 136) of men had an 80% or greater probability of having sleep apnoea and 5% (N = 26) had a 20% or lower probability.

Health condition	N
Angina	37
Anxiety	52
Asthma	55
Depression	68
Diabetes	50
Enlarged prostate	46
High cholesterol	179
High blood pressure	159
Insomnia	58
Osteoarthritis	53
Rheumatoid arthritis	25
Thyroid problems	8
Prostate cancer	10
Other cancers	41
Any other condition	214
No health condition	138

Table 4.24 The frequency of self-reported health conditions in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

Body System	N
General	13
Blood, blood forming	1
Digestive	111
Eye	24
Ear	36
Circulatory	133
Musculoskeletal	175
Neurological	42
Psychological	67
Respiratory	53
Skin	24
Metabolic, endocrine, nutrition	56
Urinary	38
Male genital	4
Social	0

Table 4.25 The frequency of "other health conditions" reported in men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

Health conditions are classified by body system, using the ICPC medical conditions coding specification.

Body Systems	N
General	0
Blood, blood forming	0
Digestive	22
Eye	0
Ear	0
Circulatory	0
Musculoskeletal	8
Neurological	7
Psychological	0
Respiratory	22
Skin	61
Metabolic, endocrine, nutrition	0
Urinary	9
Male genital	2
Social	0

Table 4.26 The frequency of "other cancers" reported in men aged 35 – 79, randomly recruited from the north and west suburbs of Adelaide.

Cancers are classified by body system, using the ICPC medical conditions coding specification.

Urogenital surgery	N
Prostatectomy	12
TURP	17
Vasectomy	163
Unilateral orchidectomy	3
Penile surgery (excluding circumcision)	14
Bladder surgery	15
Other pelvic surgery	62
No abdominal/pelvic surgery	324

Table 4.27 The frequency of self-reported urogenital surgery in 568 men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

Body Systems	N
General	0
Blood, blood forming	6
Digestive	144
Circulatory	9
Musculoskeletal	6
Neurological	0
Psychological	0
Respiratory	0
Skin	6
Metabolic, endocrine, nutrition	8
Urinary	15
Male genital	15
Social	0

Table 4.28 The frequency of “other pelvic surgery” by body system, reported in men aged 35 – 79 years, randomly recruited from the north and west suburbs of Adelaide.

Surgical procedures are classified by body system, using the ICPC medical conditions coding specification.

MEDICATION USE

Overall, 32% (184 /568) of men reported taking no medication at the time of their clinic visit, including over-the-counter medications such as vitamin and mineral or other dietary supplements. The frequencies of the indications for the medications used are shown in Table 4.29.

Body Systems	N
General	193
Blood, blood forming	2
Digestive	105
Eye	7
Ear	5
Circulatory	344
Musculoskeletal	140
Neurological	57
Psychological	65
Respiratory	133
Skin	39
Metabolic, endocrine, nutrition	219
Urinary	12
Male genital	27
Social	0

Table 4.29 The frequency of indications for medication use.

Indications are classified by body system, using the ICPC medical conditions coding specification.

DISCUSSION

RESPONSE RATES

The response and participation rates for the study were slightly lower than those reported for other large population based studies (Table 4.30). Response rates are often difficult to interpret as the methods used to calculate them are often not specified. Some studies report response rates as a percentage of eligible people in the sample, while others report it as a percentage of the entire sample. The former often leads to much higher rates. Interestingly, a study using very similar sampling procedures reported a response rate of 29% (Table 4.30 [206]). The reasons given for refusing to be involved in the study were as expected, with households simply indicating that they were not interested and others that they were too busy, being the major reasons. Interestingly, no households sighted being too old as a reason for not being involved and having no health problems or being too sick were only minor contributors to non-participation. In the present study, where extremely private information on sexual feeling and behaviour was sought, the response rate was surprisingly high. The telephone recruitment method obviously limited the sample to those households with a telephone. It is probable that use of this method resulted in missing the highly transient and homeless portion of the population.

Study name	Sampling procedure	Response rate
FAMAS	Random households from EWP's. Aged 35 - 80. Within household person to last have birthday selected.	52%
Australian Longitudinal Study of Ageing	Random from Adelaide statistical division. Included institutionalised and multiple members from households.	53%
The Dubbo Study	Non-institutionalised residents of Dubbo local government area born before January 1 1930.	73%
Canberra Longitudinal Study of Ageing	Community volunteers plus oversampling of older ages from nursing homes.	69%
PATH through life	Random from Canberra and Queanbeyan electoral rolls. Aged 20 - 64.	62%
Negotiating the life course	Random households from White Pages. Aged 18 - 54. Within household member to have next birthday selected.	29%
HILDA	Sampled from 12,252 households from 488 neighborhood regions of Australia.	66%
SA Dental Longitudinal Study	Random from electoral database.	60%
Longitudinal survey of Immigrants to Australia	Offshore visaed immigrants aged 15+.	60%
AusDiab [207]	From 6 randomly selected districts in each Australian state and the northern territory. Aged 25+.	55%

Table 4.30 Response rates from Australian longitudinal population-based studies.

Data comes from a governmental review of Australian longitudinal studies [206].

NEGATIVE VERSUS POSITIVE RESPONDERS

In comparison to negative responders, men who participated in the study came from households with more members under the age of 18. Compared to Australian Census data from 2001, the cohort consisted of proportionately less men who had never married in each age group. This suggested that men living with a spouse and children as opposed to single men, or men in other living situations were more likely to participate in the study.

In terms of health, for most of the chronic diseases specified, prevalence was only marginally higher in participants compared to negative responders. The cohort had a much lower proportion of men with known high cholesterol and blood pressure problems, fewer current smokers and more past smokers who had quit than negative responders. Interestingly, the proportion of men with “no health problems” was greater in the enrolled cohort. This most likely reflects the lack of health information that was able to be collected on non-responders. This is an important consideration in the context of this study as the “real” state of health in the area should not be assumed to reflect that which was estimated in this cohort.

Taken together, these data suggested that the cohort had an over-representation of men who had families and an under-representation of single men. Furthermore, this may coincide with the selection of men who have altered health behaviours as a result of family life. This discrepancy with population figures has implications for the overall health of the cohort as it has been demonstrated than people with live-in support systems generally have better health outcomes than people who live alone, especially in older people [208-210].

DEMOGRAPHIC CHARACTERISTICS OF THE COHORT

In the cohort, the distributions of highest qualification, gross household income, country of birth and work status closely approximated those described by the Australian Census 2001 for the male population in the north and west suburbs of Adelaide. It is possible that the telephone recruitment methods limited the likelihood of recruitment of Aboriginal members of the community and of non-English speaking members who often don't answer unexpected telephone calls (unpublished pilot data from Population Research and Outcome Studies Unit, South Australia Department of Human Services).

HEALTH CHARACTERISTICS OF THE COHORT

The prevalence of overweight and obesity based on BMI and waist circumference, hypertension and hypercholesterolaemia in the current cohort were higher than previously reported in other Australian [204, 211-213] and international [214-218] population based studies. However, the direct comparison with such studies is difficult as many included males from age 18 years and some studies included females in the same analysis. Alarmingly, there was a high rate of undiagnosed hypertension and hypercholesterolaemia in the current cohort and a high prevalence of poor control in men being treated for these conditions. This is likely due to men not seeking health care services and with poor compliance with treatment regimens and possibly not being treated aggressively enough by general practitioners in those who do. Non-linear associations between age group and serum triglycerides, total and LDL cholesterol were observed. Older school leaving age was linearly and positively associated with LDL cholesterol level. Being in the highest income bracket and not receiving a DSS pension was associated with higher LDL. Being retired was associated with lower LDL and higher HDL cholesterol. The rates of other chronic diseases in the cohort such as diabetes, depression and asthma reflected national prevalence's and medication use similarly reflected the most commonly used medications in Australia [204, 219, 220].

Rates of behavioural risk factors for disease such as smoking, high alcohol intake, and high dietary fat intakes were similar to those of other Australian population based studies in men of a similar age group [204, 221, 222]. Rates of sedentary behaviour and insufficient physical activity in the current cohort were greater than those of the Australian population in men of similar ages [185, 204].

Limitations in physical activities because of health problems were greater in the current cohort than in men of the same age in the wider South Australian population. However, limitations in usual role activities because of physical health problems were less in the current cohort of men aged 55 to 64 years than in the wider South Australian male population of the same age [205]. The current cohort also experienced greater levels of bodily pain or discomfort in the 65 – 74 year age group compared to men of the same age in the wider South Australian population [205]. Moreover, the current cohort had higher levels of psychological distress and a lower sense of wellbeing in those aged 35 to 44 and 65 to 74 years. However, limitations in usual role activities because of emotional problems were less in men aged 35 to 44 and similar in men aged 65 to 74 [205]. There was also a lower perception of general health status, lower energy and greater fatigue in men aged 45 to 54 years [205]. Scores on all domains of the SF-36 were significantly modified by various demographic factors particularly age, work status and receiving a DSS pension.

Overall, from a demographic viewpoint, the current cohort is reflective of the existing male population of the northern and western Adelaide suburbs. The cohort however, appeared to have an under-representation of men who had never married and this was true for all but the oldest age group. The cohort also included proportionately more men from households where more members were under the age of 18 years. This suggested that men living in a family situation were more likely to be involved in the study than men living alone or in other circumstances. From a health perspective the cohort had a similar prevalence of chronic disease and even though they were treated, treatment targets were not adequately met in many men. Self-reported risk factors such as high cholesterol, high blood pressure

and smoking were more prevalent in men who refused to participate. However, within the cohort, laboratory and clinical tests revealed a high prevalence of high cholesterol and high blood pressure in men who did not know they had the diseases, bringing the prevalence in the cohort in-line with that of negative responders. The current cohort appears to be more overweight and obese than previously reported Australian and international cohorts. These comparisons provide a contextual framework through which to view and interpret the findings presented subsequently in Chapters 5.1 – 5.5.