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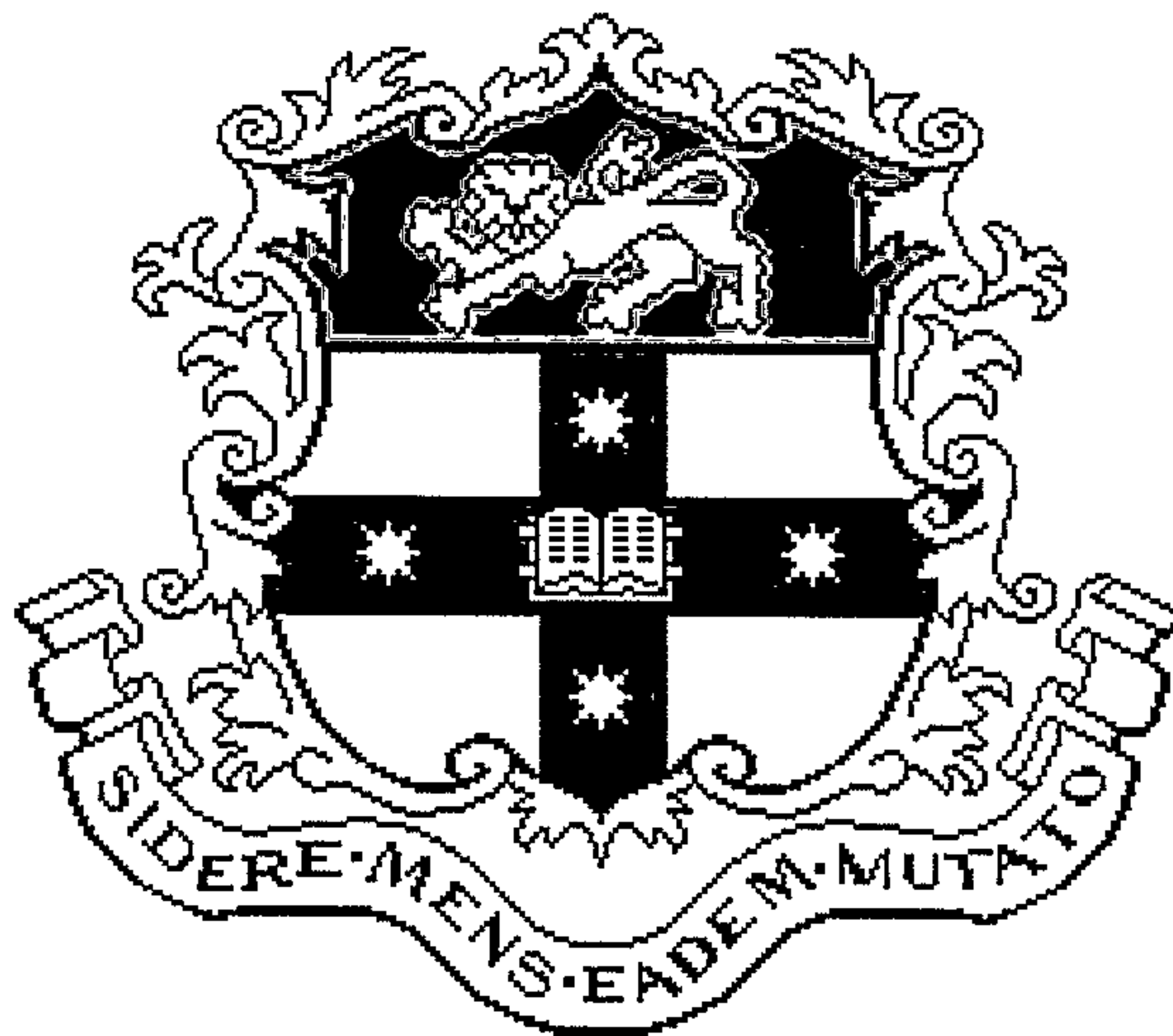
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**Craniofacial and anthropometric characteristics of
subjects with Obstructive Sleep Apnoea in Chinese and
Caucasians.**

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A thesis submitted in partial fulfilment of the
requirements for the degree of
Master of Dental Science
(Orthodontics)

Discipline of Orthodontics
Faculty of Dentistry
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DEDICATION

To my sweetheart, Sally.

For your love, understanding, and patience. You never lost faith in my ability and have supported me untiringly throughout the preparation of this thesis and during the Masters program. Without you, this could have never been possible.

To my wonderful mother, Susan, and darling sister, Sharmini.

You both have supported me in every way. Your unending love, strength and devotion to me has ensured my success through life's challenges. For all the time I have been away, I will make it up to you.

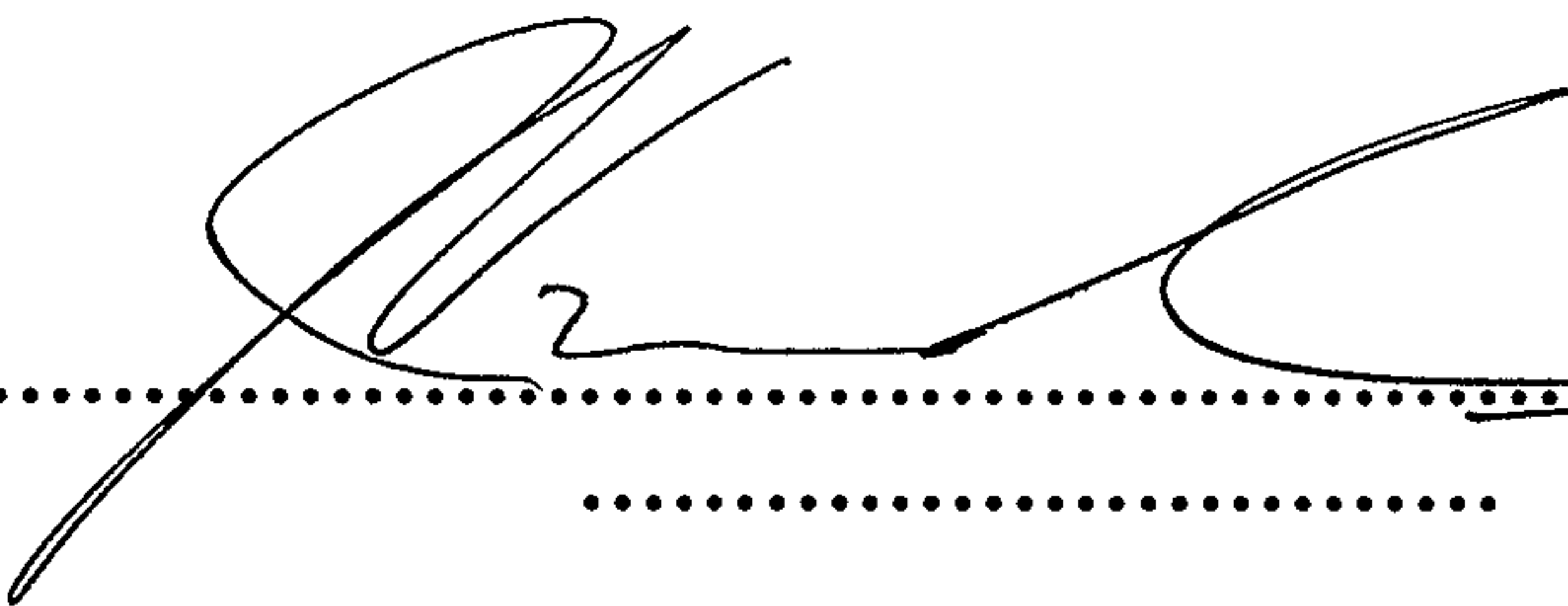
To Mithran.

Thank you for being the inspiration that started me on this path, and for your unending support and friendship throughout this entire journey. I could have not wished for a better mentor

DECLARATION

CANDIDATE CERTIFICATE

This is to certify that the candidate carried out the work in this thesis in the Orthodontic Department, University of Sydney, and has not been submitted to any other University or Institution for a higher degree.



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ABBREVIATIONS AND DEFINITIONS

AHI	Apnoea-Hypopnoea Index: the frequency of apnoeas and/or hypopneas per hour of recorded sleep.
ANOVA	Analysis of Variance
BMI	Body Mass Index
ECG	ElectroCardioGram
EEG	ElectroEncepheloGram
EMG	ElectroMyoGram
EOG	Electro-OculoGram
ESS	Epworth Sleepiness Scale: a standardised self-rating scale of subjective sleepiness.
Kg/m ²	KiloGrams per square Metre
Min	Minutes
MinSaO ₂	Minimum Arterial Oxygen Saturation level
mm	Millimetres
NREM	Non-Rapid Eye Movement
ns	Non-significant
OSA	Obstructive Sleep Apnoea: breath cessation for no less than 10 seconds (in adults) caused by upper airway obstruction in sleep; also, a generic term for a clinical condition of complete or partial obstructed breathing events that cause impaired sleep and breathing.
OSAS	Obstructive Sleep Apnoea Syndrome
P	Level of significance (Probability value)
PCA	Principal Component Analysis
PSG	Polysomnography
RDI	Respiratory Disturbance Index

REM	Rapid Eye Movement
Sd	Standard Deviation
SE	Standard Error
SEM	Standard Error of the Mean
%	Percent

ABSTRACT

Ethnic variation combined with craniofacial variation has been implicated in contributing to the severity of Obstructive Sleep Apnoea (OSA). Patients with OSA have significant craniofacial and upper airway abnormalities when compared with age-matched and sex-matched controls. This study attempted to compare the relative contributions of craniofacial skeletal characteristics and anthropometric variables such as age, sex, weight (kg), height, body mass index and neck circumference, on the severity of OSA between Caucasian and Chinese patients.

One hundred and sixty obstructive sleep apnoea (OSA) patients were divided into two groups on the basis of ethnicity: 76 Caucasian and 84 Chinese patients. A comprehensive cephalometric analysis with a multivariate statistical method was performed in order to define the different principal components (PCs) of cervico-craniofacial skeletal and upper airway soft tissue morphology in each group and how they contributed to selected indices of sleep-disordered breathing (apnoea-hypopnea index – AHI and minimum oxyhaemoglobin saturation) and demographic data (BMI.) Stepwise multiple regressions showed that ethnicity itself, once adjusted for craniofacial and anthropometric measures, does not play a significant role in differentiating OSA between the two ethnic groups. However, ethnicity expressed through differences in craniofacial characteristics between the two patient samples was found to be significant.

Twenty-eight cephalometric variables of cervico-craniofacial skeletal morphology were reduced to seven and eight PCs. Six soft tissue cephalometric variables were reduced to two PCs describing 52.6% and 63% of the total variance in the Caucasian and Chinese patients, respectively. Ten hard tissue linear cephalometric variables were reduced to two and three PCs for the Caucasian and Chinese patients, respectively accounting for 70.9% and 63.4% of the cumulative variance. The hard tissue angular linear combination of cephalometric variables was reduced to three PCs and accounted for the greatest cumulative variance, with 71.7% and 75% for the Caucasian and Chinese groups respectively. Two canonical variables and their correspondents with different loadings were established differently for the individual

OSA groups. The Caucasian group correlated highly with different canonical variables, as compared to the Chinese group.

A canonical correlation successfully clarified the complexity of the simultaneous relationship of the relevant variables by finding the linear combination of predictor variables that best explained a linear combination of response variables. These analyses are proved useful to demonstrate the relationship of cervico-craniofacial skeletal and upper airway soft tissue morphology and selected demographic data. This lays down a basis for understanding the complicated pathogenic components of ethnicity and underlying craniofacial pattern in Australian Caucasian and Hong Kong Chinese OSA subjects.

Key words: Obstructive Sleep Apnoea, Craniofacial, Ethnicity, and Body Mass Index.

1. INTRODUCTION

Respiration is a primary factor influencing posture of the jaws and tongue, and to a lesser extent the head. The normal physiological resting posture of the tongue is said to be relatively high in the mouth, touching the palate. Vig *et al* (1980) found that induced total nasal obstruction over a two-hour period results in progressive extension of the head. Degree of extension was variable. The cranio-vertebral angle typically opened by approximately 5°. Respiratory needs dominated sight as a determinant of cranial orientation. The cranial postural features studied by Solow and Tallgren (1977) showed statistical associations with both craniofacial and dento-alveolar morphology. Whilst it is supported that mouth breathing alters posture the significance of that is harder to quantify, lowered tongue and mandible may alter resting soft tissue pressures on the dentition. Kluemper *et al* (1995) stated that there was no conclusive evidence of a *causal relationship*, and found facial morphology to be unrelated to mode of respiration.

Sleep apnoea was described as early as 360BC (Aelianus 1666). One of history's greatest story tellers, Charles Dickens, in 1837, referred to the character 'Joe' from his novel 'The Posthumous Papers of the Pickwick Club', "Joe-damn that boy, he's gone to sleep again... In response to the firing of enormous guns at a military exercise, everybody was excited except the fat boy, and he slept soundly as if the roaring of the cannon were his ordinary lullaby ... Be good enough to pinch him, sir – in the leg, if you please; nothing else wakes him ... (Joe) snores as he waits at the table ... the snoring of the fat boy penetrated in a low and monotonous sound from the distant kitchen." (Dickens 1837)

OSA is caused by a partial or complete collapse of the pharyngeal airway during sleep (McNamara *et al*, 1994.) Gastault *et al*. (1965) noted that "Pickwickian" patients had repetitive apnoea events while asleep. Sleep apnoea was first noted as a syndrome in the early to mid 1970s (Guilleminault *et al*, 1973.), describing the interaction between sleep, the respiratory muscles of the chest, and the muscles of the upper airway. These early research pieces generally described the interaction between sleep and the

respiratory muscles of the chest and upper airway, which partially explained why the upper airway collapses during sleep, leading to OSA.

The daytime symptoms and clinical features of OSA may be accounted for by episodes of the upper airway narrowing and terminated by arousal, which may recur many hundred times in a night, and the recurrent sleep disruption (Douglas, 1993.) Decreased muscle tone during sleep and upper airway narrowing are aetiological factors (Cistulli, Grunstein *et al.* 1994) (Cistulli and Sullivan, 1994.)

During the 1980's, it was estimated that OSA affected approximately 4% of men and 2% of women in the middle-aged workforce (Young *et al.*, 1983.). Prior to the 1980s, tracheostomy was considered to be the only effective mechanism of treatment for OSA (Westbrook and Millman, 1994.) In 1981, Sullivan *et al.* (Sullivan, Issa *et al.* 1981) described the use of continuous positive airway pressure (CPAP) therapy for patients diagnosed with OSA, initiating the most common and successful treatment modality currently available (Sullivan, Issa *et al.* 1981). Subsequent to this, a plethora of research into the pathophysiology, incidence and treatment for sleep apnoea has been triggered.

The US National Commission on Sleep Disorders Research estimated in 1993, that 40 million Americans suffered from chronic disorders of sleep, including OSA, insomnia and narcolepsy (NIH, 1993.) Sleep apnoea accounted for 50% of this described population, or approximately 20 million people. Of these 20 million people, it was estimated that more than 30% of those aged over 30 years experienced moderate to severe forms of sleep apnoea. The prevalence of OSA (estimated at 7.5% of the population) was comparable to that for asthma and diabetes (6% to 12%). In 2001, JP Morgan Securities used these statistics as a guide, and with the assumption of worldwide prevalence of OSA at 7.5%, estimated that more than 50 million people in the world suffered from varying degrees of OSA, including 1.5 million people in Australia (Gentle, 2001).

The prevalence of OSA amongst different racial populations, may lend support to the theory that ethnicity may be an important risk factor in obstructive sleep apnoea syndrome (OSAS). African-Americans have a higher prevalence and increased

disease severity compared to Caucasians(Ancoli-Israel, Klauber et al. 1995; Redline, Tishler et al. 1997). Kripke et al. (1997) estimated that 16.3 percent of the US Hispanics and racial minorities have OSA as compared with 4.9% of non-Hispanic whites aged 40 to 64 years(Kripke, Ancoli-Israel et al. 1997).

Global migration has occurred in a large scale in recent decades and has affected the local distribution of ethnicity in many large cities. This phenomenon has resulted in 145 million people, world-wide, living outside their native countries in the mid 1990s, and the number is increasing by anywhere from two to four million each year (Population Reference Bureau.) This trend has been emphasised in the population census reports in both America and Australia. The United States (US) Census Bureau's report released in August 2004 revealed that in March 2003, 33.5 million or 11.7% of the US population has been born overseas. Among these foreign born, majority were Latin Americans, 25% were Asians while the rest were Europeans and from the other regions of the world (US Census Bureau.) In October 2005, the Australian population reached 20.4 million of which 24 percent has been overseas. Over the last decade, an average of 40% of Australia's settlers has migrated from Asian regions. Over the same period, the Asian born component of Australia's resident population has grown from 3 to 5% (Australian Bureau of Statistics.)

This literature review summaries the current body of knowledge relating to obstructive sleep apnoea (OSA), and will form the basis of the thesis topic "Craniofacial and anthropometric characteristics of Caucasians and Chinese patients with Obstructive Sleep Apnoea in Sydney". The primary focus of this review will be the determinants of variations in the incidence of OSA between different ethnic populations. However, to form a solid theoretical foundation from which to research OSA, the prevalence, pathophysiology, clinical features, consequences and diagnosis will also be explored.

2. LITERATURE REVIEW

2.1 SLEEP AND BREATHING

Sleep is not a homogenous phenomenon but rather consists of two distinct states (Rechtschaffen and Kales, 1968), distinguished by a combination of behavioural and electrographic criteria:

2.1.1 Rapid eye movement (REM) or active sleep

REM sleep, during which dreaming occurs, is characterised by intense cerebral metabolic activity and central nervous system excitation, despite which incoming sensory information and outgoing motor activity are actively inhibited.

2.1.2 Non-rapid eye movement (non-REM) or quiet sleep.

Non-REM sleep consists of four stages that are thought to represent progressively deeper sleep, with the deepest stages (3 and 4) being referred to as slow-wave sleep.

In the normal adult, non-REM sleep and REM sleep alternate cyclically, with periods of REM sleep lasting 10 to 20 minutes and occurring every 90 to 120 minutes (Somers *et al*, 1993.) Normal sleep is characterised by (Carskadon and Dement, 1994.):

- 2% to 5% of stage 1 sleep;
- 45% to 55% percent of stage 2 sleep;
- 13% to 23% percent of slow-wave sleep; and
- 20% to 25% of rapid eye movement sleep in young adults.

Non-REM sleep and REM sleep have several important physiological influences on breathing, particularly on respiratory drive, stability and ventilatory mechanics (Phillipson and Bowes, 1986). Overall respiratory drive is decreased during non-REM sleep, while during REM sleep, respiratory drive is often irregular. The influences of non-REM and REM sleep on respiratory drive and muscle activity are exerted on the muscles of the upper airway in addition to those of the chest wall. Upper airway

resistance is increased during non-REM sleep compared with wakefulness, and increased even more during REM sleep (Phillipson and Bowes, 1986).

Since 1990, respiratory disturbances during sleep have come to be recognised as extremely common disorders with important clinical consequences. Sleep related breathing disorders covers a broad spectrum of conditions in which individuals have a complete cessation of breathing (apnoea) or a marked reduction in airflow (hypopnea) while asleep (Collard *et al*, 1996; Carskadon and Dement, 1994.).

2.2 SNORING

2.2.1 Definition

Snoring is the hallmark symptom of sleep apnoea because it reflects the basic pathophysiology underlying the disorder, critical narrowing of the upper airway. Snoring is defined as the noise generated by the vibration of the relaxed soft palate, uvula and faucial pillars on inspiration during sleep (Lugaresi, Cirignotta *et al.* 1984). Bailey (1997) described it as the noise emanating from the soft tissue portion of the oropharyngeal walls that occurs during inspiration. Muscle relaxation narrows the airway space and the increased air velocity causes relaxation vibration of the soft tissue structures (Cistulli, Barnes *et al.* 1994). It is common in overweight, middle-aged and elderly adults.

“Primary snoring” refers to snoring that is not accompanied by apnoea, hypoventilation or excessive sleepiness. However, snoring in some patients without apnoea has been associated with significant sleep disturbance, which leads to excessive daytime sleepiness. This is known as “upper airway resistance syndrome” (Guilleminault *et al.*, 1992) and is characterised by repeated arousals without recognisable hypopnea or apnoea. (Lam, Ip *et al.* 2005)

2.2.2 Pathophysiology

Snoring is an example of a flutter valve in which elements of the upper pharyngeal airway vibrate under the force of inspiratory pressure (Cistulli and Sullivan, 1994). The soft palate is the structure most important for the fluttering to occur.

During sleep, the muscles and soft tissues in the throat and mouth relax which causes narrowing of the airway. This decrease in the airway space increases the velocity of air flowing through during breathing. This causes the soft palate and uvula to vibrate resulting in snoring (Isono and Remmers, 1994.)

2.2.3 Incidence

Gislason (1993) estimated habitual snoring has to affect 20% of middle-aged men and 10% of middle-aged women, and Lugaresi (1984) found a slightly increased prevalence with 25% of men and 15% of women afflicted, and is a sign of partially obstructed upper airway during sleep (Lugaresi, Cirignotta *et al.* 1984; Gislason, Benediktsdottir *et al.* 1993). Ohayon *et al.* (1997) reported that 40% of the UK population snored with Young *et al* reporting a higher prevalence of apnoea and hypopnea amongst habitual snorers (Young 1993; Young, Palta *et al.* 1993; Ohayon, Priest *et al.* 1997).

Risk factors for being a habitual snorer include age, body mass index (BMI), weight gain, smoking habits, and physical activity (Koskenvuo *et al*, 1987). The prevalence of snoring increases progressively with age then plateaus after age 65 (Figure 1); 60% of men and 40% of women between the ages of 41 and 65 years of age habitually snore (Lugaresi, Cirignotta *et al.* 1994). Weight gain is a risk factor for snoring in all age groups, while smoking is mainly associated with snoring in men before 60 years of age (Lindberg *et al*, 1998.).

FIGURE 1. PREVALENCE OF SLEEP DISORDERED BREATHING AND INCREASING AGE.
SOURCE (MCNICHOLAS AND PHILLIPSON 2002)



2.2.4 Clinical Consequences of Snoring

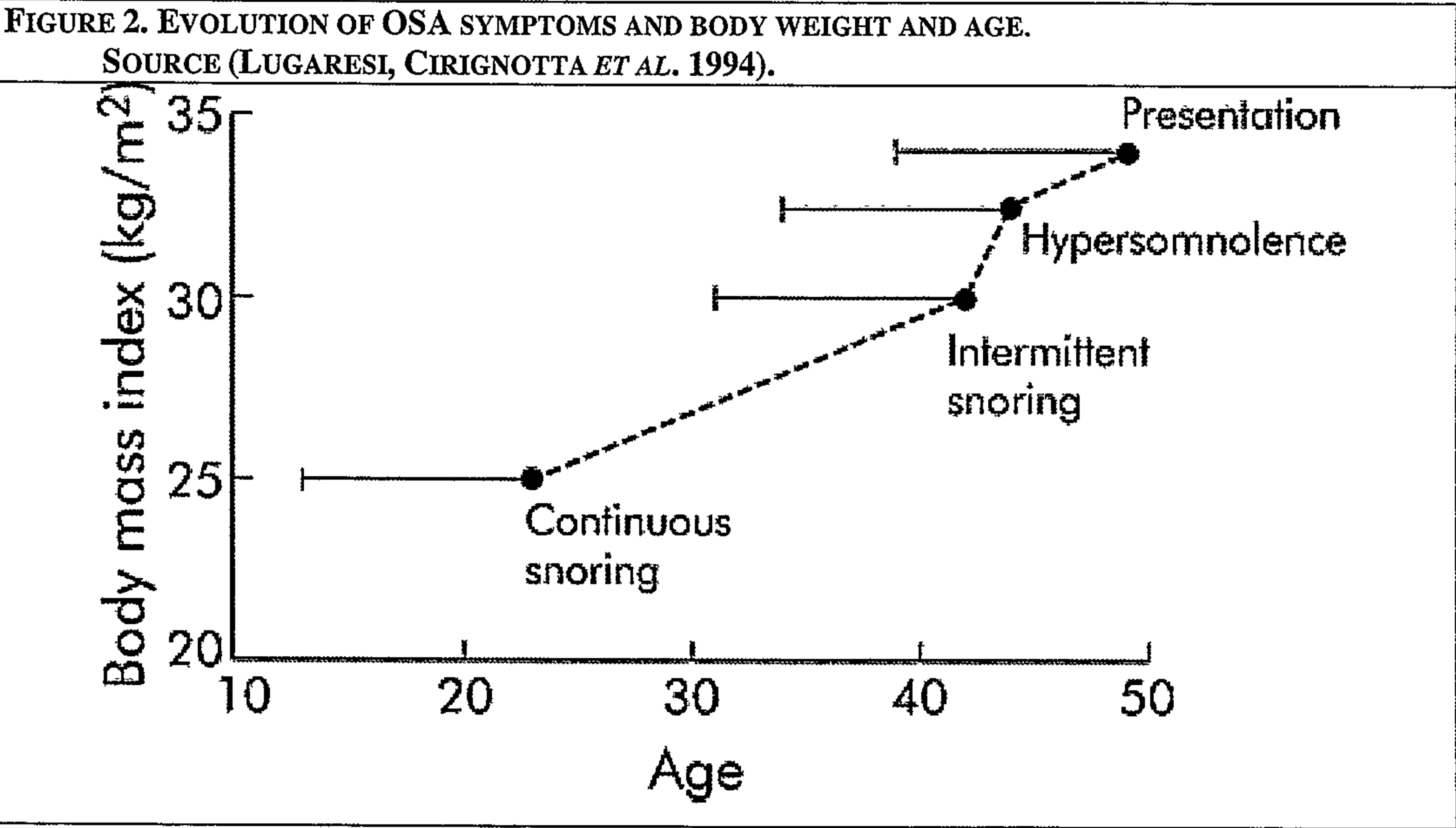
Historically, snoring was regarded as a harmless condition with certain social consequences. The recognition of OSA during the 1970s markedly increased interest in snoring as the most frequent complaint in patients with OSA. Currently, snoring is recognised as a symptom that may be related to clinical conditions with significant morbidity. Specifically, snoring is a possible risk factor for hypertension, ischaemic heart disease and stroke, although its aetiological role in these conditions is not clear (Waller and Bhopal 1989). It has been argued that age and obesity could confound the association between snoring and cardiovascular disease. However, the increased risk of these conditions is still demonstrated after adjusting for age and body mass index (Koskenvuo and Telakivi 1987; D'Alessandro, Magelli *et al.* 1990).

Snoring is recognised as a symptom that may be related to clinical conditions with significant morbidity. It is for this reason that treatment may be necessary, in addition to the fact that snoring is a social embarrassment and can be disturbing to family members.

2.2.5 Relationship of Snoring with OSA

Although not all snorers have sleep apnoea, snoring is a cardinal symptom of almost all OSA patients (Chaudhary and Smith 1991; Ryan, Lowe *et al.* 1991; Stradling, Crosby *et al.* 1991; Boudewyns and Van de Heyning 1995). Lugaresi (1994) suggested that snoring was the initial symptom, eventually progressing to OSA with onset of age and increased BMI. While good data are available on the prevalence of OSAS, there is less information available on the progression of the disease.

Several studies suggest that the severity of apnoea worsens over time. In the Wisconsin Sleep Study the mean apnoea-hypopnoea index (AHI) increased from 2.6 to 5.1 events per hour over 8 years (Young, Palta *et al.* 1993). The increase in AHI was substantially greater in obese individuals and in those who reported habitual snoring at baseline. The reason for worsening severity of apnoea over time is incompletely understood, but several factors must be considered. Primarily, snoring and repeated upper airway occlusion can lead to oedema and swelling of upper airway soft tissue structures, which may contribute to further narrowing of the upper airway, making it more susceptible to collapse. Secondly, pharyngeal muscle dysfunction may contribute to the development or progression of apnoea.



2.2.6 Craniofacial variation between snorers and OSA

Andersson and Brattstrom (1991) investigated the craniofacial morphology of 51 heavily snoring patients, with and without obstructive sleep apnoea, compared with 28 healthy control patients. The apnoea group showed a reduced posterior airway and a posterior rotation of the mandible. Reduction of the anterior-posterior diameter of the cranial base, maxilla and mandible and vertical reduction of the posterior facial height appeared to be common facial characteristics in both snoring and apnoea patients (Andersson and Brattstrom 1991).

Zucconi *et al.* (1993) recorded craniofacial bone measurements in a sample of 28 male habitual snorers with and without OSA, and 10 healthy non-snorers. Habitual snorers showed a significant decrease in sagittal dimensions of the cranial base and mandibular bone; there was also a shorter maxilla in the OSA group as compared to the snoring group. Facial height and angle dimensions were not different between snorers and non-snorers, indicating that some habitual snorers may have some anatomic disposition to upper airway obstruction during sleep (Zucconi, Ferini-Strambi *et al.* 1993).

Mayer *et al.* (1996) evaluated anatomical pharyngeal and craniofacial abnormalities using upper airway imaging in snorers with and without obstructive sleep apnoea (OSA), and attempted to ascertain the influences of the age and weight of the patient. They found that OSA patients had more upper airway abnormalities than snorers. However, when divided for BMI and age, only lean or younger OSA patients were significantly different from snorers as regards to their upper airway anatomy. The shape of the oropharynx and hypopharynx changed significantly with BMI both in OSA patients and snorers, being more spherical in the highest BMI group due mainly to a decrease in the transverse axis. Older patients (> 63 years old), whether snorers or apnoeics, had large upper airways at all pharyngeal levels than the youngest group of patients (< 52 years old.) For the total group of patients, upper airway variables explained 26% of the variance in apnoea/hypopnoea index (AHI), whereas in lean (BMI < 27 kg/m²) or youngest (age < 52 years old) subjects upper airway variables explained, respectively 69 and 55% of the variance in AHI. The authors concluded

that in lean or young subjects, upper airway abnormalities explain a major part of the variance in apnoea/hypopnoea index and are likely to play an important pathogenic role. They also suggested that the shape of the pharyngeal lumen in awake subjects is more dependent on body mass index than on the presence of OSA (Mayer, Pepin et al. 1996).

Battagel *et al.* investigated the craniofacial and pharyngeal anatomy of a group of OSA subjects, and compared these values from groups of both snoring and normal individuals, matched on basis of sex and ethnicity (Battagel, Johal *et al.* 2000). A sample of 115 dentate patients were investigated with lateral cephalometry, with a comparable number of OSA ($n = 45$) subjects and ($n = 46$) snorers. A common denominator amongst both of the sleep-disorder groups as compared to control subjects was the finding of a reduced mandibular body length. No other statistically significant differences were found for snoring and OSA subjects when dento-skeletal measurements were recorded. However, several soft tissue differences were noted, with OSA subjects having a significantly ($p < 0.05$) larger and thicker soft palate, increased lingual ($p < 0.01$) and oropharyngeal ($p < 0.05$) areas and increased mandibular plane to hyoid distances ($p < 0.05$.) They concluded that morphological differences were present between snorers, control and OSA subjects, but most relate to soft tissue structures. Moreover, whilst a cephalometrically recognizable predisposition toward sleep disordered breathing may exist, it is one aspect of consideration in this multifactorial condition (Battagel, Johal *et al.* 2000).

2.3 SLEEP APNOEA

2.3.1 Definition

An apnoea is delineated as a suspension of breathing during sleep for 10 seconds or more. The Apnoeic index is the average number of episodes of apnoea per hour of sleep, with at least 5 episodes occurring per hour during seven hours of nocturnal sleep in the diagnosis of OSA (Guilleminault and Dement 1978).

A hypopnoea is when a 50% or greater reduction in tidal volume occurs, simultaneously with a 4% or greater reduction in blood oxygen saturation, lasting 10 seconds or more (Wynne, Block *et al.* 1979; Guilleminault, Cumiskey *et al.* 1980). The Apnoea Hypopnoea Index (AHI) is the average number of episodes of apnoea plus hypopnea per hour during sleep. AHI is used to quantify the degree of severity of OSA and to evaluate the efficacy of treatment by measuring the change in this index before and after therapy (Parisi, Santiago *et al.* 1988). The Respiratory Disturbance Index (RDI) is the same as AHI but considers the average number of arousal per hour of sleep (Loube, Gay *et al.* 1999). The criteria for classification of severity of OSA is outlined in Table 1.

The term 'sleep apnoea syndrome', is when cessation of breathing occurs repeatedly during sleep for long enough periods to cause measurable blood deoxygenation (Robert 1992). It refers to the occurrence of at least 5 apnoea or hypopneas per hour of sleep, when combined with two or more of the following features: loud snoring, excessive daytime sleepiness, witnessed apnoeas by the bed partner or unrefreshing sleep (Naughton 1997).

The Wisconsin Sleep Cohort Study estimated the prevalence of sleep-disordered breathing, defined as an RDI of five or higher, at nine percent for women and twenty-four percent for men. OSA has been conservatively estimated to affect four percent of men and two percent of women in the middle-aged work force (Young 1993; Young, Palta *et al.* 1993).

2.3.2 Classification of Sleep Apnoea

Obstructive sleep apnoea, the most common of the three types of apnoea, is related to upper airway blockage despite impulses being sent from the brain. It is a progressive and potentially life-threatening disorder in which breathing stops repeatedly for at least 10 seconds for each apnoeic event, during 7 hours of nocturnal sleep in both rapid eye movement (REM) stage and non-rapid eye movement (NREM) stage.

Central sleep apnoea is characterised by the cessation of airflow and respiratory movements. It occurs when the brain fails to send impulses to the respiratory muscles so that breathing is not initiated.

Mixed apnoea occurs when initially there is no inspiratory effort but subsequently when efforts are initiated the apnoea persists because the upper airway is collapsed (Guilleminault and Dement 1978). Mixed apnoea occurs more often than central but less frequently than the obstructive type (Robert 1992).

Current opinion has moved away from the early rigid definitions that, although useful for research, excluded many patients with disabling symptoms (Physicians. 1993) For example, the individual with one or two apnoeas per hour, oxygen desaturation to 60-70% and impaired arousal reflexes due to autonomic neuropathy, can be far more vulnerable to the consequences of OSA than a healthy, asymptomatic 75 year old with 15 apnoeas per hour (Guilleminault, Tilkian *et al.* 1977).

Table 1. Proposed severity criteria for OSAHS

A. Sleepiness 1. <u>Mild</u>: Unwanted sleepiness or involuntary sleep episodes occur during activities that require little attention (such as watching TV or reading). Symptoms produce only minor impairment of social or occupational function. 2. <u>Moderate</u>: Unwanted sleepiness or involuntary sleep episodes occur during activities that require some attention (such as concerts or meetings). Symptoms produce moderate impairment of social or occupational function. 3. <u>Severe</u>: Unwanted sleepiness or involuntary sleep episodes occur during activities that require active attention (such as eating, driving). Symptoms produce marked impairment in social or occupational function. B. Sleep-related obstructive breathing events (apnoea, hypopnoea and respiratory effort-related arousals.) 1. <u>Mild</u>: 5-15 events/hour of sleep. 2. <u>Moderate</u>: 15-30 events/hour of sleep. 3. <u>Severe</u>: greater than 30 events/hour of sleep.

2.3.3 Prevalence of Sleep Apnoea

Prevalence studies vary widely, ranging from 1 to 24%, for groups of middle aged adults (Gisalon, Almqvist *et al.* 1988; Cirignotta, D'Alessandro *et al.* 1989; Young 1993; Young, Palta *et al.* 1993) These studies have concluded that 4% of males and 2% of females in the USA, have a degree of sleep apnoea severe enough to warrant treatment. More recent figures of up to 4% established OSA as second only to asthma in the prevalence of chronic respiratory disorders, depending on the diagnostic criteria employed (McNicholas 2003). "The largest studies in middle-aged adults were done in Wisconsin (the Wisconsin Sleep Cohort); the town of Busselton, Australia; and in Dauphin and Lebanon counties in Pennsylvania, USA" (Pack 2006).

Additionally, it has been demonstrated that OSA progressively worsens with age till 60 years (Figures 3 and 4.) "Most data on the evolution of OSAS comes from cross-sectional surveys which assume that age related differences are due to the ageing process itself. Cross-sectional studies on prevalence do show effects of age, independent of the unfortunate propensity of a rising BMI with age. Some studies show an approximate doubling of AHI every 10 years or so. Prevalence seems to fall above the age of 60 or so."

The wide range in prevalence of OSA reported could be attributed to differences in the diagnostic criteria employed, patient groups studied or methodologies used. For instance, the percentage of the population with heavy snoring doubles when the bed partner contributes to the questionnaire (Stradling, Crosby *et al.* 1991) Population differences in age, obesity, alcohol consumption and genetic variability could also have a bearing on prevalence figures. OSA prevalence has been found to increase with age (Roehrs, Zorick *et al.* 1983) and obesity (Battagel and L'Estrange 1996).

The varying prevalence of OSA amongst different racial populations, may lend support to the theorem that ethnicity may be an important risk factor in obstructive sleep apnoea syndrome (OSAS) (Table 2.) African-Americans have a higher prevalence and increased disease severity compared to Caucasians (Redline, Tishler *et*

al. 1997). Kripke *et al.* (1997) estimated that 16.3 percent of the US Hispanics and racial minorities have OSA as compared with 4.9% of non-Hispanic whites aged 40 to 64 years.

Several studies on the prevalence of SDB have been conducted in Asian countries. Ip *et al* (2001) demonstrated that OSA is as common among the middle-aged Hong Kong Chinese men as the Caucasians with prevalence rates of sleep disordered breathing and OSAS using full polysomnography to be 8.1 and 4.1% (Ip, Lam *et al.* 2001). Similar to the dichotomy present between Caucasian male and female OSA prevalence rates, Ip *et al* (2004) found a reduced prevalence of sleep disordered breathing and OSAS amongst middle-aged Hong Kong women of 3.7% and 2.7% respectively (Ip, Lam *et al.* 2004). Kim *et al* (2006) found the prevalence of OSAS to be 4.5% in men and 3.2% in women (Kim, In *et al.* 2004). Most Asian OSA patients are said to have a relatively lower body mass index (BMI) than the Caucasian counterparts despite suffering from a similar degree of OSA i.e. they tended to be affected to a greater extent.

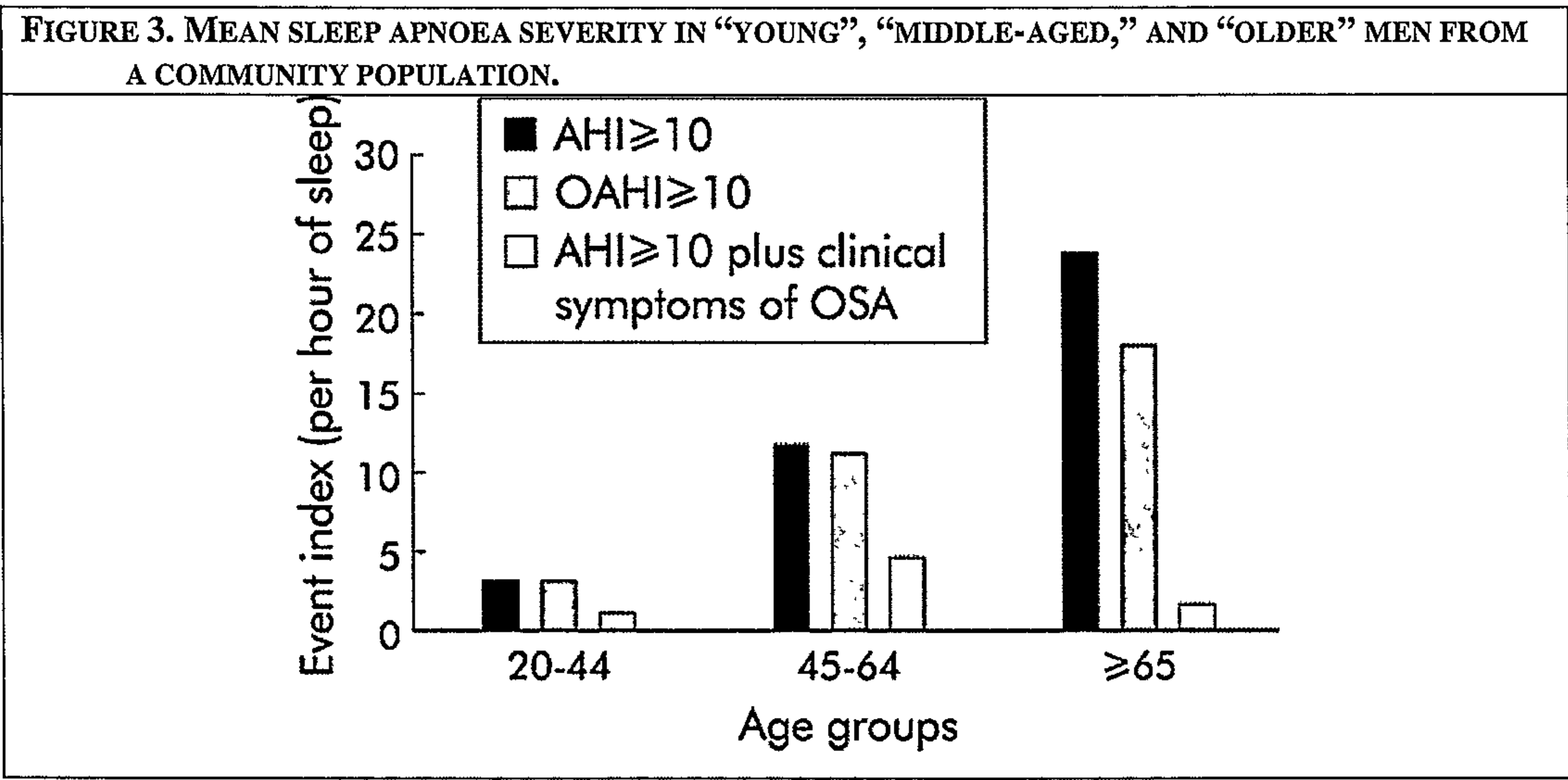
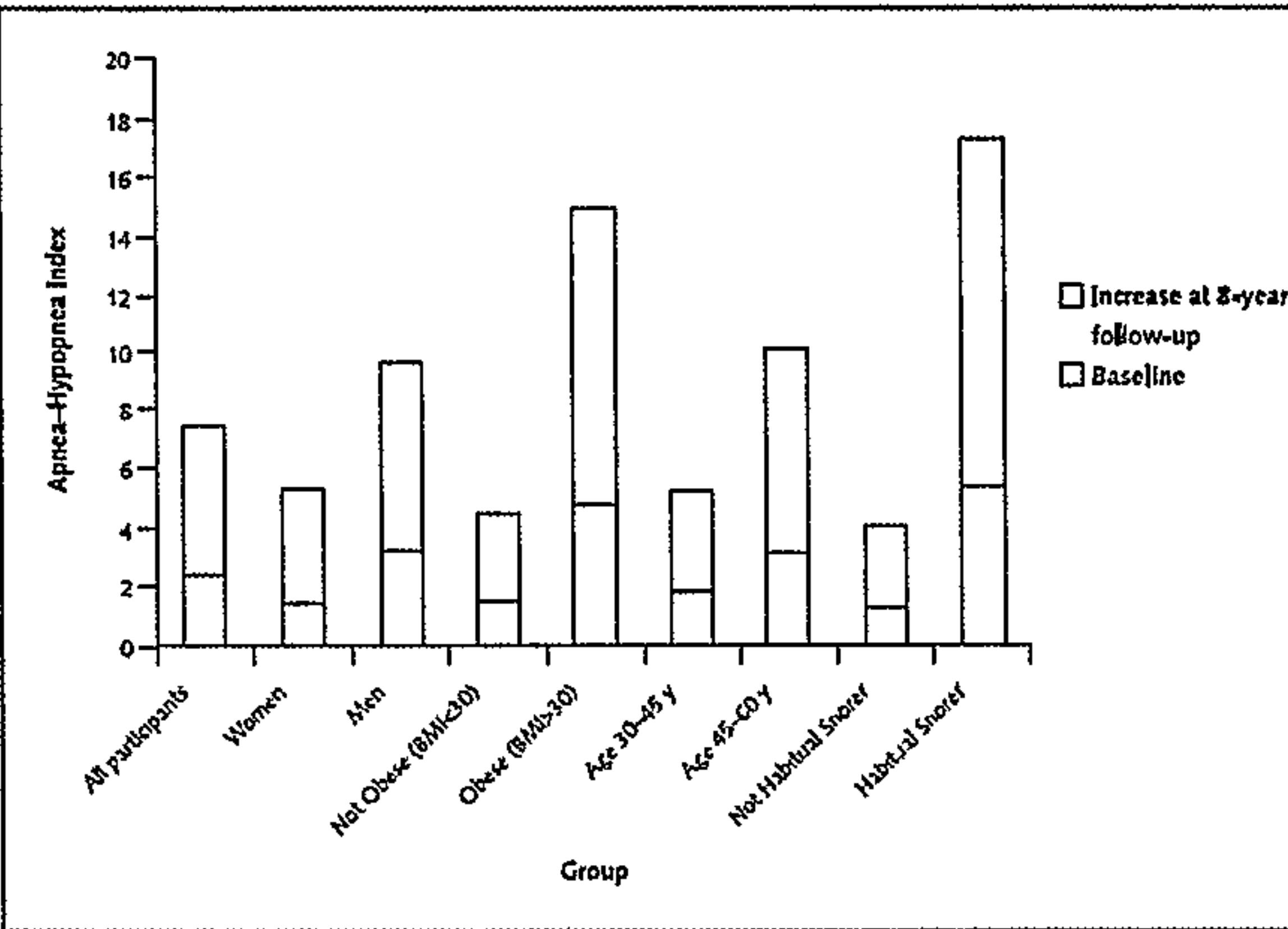


FIGURE 4. MEAN APNOEA-HYPOPNEOA INDEX AT BASELINE AND INCREASE 8 YEARS LATER.
SOURCE (YOUNG, PALTA ET AL. 1993).

Figure 1. Mean apnea-hypopnea Index at baseline and the increase 8 years later in 282 participants in the Wisconsin Sleep Cohort.



Subgroup analysis showed greater progression of disease in patients who were obese, 45 to 60 years of age, or habitual snorers at baseline. Sex did not correlate with disease progression. Data obtained from reference 7. BMI = body mass index.

Table 2. Prevalence estimates for any OSA (mild to severe, AHI≥ 5) and OSAS (any OSA and excessive daytime sleepiness).

Reference	Population	N	Monitoring Method	Prevalence estimates for: AHI≥ 5 AHI≥ 5 & excessive sleepiness	
Lavie	Israel, men	78	Polysomnography	5.3%	0.9%
Gislason <i>et al</i>	Sweden, men	61	Polysomnography		1.4%
Marin <i>et al</i>	Spain – Men	597	Home oximetry	15%	2.2%
	Women	625	Home oximetry	6%	0.8%
Stradling and Crosty	UK Men	1001	Home oximetry	5.1%	1.3%
Bearpark <i>et al</i>	Australia, Men	311	Respiratory monitor	26%	3%
Young <i>et al</i>	US Men	352	Polysomnography	24%	4%
	Women	250	Polysomnography	9%	2%

2.3.4 Anatomy of the Airway

2.3.4.1 The Pharynx

The pharynx is a muscular tube that extends superoinferiorly from the base of the cranium to the level of the inferior surface of the body of the 6th cervical vertebrae. The pharynx lies dorsal to the nasal cavity, the oral cavity and the larynx. The nasal part of the nasopharynx resembles the nasal cavity in possessing a highly vascular mucosa that is rich in lymphoid tissue. The mucosa of the nasal section of the nasopharynx is of the respiratory type, while the posterior part resembles the oropharynx in having a stratified squamous epithelium. The nasal portion of the nasopharynx has bony elements in its wall is thus rigid, whereas the pharyngeal part is contractile as a result of the musculature nature of its wall. The pharyngeal walls contain the same four basic layers as other the organs of the gut:

- An areolar coat – covers exterior of the pharynx. Continues with the areolar fascia overlying the buccinator muscle – buccopharyngeal fascia. Acts as a neurovascular transport medium. Running through the fascia is a pharyngeal plexus of veins & nerves.
- Muscular coat – consists of 5 paired muscles, which form an outer semicircular layer, and two inner longitudinal muscles.
- Submucosa, or pharyngobasilar fascia – tough, fibrous coat. Anchors the pharynx to the base of the skull at a U-shaped attachment.
- Mucosa – coats the internal aspect of the pharynx.

2.3.4.1.1 Nasopharynx

The nasopharynx begins superiorly at the attachment of the superior constrictor muscle to the pharyngeal tubercle on the basilar part of the occipital bone and ends at the level of the soft palate. It should be recorded that this is the widest part of the pharynx and it is in communication with the nasal cavity via the choanae and with middle ear cavities via the Eustachian tubes. Inferiorly, air passes through the more anteriorly placed larynx on its way to the trachea and the bronchial tree.

- Is the superior portion of the pharynx lying above the soft palate and communicates with the nasal cavity anteriorly through the choanae.
- Following features are found within the nasopharynx:
 - Mouth of the auditory (pharyngotympanic) tube bulges out into lateral wall of nasopharynx. Raised mouth is mucous membrane-covered cartilage.
 - Salpingopharyngeal fold – consists of a small muscle covered with mucous membrane. Fold continues inferiorly from the posterior aspect of the salpinx and blends with the lateral wall of the nasopharynx. Salpingopharyngeus muscle is a small portion of the palatopharyngeus muscle.
 - Pharyngeal recess – vertical cleft between salpingopharyngeal fold and the posterior wall of the pharynx.
 - Pharyngeal tonsils or adenoids – collection of nodular lymphoid tissue found on the supero-posterior wall of the nasopharynx. Also extends laterally into the pharyngeal recess.

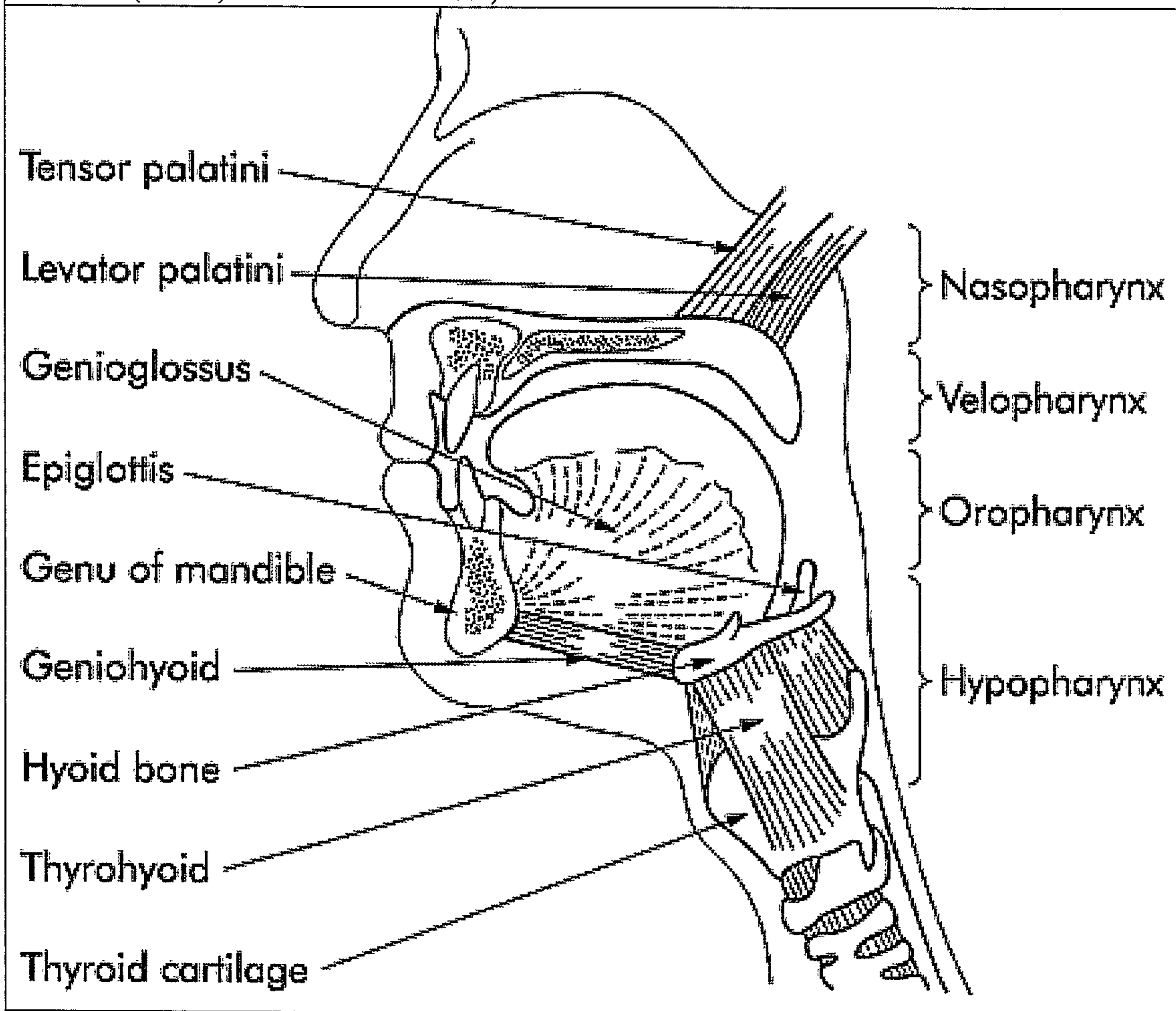
2.3.4.1.2 Oropharynx

- Extends from the soft palate to the level of the epiglottis.
- Lies below the soft palate and communicates anteriorly with the oral cavity.
- Following features found within oropharynx:
 - Anterior and posterior pillars – 2 folds of mucous membrane extending laterally and inferiorly from the soft palate. More anterior fold is the palatoglossal arch running down to the lateral aspect of the tongue.
 - Posterior fold runs from the soft palate to the lateral wall of the pharynx as the palatopharyngeal arch.
 - Palatine tonsil – rounded elevation of lymphoid tissue covered by mucous membrane. Sits in the triangular interval between the anterior and posterior pillars.
 - Blood supply to the palatine tonsil is from tonsillar branches of the ascending palatine artery and facial artery.

2.3.4.1.3 Laryngeal Pharynx

- Larynx projects upward into pharynx, and that part of the pharynx adjacent to the larynx - laryngeal pharynx; ends inferiorly at vertebral level C6 by funnelling downward into the oesophagus.
- Following features:
 - Epiglottis – leaf like, elastic cartilage structure that guards the oval opening into the larynx.
 - Glossoepiglottic folds – 3 folds of mucous membrane that run anteriorly from the epiglottis to the base of the posterior 1/3 of the tongue; median fold and two lateral folds on either side.
 - Valleculae – 2 small depressions created by 3 folds; lie on the either side of the median glossoepiglottic fold.
 - Piriform recess – vertical gutter on the lateral wall of the laryngeal pharynx; lies between the lateral glossoepiglottic fold and the sidewall of the pharynx and continues downward on either side of the larynx like 2 troughs to the oesophagus below.

FIGURE 7. ANATOMICAL REPRESENTATION OF THE UPPER AIRWAY AND THE IMPORTANT MUSCLES CONTROLLING AIRWAY PATENCY.
SOURCE - (FOGEL, MALHOTRA *ET AL.* 2004)



2.3.5 Pathophysiology of Sleep Apnoea

The upper airway includes the structures of the *nasopharynx*, *oropharynx* and *hypopharynx* (Worsnop, Pierce *et al.* 1998). The upper airway is a soft tissue structure with minimal bony support (Figures 1,2). Each structural segment has been considered as a possible site of obstruction in OSA (Solow 1992). The definitive event in OSA is posterior movement of the tongue and palate into apposition with the posterior pharyngeal wall, resulting in occlusion of the nasopharynx and oropharynx (Hudgel 1992). As a result of apnoea, progressive asphyxia develops until there is a brief arousal from sleep, restoration of upper airway patency and resumption of airflow (Bradley 1985). With the relief of asphyxia, the patient quickly returns to sleep, only to have the sequence of events repeated (Guilleminault, Cumiskey *et al.* 1980).

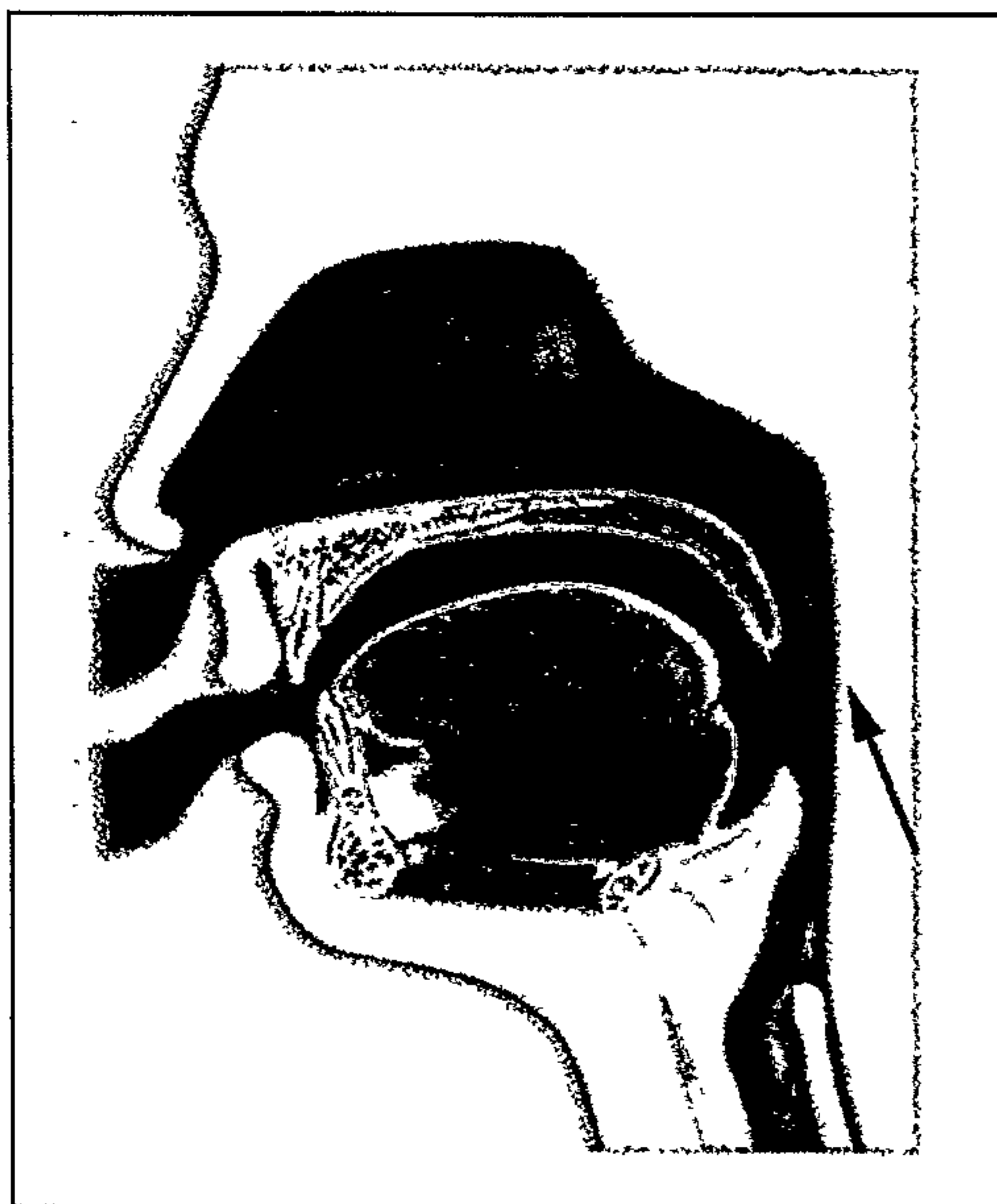


FIGURE 4. ANATOMY OF NORMAL AIRWAY

Source: (Ivanhoe, Cibirka *et al.* 1999)

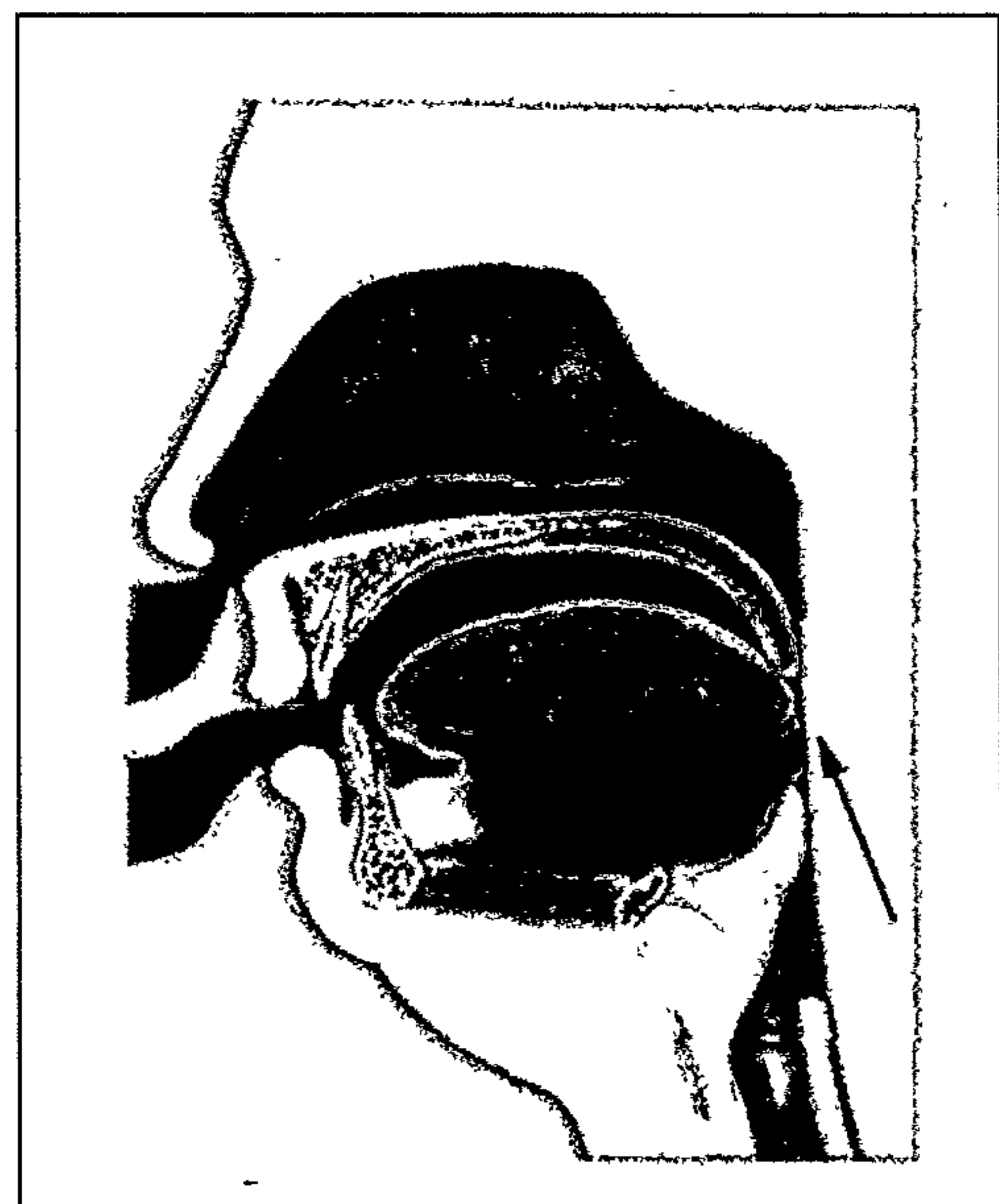
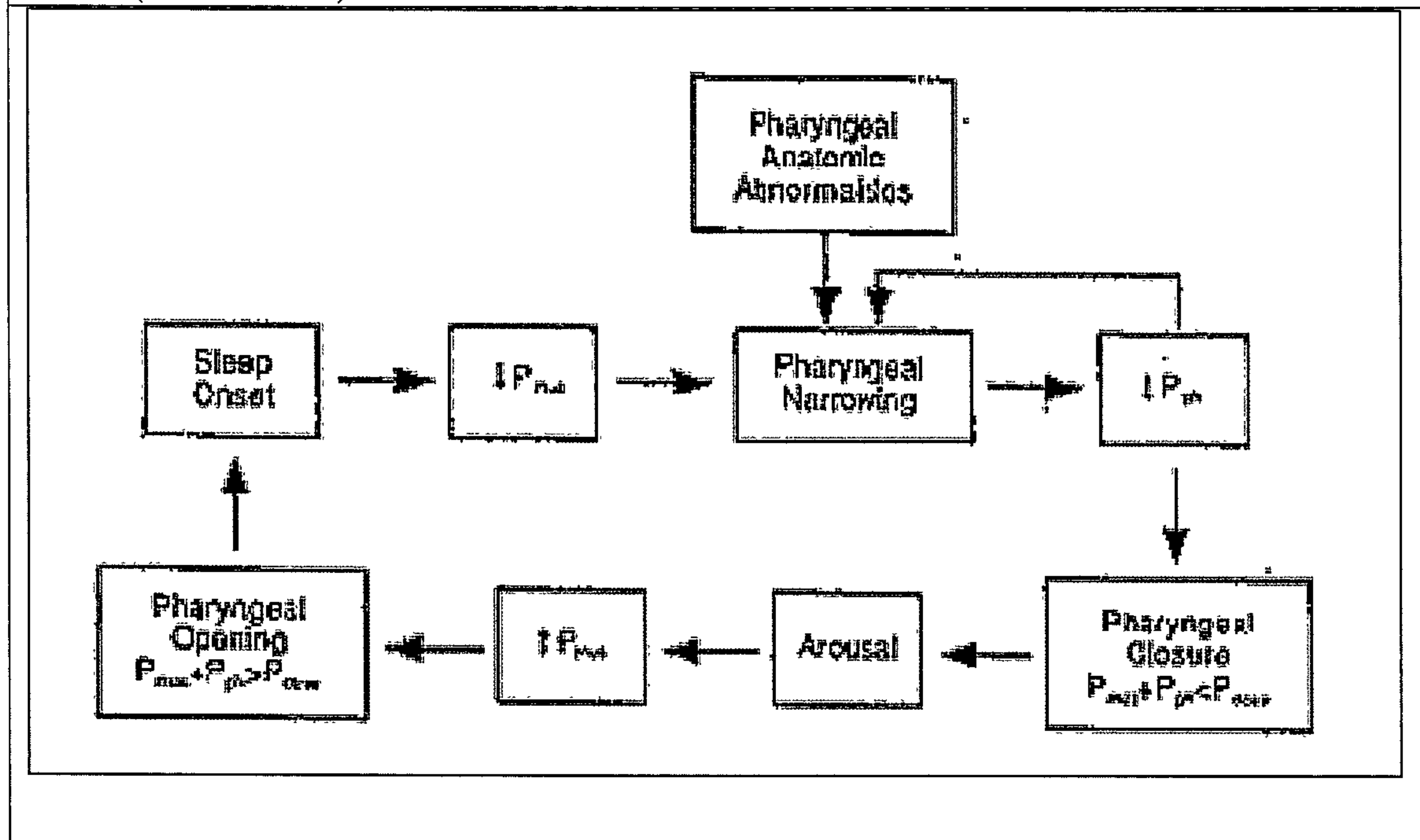


FIGURE 5. ANATOMY OF AN OSA PATIENT DURING AN APNOEA.

FIGURE 6. PATHOLOGIC SEQUENCE OF UPPER AIRWAY OCCLUSIONS DURING SLEEP.
SOURCE (REMMERS 1989).



The precise mechanism of OSA is complex and its understanding is incomplete. A multifactorial aetiology is supported by the current weight of evidence available (Anch, Remmers *et al.* 1982; Lowe, Gionhaku *et al.* 1986; Lowe, Santamaria *et al.* 1986; Rodenstein, Doms *et al.* 1990; Hudgel 1992; Cistulli, Barnes *et al.* 1994; Cistulli, Grunstein *et al.* 1994):

- Predisposing factors.
- Anatomical structures which may affect upper airway size.
- Functional processes related to upper airway muscle activity.

These aetiological factors in combination are thought to lead to a narrowing of the airway with repetitive closure during sleep.

2.3.5.1 Predisposing Factors to OSA

Several factors are influential to the severity of OSA. Pre-existing pulmonary disorders result in breathing becoming more difficult, leading to decreased blood oxygen tensions. Central nervous system depressants such as alcohol, sedatives and sleep pills induce relaxation of the pharyngeal airway musculature, which can result in airway occlusion (Issa and Sullivan 1982; Chaudhary and Smith 1991; Battagel and L'Estrange 1996).

2.3.5.1.1 Obesity

Few epidemiological studies of correlates of OSA fail to implicate a relationship with obesity. In 1999-2000, the prevalence of overweight and obesity in Australia (BMI $\geq 25.0\text{kg/m}^2$; waist circumference $\geq 80.0\text{cm}$ [women] or $\geq 94.0\text{cm}$ [men]) in both sexes was almost 60% defined by either BMI or waist circumference. Lower educational status, higher television viewing time and lower physical activity time were demonstrated to be strongly associated with obesity (Cameron, Welborn *et al.* 2003).

Obesity has been hypothesised to alter breathing during sleep via multiple mechanisms including alteration of upper airway structure and function, disturbance of the relationship between respiratory drive and load compensation, and obesity related hypoxemia (Strobel and Rosen 1996). Obesity and excess fat in peripharyngeal and subcutaneous regions serve to further diminish the available airway space, encouraging its occlusion nocturnally, whilst the subject is supine and may be involved in the lack of control of the oral and pharyngeal musculature (Battagel and L'Estrange 1996).

Obese patients with large necks have a more collapsible velopharynx during wakefulness, which may predispose to upper airway obstruction during sleep (Ryan and Love, 1996). Obesity and neck circumference may be a significant predictor of OSA (Davies and Stradling 1990; Katz, Stradling *et al.* 1990). Davies *et al.* found that

men and women were at greater risk for OSA if they had neck circumference of 17 and 16 inches or greater, respectively (Davies and Stradling 1990).

‘A variety of body habitus measures including neck morphology, general obesity, and central obesity have been cross-sectionally associated with OSA in convenience samples of patients from sleep-disorders clinics or population-based studies. Although some of these studies seem to conflict with regard to what measure of obesity or body habitus is the ‘best’ predictor of OSA, it should be noted that all measures of body habits are correlated, some highly so. Thus, any degree of ponderosity should be viewed as a risk factor or harbinger of OSA, whatever the measure used to assess body habitus’ (McNicholas and Phillipson 2002).

2.3.5.1.2 Genetics

Research linking specific genetic syndromes and polymorphisms with OSA is scarce in the literature. ‘A Japanese study found a statistically significantly higher prevalence (81%) of HLA-A2 antigen in 32 obstructive sleep apnoea syndrome patients relative to a normal control group and to the Japanese population, suggesting a genetic basis for sleep apnoea’ (McNicholas and Phillipson 2002). Familial clustering of OSA or symptoms of OSA have been reported (Redline, Tishler *et al.* 1995). Redline *et al.* found, compared with subjects having no relative with OSA, subjects having one relative with OSA had 1.6 times the odds of having SAS. They concluded that roughly 40% of OSA variability could be explained by familial factors (Redline, Tishler *et al.* 1997).

2.3.5.1.3 Other associated risk factors

Increasing age has been demonstrated to predispose to OSA (Prinz 1995; Strohl and Redline 1996). Other factors associated with metabolic and endocrine disorders, in particular hypothyroidism, male gender (Young 1993), sleeping supine (Pae, Lowe *et al.* 1994), familial tendency (McNamara, Cistulli *et al.* 1994; Redline, Tishler *et al.* 1995), Marfan’s syndrome (Cistulli and Sullivan, 1993), acromegaly (Rosenow *et al.*, 1994), non insulin dependent diabetes (Brooks *et al.*, 1994) and heaving smoking (Wetter, Bidwell *et al.* 1994) have been associated with obstructive sleep apnoea.

“Smoking is often mentioned as a risk factor for OSA, but few studies have been conducted to investigate this association. There are several mechanisms for a role of smoking in OSA. The upper airway inflammation and airway disease associated with smoking may increase vulnerability to OSA. The decline in nicotine blood levels during sleep may cause sleep instability, which in turn has been linked to OSA” (McNicholas and Phillipson 2002).

2.3.5.2 Anatomical Structures Affecting Upper Airway Size

‘Various abnormalities of the bony and soft tissue structures of the head and neck may predispose to OSAS. Dysmorphisms related to mandibular size and position and to palatal height have been observed in OSAS patients, particularly those of normal body weight. Craniofacial risk factors may be endogenous or exogenous’ (McNicholas and Phillipson 2002).

Many cephalometric studies have been performed to explore the craniofacial architecture of patients with obstructive sleep apnoea syndrome (Paoli, Lauwers *et al.* 2001). A large number of cephalometric case-control studies have compared apnoeic patients with chronic snorers or controls. This type of comparison causes problems related to the selection of patients, with Miles conducting a meta-analysis to conclude that a direct causal relationship between craniofacial structure and OSA has not been established (Miles, Vig *et al.* 1996). However, studies using fluoroscopy (Surratt, Dee *et al.* 1983), acoustic reflection (Katz, Stradling *et al.* 1990), fiberoptic endoscopy (Borowiecki, Pollak *et al.* 1978), cephalometric radiographs (deBerry-Borowiecki, Kukwa *et al.* 1988), computerised tomography (Lowe and Fleetham 1991), cinematographic computerised tomography (Shepard 1990) and magnetic resonance imaging (Abbey, Block *et al.* 1989) have demonstrated that OSA patients have narrower airways than control subjects.

Lowe *et al.* (1986) found that sleep apnoea subjects had a posteriorly positioned maxilla and mandible, a steep occlusal plane, overerupted maxillary and mandibular teeth, proclined incisors, a steep mandibular plane, a large gonial angle, high upper and lower facial heights, and an anterior open bite in association with a long tongue and a posteriorly placed pharyngeal wall (Lowe, Santamaria *et al.* 1986). They concluded that subjects with sleep apnoea demonstrated several alterations in craniofacial form that may reduce the upper airway dimensions and subsequently impair upper airway stability (Lowe, Santamaria *et al.* 1986).

These studies have limitations, such as the subjects studied were awake and often in the erect posture. Despite this, they have implicated various skeletal and soft tissue craniofacial structures in the narrowing of the upper airway in patients with OSA. The sites of minimum cross-sectional area during wakefulness can vary between individual patients but the majority demonstrate narrowing in the velopharyngeal (retropalatal) segment (Shepard, Gefter *et al.* 1991).

To account for possible differences in anatomic architecture between awake and sleeping patients, Lowe *et al* (1996) compared 347 Caucasian OSA subjects and 101 control subjects in the upright and supine position, dividing the sample by gender and malocclusion. They found that in the upright position, the most atypical craniofacial and upper airway structure was shown in male patients with Class 1 occlusion and OSA. Furthermore, in patients with OSA, the degree of upper airway abnormalities was less in the supine position regardless of the skeletal subtype. In the supine position, the most atypical craniofacial and upper airway structure was also shown in male patients with Class 1 occlusion and OSA. No significant differences were noted between Class II Division II malocclusion male OSA patients and control subjects. Similarly, no significant differences were noted Class I occlusion female OSA patients and control subjects. When patients change position to the supine, distinctive changes in the UA structure in both patients with OSA and control subjects occurred, according to skeletal subtype and gender. The authors concluded that there are a series of characteristics of craniofacial and upper airway structure that differ between patients with OSA and control subjects matched for skeletal subtype and gender. Moreover, these differences may predispose to upper airway obstruction during sleep in patients with OSA (Lowe, Ono *et al.* 1996).

Ono *et al.* (1996) identified differences in cephalometric variables in 61 adult Class 1 skeletal type male subjects, in the upright and supine position. When patients with OSA changed their posture from upright to supine, significant correlations were observed between the cranial base to upper cervical column angle and the hypopharynx cross-sectional area and BMI. Namely, the mandibular plane angle and the sella-nasion was significantly correlated with BMI. Additionally, a significant positive correlation between the sella-nasion plane angle and BMI and a significant inverse correlation between the mandibular plane angle in reference to the absolute

vertical and horizontal planes, with BMI after the positional change. The authors concluded that changes in body position from the upright to supine, lead to the patients neck being more extended, and the hyoid bone moving more anterosuperior in conjunction with an upward and forward rotation of the mandible (Ono, Lowe *et al.* 1996).

Anatomical structures affecting upper airway size can be divided into skeletal and soft tissue structures. Skeletal structures implicated are the *cranial base, maxilla, mandible, hyoid bone and head posture.*

2.3.5.2.1 Cranial Base

A decrease in the sagittal dimension of the cranial base in OSA subjects has been reported in several publications (Tangugsorn, Skatvedt *et al.* 1995; Tangugsorn, Skatvedt *et al.* 1995; Battagel and L'Estrange 1996; Redline, Tishler *et al.* 1997; Liu, Lowe *et al.* 2000). A reduction in cranial base angulation (Ba-SN) has also been reported in OSA subjects.(Jamieson, Guilleminault *et al.* 1986; Battagel and L'Estrange 1996; Battagel, Johal *et al.* 2000)

2.3.5.2.2 Maxilla and Mandible

Bimaxillary retrusion(Lowe, Santamaria *et al.* 1986) or retrognathia of the mandible has been reported in OSA subjects (Jamieson, Guilleminault *et al.* 1986; Series, St Pierre *et al.* 1992; Hochban and Bradenburg 1994). Other studies however, have found no evidence of mandibular retrognathia in OSA subjects(deBerry-Borowiecki, Kukwa *et al.* 1988; Zucconi, Ferini-Strambi *et al.* 1992). Tsuchiya found mandibular retrognathia in patients with a high Apnoeic index (AI) and low Body Mass Index (BMI)(Tsuchiya, Lower *et al.* 1992), suggesting that skeletal abnormality may be an important aetiological factor in OSA in non-obese patients with a high AI. Tangugsorn observed a reduced maxillary length with normal height in 100 male patients with OSA(Tangugsorn, Skatvedt *et al.* 1995).

Although a reduction in the length of the body of the mandible in OSA patients was reported by some authors (Battagel and L'Estrange 1996; Battagel, Johal *et al.* 2000),

whilst other workers did not find any such reduction (Bacon, Turlot *et al.* 1990; Tangugsorn, Skatvedt *et al.* 1995; Trenouth and Timms 1999). Therefore, in the anteroposterior dimension the cranial base, maxilla and mandible have been implicated as being shorter or repositioned (Battagel and L'Estrange 1996).

In the vertical dimension most studies have reported an increase in the lower anterior facial height with a concomitant increase in the maxillo-mandibular plane angle (Lowe, Santamaria *et al.* 1986; Bacon, Turlot *et al.* 1990; Tsuchiya, Lower *et al.* 1992; Tangugsorn, Skatvedt *et al.* 1995; Liu, Lowe *et al.* 2000).

2.3.5.2.3 Head Posture and Hyoid Bone

Flexion or extension of the head has been postulated by some authors to influence the dimensions of the oropharyngeal airway (Hellsing 1989; Davies and Stradling 1990). Solow and Tangugsorn found that the average craniocervical angulation of OSA patients in the standing position was significantly greater than in controls (Solow, Ovesen *et al.* 1993; Tangugsorn, Skatvedt *et al.* 1995). This was mainly mediated by a forward inclination of the cervical column and confirmed by Petri *et al.* and Solow (Petri, Suadiciani *et al.* 1994; Solow, Skov *et al.* 1996). A deviated head posture was reported to be observed in OSA subjects (Lowe, Fleetham *et al.* 1995; Tangugsorn, Skatvedt *et al.* 1995; Ozbek, Miyamoto *et al.* 1998).

The position of the hyoid bone has been found to be more inferior in relation to the mandibular plane for OSA subjects (Jamieson, Guilleminault *et al.* 1986; Lowe, Gionhaku *et al.* 1986; Lowe, Santamaria *et al.* 1986; deBerry-Borowiecki, Kukwa *et al.* 1988; Tangugsorn, Skatvedt *et al.* 1995). During normal growth and development, the position of the hyoid bone becomes inferior and at adulthood it is at the level of C4 in normal subjects (Durzon and Brodie 1962). In OSA patients it has been found between C4-C6 (Tangugsorn, Skatvedt *et al.* 1995).

The position of the hyoid bone however is subject to a high degree of variation because of physiological adaptations and changes of head position. During normal growth, Winnberg *et al.* demonstrated that a more extended head posture dropped the hyoid apparatus inferiorly and anteriorly (Winnberg, Pancherz *et al.* 1988). Pae

investigated the relationship between airway size and body position and suggested that patients with OSA had an inferiorly positioned hyoid bone and extended head postures, and concluded that a smaller than optimal airway induced an extended head posture for better airway patency and that an extended head posture elicited an inferiorly positioned hyoid bone (Pae 1989). The contemporary view regarding an inferiorly positioned hyoid bone and an extended head position suggests that, rather than predisposing factors, there are physiological adaptations to lift away the base of the tongue and the soft palate from the posterior pharyngeal wall in order to alleviate the obstructive condition.

Hoekema *et al.* have implicated several factors in the explanation of an inferior hyoid bone position amongst OSA subjects (Hoekema, Hovinga *et al.* 2003). Namely, this group cite the work of Maltais *et al.* (1991), who observed a relationship between age and hyoid bone position, with the hyoid bone in older subjects tending to be located more inferiorly than in younger subjects. Furthermore, Hoekema *et al.* proposition is strengthened by evidence from Brown *et al.* (1981) who observed a decrease in pharyngeal size with age in healthy males, and the recognised relationship between pharyngeal size, hyoid bone position and age observed in healthy males.

Several mechanisms have been postulated to explain an inferior position of the hyoid bone in OSA patients (Hoekema, Hovinga *et al.* 2003). However, their findings need to be considered carefully as the study population was limited to that of a Scandinavian ethnicity, and quite small in number and limited to male gender only ($n = 31$.) Sforza *et al.* found that the distance between the hyoid bone and the mandibular plane predicted collapsing pressure (P_{crit}) in a group of men with OSAS (Sforza, Bacon *et al.* 2000). Verin *et al.* found the mandibular plane to hyoid distance to be the best predictor of upper airway resistance in awake apnoea patients and controls (Verin, Tardif *et al.* 2002).

Soft tissue factors implicated as possible aetiological factors for OSA are the *tongue, soft palate and pharyngeal dimensions*.

2.3.5.2.4 Tongue

It is unclear on exactly what role the tongue plays in the aetiology of OSA. A larger tongue length and area in OSA patient has been reported (Lowe, Gionhaku *et al.* 1986; Lowe, Santamaria *et al.* 1986; deBerry-Borowiecki, Kukwa *et al.* 1988; Tangugsorn, Skatvedt *et al.* 1995; Battagel, Johal *et al.* 2000). Prachartam *et al.* found tongue size and area is normal by the functional space of the tongue is reduced, forcing the tongue backwards into the pharynx and diminishing airway space at this level (Prachartam, Hans *et al.* 1994). Battagel *et al.* confirmed the reduced oropharyngeal area in OSA groups, resultant of a larger and thicker tongue (Battagel, Johal *et al.* 2000). Tangugsorn *et al.* (1995) found that the tongue position was more upright and caudally extended (Tangugsorn, Skatvedt *et al.* 1995). Ryan *et al.* found that obese OSA patients have larger tongues and smaller airways (Ryan, Lowe *et al.* 1991). Do *et al.* (2000) found that tongue volume only positively correlated with BMI and neck circumference but there was no correlation with age or AHI (Do, Ferreyra *et al.* 2000). The residual oropharyngeal area was reduced by 9 percent due to a larger tongue and soft palate (Tangugsorn, Skatvedt *et al.* 1995).

2.3.5.2.5 Soft Palate

OSA patients have longer and thicker soft palates, with an area approximately 20% greater than normal subjects which results in further reduction of the airway (Jamieson, Guilleminault *et al.* 1986; Battagel and L'Estrange 1996; Lowe, Ono *et al.* 1996; Battagel, Johal *et al.* 2000) (Lyberg *et al.*, 1989;). Tangugsorn *et al.* (1995) found an increased length, thickness and sagittal area of the soft palate and 15% more pharyngeal area occupation (Tangugsorn, Skatvedt *et al.* 1995). OSA subjects have significantly ($p < 0.05$) thicker and larger soft palates as compared to individuals that snore and who do not have OSA symptoms (Battagel, Johal *et al.* 2000).

Pae showed that the thickness of the soft palate increases and the oropharyngeal cross-sectional area decreases when a patient changes from an upright to supine position (Pae, Lowe *et al.* 1994). Johnston and Richardson studied the longitudinal changes of the airway in 16 adults with a mean age of 20 years (Johnston and

Richardson 1999). A lateral cephalometric radiograph was taken at this stage and 32 years later. They found that the soft palate became longer and thicker and the oropharynx became narrower, which may explain the increased prevalence of OSA in advancing years.

2.3.5.2.6 Pharyngeal Dimensions

The dimensions of the pharynx are reduced (Battagel, Johal *et al.* 2000), whether the subjects are investigated in the upright or supine position (Yildirim, Fitzpatrick *et al.* 1991) and independent of the assessment technique (deBerry-Borowiecki, Kukwa *et al.* 1988; Lowe, Fleetham *et al.* 1995). Haponick and co-workers (1983) used computerised tomography to identify a reduced posterior airway space in OSA subjects. A recent study by Isono *et al.* used endoscopic techniques to assess pharyngeal airway size in both patients with apnoea and controls under general anaesthesia with full muscle paralysis and found a smaller pharyngeal airway and increased airway collapsibility in apnoea patients than in controls (Isono, Remmers *et al.* 1997). However, Lyberg (1989) and Pae (1997) (Pae, Lowe *et al.* 1997) found that the pharynx becomes considerably longer in the apneic group after a body position change from upright to supine (Lyberg, Krogstad *et al.* 1989; Pae, Lowe *et al.* 1997).

A number of publications have demonstrated that the linear measurement of the most constricted area in the pharynx can be an indicator of OSA severity in conventional upright cephalograms. The narrowest pharyngeal diameter is located behind the soft palate (Borowiecki, Pollak *et al.* 1978; Rojewski, Schuller *et al.* 1984) with about 50% reduction of the pharyngeal diameter in OSA patients compared to controls. Pae found that the pharyngeal length in the supine position may be more important than a one-dimensional measurement of the most constricted area in the diagnosis and treatment of OSA (Pae, Lowe *et al.* 1997).

Pae concluded that the longer the pharynx, the greater the severity of the OSA symptoms (Pae, Lowe *et al.* 1997). They postulated that as long as there is no significant difference in the cross-sectional area of the pharynx, air in a longer pharynx should travel faster than in air in a shorter one because the same volume of tidal air must pass through each conduit during the same respiration duration. Hence,

the velocity of the air in a longer pharynx is increased as compared to a shorter pharynx. The faster air stream in a longer pharynx generates more negative intraluminal pressure than that in a shorter one. Thus the longer pharynx becomes more collapsible(Pae, Lowe *et al.* 1997).

Some authors (Djupestrand, Lyberg *et al.* 1987; Strelzow, Blanks *et al.* 1988) have suggested that soft tissue abnormalities are more important than skeletal factors in patients with OSA. It has not yet been established whether the soft tissue abnormalities are in fact a consequence of the vibratory trauma associated with OSA, rather than the cause.

The PAS was first described by Riley (Riley, Guilleminault *et al.* 1983), and is defined as the distance between the posterior pharyngeal wall and the dorsal surface of the base of the tongue, measured on the line that intersects point Go and B point. Whilst most studies measuring airway diameters in OSA patients report a reduction in the measurement of PAS compared to the controls, conjecture in the literature exists with some studies finding a significantly reduced PAS (Jamieson, Guilleminault *et al.* 1986; Tangugsorn, Skatvedt *et al.* 1995), whereas other studies found no significant differences in the PAS between the OSA patients and controls (Yildirim, Fitzpatrick *et al.* 1991; Solow, Skov *et al.* 1996).

Riley (1990) proposed three categories of OSA have been based on the anatomical site of obstruction:

- Type I (oropharynx): Patients with larger soft palate and related factors, such as a longer hard palate with the resultant reduction of this region of the airway.
- Type II (hypopharynx): Patients who are retrognathic with a concurrent reduced posterior airway space due to the posterior positioning of the tongue and/or macroglossia.
- Type III: is a combination of oro- and hypopharyngeal obstruction (Types I and III.)

2.3.5.3 Functional Processes Related to Upper Airway Muscle Activity

2.3.5.3.1 Breathing

Breathing occurs when the intercostal muscle sand the diaphragm receive electrical impulses from the brain, causing them to contract. This leads to expansion of the thorax and creates a negative pressure inside the chest, drawing air into the lungs. This negative intraluminal pressure is transmitted to the upper airway dilator muscles such as the genioglossus and tensor palatini prevent this. The patency of the airway at any time is influenced by the balance of forces generated by the dilator muscles of the airways and the forces of inspiration that tend to occlude it. Normally, the upper airway remains patent during breathing because the dilating force exerted by the upper airway muscles exceeds the subatmospheric intraluminal pressure generated during inspiration (Remmers, DeGroot *et al.* 1978; Surratt, McTier *et al.* 1985; Howell, Jensen *et al.* 1989).

There is greater predisposition to closure in a narrower airway and a greater dependence on the dilator muscle activity to maintain patency, due to a greater subatmospheric inspiratory pressure that is generated in an attempt to achieve adequate airflow through a narrow airway (Cistulli and Sullivan 1994).

2.3.5.3.2 Breathing and Sleeping

The awake person is capable of making the upper airway muscles contract sufficiently so that the upper airway doesn't collapse when they are lying down. Studies have indicated that the genioglossus and tensor veli muscles may have increased activity in the awake OSA patients and thus help maintain the shape of the upper airway(Mezzanotte, Tangel *et al.* 1992; Mezzanotte, Tangel *et al.* 1996). This is clearly demonstrated in OSA patients during wakefulness where genioglossus electromyographic (EMG) activity is reduced significantly following the application of continuous positive airway pressure. In normal controls, there is only a small reduction in EMG activity (White and Mezzanotte 1993). White and Ballard (1990) also found that patients with sleep apnoea had considerable phasic inspiratory-linked

electromyographic activity in the genioglossus, both awake and asleep, whereas little or no activity could be found in normal subjects (White and Ballard 1990).

However, when the patient assumes a supine position and goes to sleep, there is a decrease in the activity of the genioglossus and tensor veli palatini muscles that result in a decreased airway space (Adachi, Lowe *et al.* 1993), which may result in an increase in the velocity of the air passing through the airway, increasing the degree of subatmospheric pressure. The combination of decreased negative pressure and decrease in muscle activity allows the tongue and soft palate to move toward and often contact the posterior wall of the oropharynx, resulting in a decreased airway space. If the blockage is not complete, the increase in airflow velocity during inspiration and expiration may cause the soft tissues, particularly the uvula, to vibrate. For others, this combination of negative pressure, decreased muscle activity and movement of the tongue and soft palate toward the posterior wall of the pharynx results in a complete blockage of the airway. The resulting conditions may be snoring and/or OSA (Surratt, Dee *et al.* 1983).

When there is a 50% or greater reduction in resting tidal volume a hypopnoea occurs and if the airway closes completely for 10 seconds or more then apnoea results. This leads to a drop in the body's blood oxygen levels (hypoxemia), an increase in the blood carbon dioxide concentration (hypercapnia) as well as an increase in blood pressure and heart rate (Ivanhoe, Cibirka *et al.* 1999).

An apnoea is terminated by a brief arousal from sleep. During this arousal the subject partially awakes and the brain increases the stimulus to the upper airway muscles causing them to contract harder and thus open the upper airway. This enables the subject to take several large breaths and quickly corrects the oxygen and carbon dioxide levels. Normally, the subject will quickly return to sleep without any recollection of arousal, with this cycle of apnoea and arousal repeating itself for part or all of the sleep period.

In summary, these studies lend support to the theory that the main underlying cause of sleep apnoea is airway narrowing due to relaxation of the upper airway muscles.

2.3.6 Clinical Features of OSA

2.3.6.1 Symptoms of OSA

Patients describe the number of symptoms that may be considered typical of OSA. Many of these symptoms are observed and reported by the spouse or partner and include (McNamara, Cistulli *et al.* 1994):

- Snoring.
- Excessive daytime somnolence (sleepiness) (Guilleminault and Dement 1978).
- Witnessed apnoeas.
- Nocturnal choking episodes.
- Nocturnal arousals.
- Sleep disruption/insomnia.
- Abnormal motor activity in sleep.
- Nocturia.
- Gastroesophageal reflux.
- Headaches (morning; nocturnal)
- Atypical chest pain
- Nocturnal sweating
- Diminished libido/impotence.
- Concentration and memory deficit.
- Personality changes/depression.

Snoring and daytime sleepiness are the most likely reasons for a patient to consult a clinician. The symptoms of OSA can be divided into nocturnal, daytime and neuropsychological. A list of symptoms and their relative impact upon OSA subjects is provided in Table 3.

2.3.6.2 Nocturnal Symptoms

The most common nocturnal symptom is loud snoring which has usually been present for years before other symptoms develop (Schwab, Gupta *et al.* 1996). The snoring takes on a temporal character, being interrupted periodically by episodes of silence corresponding to the occlusive events (Lugaresi, Cirignotta *et al.* 1984). The snoring typically crescendos whilst futile respiratory movements occur and then breaks off suddenly, as air finally enters the lung. At this point, the subject's sleep becomes lighter, they may wake up or the event may be accompanied by a period of choking. Some subjects complain that they wake up with a very sore and/or dry throat.(Battagel and L'Estrange 1996)

It is not uncommon for patients to wake up numerous times per night as a consequence of apnoeic events, however most patients do not recall these events when they finally arise in the morning, often complaining of a disturbed or restless sleep, as does the bed partner (Flemons and Remmers 1996). An increased frequency of nocturia is a further symptom, waking the subject. OSA subjects and their partners also complain of restlessness that is manifested by involuntary kicking movements of the legs.

The chemical changes resulting from an apnoeic event (hypoxemia and hypercapnia) are partially responsible for an increased cardiac workload together with an increase in blood pressure. The body's attempts to continue to breathe with an obstructed upper airway, places strain on the respiratory muscles and diaphragm. Severe medical conditions can result, including tachycardia, systemic hypertension, pulmonary hypertension, acute pulmonary oedema, reversible high grade protein-urea and possibly Sudden Infant Death Syndrome (Rapoport, Garay *et al.* 1986; Chaudhary and Smith 1991; Boudewyns and Van de Heyning 1995; Fletcher 1995).

2.3.6.3 Daytime Symptoms

Daytime somnolence is the most common daytime symptom of OSA patients. This is due to the frequent arousals from sleep, which interferes with the amount and quality of sleep (Ivanhoe, Cibirka *et al.* 1999). Sleep apnoea also interferes with the normal architecture and stages of sleep (Flemons and Remmers 1996). Many OSA patients spend an inordinate amount of time in Stages 1 and 2 NREM sleep and much less time in Stages 3 and 4 NREM and REM sleep. Nasal obstruction and headaches are common during the day for patients who suffer from OSA (Ferguson, Ono *et al.* 1995).

Daytime hypersomnolence can be extreme and the subject may fall asleep at unexpected and inappropriate moments. Driving a car or operating machinery therefore presents a danger. Epidemiological studies have shown an increased motor vehicle accident rate in OSA patients including those with mild disease (Young, Blustein *et al.* 1997). In a study by Findley *et al.* (1988), 24% of a sample of OSA sufferers reported falling asleep whilst driving, at least once per week. Aldrich (1989) found that 31% of drivers with OSA had been involved in a road traffic accident within the last 5 years. Drivers suffering from excessive sleepiness were up to seven times as likely to be implicated in an accident than normal individuals (Findley, Unverzgat *et al.* 1988; Aldrich 1989; Haraldsson, Carenfelt *et al.* 1990). Findley *et al.* (2000) studied 50 OSA patients, of which 36 were using CPAP. Using traffic records, the CPAP treated patients had no motor vehicle accidents in the 2-year study period compared with a significant 0.07 amount of accidents with those not using CPAP (Findley, Smith *et al.* 2000).

Driving simulator data suggest that sleepiness due to OSA is associated with a marked driving impairment comparable to that produced by a blood alcohol level above the legal limit for driving in the United Kingdom. This impairment was shown to respond to CPAP therapy in a controlled study (Hack, Choi *et al.* 2001).

2.3.6.4 Neuropsychological Symptoms

Poor memory and difficulty concentrating are further consequences of patients suffering from OSA, leading to an inability to remember everyday items. Some OSA subjects have been described as short-tempered or as having undergone a personality change. OSA patients may even experience depression. These symptoms are thought to be the result of the change in sleep quality (Kales, Caldwell *et al.* 1985; Bedard, Montplaisir *et al.* 1991).

Table 3. Items ranked by sleep apnoea patients as having the most impact on their quality of life.

Item	Frequency (%)	Mean importance	Male rank	Female rank
Normal Daily Routine				
Having to push yourself to remain alert	73	3.21	3	1
Decreased ability to concentrate	78	3	2	2
Having to fight to stay awake	71	3.22	1	9
Decreased ability to remember things	66	3.18	4	6
A decrease in your motivation to do exercise and leisure type activities	65	3.21	5	5
Having to force yourself to go to work, school etc.	58	3.25	7	3
Giving what energy you have to accomplish only work-related activities	53	3.45	6	7
Social Interaction				
Being told that your snoring disturbs your spouse or partner's sleep.	80	2.96	1	4
Being told that your snoring was bothersome pr irritating to your spouse or partner.	79	2.95	2	3
Less interest in socialising	58	3.13	3	1
Wanting to be left alone	50	3.04	6	2
A decrease in sexual intimacy	41	3.24	5	8
Emotional State				
Frustration	66	3.30	3	2
Irritability	70	3.10	2	3
A feeling of depression or being down	64	3.33	1	1
Impatience	56	3.10	4	5
A decreased ability to cope with every day issues	53	3.17	6	4

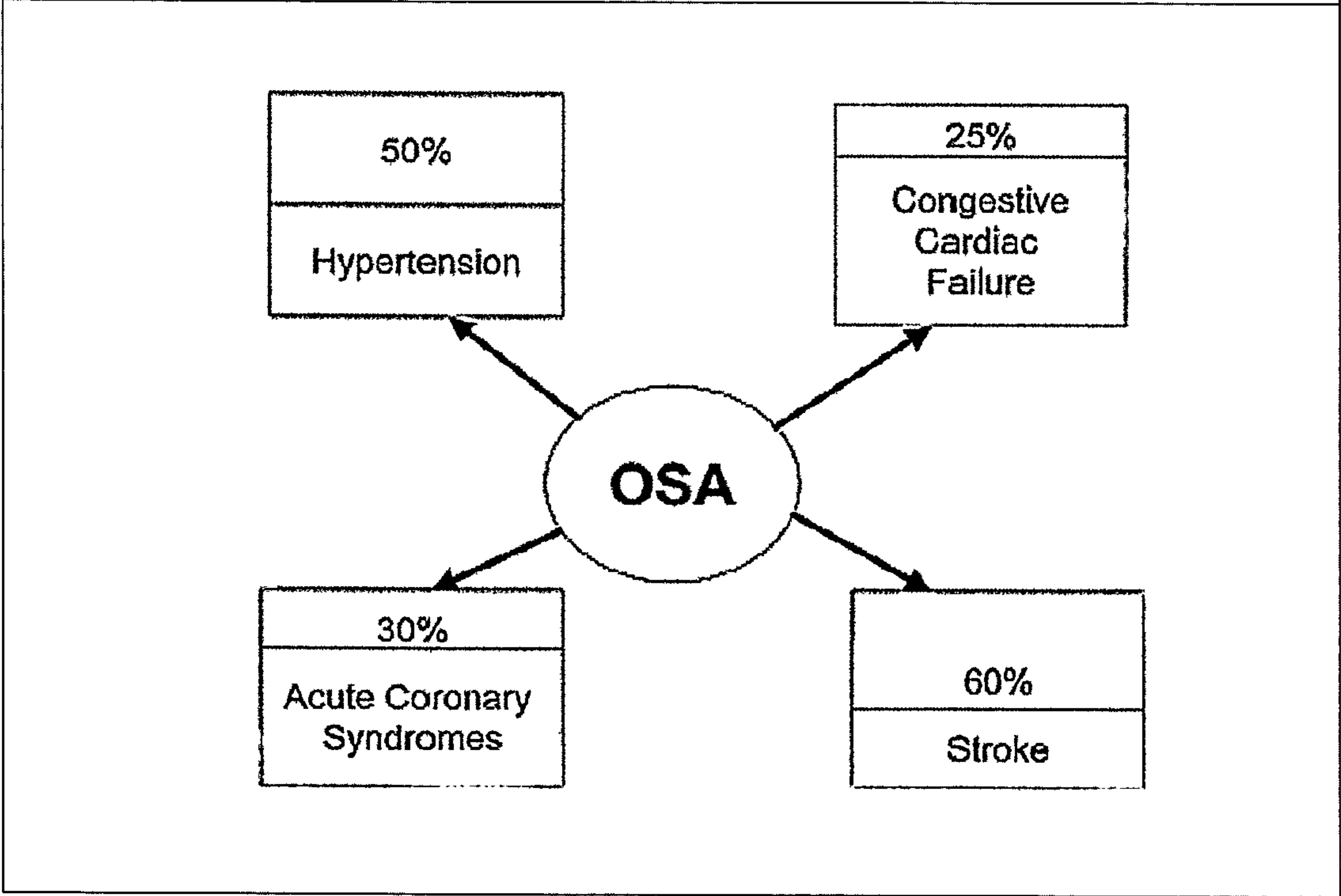
Symptoms				
Daytime:				
Decreased energy	80	3.28	1	1
Excessive fatigue	71	3.47	2	2
Difficulty in staying awake while reading	78	2.93	3	4
Ordinary activities require an extra effort to perform or complete	65	3.18	5	3
Falling asleep if not stimulated or active	61	3.10	6	5
Fighting the urge to fall asleep while driving	58	2.94	4	6
Nocturnal:				
Waking up often (more than twice) during the night.	77	3.06	1	1
Restless sleep	69	3.17	2	2
Concern about the time you stop breathing at night	52	3.22	4	3
Waking up at night feeling like you were choking	50	3.02	3	4

2.3.6.5 Clinical Consequences of OSA

Many patients with sleep apnoea are overweight and therefore it is unclear to what extent the medical problems are a direct result of obesity or the effects of sleep apnoea itself.

The morbidity of OSA relates principally to the cardiovascular system. Rigorous epidemiologic studies have demonstrated that sleep apnoea is a risk factor for the development of arterial hypertension, independent of associated obesity, alcohol intake, sex and age (Nocturnal hypoxemia (inadequate blood and tissue oxygenation during sleep) occurs with sleep apnoea and if this is prolonged, hypertension and cardiac abnormalities may develop or be exacerbated, if these conditions already exist (Klitzman and Miller 1994; Rapoport 1994).

FIGURE 8. PREVALENCE OF OBSTRUCTIVE SLEEP APNEOA (OSA) IN PATIENTS WITH CARDIOVASCULAR AND CEREBROVASCULAR DISEASE.
SOURCE: (Basetti and Aldrich 1999; Peker, Kraiczi *et al.* 1999; Sin, Fitzgerald *et al.* 1999; Parati, Ongaro *et al.* 2002)



Cardiac arrhythmia, nocturnal angina and myocardial ischaemia may result, with the possibility of the latter culminating in a myocardial infarction ((Guilleminault, Stoohs *et al.* 1994). Although hypertension in patients with OSA is often confounded by the presence of obesity and increased age, some studies implicate sleep apnoea as an independent contributor to the development of hypertension (Hoffstein, Chan *et al.* 1991; Carlson, Hedner *et al.* 1994).

Cerebral blood flow reduction is a further complication and there is an increased risk of suffering a cerebrovascular accident. An increase in the frequency of OSA in patients with recent stroke has been reported (Dyken, Somers *et al.* 1996), however, there is less evidence for this condition (Hedner, Wilcox *et al.* 1994).

In summary, OSA patients are at increased risk of injury and cardiovascular disease compared to normal subjects, as well as poorer quality of life (AHTAC 1993). These consequences highlight the importance of OSA research and the rationale for adequate management of this condition.

2.3.7 Diagnosis of Obstructive Sleep Apnoea

2.3.7.1 Clinical Examination

A careful history and clinical examination are the essential first steps in diagnosing OSA. Wiggins *et al.* suggested that information obtained from a bed partner may significantly improve the accuracy of responses to questions about sleep and sleepiness (Wiggins, Schmidt-Nowara *et al.* 1990). However, clinical evaluation has significant limitations and does not identify all OSA patients. One study identified only 52% of OSA patients based on history and physical examination (Viner and Hoffstein 1991).

The clinical examination should include an ear, nose and throat assessment, so that any physical obstructions to breathing may be identified. Height and weight recordings are recommended to calculate the subject's body mass index (BMI) (Battagel and L'Estrange 1996). This is calculated as the weight in kilograms divided by the square of height in metres. The normal range for BMI is considered to be between 20 and 25. Subjects with a BMI of greater than 25 are overweight, while those whose index is greater than 30, are obese (Hoffstein 1993). The likelihood ratios, or ability, of a clinical examination to identify physical and anthropometric characteristics diagnostic of OSA are provided in Table 4.

Table 4. Diagnosis of sleep apnoea likelihood ratios (LR) for symptoms and physical characteristics

Symptoms or Physical Characteristics	Level	LR
<i>Nocturnal</i>		
Snoring frequency	< 3 nights/week	0.4
	≥ 3 nights/week	1.4
Loud, disruptive snoring frequency	< 3 nights/week	0.5
	≥ 3 nights/week	1.7
Snoring intensity	Extremely loud	3.6
	Louder than talking	1.3
	Slightly louder than heaving breathing	0.3
Partner's report of choking or gasping	< 1 night/month	0.5
	1-8 nights/month	1.1
	≥ 3 nights/week	1.9
Partner's report of apnoea	Yes	1.4,1.5
	No	0.2,0.5
Nocturia	Yes	1.5
	No	0.6
<i>Daytime</i>		
Excessive daytime sleepiness	Yes, against the person's will	1.4
	Yes, but willingly	1.2
	None	0.8
Weight gain over previous 2 years	< 10 pounds	0.8
	≥ 10 pounds	1.4
Impotence	Yes	3.2
	No	0.9

<i>Physical examination</i>		
Pharyngeal examination	Abnormal	1.4
	Normal	0.8
Hypertension	Yes	1.6, 2.2, 2.4
	No	0.4,0.6,0.8
Body mass index	< 25(kg/m ²)	0.3
	25-30(kg/m ²)	0.7
	>30(kg/m ²)	2.0,2.3
Waist circumference	<90cm	0.3
	90-110 cm	1.1
	>110cm	3.2
Waist: hip ratio	<0.8	0.2
	0.8-1.0	1.0
	>1.0	2.8
Neck circumference	<38cm	0.5
	38-44cm	1.1
	>44cm	4.1
<i>Clinical Prediction Rule</i>		
Sleep apnoea clinical score (SACS)	<5.0	0.3
	5-10.0	1.11
	10.1-15.0	2.2
	>15.0	5.2

2.3.7.2 Polysomnography

Polysomnography is an objective measure of respiration during sleep and is the most accepted diagnostic investigation distinguishing between simple snoring and true obstructive sleep apnoea (Martin and Cohn 1985; Aboussouan, Golish *et al.* 1997). It monitors a wide range of parameters while the subject is asleep, including assessment of respiratory and cardiac function (Figure 4.) and provides detailed data on abdominal and thoracic respiratory effort, nasal and oral airflow, blood oxygen saturation, sleep stage and neurophysiological recordings (Ryan and Boldy 1995). Body position, leg and body movements and sounds can also be recorded (Battagel and L'Estrange 1996).

FIGURE 9: PARAMETERS ASSESSED DURING POLYSOMNOGRAPHY.

Electroencephalogram (EEG)	<i>To monitor brain wave activity.</i>
Electro-oculogram (EOG)	<i>To monitor eye movements.</i>
Electromyogram (EMG)	<i>Attached below the chin and to each leg, to monitor throat muscle and leg muscle activity respectively.</i>
Electrocardiogram (ECG)	<i>To monitor the heart's electrical activity, in particular arrhythmia.</i>
Pulse oximetry	<i>To monitor the peripheral arterial oxygen saturation.</i>
Respiratory thermistors	<i>To indicate whether the subject is breathing, by detecting the temperature of expired air.</i>
Measurements of respiratory effort	<i>By measuring chest and abdominal wall movement.</i>
Snore microphone	<i>Snoring and choking sounds are charted.</i>

The data is recorded, allowing the number of apnoeas and hypopneas to be quantified, enabling a definitive diagnosis to be made and permits an evaluation of the severity of the OSA (Battagel and L'Estrange 1996). The severity is established in order to make an appropriate treatment decision (ASDA, 1995.)

There are limitations of polysomnography. The studies are carried out in a sleep laboratory and not in the patient's home. Portable monitoring devices are available, however, these systems do not record all data (Flemons and Remmers 1996).

Secondly, there is significant night-to-night variability in the apnoea index. Studies however have demonstrated that one overnight polysomnography is sufficient and identifies OSA in 94% of subjects that would be detected by two consecutive overnight studies (Mendelson, 1994.) The sensitivity and specificity of polysomnography in diagnosing OSA is provided in Table 5.

Table 5. Results of a positive summary score for a high risk of OSAS

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
AHI > 5	89%	23%	89%	77%
AHI > 15	92%	50%	52%	93%
AHI > 30	65%	65%	20%	93%

2.3.7.3 Questionnaires

Different types of questionnaires have been used in different centres to assess symptoms of OSA and for use in epidemiological studies. Kump *et al.* (1994) evaluated the ability of a questionnaire in 465 participants in an epidemiological study of OSA. Subjects and their roommates each completed a questionnaire and underwent home sleep studies. Five main factors; functional impact of sleepiness, self-reported breathing disturbances, roommate-observed breathing disturbances, driving impairment and insomnia explained 67 percent of the total variance in the questionnaire data. Use of symptoms with data on gender and BMI improved predictive ability by 10 percent. The study confirmed that questionnaire data provide a valid means of characterizing symptoms in epidemiologic surveys of OSA (Battagel and L'Estrange 1996). Predictive ability was not significantly improved with multiple questions or a separate roommate questionnaire, but was improved with consideration of data on BMI and gender.

Excessive daytime sleepiness can be evaluated with both subjective and objective methods. Of the objective methods, the multiple sleep latency test (MSLT) is generally considered the gold standard (Carskadon and Dement, 1985). This test is based on the principle that degrees of sleepiness can be measured by how quickly one falls asleep (sleep latency) when given the opportunity to do so. However, the multiple sleep latency test is cumbersome and costly taking a day for both patient and polysomnographer.

The Epworth Sleepiness Scale (ESS) is a subjective questionnaire consisting of eight questions and yields a score of 0 to 24 (Johns, 1991.) It is easy to administer and is currently the most widely used subjective test for sleepiness (Benbadis *et al.*, 1999). Whilst polysomnography provides a definitive diagnosis, the ESS is merely a suggestive indicator of OSA. The sleepiness score is determined from a questionnaire designed to assess how likely a person would be to doze off in the following eight specific situations:

- 1) Sitting and reading.

- 2) Watching TV.
- 3) Sitting indicative in a public place (eg in a lecture.)
- 4) As a passenger sitting in a car for an hour.
- 5) Lying down to rest in the afternoon.
- 6) Sitting and talking to someone.
- 7) Sitting quietly after lunch, without having consumed any alcohol.
- 8) As the driver of a car, stopped for a few minutes in traffic.

Scores of more than 12 (that is over 50 percent) suggest that the subject is sleepier than would be considered normal. The mean ESS score for normal subjects is 6 ± 2 . OSA is rated at a score of 11.7 ± 4.6 (Johns, 1991.) The reliability of ESS item scores for a particular subject has been reported to be high whether repeated by the same subject at different times or by another person such as a spouse. This reliability is only slightly less than that for measurements of sleep latency on the same day in the MSLT. The reliability of total ESS scores is higher than again for the separate item scores (Johns, 1994.)

Chung (2000) validated the use of the Epworth Sleepiness Scale in the assessment of Chinese patients with Obstructive Sleep Apnoea. The investigation consisted of 61 healthy controls and 100 patients with OSA, and an analysis of the test-retest reliability, internal consistency and concurrent validity of the Chinese version of the ESS. Chung (2000) found the Chinese version of the ESS to be reliable and valid measure of daytime sleepiness, and concluded that it be included as one of the methods of assessment of sleepiness in clinic samples of Chinese patients with OSA (Chung 2000).

Ong and Clerk (1998) conducted a cross-sectional study at the Stanford University Sleep Disorders Clinic. Their investigation involved 106 Asian-American patients, diagnosed with Sleep Disordered Breathing following polysomnographic examination, and 99 Caucasian-American diagnosed patients matched for age, gender and body mass index (BMI.) Ong and Clerk (1998) found a significantly larger proportion of Asians compared to Caucasians with severe OSA, with an estimated odds ratio for Asians having severe OSA as compared with Caucasians as 2.51.

Hence, Asian patients, based on polysomnographic examination, experienced a greater severity of OSA as compared to matched Caucasian patients. However, there was no significant difference in the severity of questionnaire-based symptoms of snoring, apnoeas during sleep and the median Epworth scores between Asian and Caucasian patients (Ong and Clerk 1998).

A study by Ip and colleagues (2001) was performed to identify the prevalence of Sleep Disordered Breathing in Chinese middle-aged office-based male workers in Hong Kong. The investigation commenced with the distribution of sleep questionnaires, and a follow-up polysomnographic examination on a reduced sample of questionnaire respondents. Findings from the questionnaire identified respondents to be of a similar age and body mass index (BMI) to the general community in the target age range and gender, with a prevalence rate of 23% for habitual snoring, which was associated with excessive daytime sleepiness (EDS), hypertension, witnessed abnormal breathing pattern, BMI, and leg movements during sleep. This study demonstrated an estimated prevalence of OSA ($AHI \geq 5$ and EDS) at 4.1%. Increasing BMI and age were associated with sleep disordered breathing (Ip, Lam *et al.* 2001).

2.4 Anatomical Differences in the Chinese Mongoloid Population

Moate *et al.* reviewed an article by Wei, who reported on a study of 107 (84 male and 23 female) young adults of Chinese ethnic descent. The subjects were taken from a sample of 253 who were selected on the criteria of facial harmony, no history of previous orthodontic treatment, and being of Chinese ethnic descent. The average of the males was 23 years and the females 21 years. The sample showed a shorter length of the anterior cranial base both in males (65mm) and females (63mm) (Moate and Darendeliler 2002).

Furthermore, they found “the strongest difference between the Chinese and Caucasian groups at all ages is the length of the anterior cranial base, which has been shown to be much shorter in Chinese than in Caucasians. The mean length of the anterior cranial base of Caucasians is 83 ± 4 mm for the adult male and 77 ± 4 mm for the adult female. The Chinese consistently show a small anterior cranial base length at all ages and in both the sexes, as show in large samples from a broad cross-section of age groups that have strongly corroborated and complimented such findings. The mean length of the anterior cranial base is 65 ± 4 mm in Chinese adult males and 63 ± 4 mm in Chinese adult females.”(Moate and Darendeliler 2002)

Moate *et al.* (2002) concluded that skeletal parameters are consistently different between healthy non-OSA Chinese and Caucasians, including variables SNA, SNB and ANB. They concluded that “the Chinese craniofacial denture pattern is established early, and is characterised by a relatively larger ANB angle (5°) and a larger lower incisor mandibular plane angle (IMPA) and, thereby, a smaller interincisal angle.”

2.5 Craniofacial differences in various ethnicities diagnosed with Obstructive Sleep Apnoea

Ethnicity can be regarded as a risk factor for sleep-disordered breathing (SDB), with increased severity and heightened prevalence observed in specific racial groupings. Several studies have been performed assessing the craniofacial differences amongst various ethnic groups, that warrant further discussion (Lee, Ramirez *et al.* 1997; Redline, Tishler *et al.* 1997; Li, Powell *et al.* 1999; Li, Kushida *et al.* 2000; Liu, Lowe *et al.* 2000; Cakirer, Hans *et al.* 2001; Hoekema, Hovinga *et al.* 2003; Hui, Ko *et al.* 2003).

2.5.1 Caucasian population.

Investigations into the craniofacial pattern of OSA subjects, began with assessment of Caucasian subjects (Riley, Guilleminault *et al.* 1983). Recognized craniofacial risk factors for OSA amongst Caucasians include bony and soft tissue measures: reduced anterior-posterior dimensions, reduced middle cranial fossa length, reduced intermaxillary length, increased tongue area, and increase soft palate length (Redline, Tishler *et al.* 1997).

2.5.2 Scandinavian Caucasian population

Tangugsorn *et al.* undertook a cephalometric investigation of obese and non-obese OSA Scandinavian patients compared to a control population, with the purpose of examining the differences in the cervico-craniofacial skeletal and upper airway soft tissue morphology. Demographically, highly significant differences in the two patient groups were noted amongst weight, BMI, severity of OSA and oxyhaemoglobin saturation, with the authors concluding that the obese OSA patients appeared to possess a more serious clinical condition than the non-obese patient group (Tangugsorn, Krogstad *et al.* 2000).

The non-obese OSA patients had more maxillo-mandibular discrepancy than the controls and the obese group due to a more posteriorly positioned and rotated

mandible. The non-obese group had an increased anterior lower facial height and decreased posterior lower facial height than the obese group. A significantly longer, thicker and larger soft palate was clearly observed in both OSA groups, when compared to the controls. The obese patients were found to have larger and longer tongues than the other two groups, with the tongue morphology in non-obese group not being different from that of the controls (Tangugorn, Krogstad *et al.* 2000).

Tangugorn *et al* state recognise the difficulty in defining the causal relationship between the excess body weight and sleep-disordered breathing, with implicating factors including alterations in upper airway structures, upper airway function, the balance between ventilatory drive and load and obesity-induced hypoxemia (Tangugorn, Krogstad *et al.* 2000). The authors concluded that both OSA groups had aberrations of cervico-craniofacial skeletal as well as upper airway soft tissue morphology when compared with the controls, with the non-obese OSA patients having cervico-craniofacial skeletal abnormality and the obese OSA patients possessing more abnormalities in the upper airway soft tissue morphology, head posture and position of the hyoid bone (Tangugorn, Krogstad *et al.* 2000).

As previously stated, the causal relationship between the excess body weight and sleep-disordered breathing is difficult to define. Consequently, Tangugorn *et al* performed a second, advanced statistical investigation to define the simultaneous relationships between OSA severity, BMI, oxygen haemoglobin saturation, and cervico-craniofacial skeletal and upper airway soft tissue morphology (Tangugorn, Krogstad *et al.* 2001).

“Canonical correlation analysis is a multivariate statistical model that facilitates the study of interrelationships among sets of multiple dependent and independent variables. Canonical correlation analysis identifies the optimal structure or dimensionality of each variable set that maximises the relationship between composites of sets of multiple dependent and independent variables. In doing so, it develops a number of independent canonical functions that maximise the correlation between the linear composites, also known as canonical variates, which are sets of dependent and independent variables.” (Tangugorn, Krogstad *et al.* 2001) Canonical correlation analysis has been applied to morphometric studies in an attempt to solve

the complexity of the inter-relationships between craniofacial structures and their related function.

Eight principal components were obtained for the 30 original variables in both groups of obese and non-obese OSA patients. Principal Component analysis was able to demonstrate the disconfiguration of the craniofacial skeleton in both groups. The predominant craniofacial characteristics in the obese OSA group were due to the combination of an increased anterior facial height (AFH), anterior lower facial height, mandibular length and mandibular plane angle. Conversely, in the non-obese group, a narrow antero-posterior dimension of the maxilla and mandible and retruded chin proved to be a significant combination of variables. The hyoid bone was located inferiorly in both OSA groups, but assumed an anterior position away from the cervical column only in the obese OSA patients. The soft tissue airway analysis expressed different leading elements of upper airway soft tissue between the obese and non-obese groups, with the linear combination of increased size of tongue, oral area and oropharyngeal area featuring prominently in the obese OSA patients. In the non-obese group, a narrow minimal posterior pharyngeal airway space, nasopharynx, velopharynx and decreased angulation between the uvula and palatal plane. The principal component analysis demonstrated that both obese and non-obese OSA patients had atypical cervico-craniofacial skeletal as well as upper airway soft tissue morphology (Tangugsorn, Krogstad *et al.* 2001).

Tangugsorn *et al.* established that three canonical variables and their correspondents with different loadings existed for both OSA groups, and that a canonical correlation successfully clarified the complexity of simultaneous relevant variables. They concluded that different morphologic components and their relevance to the diagnostic data obtained from sleep laboratories must be taken into consideration before treatment selection (Tangugsorn, Krogstad *et al.* 2001).

Hoekema *et al.* (Hoekema, Hovinga *et al.* 2003) performed a cephalometric investigation, assessing the craniofacial morphology of OSA patients and healthy subjects, to ascertain which cephalometric variables of craniofacial morphology discriminated between OSA patients and non-OSA subjects. Multiple regression analysis was used to determine that the hyoid bone was inferiorly positioned in the

OSA group as compared to the non-OSA subjects, a finding consistent with Tangugorn *et al* (Tangugorn, Krogstad *et al.* 2000; Tangugorn, Krogstad *et al.* 2001), and a number of other published studies (Jamieson, Guilleminault *et al.* 1986; Lowe, Gionhaku *et al.* 1986; Lowe, Santamaria *et al.* 1986; deBerry-Borowiecki, Kukwa *et al.* 1988; Tangugorn, Skatvedt *et al.* 1995).

2.5.3 Hispanic population

Will *et al* (1995) studied anatomical measurements as a function of ethnicity in three population groups:

1. Caucasian – 20 patients.
2. Hispanic – 13 patients.
3. African American – 15 patients.

The study utilised cephalometric analysis specific for the evaluation of OSA patients. Statistically significant differences between Steiner's SNA and SNB values were noted between the African-American and Hispanic groups, when compared to the Caucasian group. Hispanic OSA patients displayed statistically significant bimaxillary retroposition, with lower SNA and SNB values as compared to their ethnic means (Will, Ester *et al.* 1995). Lee *et al* demonstrated that non-OSA Hispanics had a reduced SNA value of 0.37% lower than their Caucasian counterparts (Lee, Ramirez *et al.* 1997).

Will *et al* (1995) concluded that their findings could have possible implications in the approach to surgical treatment of OSA, and indications for orthognathic surgery as opposed to soft palate and soft-tissue surgical intervention. Furthermore, the authors recommended that Hispanic OSA patients may require bimaxillary advancement earlier in the sequence of surgical therapy to achieve definitive resolution of OSA (Will, Ester *et al.* 1995).

2.5.4 Polynesian Maori population

A cross-sectional study was performed, with lateral and posterior-anterior cephalometric radiography used to assess New Zealand Maori (Polynesian) and European (Caucasian) males for the relative contributions of craniofacial form and anthropometric factors to OSA (Coltman, Taylor *et al.* 2000). Both groups were markedly obese and had a similar mean respiratory disturbance index (RDI.) Unpaired statistical t-tests were used to compare the anthropometric and RDI data for the Polynesian and Caucasian subjects. The Polynesian men proved to have broader craniofacial skeletons, larger and more prognathic mandibles, greater neck extension and some larger airway dimensions than the Caucasian men.

Approximately thirty-six percent of variation in RDI was explained by independent contributions of the nasal aperture width, and mandibular position relative to the cranial base. OSA severity in the Polynesian group increased with a wider anterior nasal aperture, and a more retrognathic mandible. In comparison, the Caucasian men, had neck circumference as the only positively associated with RDI, while retropalatal airway was negatively associated with RDI i.e. OSA severity increased as neck circumference increased and the retropalatal airway width decreased. Soft palate length (PNS-U) and maximum soft palate thickness were not significantly different between the groups. The authors concluded that the thickness of the soft palate and tongue size are weight-related and contribute to airway narrowing, with the soft palate thickness values comparable to other published studies (Tangugsorn, Skatvedt *et al.* 1995; Tangugsorn, Krogstad *et al.* 2000; Tangugsorn, Krogstad *et al.* 2000).

Thus, the results indicate that OSA in these two racially distinct groups was attributable to different aetiological factors. Interestingly, OSA in the Polynesian sample was found not to be associated with any of the weight-related factors (Coltman, Taylor *et al.* 2000).

2.5.5 African-American (Negroid) population

Will *et al* found that African American OSA patients presented with a statistically significant bimaxillary prognathism compared to the maxillary and mandibular positions seen in Hispanic and Caucasian subjects, and approximately 3.5% above the mean for their ethnic group (Will, Ester *et al.* 1995). Accordingly, the authors recommended that African-American OSA patients may not be as appropriate as their counterparts for bimaxillary advancement surgery for primary surgical treatment, and suggested that soft tissue surgical intervention eg uvulopharyngoplasty, tonsillectomy, partial glossectomy and hyoid suspension might be contemplated for the management of OSA (Will, Ester *et al.* 1995). However, it is important to note that this study involves a small sample size of various ethnic groups studied, and further studies with larger sample sizes may serve to verify these initial findings.

Lee *et al* assessed gender and race variations in normal soft-tissue measurements in a non-OSA population (Lee, Ramirez *et al.* 1997), and found no difference in posterior airway space, soft palate length and hyoid position between different ethnics groups of men. Gender consideration revealed that only Caucasian women differed from their male counterparts in posterior airway space, soft palate length and hyoid position.

Redline *et al* (1997) found only soft tissue measures of increased tongue area and increased soft palate length to be significant craniofacial risk factors in a group of 41 African-American OSA patients (Redline, Tishler *et al.* 1997). Cakirer *et al* (2001) used head and facial forms to investigate the relationship between non-morbidly obese subjects with and without OSA, and to identify a possible relationship between American Caucasians and African-Americans. They used cranial (CI) and facial (FI) indices, and found that these parameters did not differ in OSA versus non-OSA groups of African-Americans. In OSA subjects, the CI in Caucasians was again greater and the FI smaller than those in African Americans. The authors concluded that brachycephaly is associated with an increased AHI in whites but not in African Americans, with other anatomic features eg neck circumference, and soft tissue

structures in the airway eg tongue size, being relatively more important risk factors in the African American population (Cakirer, Hans *et al.* 2001).

2.5.6 Japanese Population

To clarify that factors besides obesity play an important role in the development of obstructive sleep apnoea syndrome (OSAS) in Japanese patients, Ito *et al.* (2001) compared craniofacial structures in patients with severe OSAS with those of normal controls. The craniofacial structures of 60 Japanese patients with severe OSAS and 30 normal controls were evaluated using standard cephalometric analysis. The SNA was significantly smaller in the patient groups than in the controls. The SNB and SNBa were significantly smaller in the non-obese and moderately obese patients than in controls. The MP-H distance and the PNS-P distance were significantly longer in the patient groups than in the controls. The PNS-P was significantly longer in the severely obese patients than in the non-obese group. The authors concluded that Japanese patients with severe OSAS have enlargement of the soft tissue and palate as well as craniofacial bony structural abnormalities, particularly remarkable in non-obese patients (Ito, Akashiba *et al.* 2001).

Endo *et al.* (2003) investigated the morphological characteristics of Japanese patients with OSA, with the craniofacial skeleton, soft tissue and upper airway analysed on lateral cephalograms from 103 patients with OSA and 98 control subjects. They found that micrognathia was a major risk factor of Japanese OSA patients instead of obesity; the narrowing in the hypopharynx was observed due to the inferior-located hyoid bone, especially in the obese group, an enlarged tongue and sticking of fatty-tissue to upper airway wall was noted (Endo, Mataka *et al.* 2003).

Yao *et al.* (2004) assessed the impact of craniofacial morphology and body weight on sleep-disordered breathing in Japanese men. They found that multivariate odds ratios associated with craniofacial score were higher in men with body mass index 25.0kg/m^2 or greater than in men with a lower body mass index (Yao, Tachibana *et al.* 2004).

2.5.7 Chinese (Mongoloid) population

A study of a mixed group of Asian OSA patients (Korean, Japanese and Chinese) demonstrated that the subjects had bimaxillary protrusion, narrower cranial base angle, larger posterior airway space and a more superiorly positioned hyoid bone as compared to Caucasians (Li, Powell *et al.* 1999).

Liu *et al.* investigated the differences of craniofacial and upper airway morphology between OSA adult Chinese and Caucasian males on the basis of matching age, BMI, craniofacial skeletal pattern, and respiratory disturbance index (RDI) (Liu, Lowe *et al.* 2000). The two groups selected had similar antero-posterior craniofacial skeletal patterns, i.e. a Class II division 1 malocclusion with an ANB value greater than five degrees. The Chinese group showed a shorter anterior cranial base ($p < 0.01$), smaller anteroposterior bimaxillary dimensions, more severe mandibular retrognathia, more proclined lower incisors, relatively increased upper and lower facial heights and steeper and shorter anterior cranial base. A more severe underlying skeletal discrepancy in the Chinese group was noted. The Chinese group had a significantly higher apnoea index despite no significant RDI difference relative to the Caucasian group with a higher hypopnea index. They found no significant differences between the Caucasians and Chinese, matched for age and BMI, with reference to the position of the hyoid bone or maxilla but noted a smaller midface with a smaller and more posteriorly positioned mandible in the Chinese group (Liu, Lowe *et al.* 2000). The authors did concede that further comparative studies of the two ethnic OSA groups with other craniofacial patterns and larger sample size, may serve to broaden the knowledge of the ethnic differences of craniofacial and upper airway structures in patients with OSA.

Li *et al.* found that Far-East Asian men with OSA have abnormal skeletal and soft tissue features that were similar to those found in Caucasian men with OSAS, with abnormalities including an elongated soft palate (PNS-P), inferiorly positioned hyoid (MP-H), decreased PAS, and decreased cranial base flexure (NSBa.) Far-East Asian men were found to have more anteriorly projected maxilla and mandible, than the Caucasian counterparts with OSA. Furthermore, they were found to have a

significantly shorter anterior cranial base ($p < 0.0001$) and more acute cranial base flexure (Li, Kushida *et al.* 2000).

Hui *et al.* performed polysomnographic and lateral cephalometric radiographic examination of 94 consecutive Chinese patients with OSA, comparing the cephalometric data between those with and without significant OSA (Hui, Ko *et al.* 2003). The mandibular plane to hyoid bone distance (MPH) and the perpendicular distance from hyoid bone to the line connecting C3 vertebra and retrognathion (HHI) were significantly longer in the OSA patients. The SNA angle was smaller in the OSA group, with MPH distance being the only independent variable for significant OSA with an odds ratio of 3.47. Further, they found that abnormalities of the SNA and MHP were more spectacular in OSA patients with BMI ≥ 30 kg/m². Their findings demonstrated a significant difference in craniofacial morphology between OSA patients and non-apnoeic controls, with an inferiorly positioned hyoid bone and a retropositioned maxilla possibly predisposing obese patients to more severe OSA (Hui, Ko *et al.* 2003).

Ang *et al.* measured craniofacial and head posture variables in Chinese subjects at the National Dental Centre Singapore (Ang, Sandham *et al.* 2004). They assessed 61 Chinese male subjects, comparing 25 individuals with mild OSA mild to 36 with moderate-to-severe OSA patients, and found significant differences between hyoid position in the two groups. The hyoid bone was more caudally or inferiorly positioned in moderate-to-severe sample, complementing other studies performed (Jamieson, Guilleminault *et al.* 1986; deBerry-Borowiecki, Kukwa *et al.* 1988; Tsuchiya, Lower *et al.* 1992; Lowe, Ono *et al.* 1996). The results from the Ang *et al.* study seem to suggest that craniofacial morphology in Chinese subjects does not markedly differ as severity of OSA increases, although cranial base (S-N) and cranial base angle (N-S-Ba) are smaller, and although a more retrognathic lower jaw is found in the moderate-to-severe sample, these differences are not significant when compared with the mild OSA reference group (Ang, Sandham *et al.* 2004).

The second part of the Ang *et al.* (2004) study examined the head posture variables in the group of OSA and compared them to published controls for Chinese and white

subjects. They found a marked increase in the craniocervical angulation for the total OSA study sample for craniovertical, craniocervical and craniohorizontal variables. The authors concluded that a more caudal hyoid bone position and greater craniocervical angulation was found in subjects with OSA (Ang, Sandham *et al.* 2004), and that there is a change in hyoid bone position and marked head posture adaptation in Chinese subjects with OSA, and that racial difference may exist for craniocervical posture between Chinese and white controls.

A multi-centre study assessing craniofacial profile in Hong Kong Chinese and Caucasian subjects from Vancouver with OSA conducted by Lam and co-workers (Lam, Ip *et al.* 2005), found that OSA subjects had larger thyromental angles and higher Mallampati scores than their non-apnoeic counterparts. Asians had higher mallampati scores, a reduced thyromental distance and larger thyromental angle than Caucasians. They found that a crowded posterior oropharynx and steep thryomental angle predicted OSA across two different ethnic groups and varying degrees of obesity. Additionally, risk factors for OSA eg obesity and craniofacial features that reflect structural narrowing of the upper airway are readily identified and can easily be incorporated into the routine physical examination.

2.6 Limitations in the use of Cephalometry in Sleep Apnoea Research

Many studies support the use of cephalometric analysis along with head and neck examination, polysomnography (PSG) and endoscopy to evaluate the OSAS patients and assist with the planning for non-invasive and surgical management of the syndrome(Riley, Guilleminault *et al.* 1983; Guilleminault, Riley *et al.* 1984; Riley, Guilleminault *et al.* 1985; deBerry-Borowiecki, Kukwa *et al.* 1988; Partinen, Guilleminault *et al.* 1988). However, the examination of airway dimension by cephalometric measurements can be inaccurate. A cephalometric measurement is made from a two dimensional image of a complex three-dimensional structure and this therefore creates limitations as no information is provided on the transverse dimension.

Some authors discuss the possibility that flexion or extension of the head could influence the dimensions of the oropharyngeal airway (Rubinstein *et al.*, 1987; Davies and Stradling, 1990). To take this factor into account, cephalometric radiographs of the subjects in this study were taken in the standing natural head position.

Also, it has been shown that subject posture may affect cephalometric measurements(Yildirim, Fitzpatrick *et al.* 1991). Caution must therefore be exercised when relating results of upright cephalometry to events occurring during sleep in the supine position.

Changes in airway tone and compliance from wakefulness to sleep, as well as potential unreliability of interpretation based on isolated parameters of airway calibre tone, are other confounding factors in the use of standard cephalometry.

Assessment of dynamic structures of the airway, such as the tongue and soft palate present many difficulties, which influences the reliability of these measurements (Miles *et al.*, 1995).

The analysis of a lateral cephalogram of a Chinese face presents a unique problem with the accurate identification of the point Nasion, because the image of the shallow nasal bridge is frequently super-imposed by the image of the tarsal plates of the upper eyelids.(Moate and Darendeliler 2002)

A major consideration in all cephalometric studies is the control population used for comparison. The normative data used in this study are from a recently published manual by Bhatia and Leighton (1993), and from other published papers(Solow and Kreiborg 1977; Guilleminault, Riley *et al.* 1984; Guilleminault, Riley *et al.* 1984; Tangugorn, Skatvedt *et al.* 1995; Solow, Skov *et al.* 1996).

Despite these drawbacks, the upright cephalogram remains the most popular clinical tool to assess upper airway size for preliminary diagnostic purposes because it is simple and cost effective to use.

2.6.1 Cephalometric Errors

Landmark identification in cephalometric analysis has traditionally been carried out on an acetate sheet showing the specific points chosen for analysis. During the cephalometric analysis there are many possible sources of error of varying degrees depending upon the method use in the landmark identification and measuring process, with landmark identification being found to be the greatest source of error in the use of lateral cephalograms (Hixon 1956; Hatton and Grainger 1958; Bjork and Solow 1962; Richardson 1966; Savara, Tracy *et al.* 1966; Baumrind and Frantz 1971; Baumrind and Frantz 1971; Gravely and Benzies 1974; Mitgard, Bjork *et al.* 1974; Bondevik, Rosler *et al.* 1981; Broch, Slagsvold *et al.* 1981; Stabrun and Danielsen 1982; Houston 1983; Cohen, Ip *et al.* 1984; Houston, Maher *et al.* 1986; Vincent and West 1987). There is a characteristic pattern of error for each individual landmark (Baumrind and Frantz 1971; Baumrind and Frantz 1971; Vincent and West 1987).

The three stages in obtaining the lateral cephalometric radiograph lead to three possible sources of error:

1. Projection error.
2. Landmark identification error.
3. Tracing and measurement error.

Radiological error falls into two main categories, systematic and random (Houston 1983).

Systematic errors result from magnification and distortion effects whilst obtaining the radiographic film or during the measuring process. Random errors arise mainly from uncertainty in the visual identification of the radiographic landmarks, and can be due to lack of image sharpness, inadequate contrast and the subjective inter-operator differences involved landmark identification.

2.6.1.1 Projection Error

Errors of projection produce dimensional differences between the original object and resultant image. Projection errors can be explained by the fact that any radiographic film is a mere two-dimensional representation of a three-dimensional object and the non-parallel nature of the x-ray beam. The films are distorted further by foreshortening of distances between points lying in the different planes and not lying in the same central ray. These distortions can be calculated from the geometry of the apparatus or via the use of standard scales in the field of view. Further using angular measurements rather than linear measurements can lessen the impact of these errors.

It is recognised that a generalised magnification and distortion of the image occurs with varying degree dependent upon the specific area of the radiograph examined.

Distortion is the inaccurate representation of a structure as a result of different target-object-film distances for different portions of the radiograph, and signifies that the enlargement of the image is not directly proportional to the object size. Distortion, whilst considered to be a minimal error, needs to be borne in mind when interpreting results of cephalometric studies.

Peripherally located landmarks are considered to be the most significantly, due to the greatest area of central beam dispersion. Adams demonstrated that using the Broadbent five foot target-object distance, that all angular measurements opened on average 1°, with those of the cranial base opening the least and the mandibular angles the most (Adams 1940). Thurow contends that enlargement is usually between 5-8% in the mid-sagittal plane and up to 15% at the periphery (Thurow 1951).

The relations between the different components of the cephalometric equipment are affected by a number of factors.

These are:

- The focal spot; the cephalostat and the film may be linearly displaced in relation to each other.

- The cephalostat and the film may be rotated with respect to one another, and
- The patient may be linearly displaced and/or rotated in relation to the rest of the system.

Bilateral skeletal structures such as the gonial angle, represent an obvious difference between the object and the respective sides of the projected image. The gonial angle is defined by the landmarks on the lower and posterior borders of the mandible, with the two halves of the mandibular corpus invariably angulated to the median plane so that the forward extending leg of the gonial angle is oblique to the film. The bilateral ascending rami are similarly implicated. Distortion also occurs, and this can be distinguished from enlargement in that it is an inaccurate duplication of the structure, whilst enlargement is a proportional expansion of the structure. To overcome distortion is an attempt to relate two lateral points to the mid-sagittal plane, although the side nearest the film will actually give the most accurate representation. Johnston advocates where bilateral landmarks present as two images, the average of the two be used, with a custom template of the bilateral structures employed to ensure accurate reproduction (Johnston 1996).

Projection errors involving head rotation of $\pm 5^\circ$, resulted in errors of length measurement that were usually less than 1% (Alqvist, Eliasson *et al.* 1986), and can be deemed insignificant and may be concealed by other errors. Three main studies have focussed on projection error obtained at the first stage of taking a lateral cephalometric radiograph (Hatton and Grainger 1958; Houston, Maher *et al.* 1986; Cooke and Wei 1991).

Hatton and Grainger recorded two radiographs of 15 three-year-old children and trace each radiograph on two separate occasions. Only one conventional measurement, Nasion-Bolton point distance, was used. The error variance of tracings from the pairs of radiographs was almost double that of the tracings repeated from the same radiograph. Therefore, it was concluded that the error introduced in taking the radiographs was almost as great as that of tracing measurement (Hatton and Grainger 1958).

Houston *et al* examined the lateral cephalometric radiograph of 24 patients who were having the films taken for another reason. The patients were removed from the cephalostat between the two films to test the projection error involved. The authors found that the greatest errors were those of the landmark identification and that errors arising in obtaining radiographs can be quite small provided due care is given to positioning the patient in the cephalostat. The authors suggested that the reason for the difference between their results and those of Hatton and Grainger may be because Nasion-Bolton point distance is particularly sensitive to any rotation of the skull in the cephalostat (Houston, Maher *et al.* 1986).

Cooke and Wei compared landmark location errors when retaking the radiograph and when re-measuring the same radiograph (Cooke and Wei 1991). Their results compare better with those of Hatton and Grainger as they found that the error percentage doubled for measurements on the retaken radiographs. The Frankfort plane, the functional occlusal plane and the incisor long axes showed the poorest reproducibility. Error percentage is the variance of the method error as a percentage of the variance of the particular measure. As this was a different statistical analysis to the ones used by Hatton and Grainger, and Houston, who used purely the method variance, the results may not be statistically comparable (Hatton and Grainger 1958; Houston, Maher *et al.* 1986)).

2.6.1.1.1 Natural Head Position (N.H.P.)

The concept of natural head position was introduced to orthodontics in the 1950's when it was found that the Sella-Nasion or Frankfort-Horizontal differed markedly from a horizontal line taken from natural head position (Downs 1956; Bjerin 1957; Moorees and Kean 1958) .

A horizontal baseline is crucial to reduce the error involved in identifying landmarks if definitions such as "most inferior..., or highest point on..." are to be used. For example, Menton, where the definition often used is "the most inferior point on the symphyseal outline."

Most investigations into natural head position have been concerned with the extension/flexion component of head orientation and not that of lateral tilting or turning, although this is also important (Harrison 1995). NHP is of considerable importance when investigating projection errors because of the three-dimensional positioning of the head.

Two lateral photographs of patients in the natural head position were used to determine a horizontal reference line (Lundstrom and Lundstrom 1992). They looked at the inclination of Sella-Nasion, Basion-Nasion and Porion-Orbitale to this horizontal. The results showed high standard deviations (4.5 -5.6) and these exceed those for natural head position. Therefore, they concluded that the greater stability of natural head position was recommended for use as a basis in cephalometric analysis. The authors did not, however, that when the second photograph was taken the patients tended to hold their chin slightly upwards in comparison to the initial film.

Cooke and Wei, in a study of Chinese and Caucasians, examined the accuracy of their own reference line, AB/horizontal, versus standard reference planes in accurate determination of a subject's sagittal skeletal relationship. They found that this natural head position true horizontal gave a "true life" picture of the patient but they did not discuss the reproducibility of the method (Cooke and Wei 1988).

There are conflicting opinions on the accuracy of head positioning, but NHP has been shown to be as accurate as any other horizontal baseline.

2.6.1.2 Landmark identification error

This type of error is a random error, which results largely through uncertainty in visual identification(Houston 1983).

2.6.1.2.1 Radiographic interpretation

Perception of an image on a radiograph involves four aspects of visual acuity (Goaz and White 1982):

- Detection of a single thin line or grey level,
- Recognition of a pattern,
- Resolution of a smallest line pairs on a test grid, and
- Recognition of a pattern in a two dimensional representation of a three dimensional object.

Visual recognition occurs as the brain tries to match an object with the stored image of a similar object, but if insufficient information is available this may be difficult. Therefore, a thorough knowledge of the anatomy of the skull is required to accurately analyse and locate landmarks on a lateral cephalometric radiograph (Bowden 1970).

According to Ben, when trying to interpret a lateral cephalometric radiograph, the best perception is achieved in an environment free of distraction (Ben 1991).

2.6.1.2.2 Landmark identification

Errors in anatomical landmarks identification was highlighted by Baumrind (Baumrind and Frantz 1971). He found that the magnitude of error varies greatly from landmark to landmark; with each landmark has its own characteristic and non-circular envelope of error. The landmarks with sharp folding edges (e.g. incisor crown tip) have a more accurate localisation compared to landmarks with the edge is a gradual curve (e.g. Point A) (Jacobson 1990), which demonstrated a proportionally larger error and evenly distributed along the edge. Gravely suggested that the lack of landmark identification was due to the lack of clarity due to image blurring due to patient movement during exposure, lack of film contrast and emulsion grains (Gravely and Benzie 1974).

Cephalometric landmarks are points that are used to make measurements from a cephalometric radiograph. They should be reliably identified and reproducible. There are five different types of landmarks(Moyers and Bookstein 1979):

- True anatomic points – these are points, which are identified directly from local morphology. For example, Anterior Nasal spine, Sella Turcica, Nasion, incisal edges and cusp tips.
- Extremal points – these are points which require an external from reference such as “most inferior”, “lowest.” For example, orbitale, menton, porion, A point, B point. The positioning of the subject is of greatest significance for the definitions of these points to apply.
- Intersection of projected line images – these are points derived from the intersection of anatomical line images. Such points only exist in projections and will depend on subject positioning. For example, articulare and pterygomaxillary fissure.
- Intersection of constructed lines – for example, constructed Gonion, which is taken as the intersection of the two tangents to the borders of the mandible.
- Implants – these are used for superimposition studies, mainly to show treatment change and growth.

There are five main factors that contribute to errors in identification of cephalometric points. These are sharpness, contrast, operator experience, variation in landmark definition and the contour of a curved outline for location of an extremal point. Included in these factors are the radiographic bony complexity of the region and the quality of the radiographic image. Also, when considering any computerized technique, a lack of resolution prevents accurate landmark identification.

Mclure *et al* (2006) investigated differences in landmark identification on direct digital and conventional cephalometric radiographs, to determine whether direct digital lateral cephalometric radiographs are of equal value in diagnosis and treatment

planning as conventional cephalometric radiographs. Each landmark exhibited its own unique pattern of landmark identification error, the magnitude and distribution of which must be taken into consideration when selecting landmarks for use in cephalometric analysis or when interpreting these analyses for diagnostic or treatment planning purposes. The authors concluded that the present study indicated similar precision and reproducibility in landmark identification using both direct digital images and conventional lateral cephalometric head films (McLure 2006).

2.6.1.2.3 Operator experience and anatomic complexity of the region

The skill of the observer can play a major role in the differences in landmark interpretation according to a study by Kvam and Krogstad (Kvam and Krogstad 1969). In addition, it is absolutely essential to have a full understanding of bony anatomy (Yen 1960; Bowden 1970; Van der Linden 1971). These two factors are closely related.

2.6.1.2.4 Landmark definition

According to Houston (Houston 1983), some cephalometric landmark definitions were ambiguous and lacked precision. For example, random errors would be introduced if the cephalometric landmark "Menton" was defined as the most inferior point on the bony chin with no reference to head orientation. If the X and Y-axis are used to display the envelope of error for any given landmark then head orientation has to be explained if the results of various studies are to be compared.

2.6.1.2.5 Envelopes of error

Landmark identification is reported to be the greatest error in the analysis of lateral cephalometric radiographs (Bjork 1947; Hixon 1956; Hatton and Grainger 1958; Richardson 1966; Savara, Tracy *et al.* 1966; Baumrind and Frantz 1971; Baumrind and Frantz 1971; Mitgard, Bjork *et al.* 1974; Broch, Slagvold *et al.* 1981; Stabrun and Danielsen 1982; Houston 1983; Vincent and West 1987).

Baumrind and Frantz, using manual tracing techniques, found that for each cephalometric point there was a characteristic pattern of recording error in either the

vertical or horizontal direction, and that the pattern for each landmark was systematic or unique (Baumrind and Frantz 1971; Baumrind and Frantz 1971). Nasion and Pogonion had twice the error in the vertical direction when compared to the horizontal, whereas Menton varied most in the horizontal direction. Sella and Gonion had the same error in both directions but Sella had the least total error and the Gonion had the most.

A similar study found a comparable pattern of error for the various cephalometric points but the errors were smaller in magnitude (Vincent and West 1987). Richardson found that some cephalometric points could be located with greater accuracy than others and that there was a pattern in the vertical and horizontal directions similar to the previously mentioned studies (Richardson 1966). Additionally, he commented that where a curved anatomic outline is involved variations would be more in one direction than the other. For example in locating Menton, where it is possible to make a large error in the horizontal plane without effecting the vertical much at all.

Some analyses use geometrically constructed points in addition to anatomic and extremal points. Savage examined the reliability of geometrically constructed points compared to those determined directly (Savage, Showfety *et al.* 1987). They found no statistically difference between the two types of points and that the level of operator experience was unrelated to the landmark variability.

Certain cephalometric points are more difficult to locate than others. One of these is Condylion, which can be difficult to identify because of the overlying dense bony structures. Investigations into the reliability of identifying Condylion, concluded that an open-mouth cephalogram was required, in addition to the standard film, so that this point could be accurately located (Adenwalla, Kronman *et al.* 1988; Forsberg and Odenrick 1989).

With the advent of computer technology, studies have been performed looking at the envelope of error on digitised radiographs. Broch (Broch, Slagsvold *et al.* 1981), using a digitiser for landmark identification, found a pattern of error similar to Baumrind and Frantz (Baumrind and Frantz 1971; Baumrind and Frantz 1971) for each landmark. Again, whilst studying envelopes of error for landmark identification,

Stabrun *et al* (Stabrun and Danielsen 1982) compared inter- and intra-operator error using digitised cephalograms. These authors found that inter-operator discrepancy was higher than intra-operator and, again, that each landmark had its own pattern of error.

It is important in any study on cephalometric errors to perform the correct statistical analysis(Houston 1983; Battagel 1993). Houston(Houston 1983) criticised the published literature for incorrect error analysis or at least no correct evaluation of the errors of the method. He stressed the need to replicate measurements as much as possible to reduce the risks of random error. Battagel(Battagel 1993) reviewed the statistical methods used in studies on cephalometric accuracy, and based the examination on the fact measuring a lateral cephalometric radiograph is often imprecise and that the errors associated with this should be quantified and understood.

2.6.1.3 Tracing and Measurement Error

Once the landmarks have been identified they can be used in a number of analyses in order to obtain an overall description of the facial type, or for superimpositions to study treatment change and the effect of growth. Measuring or tracing errors are mechanical, systematic errors. Modern computer methods practically eliminate the error in measurement by using calculations from Cartesian coordinates (Bondevik, Rosler *et al.* 1981).

Measurement of the lateral cephalometric radiograph is the last stage in the analysis at which an error can occur. Measurements are either linear or angular and have different degrees of error depending upon the cephalometric landmarks being used. Baumrind and Frantz, examined the accuracy of linear and angular measurements, suggesting that the measurements were affected by (Baumrind and Frantz 1971; Baumrind and Frantz 1971):

- The magnitude of the landmark identification error.
- The linear distance between the points used. The shorter the distance the greater the percentage error.
- The direction of the measurement was taken from. If the landmark were approached from the direction in which its envelope of error was the greatest, for example Nasion from the horizontal, the measurement error would be increased.

Richardson (1966) and Stabrun *et al* (1982) stress the importance of using appropriate measurements, that is those involving the lowest envelope of error (Richardson 1966; Stabrun and Danielsen 1982)). The importance of this was reinforced by Cohen who suggested that linear measurements should be obtained by approaching the cephalometric point at right angles to the greatest envelope of error. An example of this is B point in a Condylion to B point measurement. This would, however, not apply to the angular reading of SNB where least error is obtained when the point is approached from the vertical direction.

Gravely and Benzies showed that inter-operator error was greater than intra-operator and that the experience led to greater stability (Gravely and Benzies 1974). The importance and expert knowledge has also been demonstrated by Kvam and Krogstad (Kvam and Krogstad 1969). They showed that one of the least reliable measurements was that of the axial inclination of incisor teeth, which is often of most use to the clinician.

2.6.2 Image Enhancement

One of the greatest advantages of digital images over conventional methods may be the ability to enhance the digital image.

Image enhancement is the ability of the computer to produce an improved digital image by various techniques (Jackson, Dickson *et al.* 1985).

- Modification of contrast and brightness allows compensation for different x-ray exposure levels and a means to increase the range of contrast for a specific area, so that fine detail can be seen. Modern systems such as Dolphin Imaging allow manipulation of the contrast on various parts of the lateral cephalometric radiograph and this is then incorporated into one final digital image.
- Spatial filtering can also be used to “deblur” and sharpen the image but many of these techniques can increase picture noise and thus lead to little overall improvement in the image.
- Positive and negative images. Radiographic images are negative images. If a positive image is formed bony areas appear black and soft tissues white. Jackson *et al* found this inversion of the image to be a less tiring method of analysing the lateral cephalometric radiograph (Jackson, Dickson *et al.* 1985).

2.6.3 Accuracy of Computer Systems

In recent years, many studies have looked at the accuracy of different computer systems, comparing them to traditional manual techniques (Houston 1979; Richardson 1981; Cohen, Ip *et al.* 1984; Jackson, Dickson *et al.* 1985; Powell 1987; Sandler 1988; Epply and Sadove 1991; Oliver 1991; Lowey 1993; Macri and Wenzel 1993; Forsyth, Shaw *et al.* 1996; Schulze, Gloede *et al.* 2002; Cohen 2005; McLure 2006; Santoro, Jarjoura *et al.* 2006). The different authors found varying results.

- Richardson compared landmark identification on a digitiser with manual methods on 50 lateral cephalometric radiographs (Richardson 1981). He found that the digitiser gave a statistically significant more accurate location, although each radiograph was only digitised twice.

When a digitiser is used for landmark identification this can either be done directly from the lateral cephalometric radiograph or from a tracing. Houston (1982) and Cohen (1984) compared these two methods. Houston's study involved double determination of four linear and seven angular measurements on 25 lateral cephalometric radiographs with immediate and delayed direct redigitization and digitisation of repeat tracings. The errors in delayed direct redigitization were found to be slightly greater than those in digitising repeat tracings.

Cohen (1984) evaluated the use of digitiser on tracings, untraced films and modified "dot" tracings. He found that errors in measurement of conventional cephalometric angles were comparable, irrespective of the method chosen. Errors in landmark location were smallest when measured directly on the radiographs without the use of an intermediate tracing.

Following on from the work of the three previously mentioned authors, Sandler (1988) further investigated the use of digitisation of tracings, direct digitisation and a manual method. Of the three methods, direct digitisation proved to be the most reproducible, particularly for angular measurements. Tracings were found to be useful

for linear measurements involving constructed points, such as Gonion and Articulare. The sample of lateral cephalometric radiographs was not randomly selected as only good quality radiographs were used. These radiographs did not have any unerupted teeth which the author thought may have made detection of incisor apices difficult.

The remaining studies examined the accuracy of a digital on-screen representation of a lateral cephalometric radiograph, in addition to the previous methods.

Jackson *et al* (1985) performed a pilot study comparing digitised images, formed from a placing the radiograph on a digitising tablet, with uptaking the image via a microdensitometer scanner. They studied inter-observer and intra-observer reproducibility. The results of these two methods were also compared to a manual method. Their findings showed that the image processing system gave reproducibility comparable to the manual method. The authors expected a more positive result for the image capture method. Therefore, they suggested that these findings may have been due to lack of familiarity with the system, and the low spatial resolution of the image processing (512 by 426 pixels.)

Cohen and Linney (1986) using television based image display, compared coordinate values of digital images obtained by a television camera to those of the original radiograph using a Reflex Metrograph. Sella and Menton were the only two landmarks used and the resolution of the screen was not remarked upon. The authors found that the digital system gave more reproducible results, but that it was limited by the quality of the original image.

Oliver (1991), using five lateral cephalometric radiographs compared a digitiser method, on-screen digitising of an enhanced video image and hand tracing techniques. The resolution of the computerised system was 512 by 426 pixels for the screen and 579 by 583 for the camera. It was possible to enhance the video image using three options: contrast and brightness, soft tissue enhancement and edge enhancement. Six angular measurements were compared comprising SNA, SNB, ANB, maxillary/mandibular plane, upper incisor to maxillary plane and lower incisor to mandibular plane. For all methods the reproducibility was poorest for the angulation of the incisors to their respective planes. Digitisation of a tracing was more accurate

than direct digitisation for both computerized methods. Overall, the video image method was found to be less accurate than the digitiser method, with the conclusion being made that the facility to enhance the radiographic image did not produce any significant improvement in precision of the cephalometric variables studied.

Using the same six angular measurements as Oliver (1991) and Jackson *et al* (1985), Davis and Mackay (1991) compared a manual tracing technique to the measurements on two different digital images. One was the original image and the other a high frequency filtered image, which increased the contrast of the image. A resolution of 512 by 512 pixels was used. Overall the least variable results were from the computer-based measurement of the unenhanced image. This investigation was, however, only a pilot study and as such the sample size was only five lateral cephalometric radiographs.

It is possible to obtain a digital image using digital image processing techniques. Eppley and Sadove (1991) compared measurements of the twenty cleft patients from one radiographic exposure on a conventional radiograph, with that of a digitally processed image. The osseous landmarks were found to be readily identifiable with both radiographic techniques, with no statistical difference between techniques. For soft tissue visualization the video image was found to be far superior.

Lowey (1993), in two consecutive papers, studied a video image capture system for cephalometric evaluation and study cast mensuration. The camera resolution was 512 by 512 pixels giving an overall linear resolution, on screen, of 0.51mm in the X axis and 0.37mm in the Y-axis. Fifty radiographs were measured and compared to a digitiser method. The results showed the digitiser method to be more accurate, but the author commented that the differences were slight and the errors due to calibration, rounding and resolution in the image capture system probably caused the difference. He concluded that the clinical advantages of direct on-screen image manipulation outweighed the limitations of system precision and that the observed difference between systems would be of limited clinical significance, but may be more important if used for research purposes. This is a questionable conclusion as high accuracy is required in some clinical situations, for example, borderline surgical patients.

In a further study, Marci and Wenzel (1993) found similar results to Lowey (1993), when comparing measurements on a video image capture system with a digitiser method. These authors were the first to comment on the intrinsic bias in the system due to the different resolutions of the two systems. The digitiser has a resolution capability of 0.1mm for both axes, whereas the digital system was 0.5mm in the X-axis and 0.3mm in the Y-axis. This difference in resolution would lead to a lower mean error for the system with the inferior accuracy. Despite this advantage of the digital system the results showed that the overall reliability of landmark location with the digital system was inferior to that obtained with the digitiser. With digital processing it was possible to improve good quality radiographs but not those that had an initial lower quality. These authors concluded that the reason their results were not in favour of the digital system was because some of the previous studies (Cohen and Linney 1984; Jackson *et al* 1985) did not take into account the precision of the different systems.

Recently, Forsyth, Shaw and Richmond (1996) also compared an image capture system with a conventional digitiser. The resolution was 512 by 512 pixels for the monitor, which was similar to all the previous studies. They found a greater error with the digital image method, with the largest error for SNA, which was on average 2.2 larger.

In summary, there have been many studies into the accuracy of commercially available computer systems using different methods for landmark location and measurement. There are so many pathways for system error that the statistics are often not adequate to accurately compare the results. As the studies use various statistical analyses it is also difficult to compare one result to one another in a different study. Furthermore, because a large amount of the error was thought to be due to the resolution of the system, further investigation into this factor is required. Macri and Wenzel (1993) suggest that a screen resolution of 1025 by 1024 pixels, with a matched camera resolution, is the minimum system required to achieve comparable accuracy to a digitiser.

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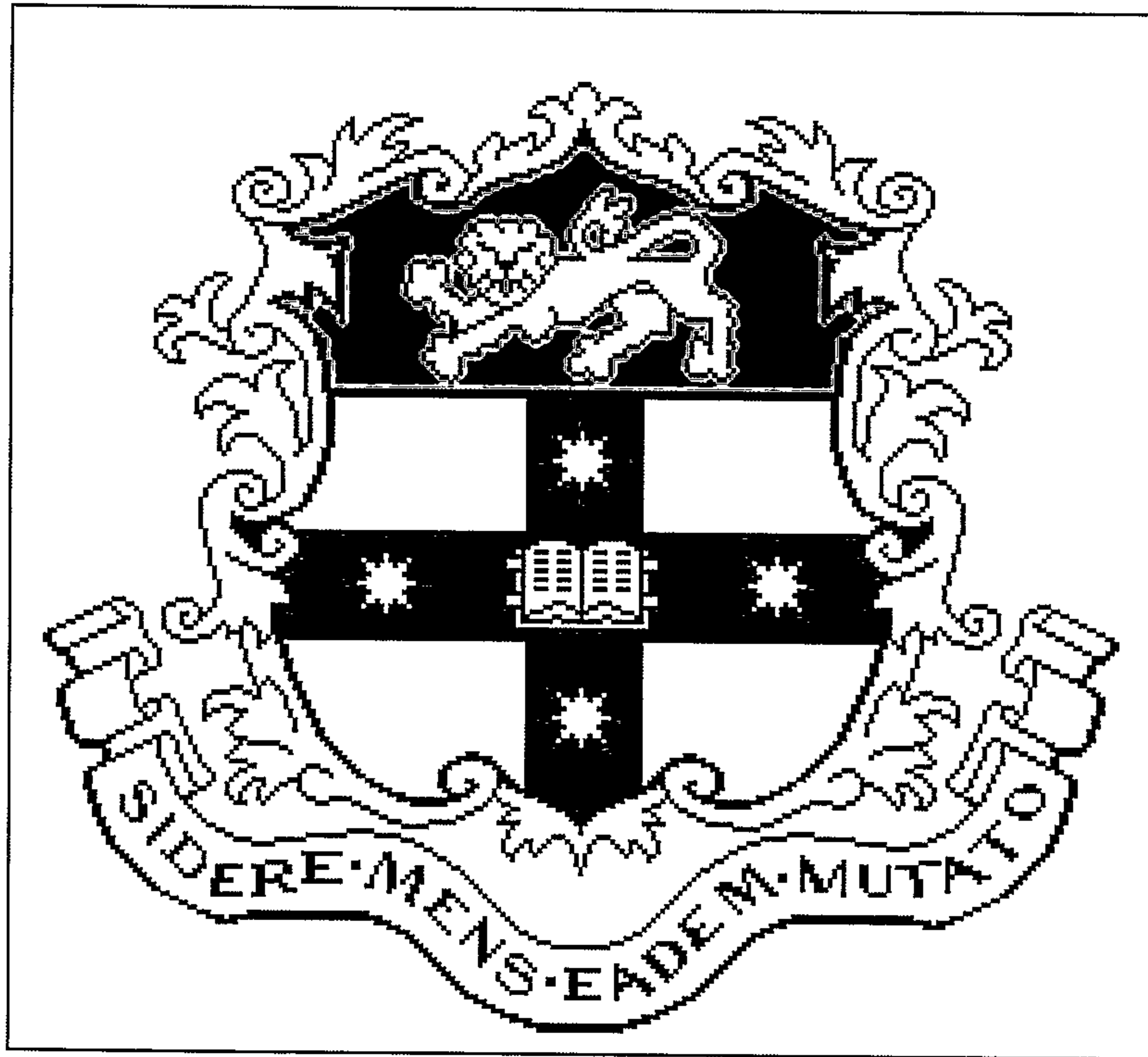
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4. Manuscript



**The role of ethnicity in Obstructive Sleep
Apnoea. A comparative study of craniofacial
morphology between Australian Caucasians and
Hong Kong Chinese subjects.**

This manuscript is to be modified prior to journal submission.

An analysis of Hong Kong Chinese and Australian Caucasian subjects with Obstructive Sleep Apnoea.

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ABSTRACT

Ethnic variation combined with craniofacial variation has been implicated in contributing to the severity of Obstructive Sleep Apnoea (OSA). Patients with OSA have significant craniofacial and upper airway abnormalities when compared with age-matched and sex-matched controls. This study attempted to compare the relative contributions of craniofacial skeletal characteristics and anthropometric variables such as age, sex, weight (kg), height, body mass index and neck circumference, on the severity of OSA between Caucasian and Chinese patients.

One hundred and sixty obstructive sleep apnoea (OSA) patients were divided into two groups on the basis of ethnicity: 76 Caucasian and 84 Chinese patients. A comprehensive cephalometric analysis with a multivariate statistical method was performed in order to define the different principal components (PCs) of cervico-craniofacial skeletal and upper airway soft tissue morphology in each group and how they contributed to selected indices of sleep-disordered breathing (apnea-hypopnea index – AHI and minimum oxyhaemoglobin saturation) and demographic data (BMI.) Stepwise multiple regression showed that ethnicity itself, once adjusted for craniofacial and anthropometric measures, does not play a significant role in differentiating OSA between the two ethnic groups. However, ethnicity expressed through differences in craniofacial characteristics between the two patient samples was found to be significant.

Twenty-eight cephalometric variables of cervico-craniofacial skeletal morphology were reduced to seven and eight PCs. Six soft tissue cephalometric variables were reduced to two PCs describing 52.6% and 63% of the total variance in the Caucasian and Chinese patients, respectively. Ten hard tissue linear cephalometric variables were reduced to two and three PCs for the Caucasian and Chinese patients, respectively accounting for 70.9% and 63.4% of the cumulative variance. The hard tissue angular linear combination of cephalometric variables was reduced to three PCs and accounted for the greatest cumulative variance, with 71.7% and 75% for the Caucasian and Chinese groups respectively. Two canonical variables and their correspondents with different loadings were established differently for the individual

OSA groups. The Caucasian group correlated highly with different canonical variables, as compared to the Chinese group.

A canonical correlation successfully clarified the complexity of the simultaneous relationship of the relevant variables by finding the linear combination of predictor variables that best explained a linear combination of response variables. These analyses are proved useful to demonstrate the relationship of cervico-craniofacial skeletal and upper airway soft tissue morphology and selected demographic data. This lays down a basis for understanding the complicated pathogenic components of ethnicity and underlying craniofacial pattern in Australian Caucasian and Hong Kong Chinese OSA subjects.

Key words: Obstructive Sleep Apnoea, Craniofacial, Ethnicity, Body Mass Index.

INTRODUCTION

Obstructive Sleep Apnoea (OSA) is a debilitating condition, affecting approximately 4% of men and 2% of women. Sleep apnoea was first noted as a syndrome in the early to mid 1960s¹. Prevalence studies on Obstructive Sleep Apnoea (OSA) vary widely, ranging from 1 to 24%, for groups of middle aged adults²⁻⁴. More recent figures of up to four percent established OSA as second only to asthma in the prevalence of chronic respiratory disorders, depending on the diagnostic criteria employed⁵. The prevalence of OSA amongst different racial populations, may lend support to the theory that ethnicity may be an important risk factor in obstructive sleep apnoea syndrome (OSAS). African-Americans have a higher prevalence and increased disease severity compared to Caucasians^{6,7}. Kripke et al. (1997) estimated that 16.3 percent of the US Hispanics and racial minorities have OSA as compared with 4.9% of non-Hispanic whites aged 40 to 64 years⁸.

Chinese racial groups comprise one quarter of the world's population and currently one million people of Chinese origin live in Australia. A further 27% of the Australian population has at least one parent born outside Australia, of which approximately one quarter are of Asian origin⁹. Several studies on the prevalence of sleep disordered breathing (SDB) have been conducted in Asian countries. Ip et al. (2001) demonstrated that OSA is as common amongst middle-aged Hong Kong Chinese men as in Caucasians with prevalence rates of SDB and OSAS using full polysomnography to be 8.1 and 4.1%¹⁰. Similar to the dichotomy present between Caucasian male and female OSA prevalence rates, Ip et al (2004) found a reduced prevalence of SDB and OSAS amongst middle-aged Hong Kong women of 3.7% and 2.7% respectively¹¹. Kim et al (2006) found that in Korea the prevalence of OSAS to be 4.5% in men and 3.2% in women¹². Most Asian OSA patients are said to have a relatively lower body mass index (BMI) than the Caucasian counterparts despite suffering from a similar degree of OSA, i.e. they tend to be affected to a greater extent.

Despite the fact that ethnicity has been included as a factor in the predisposition to OSA, few studies have been dedicated to exploring the differences in craniofacial

structures between ethnic groups that may account for diverse prevalence susceptibility and severity.

The primary aim of this study was to compare the differences in craniofacial and upper airway morphology between adult Caucasian and Chinese OSA patients. Our null hypothesis was that OSA is influenced by craniofacial and anthropometric characteristics, independent of ethnic variation. Our alternate hypothesis was OSA is influenced by craniofacial and anthropometric characteristics, independent of ethnic variation.

MATERIALS AND METHODS

Sample Selection

A total of 160 patients were included in the study, with 74 Caucasian and 86 Chinese patients. The Caucasian patients were recruited from a tertiary referral sleep disorders centre in Australia, while the Chinese patients were recruited from an equivalent centre in Hong Kong. Patients were included only if their ethnic background was clear, and they had evidence of OSA as determined by polysomnography (AHI > 10/hour). They were excluded if they were edentulous, had an ethnic background other than Caucasian or Chinese, exhibited predominantly central sleep apnoea.

Polysomnography.

Nocturnal sleep studies were performed by a trained sleep technician in a standard fashion as described previously¹. Standard nocturnal polysomnography was performed, with electroencephalogram (EEG), electrooculogram and submental electromyogram (EMG) electrodes applied in the standard fashion for sleep stage determination. Respiratory variables included chest wall and abdominal movement, diaphragm EMG, nasal airflow and pressure and oxygen saturation by pulse oximetry.

Apnoea was defined as a cessation of breathing during sleep for 10 seconds or more, with oxygen desaturation of more than 3% and/or associated with arousal. Hypopnoea was defined as a 50% or greater reduction in airflow, associated with arousal and/or a 3 % or greater reduction in blood oxygen saturation, lasting 10 seconds or more^{13,14}. The Apnea Hypopnoea Index (AHI) was calculated as the average number of episodes of apnoea plus hypopnea per hour during sleep.

Anthropometric Examinations

The anthropometric measurements included height (m) and weight (kg), enabling calculation of BMI (kg/m²), and measurement of neck circumference (cm).

Cephalometric examinations for craniofacial morphology

A lateral cephalometric radiograph was taken for each subject, according to previously described methods¹⁸. Radiographs were taken at end-expiration with the head in the natural position, achieved by asking the subjects to look into their own pupils reflected in a mirror located at eye level. Cephalometric analysis was formed looking at anatomical variables previously validated for OSA investigation. The landmarks and measurements used for the cephalometric analysis are exhibited in Figure 1, and Tables 1 and 2. All lateral head radiographs were hand traced by the primary author (SV), blinded to the subjects' clinical status, on 0.03inch matte acetate paper over a light-viewing box with a 0.3mm 2H lead pencil. Landmarks were identified and denoted with a 'X.' Where a bilateral landmark presented as two images, the average of the two was used, with a template of the bilateral structures employed to ensure accurate reproduction. All the landmarks that were identified, were verified by the corresponding author (MAD) to be accurate and true. The cephalograms were scanned using the Epson 1600 digital scanner, and imported into the Dolphin Imaging Program – Premium Version 10.0 (California, USA.) A custom analysis was constructed using the landmarks available from the Dolphin Program, and the images were digitised¹⁵. The mean enlargement factor for the cephalometric radiographs was 11% for the Australian Caucasian group and 13% for the Hong Kong Chinese group, which did not influence the angular measurements. All linear values for distances were automatically transformed by the respective enlargement factors by the Dolphin Imaging Program (California, USA.)

Measurement error was assessed in twenty randomly selected patients from both groups, whose radiographs were retraced, redigitized, and remeasured by the same examiner under the same conditions one month later. A common way of representing "measurement error" is as the standard deviation of the repeated measurements on the same subject ie 'the difference between the observed value, with measurement error, and the subject's true value will be at most two standard deviations with probability 0.95'¹⁶. Additionally, we calculated a "(within subjects) coefficient of variation"

(CV). The coefficient of variation was less than 5% for all variables. Hence, the cephalometric measurements were considered to be accurate.

Figure 1. Cephalometric variables.

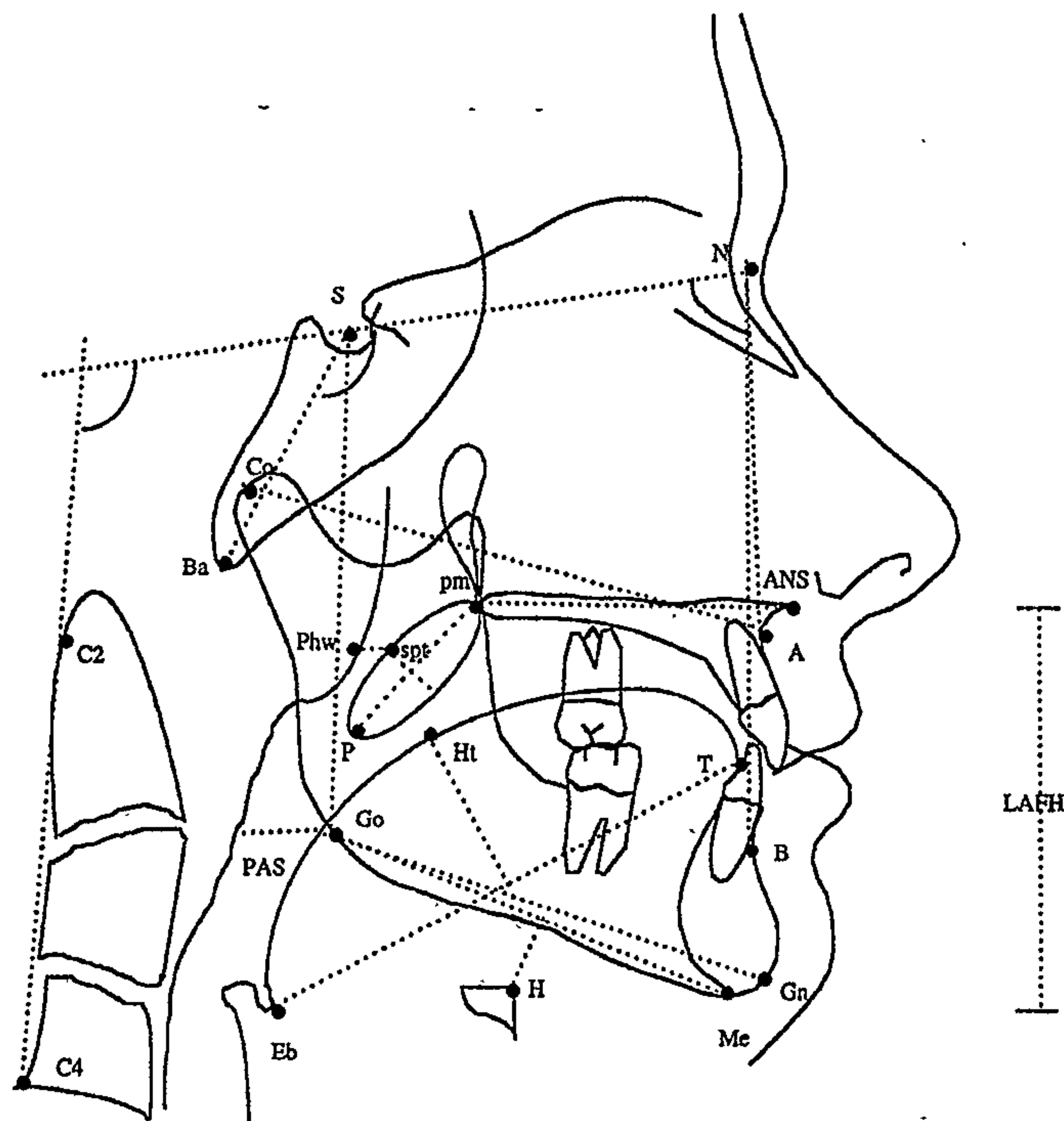


Figure 1. Definitions of cephalometric landmarks and measurements¹⁷. *Anatomical landmarks*: ANS = Anterior Nasal Spine, the tip of the median sharp bony process of the palatine bone in the hard palate. A Point = deepest midline point on the maxillary alveolus between ANS and the maxillary alveolar crest. B Point = deepest midline point between the mandibular alveolar crest and the gnathion. Ba = Basion, the most inferior point on the anterior margin of the foramen magnum in the median plane. Go = Gonion, the most lateral external point at the junction of the horizontal and ascending rami of the mandible. Gn = Gnathion, the most anteroinferior point on the bony mandibular symphysis. H = Hyoidale, the most superior-anterior point on the body of the hyoid bone. Me = Menton, the lowest point on the bony outline of the mandibular symphysis. MP = Mandibular plane, line joining Me and Go. N = Nasion, the most anterior point of the frontonasal suture. PNS = Posterior nasal spine, the tip of the posterior spine of the palatine bone in the hard palate. spt = tangent point on a line parallel to the long axis of the soft palate at the maximum width. Phw = Posterior pharyngeal wall, the point on the posterior pharyngeal wall at the same horizontal level as spt. S = Sella, the center of the sella turcica. *Measurements*: BaSN (degrees) = Cranial base angulation in midsagittal plane, SN (mm) = anterior cranial base length. Go-Gn (mm) = mandibular length. SNA (degrees) = angle from S to N to A Point. SNB (degrees) = angle from S to N to B Point. ANB (degrees) = angle from A Point to N to B Point. SN-MP (degrees) = angulation of the mandibular plane with the SN line. H-MP (mm) = perpendicular distance from the MP to H. RPAS (mm) = width of nasopharynx from Phw to spt. PAS (mm) = distance between the posterior pharyngeal wall and the dorsal surface of the base of the tongue, measured on the line that intersects Go and B point. Overjet (mm) = horizontal distance between the upper and lower central incisors measured parallel to the occlusal plane. It is measured from the labioincisal edge of one upper central incisor to the labial surface of the corresponding lower central incisor with the upper and lower teeth in centric occlusion. Overbite (mm) = vertical distance between the incisal edge of the upper central incisor and the incisal edge of the lower central incisor.

STATISTICAL ANALYSES

Data were analysed using a statistical package (SPSS for Windows Version 12.0, SPSS Inc, Chicago IL.) Independent samples t-test were used to compare the cephalometric, anthropometric and AHI data between racial groups. A multiple linear step-wise regression model was constructed to initially select important variables (such as cephalometric, BMI, neck circumference and ethnicity) predicting for OSA severity between the two groups. The regression models were then checked for their accuracy in determining the relationship between OSA and ethnicity.

A principal component analysis (PCA) was used to reduce the numerous cephalometric variables within the two populations to a few meaningful principal components (PCs) ¹⁸.

In order to analyse the relationships between the outcomes (OSA severity and minimal oxyhemoglobin saturation) and the explanatory variables (groups of cephalometric variables, BMI and neck circumference), a canonical correlation analysis was performed. Canonical correlation analysis is a multivariate statistical model that facilitates the study of interrelationships among sets of multiple dependent and independent variables. Canonical correlation analysis identifies the optimal structure or dimensionality of each variable set that maximises the relationship between composites of sets of multiple dependent and independent variables.

RESULTS

Independent T-Tests

Anthropometric, cephalometric and polysomnographic characteristics of each group are presented in Tables 1,2,3 and 4.The total average of BMI for the combined subjects was 26.7±6.0, with a neck circumference of 40.7±4.8, and AHI of 28.6±22.7. The Hong Kong Chinese group had a BMI of 29.1± 0.6, whereas the Australian Caucasian group had a BMI of 30.4±0.8. The neck circumference of the Australian Caucasian group was 40.9cm±0.4, whereas the Hong Kong Chinese group had a neck circumference of 40.5cm±0.6 (Table 1.) Although there were differences between the two groups in regards to weight and height, no statistically significant differences existed between the BMI of the two groups. The AHI values for the Caucasian group was 25.2±1.9, and the Hong Kong Chinese group had a AHI value of 31.4±2.9 (Table 4.)

Table 1: Anthropometric Measurements

Variable	Caucasian (Mean ± SD)	Chinese (Mean ± SD)	P-level
Age	46.95 ± 11.43	48.77 ± 11.65	ns
Neck	40.9cm ± 0.4	40.5cm ± 0.6	ns
Weight	92.9kg ± 17.0	79.0kg ± 16.8	****
Height	1.74m ± 0.08	1.65m ± 0.08	****
BMI	30.4 ± 0.8	29.1 ± 0.6	ns

Table 2: Skeletal and Dental Cephalometric Measurements

Variable	Caucasian (Mean ± SD)	Chinese (Mean ± SD)	P-level
SNA	82.3 ± 3.3	84.6 ± 4.5	****
ANB	3.0 ± 3.3	4.9 ± 3.2	****
UFH	58.2mm ± 5.8	54.1mm ± 4.6	****
LAFH	75.1mm ± 8.8	70.4mm ± 5.5	****
AFH	131.7mm ± 12.3	122.0mm ± 6.9	****

Jarabak	88.2% ± 6.4	82.2% ± 5.2	****
Y-Axis	67.1 ± 4.6	71.1 ± 4.9	****
Gonial Angle	126.5 ± 6.0	119.9 ± 8.2	****
Go-Me	77.9mm ± 9.4	65.8mm ± 4.1	****
SN	77.5mm ± 6.7	63.7mm ± 3.3	****
ANS-PNS	58.8mm ± 4.3	50.7mm ± 3.5	****
Co-A	96.2mm ± 8.0	83.1mm ± 4.6	****
CVTSN	108.7 ± 7.8	111.3 ± 8.4	*
SN-PP	8.3 ± 3.8	10.0 ± 4.5	**
Overbite	2.6mm ± 3.6	1.1mm ± 2.9	**
Overjet	4.22mm ± 2.42	3.95mm ± 2.37	Ns
MP-H	22.4mm ± 6.7	18.5mm ± 6.1	****

Table 3. Cephalometric Soft-Tissue Measurements

Variable	Caucasian (Mean ± SD)	Chinese (Mean ± SD)	P-level
RPAS	10.6mm ± 4.0	8.8mm ± 2.5	***
PAS	10.8mm ± 4.5	8.0mm ± 3.5	****
PNS-P	40.1mm ± 4.3	33.7mm ± 4.6	****
Mx Soft Palate	11.4mm ± 1.8	9.7mm ± 1.5	****
Tongue Length	89.4mm ± 7.6	66.9mm ± 10.7	****
Tongue Height	40.0mm ± 5.0	31.1mm ± 4.3	****

Table 4. Polysomnography Measurements

Variable	Australian (Mean ± SD)	Chinese (Mean ± SD)	P-level
AHI	25.2 ± 1.9	31.4 ± 2.9	ns
Min O ₂ Saturation	85.8% ± 5.8	93.4% ± 4.7	****

**** P < 0.001; *** P < 0.005; ** P < 0.01; * P < 0.05; ns – not significant.

Multiple Linear Stepwise Regression

Multiple linear regressions were performed, initially using an automatic procedure (step-wise regression) to select the important variables, then running the actual regressions to check the accuracy of the model produced. The last step of the procedure was to add ethnicity (and gender) to the model to see whether it was significant. Three options existed – first, with only cranio-facial variables, second with BMI and Neck in addition, and third with minimum oxygen saturation. The regression model (regression 1, 4 and 7), then the model with gender and ethnicity added (regression 2,5 and 8) and finally with ethnicity added (regression 3,6 and 9.) All nine regression models revealed that ethnicity is non-significant ie the overall conclusion is that there is no evidence to suggest differences between the ethnic groups. Hence, our initial analyses showed that ethnicity itself as a variable allowing for, and adjusted for craniofacial and anthropometric measures, doesn't play a significant role in discriminating for OSA between Australian Caucasians and Hong Kong Chinese. However, ethnicity expressed through differences in craniofacial characteristics between the two patient samples was found to be significant (Tables 2 and 3).

Principal Component Analysis

A principal component analysis (PCA) was used to reduce the numerous cephalometric variables to a few meaningful principal components (PCs)¹⁸. The first PC (PC1) is the linear combination of the original variables that accounts for the largest possible amount of variability in OSA severity. The second PC is the linear combination of the original variables uncorrelated with PC1, which explains the second largest amount of the remaining variability.¹⁸ The rule used to determine how many principal components to use was to include only those whose associated eigenvalues were greater than one.

The number of cephalometric variables was reduced to linear combinations of the original variables suggested by principal component analyses using a varimax rotation applied to logical subgroups split by ethnic group. These subgroups were defined as soft tissue linear, hard tissue linear and hard tissue angular. The soft tissue linear (STL) subgroup consisted of the variables PAS, PNSP, MxSfPl, RPAS, TL and THt.

The hard tissue linear (HTL) subgroup consisted of PFH, UFH, LAFH, AFH, GoMe, SN, ANSPNS, CoA, OJ, and OB. The hard tissue angular (HTA) subgroup consisted of SNA , SNB , ANB , Y-axis , SN-PP , SN-OP , SN-MP , PP-MP , Gonial Angle, SN-Ba , and CVT-SN .

The Australian Caucasian and Hong Kong Chinese subjects were dealt with separately because the principal components for Caucasians and Chinese subjects respectively were not similar to what was obtained when combining the two ethnic groups. In the canonical correlation analysis as well as the important principal components from these three groupings we included the variables MPH, BMI and neck circumference. A summary of the linear combinations suggested by the principal components analyses applied to the logical subgroups split by ethnicity is given below (Table 5 and Table 6). Only variables in the principal component linear combination whose coefficient absolute value greater than 0.4 are displayed.

Table 5. Caucasian Principal Components

Principal Component	Linear Combinations		
	Soft tissue linear	% Variance	Cumulative %
AUSPC1STL	PNSP + MxSfPl + TL	27.37	27.37
AUSPC2STL	PAS + RPAS - THt	25.20	52.57
	Hard tissue linear		
AUSPC1HTL	PFH + UFH + LAFH + AFH + GoMe + SN + ANSPNS + CoA	53.98	53.98
AUSPC2HTL	OJ + OB - LAFH	16.91	70.89
	Hard tissue angular		
AUSPC1HTA	Y-axis + SN-OP + SN-MP + PP-MP + Gonial Angle	25.95	25.95
AUSPC2HTA	-SNB + ANB + Y-axis + SN-MP + CVT-SN	25.24	51.19
AUSPC3HTA	-SNA + SN-PP + SN-Ba	20.50	71.69

Table 6. Chinese Principal Components

Principal Component	Linear Combinations		
	Soft tissue linear	% Variance	Cumulative %
<i>HKPC1STL</i>	PAS + PNSP + MxSfPl + TL + THt	42.69	42.69
<i>HKPC2STL</i>	-MxSfPl* + RPAS	20.30	62.99
	Hard tissue linear		
<i>HKPC1HTL</i>	UFH + GoMe + SN + ANSPNS + CoA	29.63	29.63
<i>HKPC2HTL</i>	LAFH + AFH - OB	20.96	50.58
<i>HKPC3HTL</i>	PFH - OJ	12.81	63.39
	Hard tissue angular		
<i>HKPC1HTA</i>	-SNA -SNB + Y-axis + SN-PP + SN-OP + SN-MP + SN-Ba + CVT-SN	37.12	37.12
<i>HKPC2HTA</i>	Y-axis + SN-MP + PP-MP + Gonial Angle	25.63	62.75
<i>HKPC3HTA</i>	SNA + ANB	12.27	75.02

*Absolute size of coefficient just above 0.4. Size of coefficient for THt just below 0.40.

Canonical Correlation Analysis

We then tested for significant canonical correlations between the linear combinations of the original variables suggested by the principal components for the two ethnic groups separately. Canonical correlation analysis is a multivariate statistical model that facilitates the study of interrelationships among sets of multiple dependent and independent variables ie if the variables divide naturally into two groups in a multivariate data set, we can use canonical correlation to investigate the relationship between the two groups. Canonical correlation analysis identifies the optimal structure or dimensionality of each variable set that maximises the relationship between composites of sets of multiple dependent and independent variables. In doing so, it develops a number of independent canonical functions that maximise the correlation between the linear composites, also known as canonical variates, which are sets of dependent and independent variables. Each canonical function is actually based on the correlation between 2 canonical variates, 1 variate for the dependent variables and 1 for the independent variables¹⁹.

An eigenvalue, or canonical root, provides an estimate of the amount of shared variance between the respective optimally weighted canonical variates of dependent and independent variables. Correlation between P_k and Q_k are termed *canonical correlations* (R_k). The significance of the canonical correlations can be tested by

means of Wilk’s test. Canonical variables can be interpreted by evaluating the canonical variable loadings that are the correlations of the original variables (X, Y) with canonical variables (P, Q)¹⁹.

Table 7. Caucasian Canonical correlations

	Test that remaining correlations are zero			
Canonical correlation	Wilk's	Chi-square	DF	p-value
0.581	0.565	36.280	20	0.014
0.384	0.853	10.129	9	0.340

Canonical correlations refer to the variance explained in the canonical variates. Only the first canonical correlation is of sufficient magnitude and statistically significant according to Wilk’s test (Table 7). However there are problems with multivariate normality, which may limit the interpretation (e.g. BMI values are skewed to the right). Hence, we need only interpret the first pair of canonical variables. The first canonical function is:

$$\begin{aligned}
 &-1.036AHI - 0.134MinSaO_2 = -0.002AUSPC1STL + 0.115AUSPC2STL - \\
 &0.136AUSPC1HTL + 0.078AUSPC2HTL - 0.947AUSPC1HTA - \\
 &0.052AUSPC2HTA + 0.958AUSPC3HTA - 0.194MPH - 0.201BMI - 0.366Neck \\
 &Circumference.
 \end{aligned}$$

The computation of canonical cross-loadings has been suggested as an alternative to canonical loadings. This procedure involves correlating each of the original observed dependent variables directly with the independent canonical variate, and vice versa. Cross-loadings provide a more direct measure of the dependent-independent variable relationships by eliminating an intermediate step involved in conventional loadings. The canonical cross-loadings for variables on the left hand side of the first canonical function are:

Table 8. Cross Loadings for Set-1

	1	% Explained by RHS
AHI	-.576	33.18%
Min O ₂ Saturation	.119	1.42%

AHI was determined to account for 33.18% of the variance explained by the right hand side of the first canonical function while MinSaO2 only has 1.42% so can be

ignored. AHI has an inverse relationship. The Canonical cross loadings for the variables on the right hand side of the first canonical function are:

Table 9. Cross Loadings for Set-2

	1	% Explained by LHS
AUSPC1STL	-0.118	1.39%
AUSPC2STL	0.141	1.99%
AUSPC1HTL	-0.107	1.14%
AUSPC2HTL	0.221	4.88%
AUSPC1HTA	-0.217	4.71%
AUSPC2HTA	-0.109	1.19%
AUSPC3HTA	0.202	4.08%
MPH	-0.299	8.94%
BMI	-0.023	0.05%
Neck Circumference	-0.180	3.24%

The variables of *AUSPC2HTL*, *AUSPC1HTA*, *AUSPC3HTA*, *MPH* and *Neck circumference* were determined to be of most importance. Since MPH, AUSPC1HTA and Neck Circumference are negatively loaded, the relationships are inverse except for *AUSPC2HTL* and *AUSPC3HTA*, which are direct due to their positive loading.

Table 10. Canonical correlations Chinese:

	Test that remaining correlations are zero			
Canonical correlation	Wilk's	Chi-square	DF	p-value
0.726	0.416	72.619	22	0.000
0.345	0.881	10.346	10	0.500

Only the first canonical correlation is significant however there are problems with multivariate normality, which may limit the interpretation (e.g. BMI values are skewed to the right). Hence, only the first pair of canonical variables needs to be interpreted. The first canonical function is:

$$-0.849AHI + 0.208MinSaO_2 = -0.101HKPC1STL - 0.013HKPC2STL + 0.477HKPC1HTL - 0.515HKPC2HTL - 0.140HKPC3HTL - 0.013HKPC1HTA + 0.223HKPC2HTA + 0.017HKPC3HTA - 0.173MPH - 0.460BMI - 0.381Neck Circumference.$$

The canonical cross-loadings for variables on the left hand side of the first canonical function are:

Table 11. Cross Loadings for Set-1

	1	Percentage explained by RHS
AHI	-0.718	51.55%
Min O₂ Saturation	0.565	31.92%

AHI contributes almost twice that of Minimum Oxygen Saturation to the right hand side. The relationship is direct for MinSaO₂, since it is positively loaded, and inverse for AHI due to its negative loading.

The Canonical cross loadings for the variables on the right hand side of the first canonical function are:

Table 12. Cross Loadings for Set-2

	1	Percentage explained by LHS
HKPC1STL	-0.370	13.69%
HKPC2STL	-0.125	1.56%
HKPC1HTL	-0.007	0.00%
HKPC2HTL	-0.249	6.20%
HKPC3HTL	-0.206	4.24%
HKPC1HTA	-0.201	4.04%
HKPC2HTA	-0.101	1.02%
HKPC3HTA	0.118	1.39%
MPH	-0.359	12.89%
BMI	-0.586	34.34%
Neck circumference	-0.577	33.30%

BMI, *Neck circumference*, *HKPC1STL* and *MPH* are the most important variables, and all are negatively loaded. Thus, the relationships are inverse. Thus all relationships of dependent and independent variables are inverse (due to the negative loadings) except for MinSaO₂, which is direct (due to its positive loading.)

DISCUSSION

Cranial Base Dimension (SN)

Moate⁹ et al. reviewed an article by Wei, young adults of Chinese ethnic descent, showed a shorter length of the anterior cranial base both in males (65mm) and females (63mm.)⁹. Moate⁹ et al. concluded "the strongest difference between the Chinese and Caucasian groups at all ages is the length of the anterior cranial base, which has been shown to be much shorter in Chinese than in Caucasians. The mean length of the anterior cranial base of Caucasians is 83 ± 4 mm for the adult male and 77 ± 4 mm for the adult female. Our findings revealed that the Australian sample had a larger cranial base length compared to the Hong Kong Chinese sample significant at $P < 0.001$, but had a statistically insignificantly reduced cranial base flexure (Table 2.) The Chinese sample had a statistically significantly larger cranio-cervical vertebral angulation as compared to the Australian Caucasian group to $P < 0.05$. A decrease in the sagittal dimension of the cranial base in OSA subjects has been reported in several publications^{7,20-23}. A reduction in cranial base angulation (Ba-SN) has been reported in OSA subjects²³⁻²⁵.

Hyoid Bone Position (MP-H) and Head Posture (C2C4-SN)

Flexion or extension of the head has been postulated by some authors to influence the dimensions of the oropharyngeal airway^{26,27}. Solow et al.²⁸ and Tangugsorn et al.²⁰ found that the average craniocervical angulation of OSA patients in the standing position was significantly greater than in controls, mainly mediated by a forward inclination of the cervical column and confirmed by Solow et al.²⁹. A deviated head posture was reported to be observed in OSA subjects^{20,30,31}. The position of the hyoid bone has been found to be more inferior in relation to the mandibular plane for OSA subjects^{24,31,32}. The hyoid bone was inferiorly positioned in the Australian group ($22.44\text{mm} \pm 0.78$) as compared to the Hong Kong Chinese group ($18.46\text{mm} \pm 0.65$), significant to a level of $P < 0.001$ (Table 3.) Further analysis by malocclusion, revealed that Australian Class I and Class II patients had a more inferiorly positioned hyoid bone compared to the other groups which were more consistent with one another.

The position of the hyoid bone however is subject to a high degree of variation because of physiological adaptations and changes of head position. During normal growth, Winnberg et al (1988) demonstrated that a more extended head posture dropped the hyoid apparatus inferiorly and anteriorly³³. Pae (1989) investigated the relationship between airway size and body position and suggested that patients with OSA had an inferiorly positioned hyoid bone and extended head postures. He concluded that a smaller than optimal airway induced an extended head posture for better airway patency and that an extended head posture elicited an inferiorly positioned hyoid bone³⁴. The contemporary view regarding an inferiorly positioned hyoid bone and an extended head position suggests that, rather than predisposing factors, there are physiological adaptations to lift away the base of the tongue and the soft palate from the posterior pharyngeal wall in order to alleviate the obstructive condition. Furthermore, the position of the hyoid bone relative to the mandible seems to have a direct effect on ventilation. Mayer³⁵ demonstrated that hyoid bone position was the only cephalometric parameter which had a correlation with minimal oxygen saturation and percentage change in apnoea index.

Pharyngeal Dimensions: Posterior Airway Space (PAS) and Width of Pharynx at Maximum Soft Palate Width (RPAS)

Our findings revealed that the posterior airway space was greater in the Australian Caucasian sample ($10.80\text{mm} \pm 0.53$) as compared to the Hong Kong Chinese sample ($7.99\text{mm} \pm 0.38$), significant to a level of $P < 0.001$. The Australian sample had a greater upper airway dimension as compared to the Chinese sample significant to a level of $P < 0.005$ (Table 3.) PAS is used in most studies of airway dimensions in OSA, but its validity is questionable. The measurement of PAS is based on a reference line determined by facial skeletal morphology. From a physiological point of view it would seem more relevant to have this parameter defined by the anatomy of the airway itself. Although, endoscopic^{36,37} and computer tomography³⁸ studies have reported the narrowest segment to be located most often in the retropalatal region, no studies have been carried out measuring the precise anatomical location of the narrowest sagittal pharyngeal airway diameter. A recent study, by Solow et al.²⁹, using lateral cephalometry also found the most narrow airway diameter to be behind the soft palate.

A number of publications have suggested that the linear measurement of the most constricted area in the pharynx can be an indicator of OSA severity in conventional upright cephalograms. The narrowest pharyngeal diameter is located behind the soft palate^{36,37} with about 50% reduction of the pharyngeal diameter in OSA patients compared to controls. Pae et al.³⁹ found that the pharyngeal length in the supine position may be more important than a one-dimensional measurement of the most constricted area in the diagnosis and treatment of OSA.

The dimensions of the pharynx are reduced²⁵, whether the subjects are investigated in the upright or supine position⁴⁰ and independent of the assessment technique⁴¹. Haponick and coworkers (1983) used computerised tomography to identify a reduced posterior airway space in OSA subjects. However, Pae et al.³⁹ found that the pharynx becomes considerably longer in the apneic group after a body position change from upright to supine.

Pae et al.³⁹ concluded that the longer the pharynx, the greater the severity of the OSA symptoms. They postulated that as long as there is no significant difference in the cross-sectional area of the pharynx, air in a longer pharynx should travel faster than in air in a shorter one because the same volume of tidal air must pass through each conduit during the same respiration duration. Hence, the velocity of the air in a longer pharynx is increased as compared to a shorter pharynx. The faster air stream in a longer pharynx generates more negative intraluminal pressure than that in a shorter one. Thus the longer pharynx becomes more collapsible.

Anatomical Structures Affecting Upper Airway Size

Many cephalometric studies have been done to explore the craniofacial architecture of patients with obstructive sleep apnoea syndrome⁴². Miles conducted a meta-analysis which concludes that a direct causal relationship between craniofacial structure and OSA has not been established⁴³. However, studies using fluoroscopy⁴⁴, acoustic reflection⁴⁵, fiberoptic endoscopy³⁶, cephalometric radiographs⁴⁶, computerised tomography⁴¹, cinematographic computerised tomography³⁸ and magnetic resonance imaging⁴⁷ have demonstrated that OSA patients have narrower airways than control subjects.

Lowe et al found that sleep apnoea subjects had a posteriorly positioned maxilla and mandible, a steep occlusal plane, overerupted maxillary and mandibular teeth, proclined incisors, a steep mandibular plane, a large gonial angle, high upper and lower facial heights, and an anterior open bite in association with a long tongue and a posteriorly placed pharyngeal wall⁴⁸. They concluded that subjects with sleep apnoea demonstrated several alterations in craniofacial form that may reduce the upper airway dimensions and subsequently impair upper airway stability⁴⁸.

Maxilla and Mandible

Bimaxillary retrusion⁴⁸ or retrognathia of the mandible has been reported in OSA subjects²⁴. Other studies however, have found no evidence of mandibular retrognathia in OSA subjects^{46,49}. Tsuchiya et al.³² found mandibular retrognathia in patients with a high Apnoeic index (AI) and low Body Mass Index (BMI), suggesting that skeletal abnormality may be an important aetiological factor in OSA in non-obese patients with a high AI. Tangugsorn et al observed a reduced maxillary length with normal height in 100 male patients with OSA²⁰.

Although a reduction in the length of the body of the mandible in OSA patients was reported^{23,25,50}, other investigators Trenouth and Timms (1999) did not find any such reduction²⁰. Therefore, in the anteroposterior dimension the cranial base, maxilla and mandible have been implicated as being shorter or repositioned²³. The cephalometric analysis performed in this study revealed that the Australian OSA sample had a retro-positioned maxilla and mandible compared to their Chinese counterparts, with a correspondingly larger ANB value for the Chinese OSA sample. The SNA position for the Australian group was 82.31 ± 0.38 , was reduced compared to the Chinese sample with a value of 84.66 ± 0.48 significant to a level of $P < 0.001$. The SNB value for the two groups were comparable with the Australian group possessing a value of 79.3 ± 0.39 , and the Chinese group having a value of 79.78 ± 0.49 , but this was deemed not to be of statistical significance. The difference in ANB value for the two ethnic groups was statistically different to a level of $P < 0.001$, with the Australian group having a reduced ANB value 3.01 ± 0.38 as compared to the Chinese group of 4.89 ± 0.34 (Table 2.)

Our findings revealed that the Chinese group had a consistently reduced maxillo-mandibular dimension as compared to the Australian Caucasian OSA sample, as measured by mandibular, maxillary and midface lengths. Additionally, the mandibular unit length, maxillary unit length and palatal length for the Chinese group was reduced as compared to the Australian Caucasian group significant to a level of $P < 0.001$ (Table 2.)

The vertical measurement of craniofacial dimension in this study demonstrated that the Australian Caucasian and Hong Kong Chinese group were comparable. Statistically significant differences between the two groups were detected for lower anterior facial height, with the Australian Caucasian group having a LAFH of $75.06\text{mm} \pm 1.02$, which was greater than the Hong Kong Chinese group LAFH of $70.40\text{mm} \pm 0.59$, significant at $P < 0.001$ (Table 2.) The upper face height (UFH) dimensions (figure 8.) was statistically significant between the two groups, with the Australian Caucasian group having a UFH of $58.22\text{mm} \pm 0.68$, and the Hong Kong Chinese group a UFH of 54.05 ± 0.49 to a level of $P < 0.001$. Correspondingly, the total anterior facial height was statistically significant to a level of $P < 0.001$. A number of OSA studies have reported an increase in the lower anterior facial height with a concomitant increase in the maxillo-mandibular plane angle^{20,22,32,48,50}

Overjet and Overbite

The Australian OSA subjects in this study displayed a greater overjet and overbite as compared to the Hong Kong Chinese OSA group. The overbite was a statistically significant variable between the two ethnic groups, with the Australian group having an overbite of $2.59\text{mm} \pm 0.42$, and the Chinese group of $1.14\text{mm} \pm 0.31$, to a level of $P < 0.01$ (Table 2.)

Tongue

A larger tongue length and larger cross-sectional tongue area in OSA patient has been reported^{20,25,31,48}. Our study identified that the Australian OSA sample had larger tongue dimensions as compared to the Hong Kong Chinese OSA group, with both a larger tongue length and tongue height recorded, both significant to a level of $P < 0.001$ (Table 3.) Prachartam et al. found tongue size and area is normal by the

functional space of the tongue is reduced, forcing the tongue backwards into the pharynx and diminishing airway space at this level⁵¹. Tangugsorn et al. found that the tongue position was more upright and caudally extended²⁰. Ryan et al (1991) found that obese OSA patients have larger tongues and smaller airways⁵². Do et al (2000) found that tongue volume only positively correlated with BMI and neck circumference but there was no correlation with age or AHI⁵³. The residual oropharyngeal area was reduced by 9 percent due to a larger tongue and soft palate according to Tangugsorn et al.²⁰

Soft Palate

OSA patients have longer and thicker soft palates, with an area approximately 20% greater than normal subjects which results in further reduction of the airway^{23-25,31}. Tangugsorn et al. found an increased length, thickness and sagittal area of the soft palate and 15% more pharyngeal area occupation²⁰. The soft palate dimension was greater in the Australian sample, with a larger soft palate length and maximum soft palate thickness significant to a level of $P < 0.001$ (Table 3.) Pae et al showed that the thickness of the soft palate increases and the oropharyngeal cross-sectional area decreases when a patient changes from an upright to supine position⁵⁴.

Key Statistical Findings

From the preceding discussion, it is clear that there were some statistically significant differences were found between the two groups as highlighted by the independent T-tests. However, these differences were unable to distinguish the key craniofacial and anthropometric measurements that were pivotal in discriminating the severity of OSA between our two experimental populations.

A multiple regression analysis was designed to ascertain whether ethnicity (and gender) was a significant variable in OSA as measured by the AHI after allowing for various body measurements. A regression model was constructed, initially allowing for the craniofacial variables, then allowing for the relevant body anthropometric measurements. From this model, it found that ethnicity was not a significant variable, either by itself, or after allowing for craniofacial variables, or after for craniofacial and body measurement variables. Hence, the multiple regression analysis revealed that ethnicity was not significant in discriminating for OSA between two populations.

Twenty-eight cephalometric variables of cervico-craniofacial skeletal morphology were reduced to seven and eight PCs. Six soft tissue cephalometric variables were reduced to two PCs describing 52.6% and 63% of the total variance in the Caucasian and Chinese patients, respectively. Ten hard tissue linear cephalometric variables were reduced to two and three PCs for the Caucasian and Chinese patients, respectively accounting for 70.9% and 63.4% of the cumulative variance. The hard tissue angular linear combination of cephalometric variables was reduced to three PCs and accounted for the greatest cumulative variance, with 71.7% and 75% for the Caucasian and Chinese groups respectively.

Canonical correlation analysis finds the linear combination of predictor variables that best explains (or correlates with) a linear combination of response variables. Then it looks for the second best combinations, but these have to be independent of the previous one. The canonical correlation analysis revealed the principal component variables of *AUSPC2HTL*, *AUSPC1HTA*, *AUSPC3HTA*, *MPH* and *Neck circumference* were determined to be of most importance in the Caucasian OSA group. Hence, one hard tissue linear and two hard tissue angular group of variables, and MPH and Neck circumference were of most significance in determining the severity of OSA in the Australian Caucasian group. Interesting, canonical correlation analysis revealed that different principal component variables of *BMI*, *Neck circumference*, *HKPC1STL* and *MPH* to be of greatest importance in the Chinese OSA group.

Two canonical variables and their correspondents with different loadings were established differently for the individual OSA groups. Neck circumference and MP-H was common to both OSA populations in their respective canonical functions. The Caucasian group correlated highly with different canonical variables, namely hard tissue linear and hard tissue angular variables as compared to the Chinese group, who correlated with BMI and a soft tissue variable component.

Watanabe *et al.*⁵⁵ postulated that since the pharyngeal airway is surrounded by soft tissue, enclosed by bony structures, a mechanical model to illustrate this relationship would be that of a collapsible tube surrounded by soft material within a rigid box. The

luminal size of the collapsible tube is determined by mechanical properties of the tube and transmural pressure. Obesity can be a condition in which an excess of soft material is present in the rigid box. Conversely, a small bony enclosure at the level of the pharynx may be analogous to the condition in which the size of the rigid box is small. Both obesity and craniofacial abnormalities may synergistically increase the tissue pressure surrounding the pharynx, and therefore increase the closing pressure of the passive pharynx in SDB patients.⁵⁵ In light of Watanabe's mechanical model, the findings from our study can be interpreted that the relative contributions of craniofacial abnormalities (size of the rigid box) and obesity (soft material) to severity of OSA are not equal in the two ethnic populations studied.

Liu et al.²² found no significant differences between the Caucasians and Chinese, matched for age and BMI, with reference to the position of the hyoid bone or maxilla but noted a smaller midface with a smaller and more posteriorly positioned mandible in the Chinese group.

Ang and co-workers⁵⁶ measured craniofacial and head posture variables in Chinese subjects at the National Dental Centre Singapore. They found significant differences between hyoid position in the two groups. The hyoid bone was more caudally or inferiorly positioned in moderate-to-severe sample, complementing other studies performed^{24,31,32,46}. Secondly, the study examined the head posture variables in the group of OSA and compared them to published controls for Chinese and white subjects. They found a marked increase in the craniocervical angulation for the total OSA study sample for craniovertical, craniocervical and craniohorizontal variables. The authors concluded that a more caudal hyoid bone position and greater craniocervical angulation was found in subjects with OSA.

Compared with advanced modern upper airway imaging, cephalometric analysis, together with multivariate statistical analysis, seems to provide adequate information for diagnosis and treatment planning for OSA patients as well. OSA subgroup characteristics eg ethnic craniofacial differences and anthropometric differences should be taken into consideration for selection of treatment regimens chosen because of the differences in the interdependence of craniofacial morphology and the anthropometric characteristics.

CONCLUSION

1. Several craniofacial and anthropomorphic variables exist differentiating between two ethnic groups with Obstructive Sleep Apnoea.
2. Canonical correlation successfully clarified the complexity of simultaneous relationship of the relevant variables. Canonical correlation established that craniofacial and anthropometric variables accounted for 28% of variability of AHI in Australian Caucasians, and 55.5% of AHI and 31.7% of Minimum Oxygen Saturation amongst Hong Kong Chinese.
3. For the OSA Australian Caucasian patients in our sample, the principal function involving the variables of AUSPC2HTL, AUSPC1HTA, AUSPC3HTA, MPH and Neck-circumference correlated highly with AHI.
4. Conversely, in the OSA Hong Kong Chinese patient sample, the principal function involving the variables of BMI, Neck Circumference, HKPC1STL and MPH, correlated highly with AHI and Minimum Oxygen Saturation.

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5. FUTURE RESEARCH DIRECTIONS

A new class of volumetric imaging devices specifically developed for dentistry has recently been introduced termed cone beam computerised tomography (CBCT). Essentially, these devices capitalize on recent technologies such as cone-beam principles and improved sensors combined with a small chamber volume and field of view to produce three-dimensional images of the craniofacial skeleton at much reduced radiation exposure relative to their whole-body CT counterparts used in medical imaging. The commercially available units now include The NewTomTM system (Quantitative Radiology, Srl, Verona, Italy) (Mozzo, Procacci et al. 1998)(NewTom 9000), the Morita system (J. Morita Corporation, Osaka and Tokyo, Japan), and the MercuRayTM system (Hitachi Medical Corporation, Tokyo, Japan (Arai, Tammisalo et al. 1998; Arai, Tammisalo et al. 1999), as well as Xoran Technologies, Ann Arbor, MI, USA (Sukovic, Brooks et al. 2001)(DentoCATTM).

During tomography, the NewTomTM machine creates a data file of coordinates located in 3 dimensions on the x, y and z axes of the skull being radiographed. The coordinates are recorded and stored according to their darkness on a continuous white to black scale, reflecting the radiopacity of the tissue point being imaged (Preston, Lampasso et al. 2004). Recent advances in volume rendering technology and graphic cards have provided a myriad of software to visualize CT data in three dimensions, including Amira 2.3, Volview (Kitware, Inc., Clifton Park, NY) and VolumePro (TeraRecon Headquarters, San Mateo, CA). The high flexibility of these systems allows the users to display soft tissue or bone tissue in real-time for visualization, diagnosis or treatment planning in full three dimensions (Enciso, Memon et al. 2003). The use of fine resolution is useful to visualize skeletal shapes and to obtain actual measurements of the individual teeth. The data files produced by the NewtomTM are manipulated with separate computer software capable of producing an almost endless variety of radiographs that give a 3-dimensional insight into craniofacial structures.

Stratemann (2005) using CBCT to study airway constriction concluded that specific sites of upper airway constriction are associated with specific patterns of skeletal

adaptations of the craniofacial complex in non-extreme facial types. The zygomatic processes of the maxilla and piriform rim follow the constriction patterns of the nasal airway; the chin follows the oropharynx and hypopharynx, and the mandibular body follows the hypopharynx (Stratemann 2005).

Prospective research investigations assessing ethnic differences in OSA patients, should utilise airway CBCT imaging to accurately identify relationships of craniofacial dimensions and soft tissue relationships with the underlying pharyngeal anatomy. The cosmopolitan constitution of Sydney's population readily enables such a prospective study of craniofacial variation in various ethnic OSA populations such as Middle-Eastern, Lebanese, Turkish, Vietnamese and Indians.

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6. Appendix. Statistical Analyses

FIGURE 10. DISTRIBUTION OF MALOCCLUSION BETWEEN THE TWO ETHNIC GROUPS.

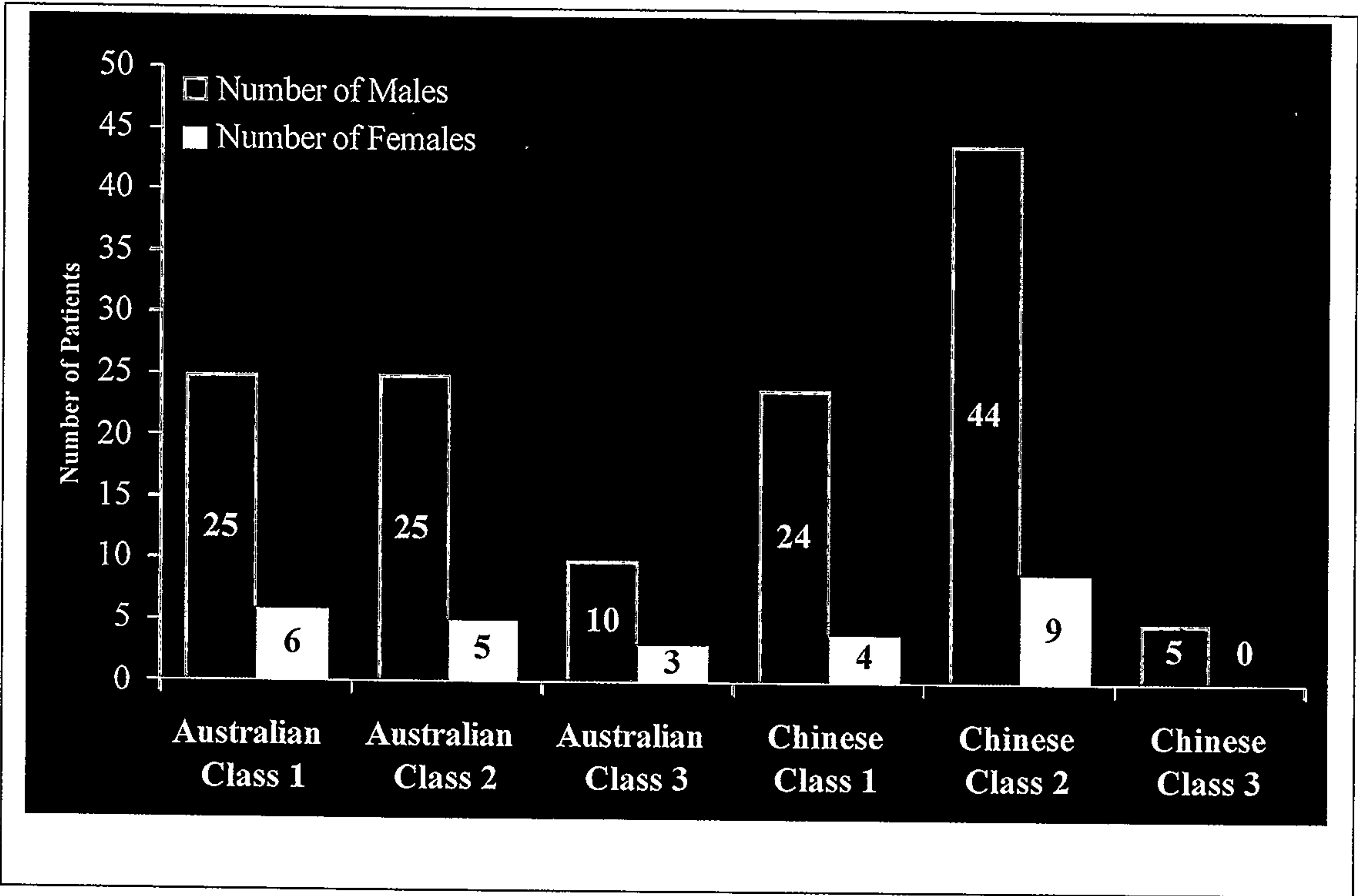


FIGURE 11. RELATIONSHIP OF BMI AND MALOCCLUSIONS BETWEEN THE TWO ETHNICAL GROUPS.

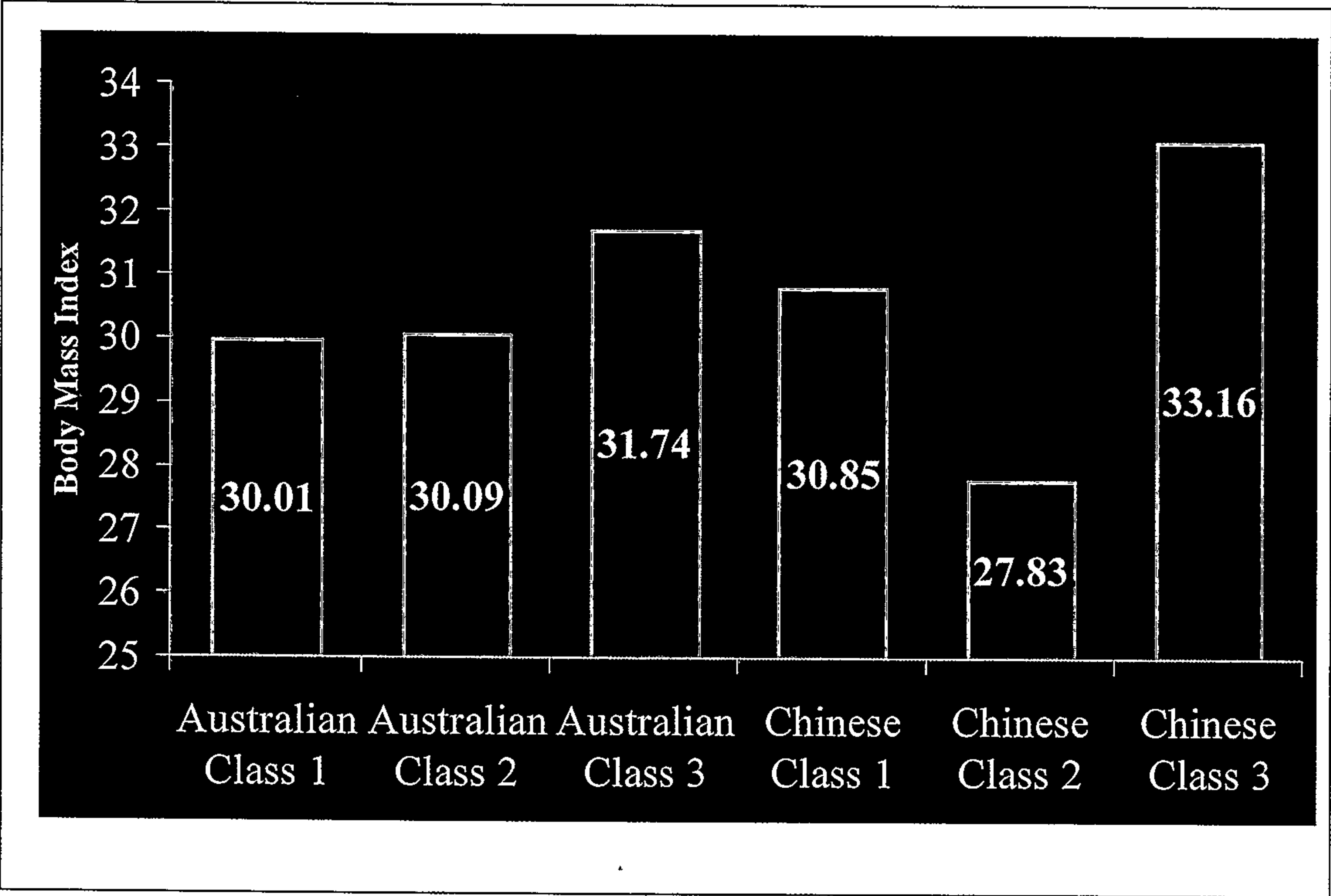


FIGURE 12.RELATIONSHIP OF AHI AND WITH MALOCCLUSIONS BETWEEN TWO ETHNICAL GROUPS.

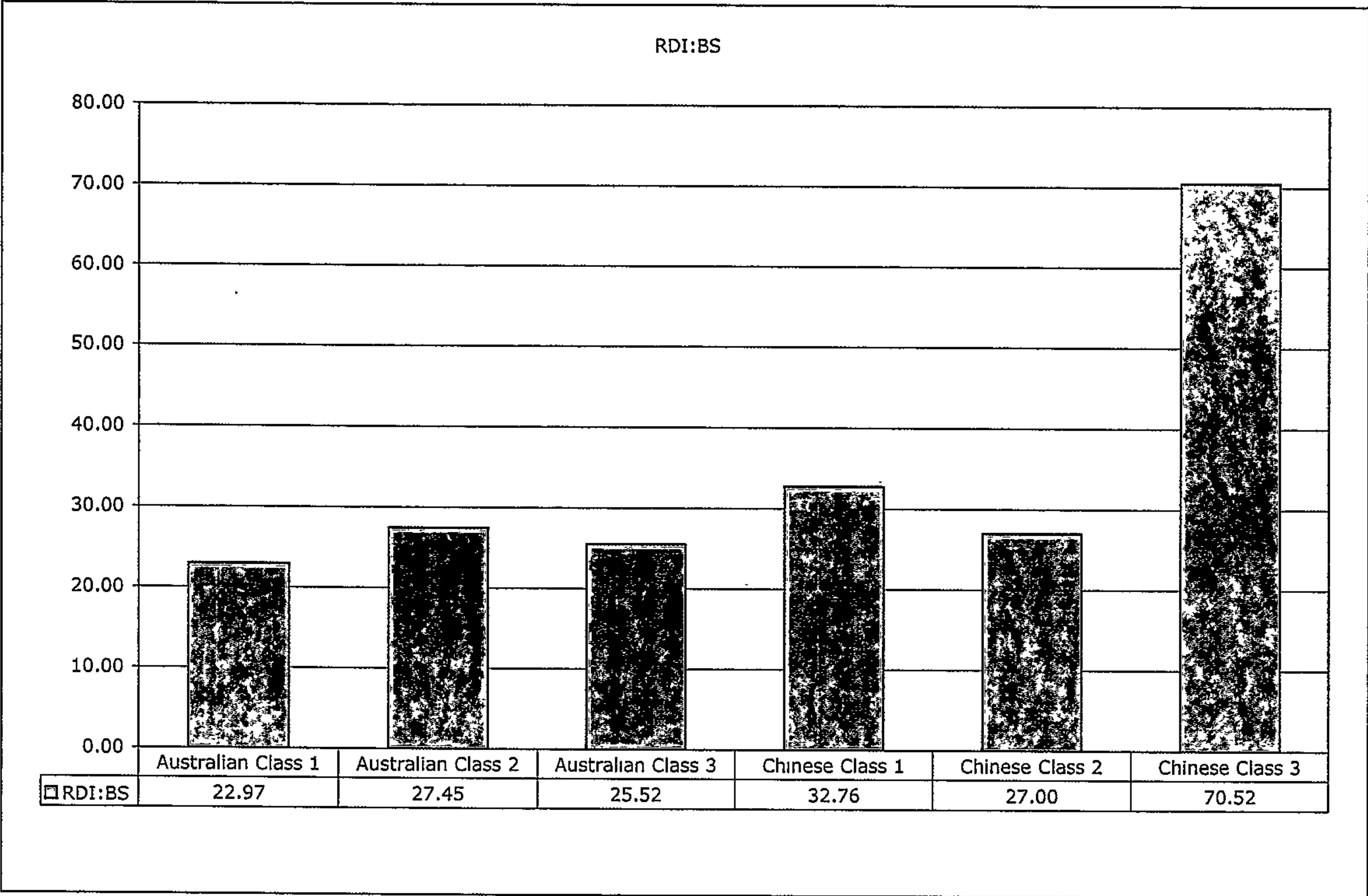


FIGURE 13. RELATIONSHIP OF NECK-CIRCUMFERENCE AND MALOCCLUSIONS BETWEEN TWO ETHNICAL GROUPS.

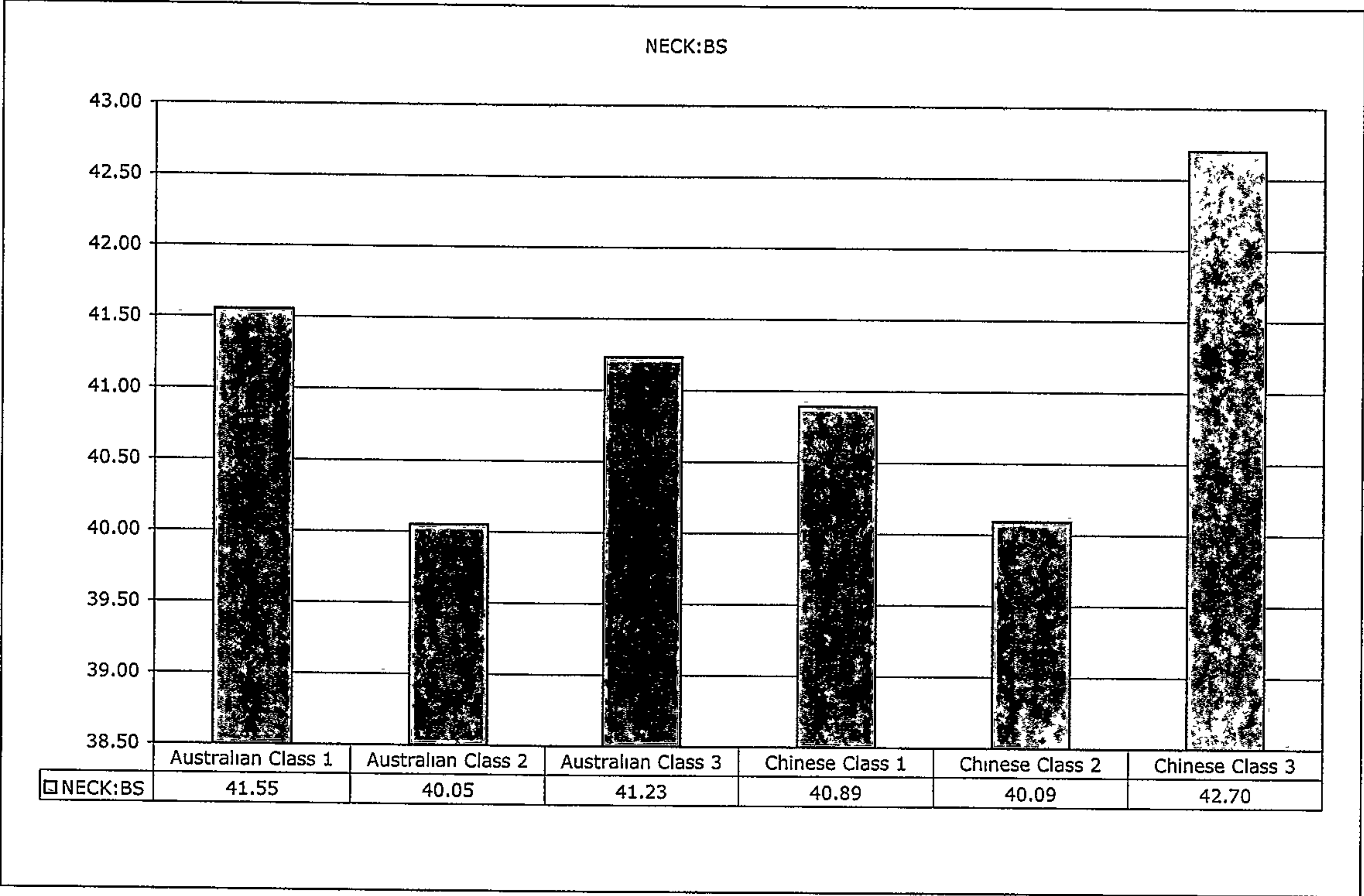


FIGURE 14. FACIAL DIMENSIONS BETWEEN THE TWO ETHNICAL GROUPS.

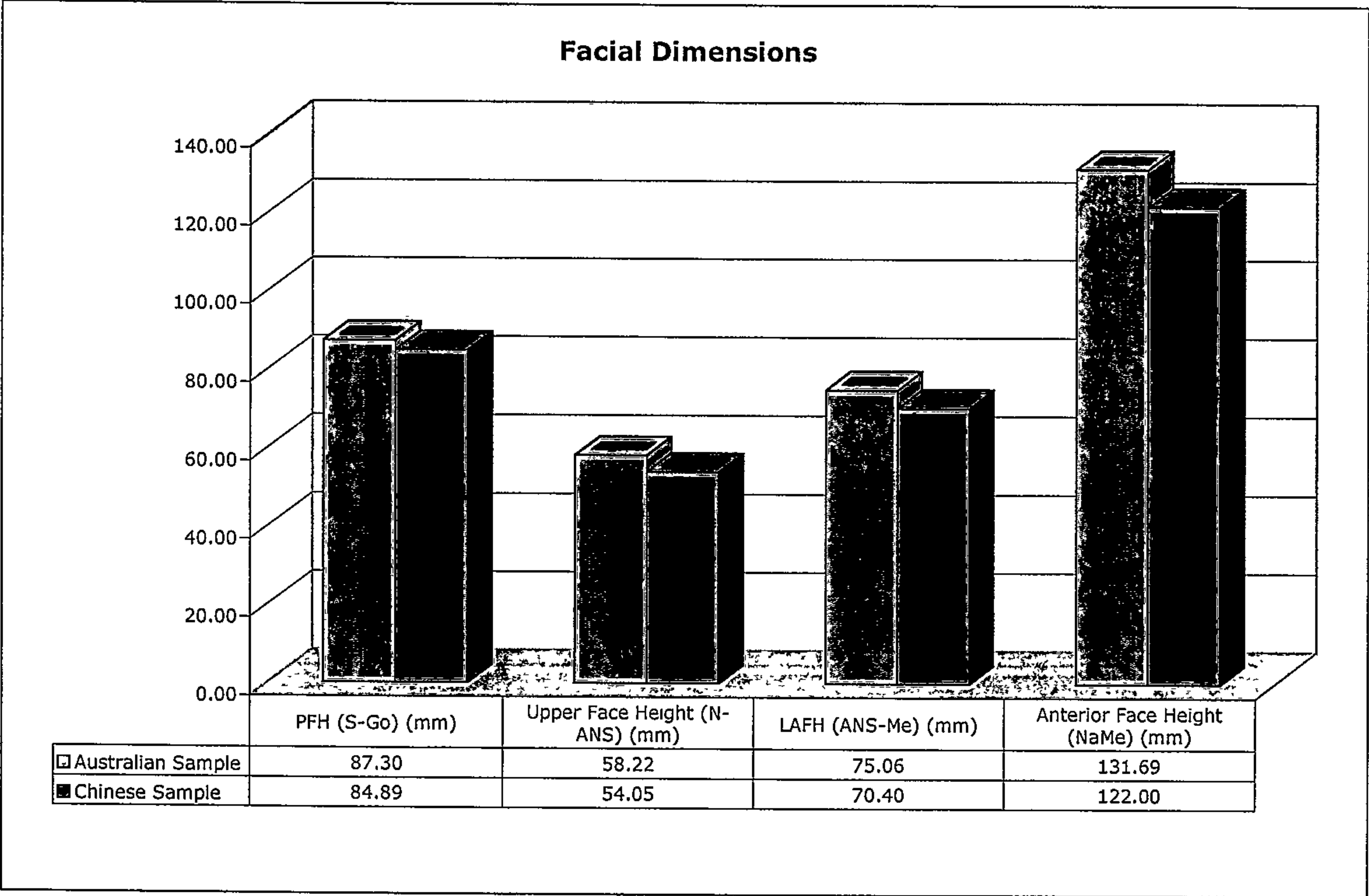


FIGURE 15. LOWER ANTERIOR FACIAL HEIGHT DIMENSIONS BETWEEN THE TWO ETHNICAL GROUPS.

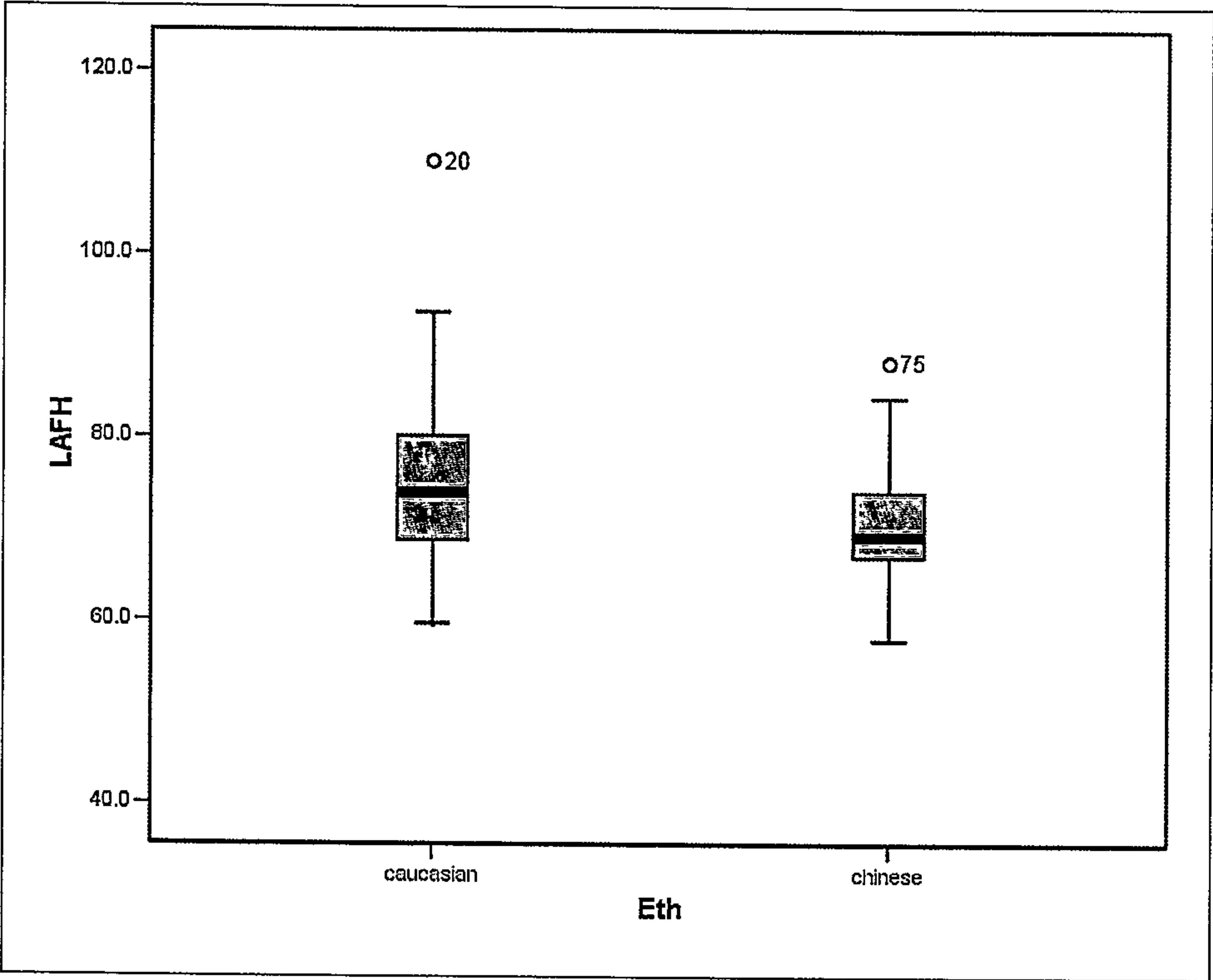


FIGURE 16. UPPER FACIAL HEIGHT DIMENSIONS BETWEEN THE TWO ETHNICAL GROUPS.

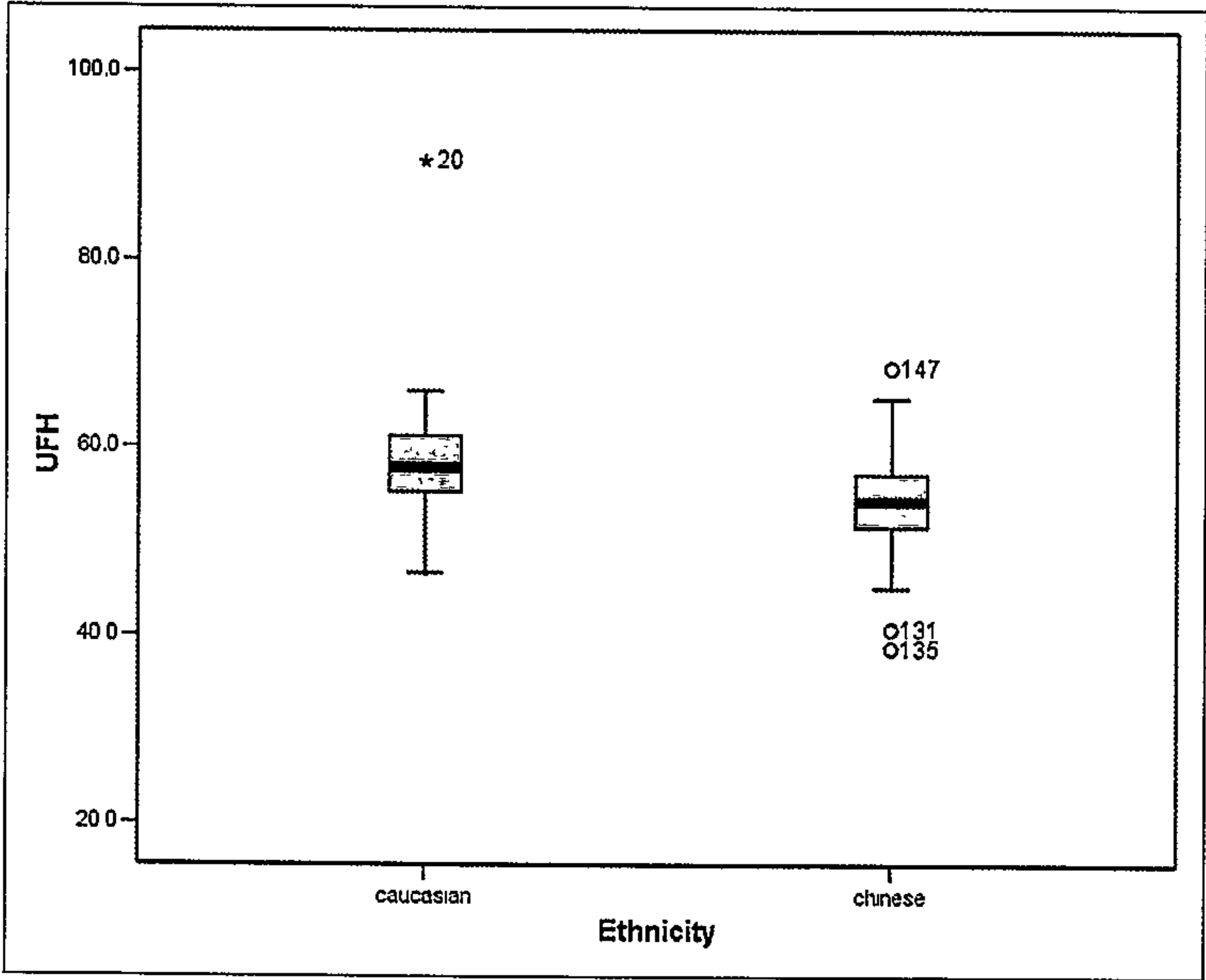


FIGURE 17. CRANIAL BASE DIMENSIONS BETWEEN THE TWO ETHNICAL GROUPS.

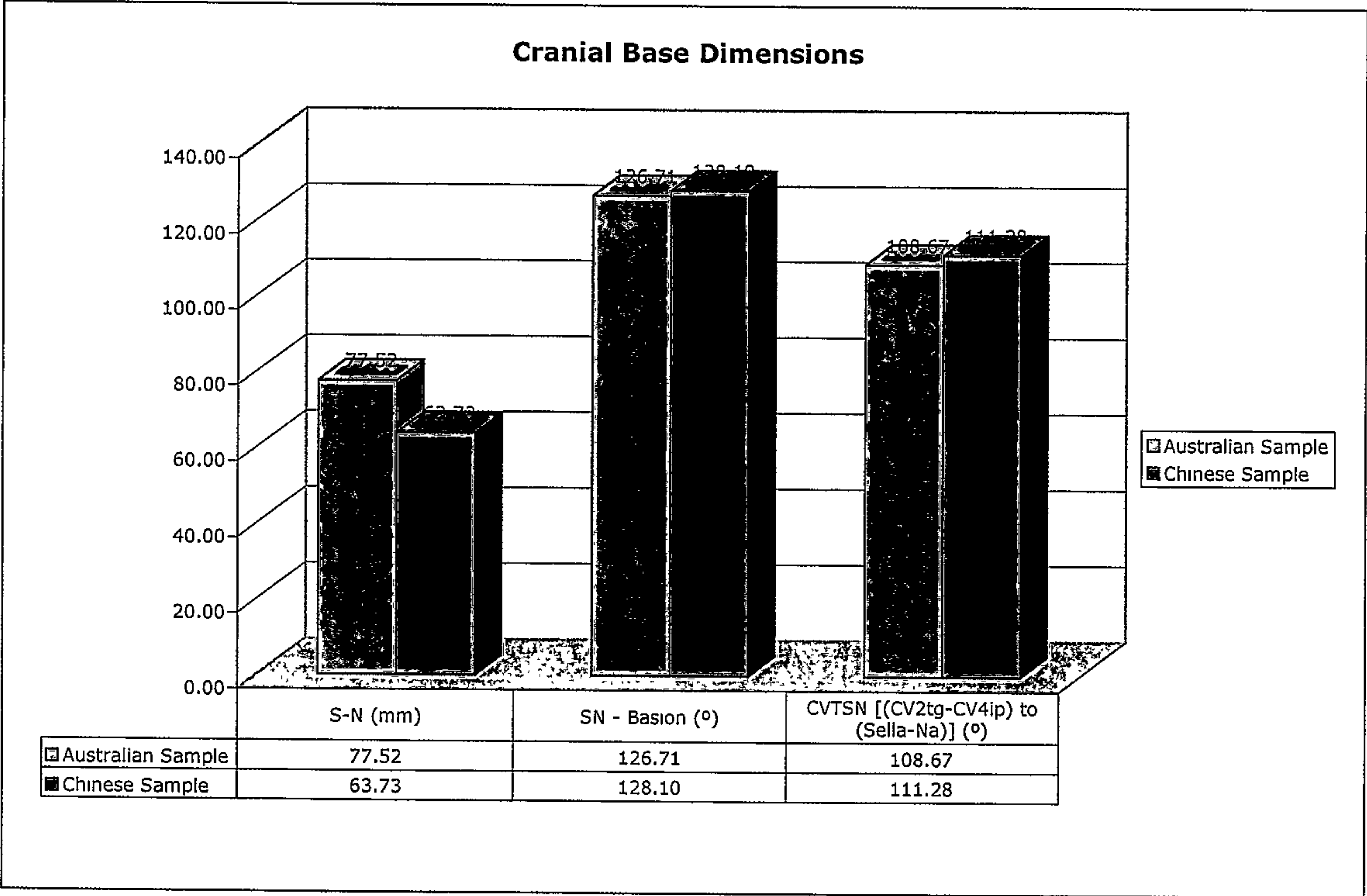


FIGURE 18. MAXILLOMANDIBULAR POSITION BY ETHNICITY

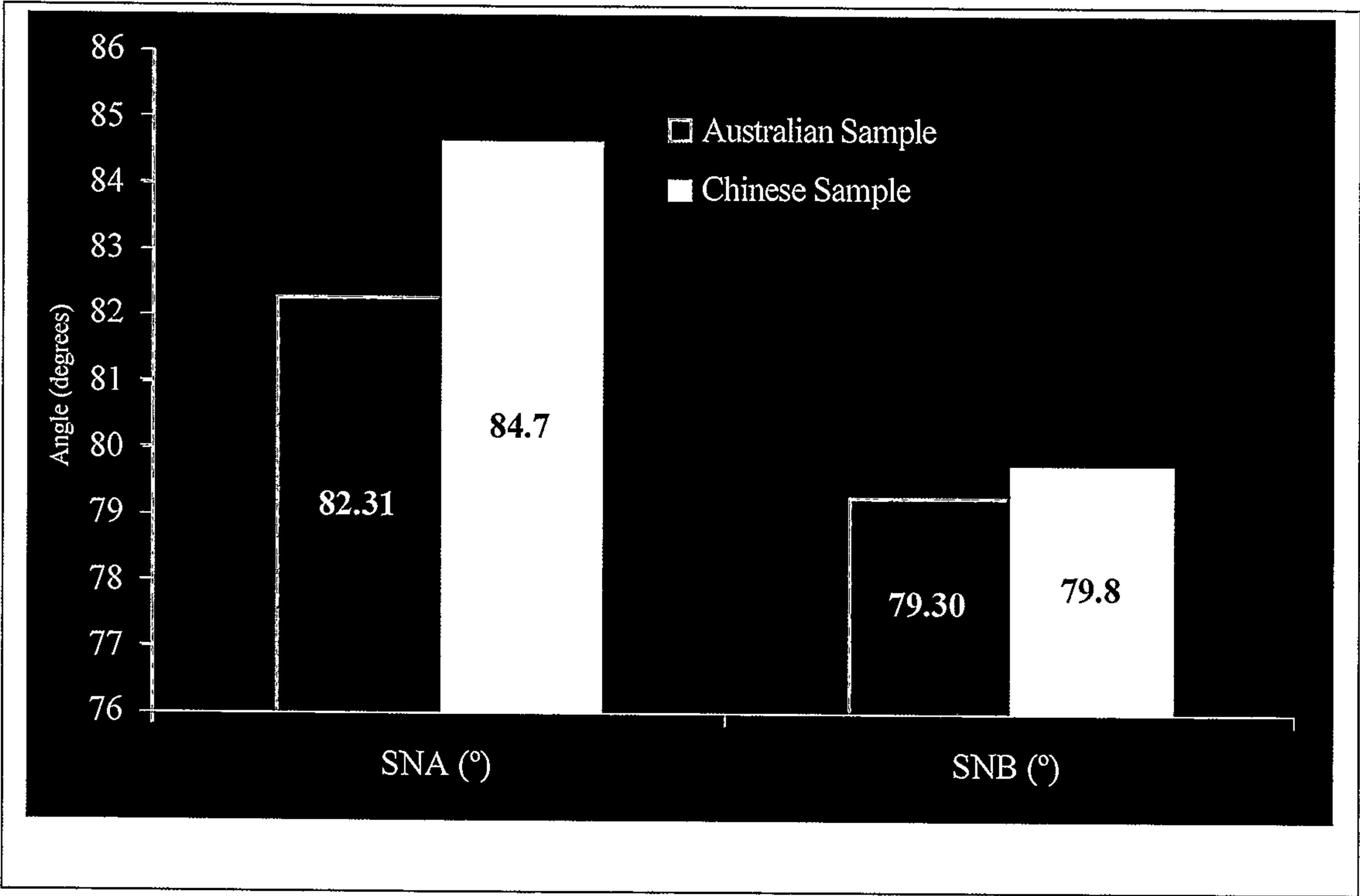


FIGURE 19. MAXILLOMANDIBULAR POSITION BY ETHNICITY

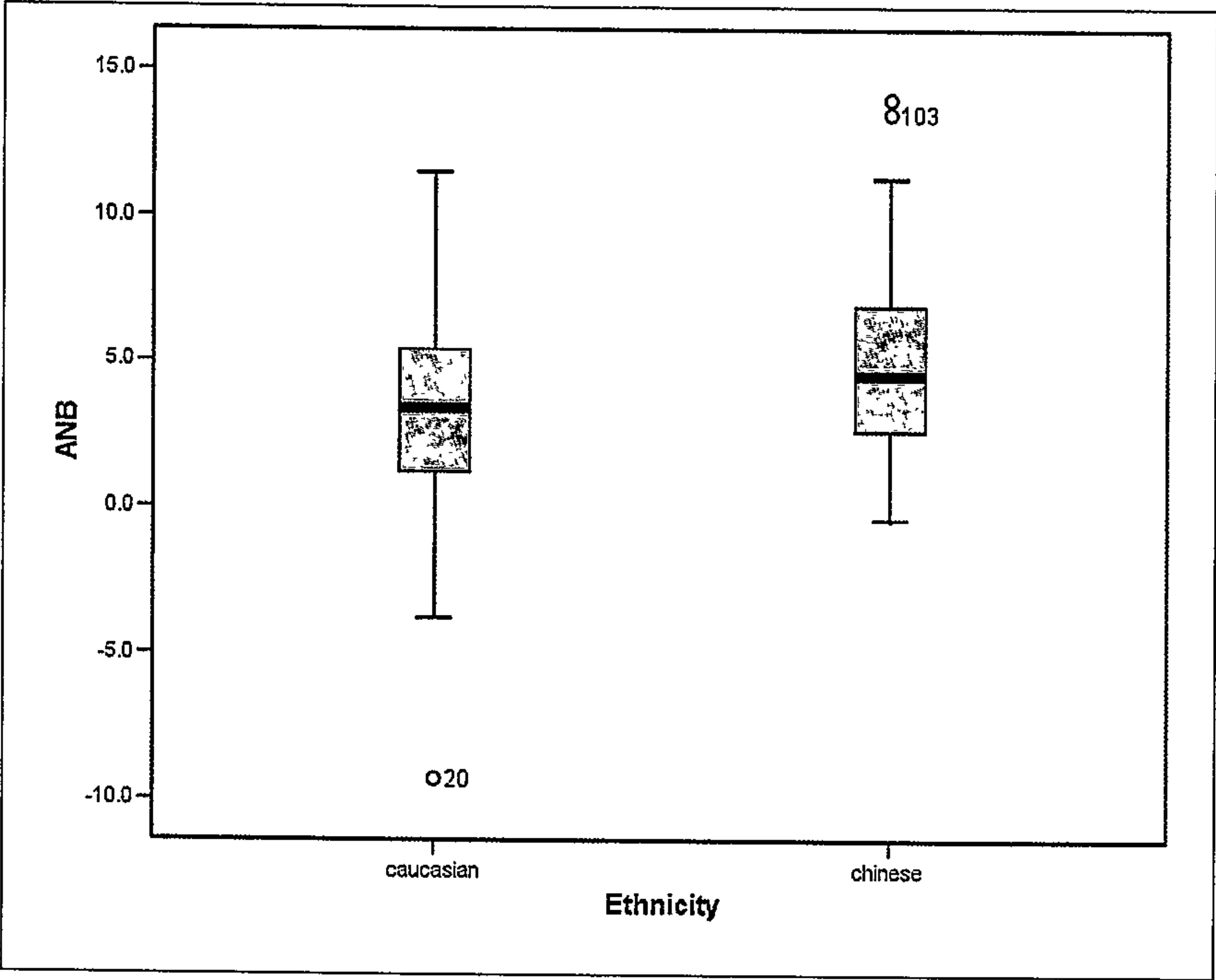


FIGURE 20. MAXILLOMANDIBULAR DIMENSIONS BETWEEN TWO ETHNICAL GROUPS.

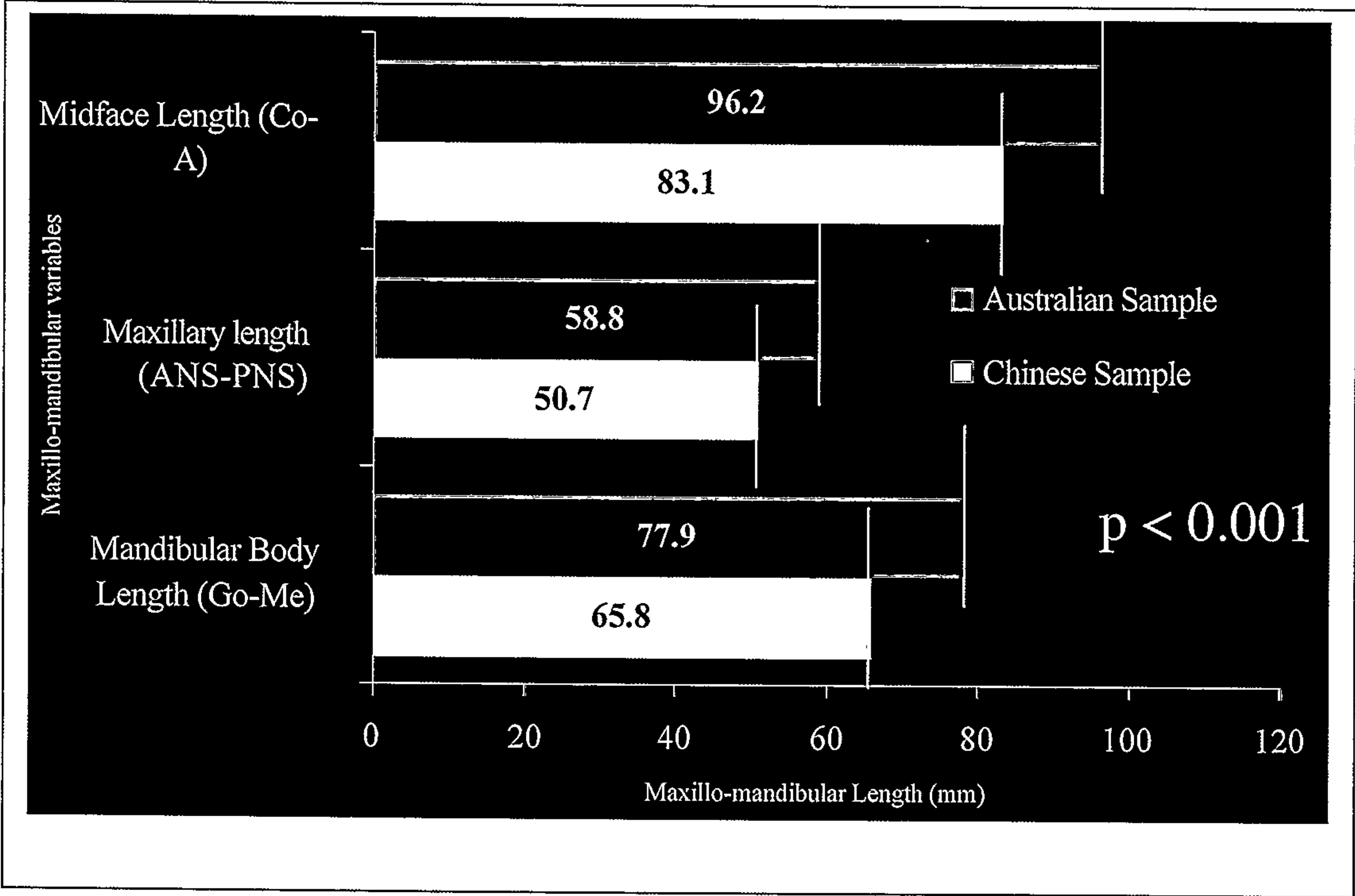


FIGURE 21. MANDIBULAR UNIT-LENGTH DIMENSIONS BETWEEN TWO ETHNICAL GROUPS.

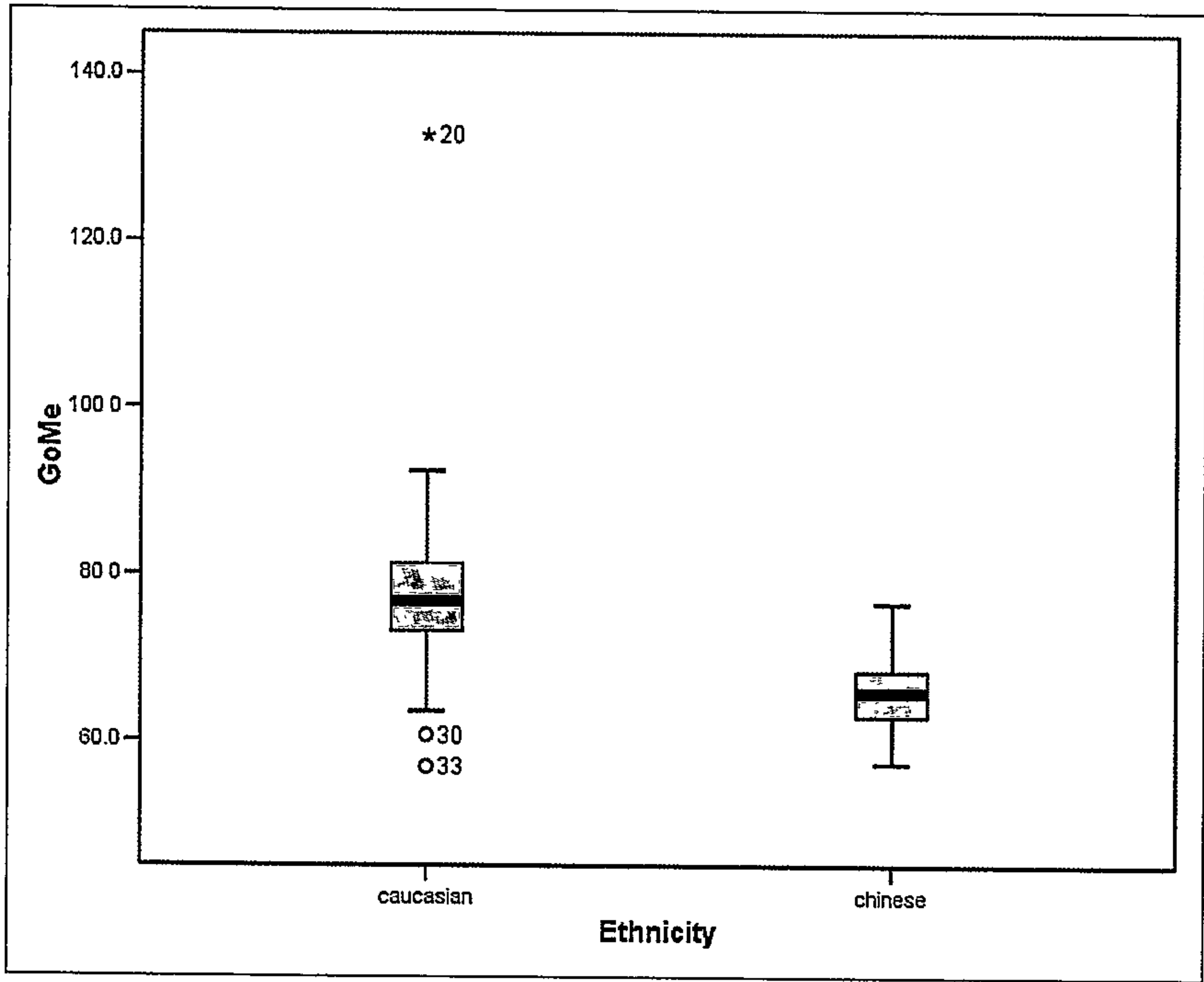


FIGURE 22. MAXILLARY UNIT-LENGTH DIMENSIONS BETWEEN TWO ETHNICAL GROUPS.

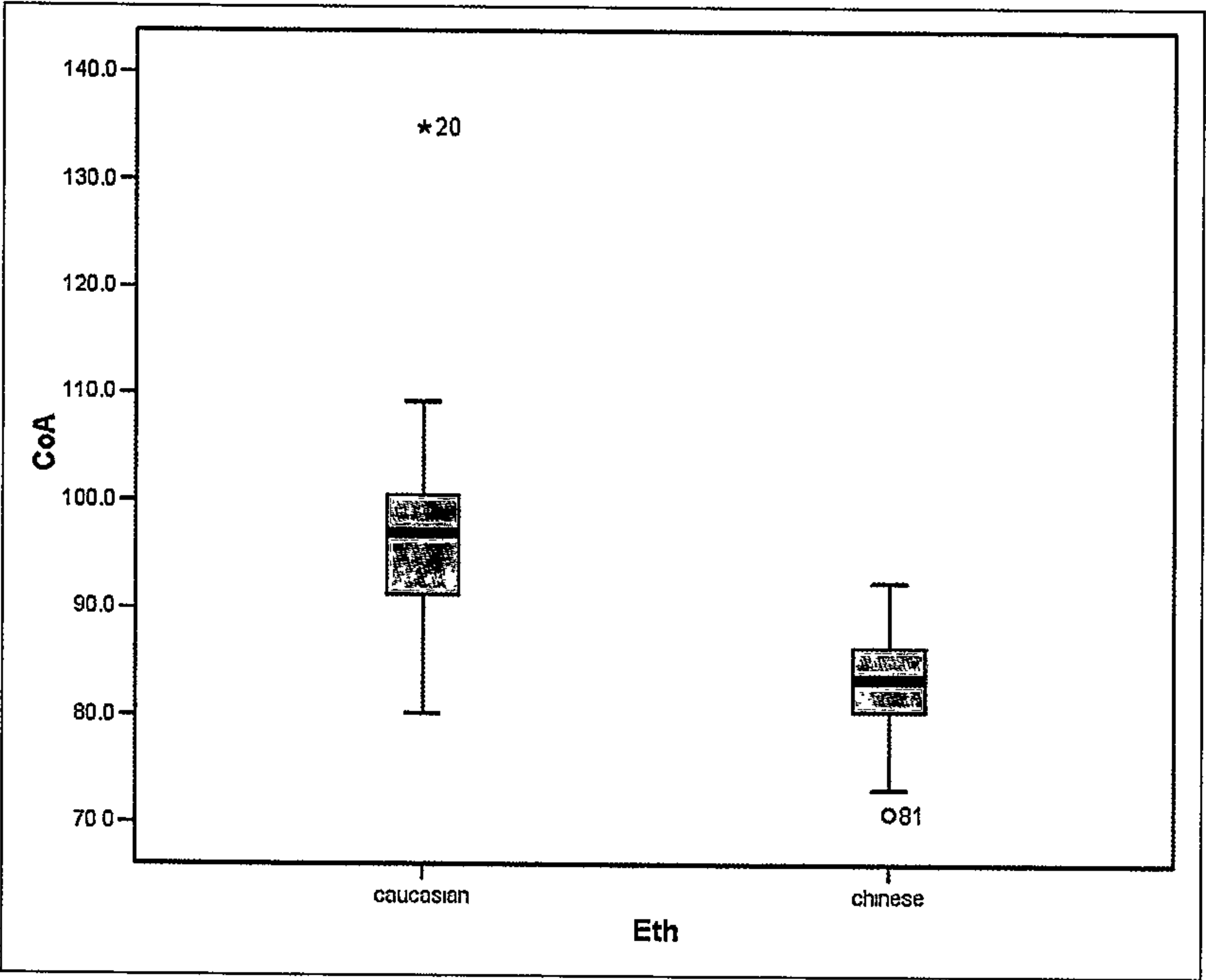


FIGURE 23. MANDIBULAR PLANE TO HYOID DIMENSION BY MALOCCLUSION BETWEEN TWO ETHNIC GROUPS.

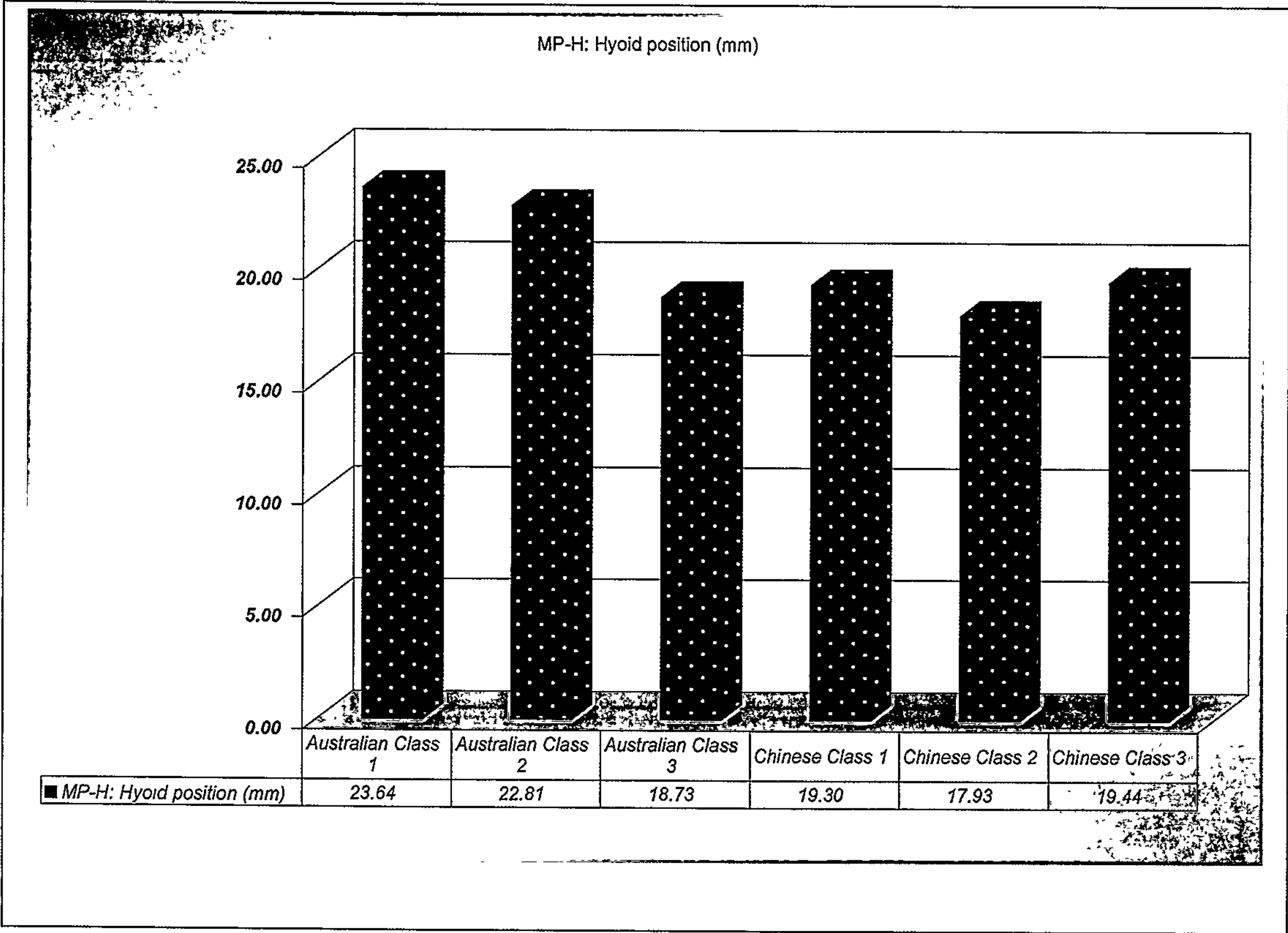


FIGURE 24. MANDIBULAR PLANE TO HYOID DIMENSION BETWEEN TWO ETHNIC GROUPS.

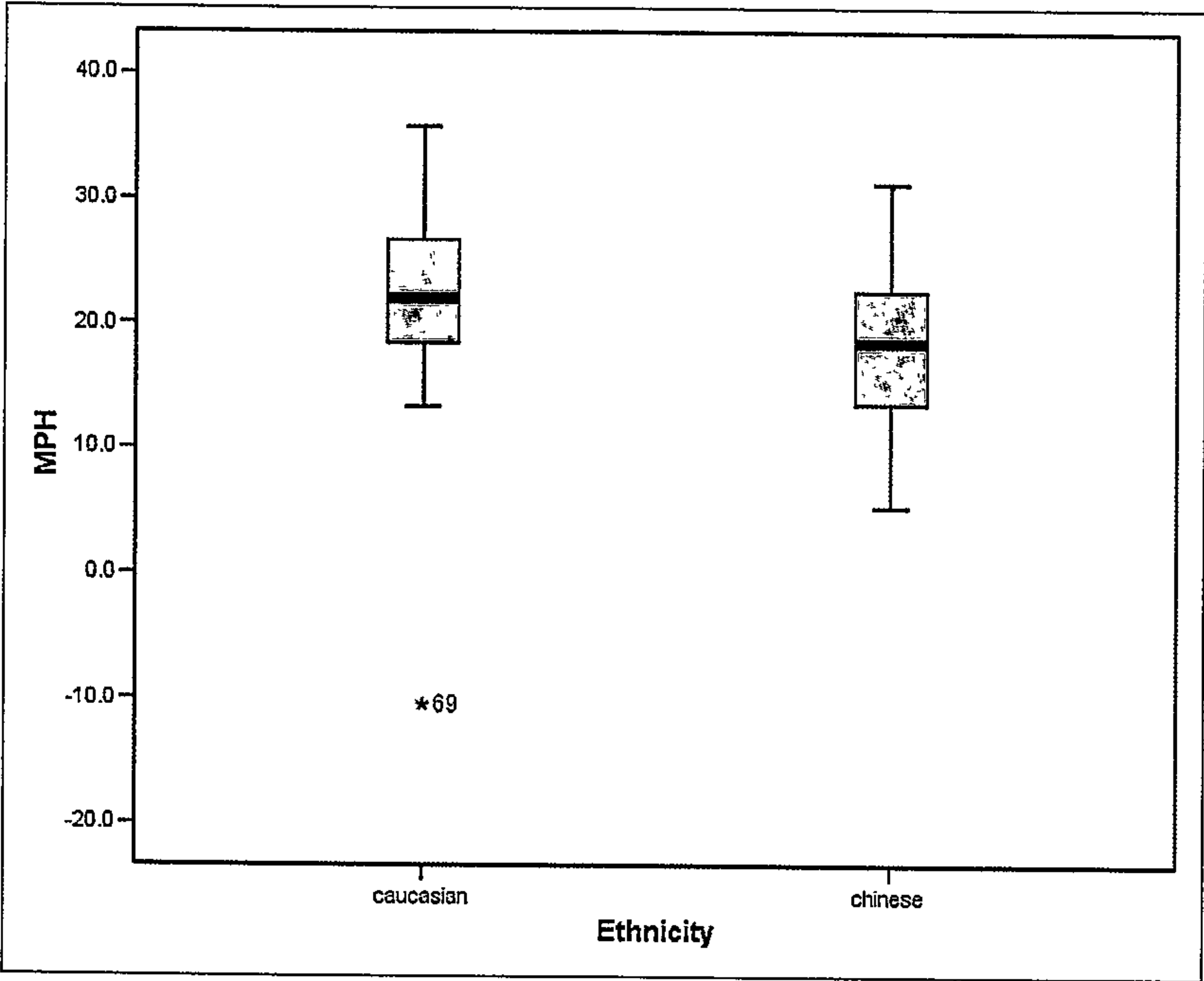


FIGURE 25. CEPHALOMETRIC AIRWAY MEASUREMENTS BY ETHNICITY.

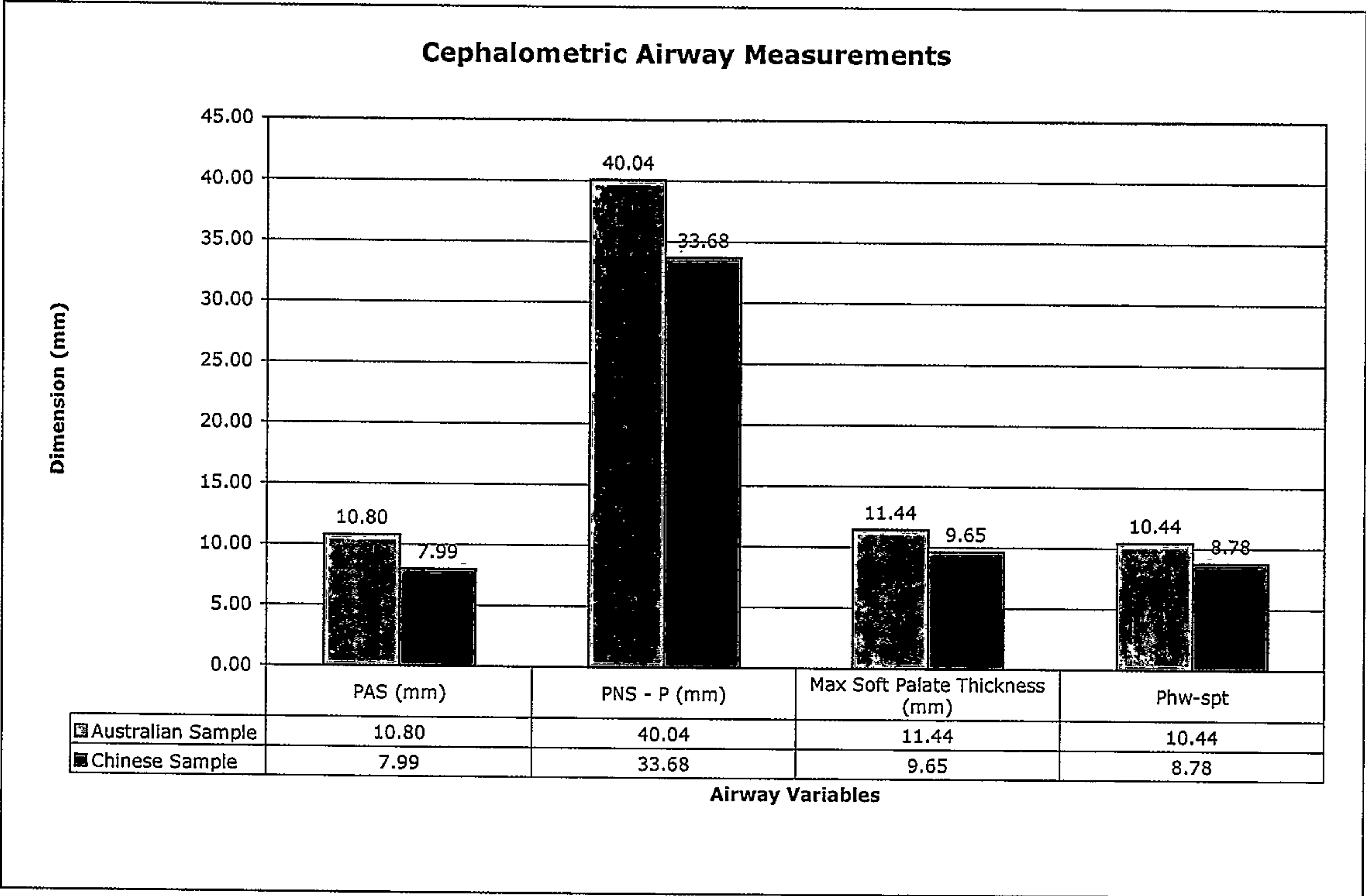


FIGURE 26. POSTERIOR AIRWAY MEASUREMENTS BY ETHNICITY.

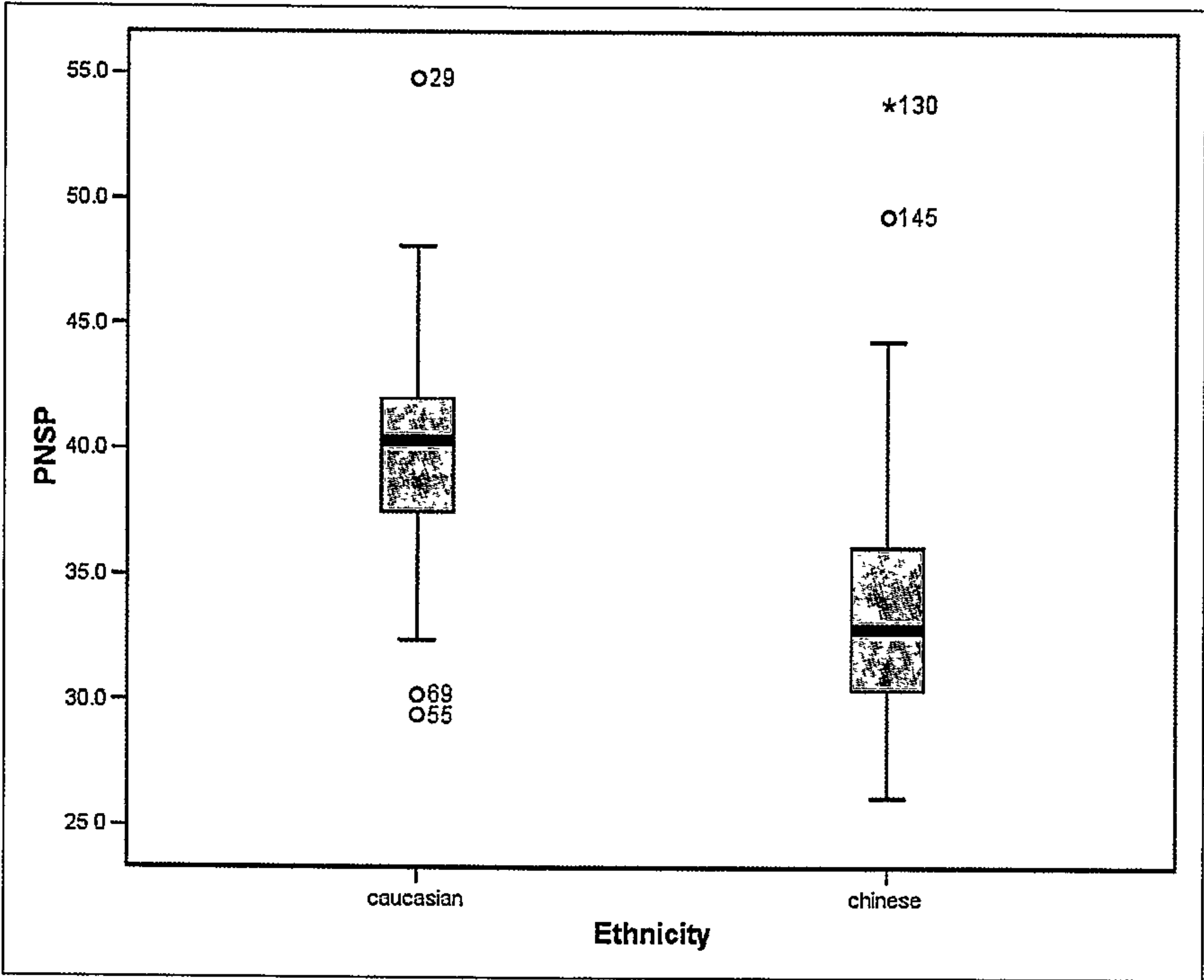


FIGURE 27. POSTERIOR AIRWAY MEASUREMENTS BY ETHNICITY

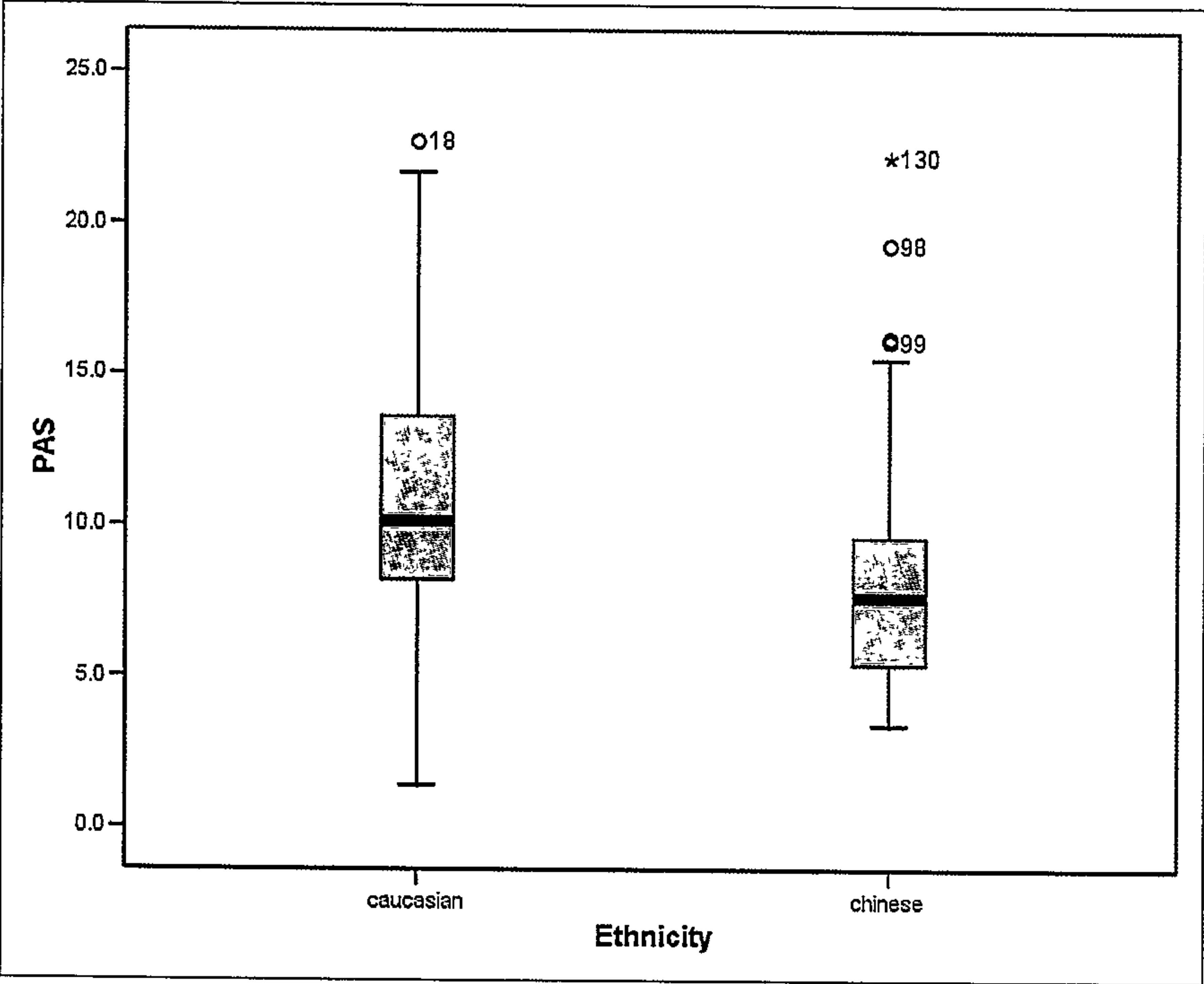


FIGURE 28. MAXIMUM SOFT PALATE DIMENSION BY ETHNICITY.

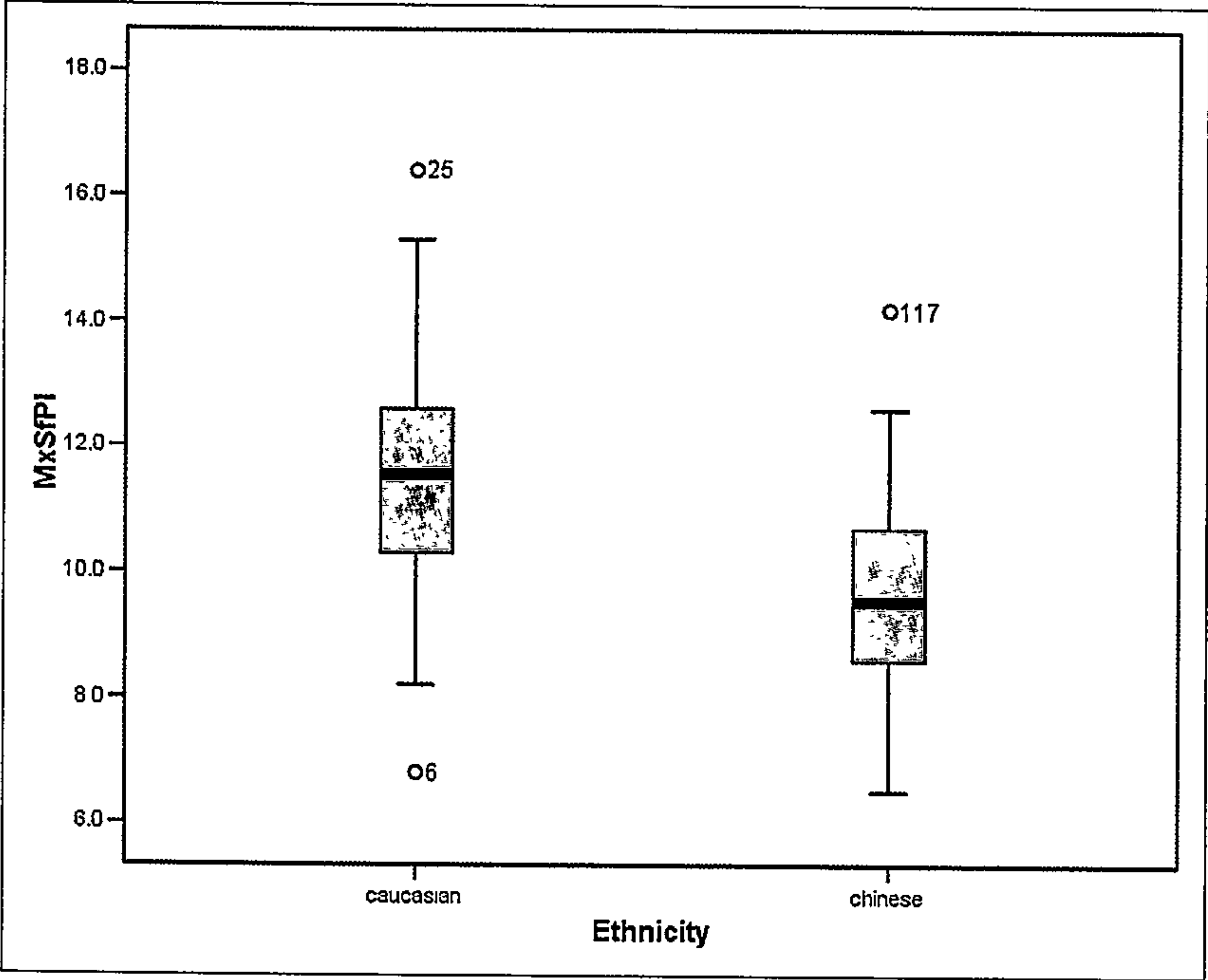


FIGURE 29. TONGUE HEIGHT BY ETHNICITY.

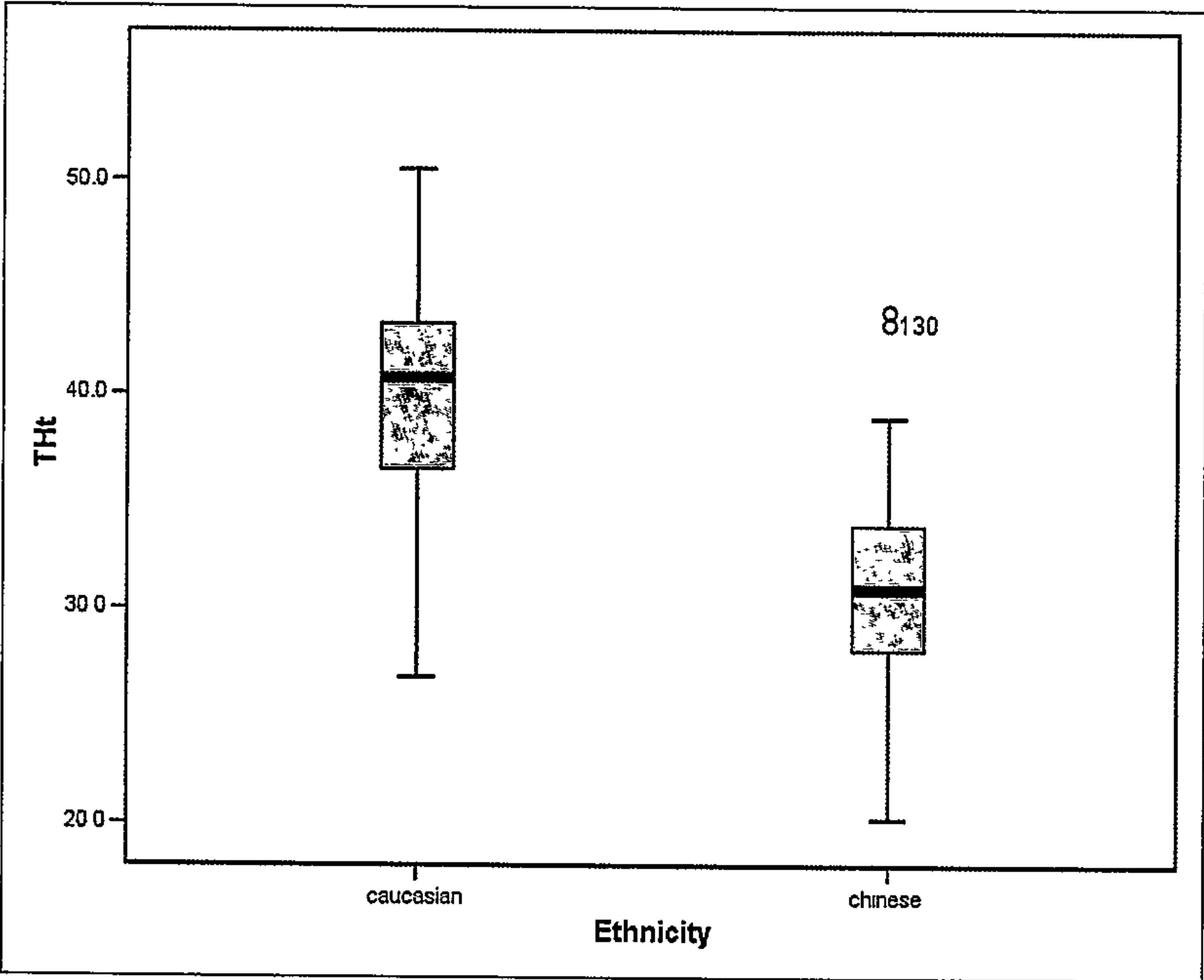
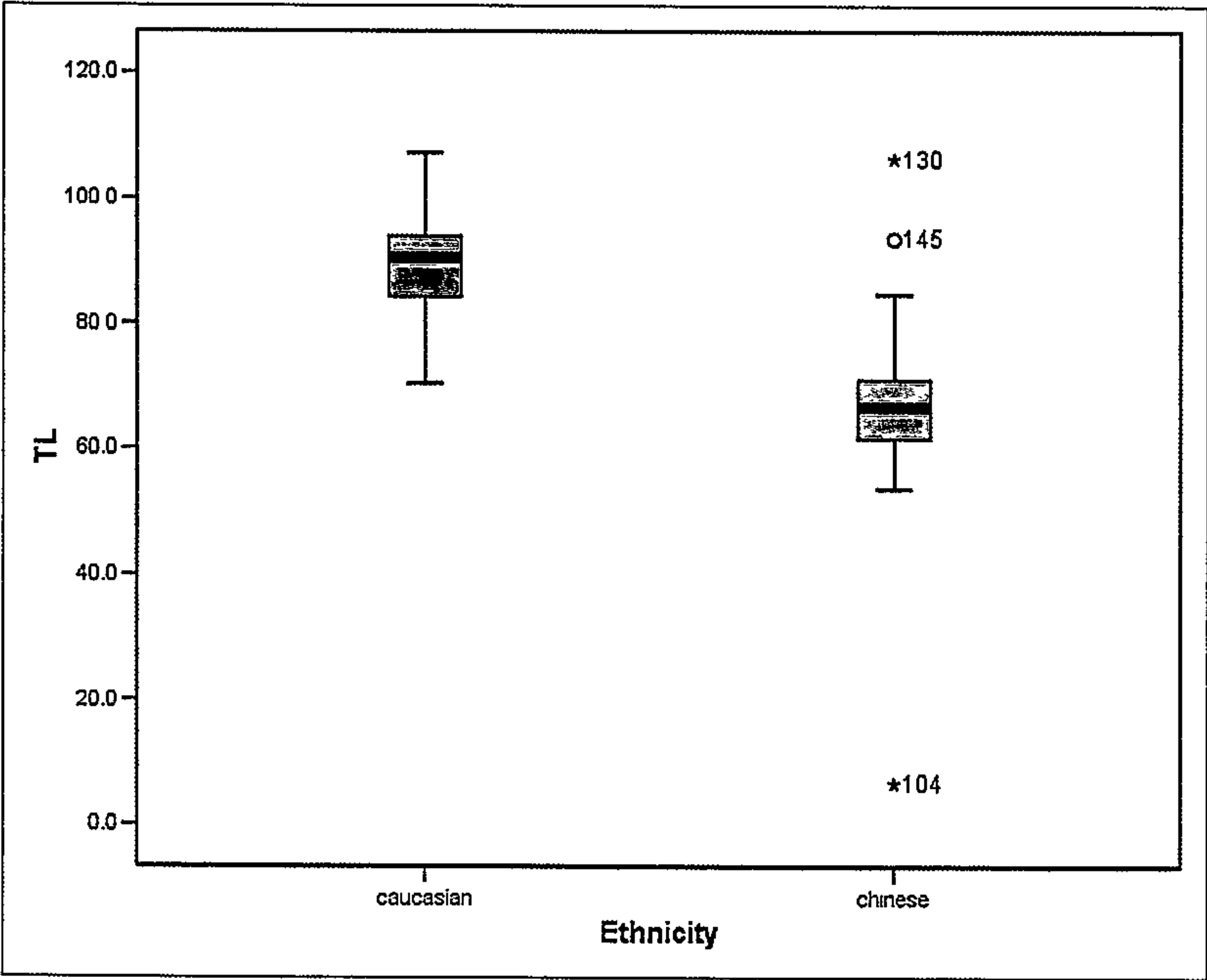


Figure 30. Tongue length by ethnicity



T-Test
Notes

Output Created		18-APR-2006 14:44:43
Comments		
Input	Data	D:\Documents and Settings\ppetocz\My Documents\Data\SPSSdata\Consult\SivaCranFac.sav
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	160
Missing Value Handling	Definition of Missing	User defined missing values are treated as missing.
	Cases Used	Statistics for each analysis are based on the cases with no missing or out-of-range data for any variable in the analysis.
Syntax		T-TEST GROUPS = Eth(1 2) /MISSING = ANALYSIS /VARIABLES = SNA SNB ANB PFH UFH LAFH AFH Jarabak Yaxis SNPP SNOP SNMP PPMP ArGoMe GoMe SNBa SN ANSPNS CoA OJ OB MPH CVTSN PAS PNSP MxSfPI Phwspt TL THt RDI Wt Ht BMI Neck Age MinSaO2 /CRITERIA = CI(.95) .
Resources	Elapsed Time	0:00:00.06

Group Statistics

	Eth	N	Mean	Std. Deviation	Std. Error Mean
SNA	caucasian	74	82.305	3.2731	.3805
	Chinese	86	84.664	4.4813	.4832
SNB	caucasian	74	79.300	3.6337	.4224
	Chinese	86	79.776	4.5687	.4927
ANB	caucasian	74	3.011	3.3362	.3878
	Chinese	86	4.890	3.1508	.3398

PFH	caucasian	74	87.300	9.8781	1.1483
	Chinese	86	84.894	6.5594	.7073
UFH	caucasian	74	58.222	5.8349	.6783
	chinese	86	54.050	4.5900	.4950
LAFH	caucasian	74	75.055	8.8165	1.0249
	chinese	86	70.397	5.4519	.5879
AFH	caucasian	74	131.685	12.3208	1.4323
	chinese	86	121.995	6.8553	.7392
Jarabak	caucasian	74	88.224	6.3882	.7426
	chinese	86	82.172	5.2323	.5642
Yaxis	caucasian	74	67.122	4.5668	.5309
	chinese	86	71.138	4.9110	.5296
SNPP	caucasian	74	8.288	3.7931	.4409
	chinese	86	10.033	4.5075	.4861
SNOP	caucasian	74	14.455	9.4563	1.0993
	chinese	85	17.742	11.0862	1.2025
SNMP	caucasian	74	30.781	6.9822	.8117
	chinese	86	29.691	7.7952	.8406
PPMP	caucasian	74	25.101	6.7274	.7820
	chinese	86	23.166	6.7617	.7291
ArGoMe	caucasian	74	126.480	5.9697	.6940
	chinese	86	119.869	8.1514	.8790
GoMe	caucasian	74	77.857	9.3568	1.0877
	chinese	86	65.757	4.1211	.4444
SNBa	caucasian	74	126.708	5.8643	.6817
	chinese	86	128.103	6.0708	.6546
SN	caucasian	74	77.518	6.7374	.7832
	chinese	86	63.731	3.2600	.3515
ANSPNS	caucasian	74	58.839	4.3099	.5010

	chinese	86	50.730	3.4756	.3748
CoA	caucasian	74	96.172	7.9811	.9278
	chinese	86	83.094	4.6113	.4972
OJ	caucasian	74	4.215	2.4226	.2816
	chinese	86	3.952	2.3746	.2561
OB	caucasian	74	2.589	3.6130	.4200
	chinese	86	1.141	2.8970	.3124
MPH	caucasian	74	22.443	6.7035	.7793
	chinese	86	18.460	6.0680	.6543
CVTSN	caucasian	74	108.666	7.7825	.9047
	chinese	86	111.283	8.4106	.9069
PAS	caucasian	74	10.803	4.5402	.5278
	chinese	86	7.987	3.4855	.3759
PNSP	caucasian	74	40.045	4.3051	.5005
	chinese	86	33.685	4.6058	.4967
MxSfPI	caucasian	74	11.439	1.7884	.2079
	chinese	86	9.645	1.4734	.1589
Phwspt	caucasian	73	10.588	3.9683	.4645
	chinese	86	8.780	2.4961	.2692
TL	caucasian	74	89.412	7.6226	.8861
	chinese	86	66.921	10.7024	1.1541
THt	caucasian	74	39.997	4.9702	.5778
	chinese	86	31.064	4.3099	.4647
RDI	caucasian	74	25.23	16.241	1.888
	chinese	86	31.41	26.790	2.889
Wt	caucasian	73	92.905	17.0383	1.9942
	chinese	86	79.045	16.7618	1.8075
Ht	caucasian	74	1.7411	.08244	.00958
	chinese	86	1.6462	.07624	.00822

BMI	caucasian	74	30.3473	6.69039	.77774
	chinese	86	29.1233	5.42371	.58485
Neck	caucasian	72	40.868	3.4015	.4009
	chinese	85	40.509	5.6752	.6156
Age	caucasian	50	46.948	11.4316	1.6167
	chinese	86	48.767	11.6485	1.2561
MinSaO2	caucasian	41	85.83	5.826	.910
	chinese	86	93.40	4.705	.507

Independent Samples Test

	Levene's Test for Equality of Variances			t-test for Equality of Means					
	F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
								Lower	Upper
Var Eq	9.418	.003	-3.748	158	.000	-2.3585	.6293	-3.6015	-1.1155
Var NE q			-3.835	154.100	.000	-2.3585	.6151	-3.5736	-1.1435
Var Eq	3.032	.084	-.720	158	.472	-.4756	.6601	-1.7793	.8281
Var NE q			-.733	157.071	.465	-.4756	.6490	-1.7574	.8062
Var Eq	.041	.841	-.3659	158	.000	-1.8787	.5134	-2.8927	-.8647
Var NE q			-.3644	151.443	.000	-1.8787	.5156	-2.8974	-.8600

Var Eq	7.945	.005	1. 83 7	15 8	.068	2.4058	1.3097	-.1810	4.9927
Var NE q			1. 78 4	12 3.6 20	.077	2.4058	1.3487	-.2637	5.0753
Var Eq	1.001	.318	5. 05 7	15 8	.000	4.1716	.8249	2.5424	5.8008
Var NE q			4. 96 8	13 7.8 68	.000	4.1716	.8397	2.5113	5.8319
Var Eq	10.866	.001	4. 07 8	15 8	.000	4.6589	1.1423	2.4027	6.9151
Var NE q			3. 94 3	11 7.9 73	.000	4.6589	1.1815	2.3191	6.9987
Var Eq	6.301	.013	6. 25 6	15 8	.000	9.6898	1.5489	6.6306	12.7489
Var NE q			6. 01 2	11 0.3 47	.000	9.6898	1.6118	6.4957	12.8838
Var Eq	3.119	.079	6. 58 7	15 8	.000	6.0522	.9189	4.2374	7.8671
Var NE q			6. 48 9	14 1.1 95	.000	6.0522	.9326	4.2085	7.8960
Var Eq	.570	.451	5. 32 7	15 8	.000	-4.0168	.7540	-5.5059	-2.5276
Var NE q			5. 35 7	15 7.0 28	.000	-4.0168	.7499	-5.4978	-2.5357
Var Eq	1.690	.195	2. 62 5	15 8	.010	-1.7447	.6648	-3.0577	-.4317

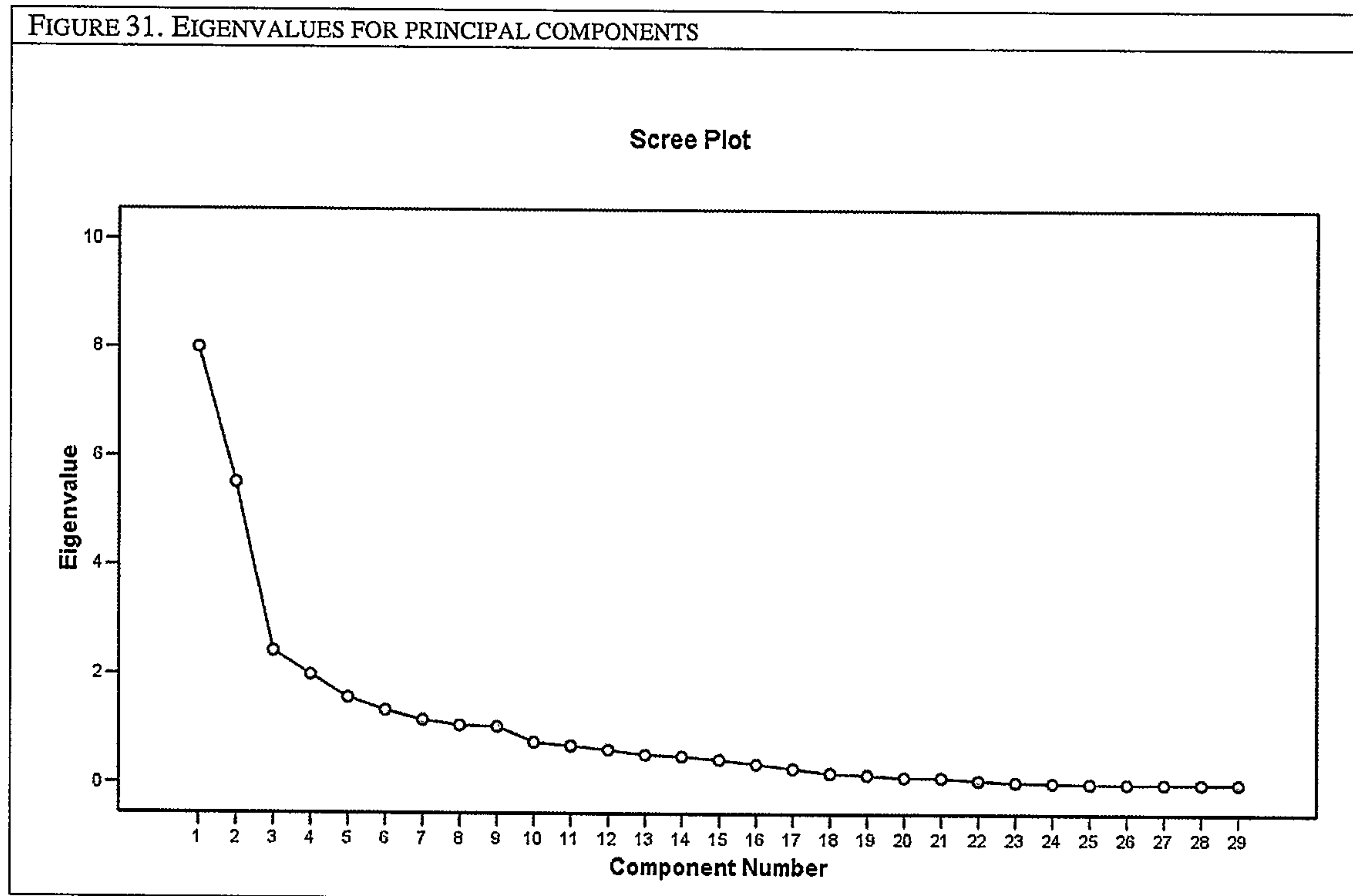
Var NE q			- 2. 65 9	15 7.9 29	.009	-1.7447	.6563	-3.0409	-.4485
Var Eq	1.404	.238	- 1. 99 5	15 7	.048	-3.2869	1.6472	-6.5405	-.0334
Var NE q			- 2. 01 8	15 6.9 41	.045	-3.2869	1.6292	-6.5050	-.0689
Var Eq	1.231	.269	.9 25	15 8	.356	1.0904	1.1782	-1.2367	3.4174
Var NE q			.9 33	15 7.7 34	.352	1.0904	1.1685	-1.2175	3.3983
Var Eq	.001	.971	1. 80 9	15 8	.072	1.9351	1.0696	-.1775	4.0477
Var NE q			1. 81 0	15 4.6 89	.072	1.9351	1.0692	-.1771	4.0472
Var Eq	6.876	.010	5. 77 0	15 8	.000	6.6111	1.1457	4.3482	8.8740
Var NE q			5. 90 3	15 4.2 20	.000	6.6111	1.1199	4.3988	8.8235
Var Eq	10.181	.002	10 .8 37	15 8	.000	12.0998	1.1165	9.8945	14.3051
Var NE q			10 .2 98	97. 08 1	.000	12.0998	1.1750	9.7678	14.4318
Var Eq	.000	.991	- 1. 47 3	15 8	.143	-1.3954	.9476	-3.2670	.4762
Var NE q			- 1. 47 6	15 5.8 74	.142	-1.3954	.9451	-3.2623	.4715

Var Eq	12.462	.001	16 .8 30	15 8	.000	13.7862	.8192	12.1683	15.4041
Var NE q			16 .0 59	10 1.8 26	.000	13.7862	.8585	12.0834	15.4890
Var Eq	3.163	.077	13 .1 69	15 8	.000	8.1090	.6158	6.8928	9.3251
Var NE q			12 .9 60	13 9.9 28	.000	8.1090	.6257	6.8719	9.3460
Var Eq	11.076	.001	12 .9 01	15 8	.000	13.0774	1.0137	11.0754	15.0795
Var NE q			12 .4 24	11 2.9 57	.000	13.0774	1.0526	10.9920	15.1629
Var Eq	.046	.831	.6 91	15 8	.491	.2625	.3801	-.4881	1.0132
Var NE q			.6 90	15 3.4 96	.491	.2625	.3806	-.4894	1.0145
Var Eq	4.508	.035	2. 81 3	15 8	.006	1.4485	.5149	.4315	2.4655
Var NE q			2. 76 7	13 9.4 56	.006	1.4485	.5234	.4136	2.4834
Var Eq	.001	.971	3. 94 4	15 8	.000	3.9828	1.0099	1.9880	5.9775
Var NE q			3. 91 4	14 8.7 30	.000	3.9828	1.0175	1.9721	5.9935
Var Eq	.159	.690	- 2. 03 0	15 8	.044	-2.6163	1.2885	-5.1613	-.0714
Var NE q			- 2. 04 2	15 7.1 47	.043	-2.6163	1.2810	-5.1466	-.0861

Var Eq	4.252	.041	4. 43 1	15 8	.000	2.8155	.6354	1.5605	4.0705
Var NE q			4. 34 5	13 5.8 16	.000	2.8155	.6479	1.5341	4.0969
Var Eq	.298	.586	8. 97 4	15 8	.000	6.3597	.7087	4.9600	7.7594
Var NE q			9. 02 0	15 6.8 98	.000	6.3597	.7051	4.9670	7.7524
Var Eq	1.677	.197	6. 95 5	15 8	.000	1.7938	.2579	1.2845	2.3032
Var NE q			6. 85 6	14 1.6 71	.000	1.7938	.2617	1.2766	2.3111
Var Eq	20.815	.000	3. 48 9	15 7	.001	1.8074	.5180	.7843	2.8306
Var NE q			3. 36 7	11 7.2 76	.001	1.8074	.5368	.7443	2.8705
Var Eq	.333	.565	15 .0 81	15 8	.000	22.4912	1.4914	19.5456	25.4368
Var NE q			15 .4 58	15 2.8 91	.000	22.4912	1.4550	19.6167	25.3658
Var Eq	1.456	.229	12 .1 77	15 8	.000	8.9333	.7336	7.4844	10.3823
Var NE q			12 .0 48	14 5.6 56	.000	8.9333	.7415	7.4679	10.3988
Var Eq	23.745	.000	- 1. 72 8	15 8	.086	-6.175	3.574	-13.233	.884
Var NE q			- 1. 78 9	14 2.7 87	.076	-6.175	3.451	-12.997	.647

Var Eq	1.314	.253	5. 15 6	15 7	.000	13.8594	2.6878	8.5505	19.1684
Var NE q			5. 14 9	15 1.9 98	.000	13.8594	2.6914	8.5420	19.1769
Var Eq	.139	.710	7. 56 2	15 8	.000	.09492	.01255	.07013	.11971
Var NE q			7. 51 8	15 0.1 43	.000	.09492	.01263	.06997	.11987
Var Eq	1.368	.244	1. 27 8	15 8	.203	1.22400	.95803	-.66819	3.11620
Var NE q			1. 25 8	14 0.3 58	.211	1.22400	.97311	-.69984	3.14784
Var Eq	.366	.546	.4 69	15 5	.639	.3586	.7640	-1.1506	1.8679
Var NE q			.4 88	14 0.4 67	.626	.3586	.7346	-1.0936	1.8109
Var Eq	.010	.920	.8 84	13 4	.378	-1.8194	2.0576	-5.8890	2.2501
Var NE q			.8 89	10 4.1 38	.376	-1.8194	2.0473	-5.8792	2.2403
Var Eq	1.730	.191	7. 83 2	12 5	.000	-7.567	.966	-9.479	-5.655
Var NE q			7. 26 4	65. 74 9	.000	-7.567	1.042	-9.647	-5.487

FIGURE 31. EIGENVALUES FOR PRINCIPAL COMPONENTS



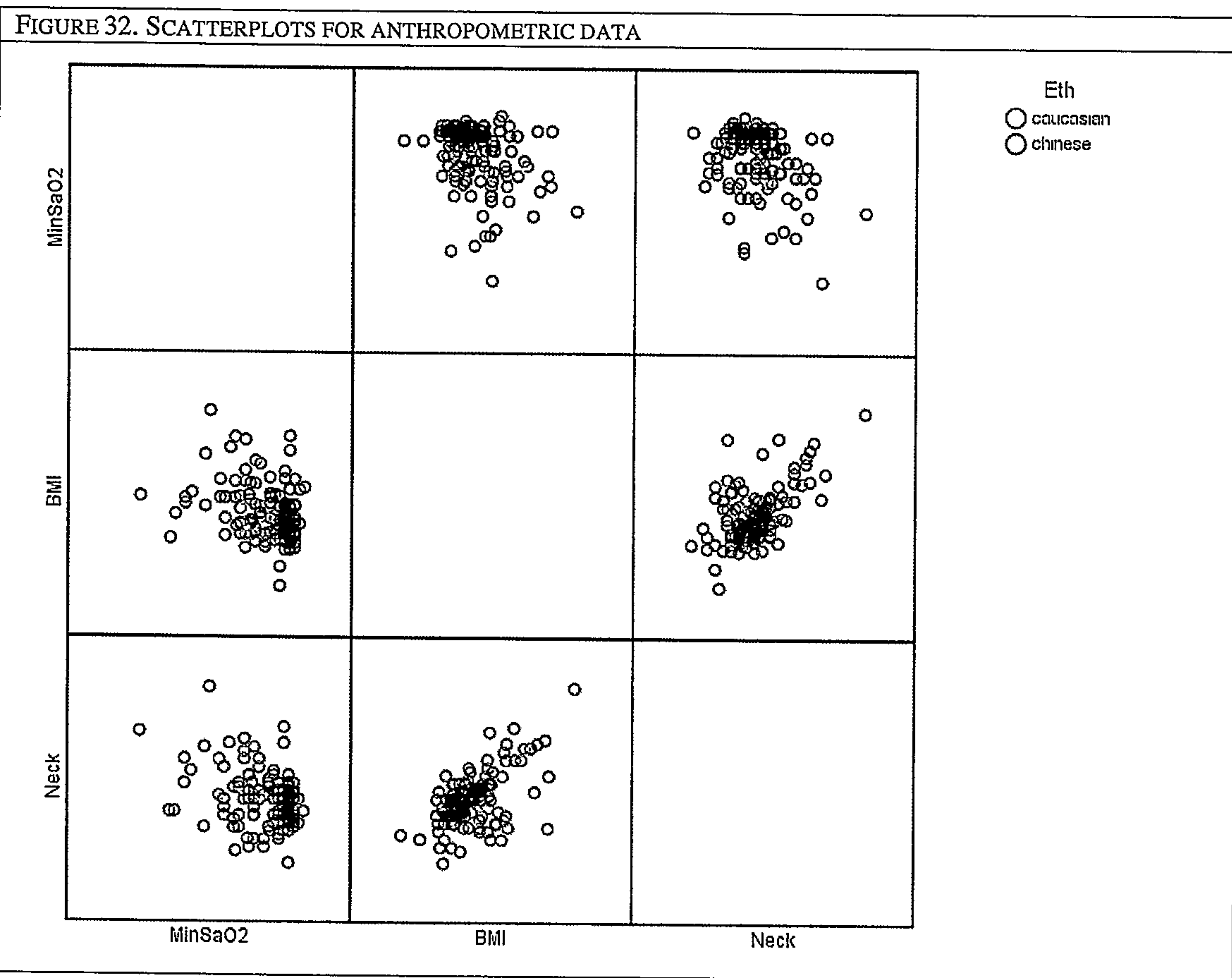


FIGURE 33. RELATIONSHIP OF RDI AND MINIMUM OXYGEN SATURATION.

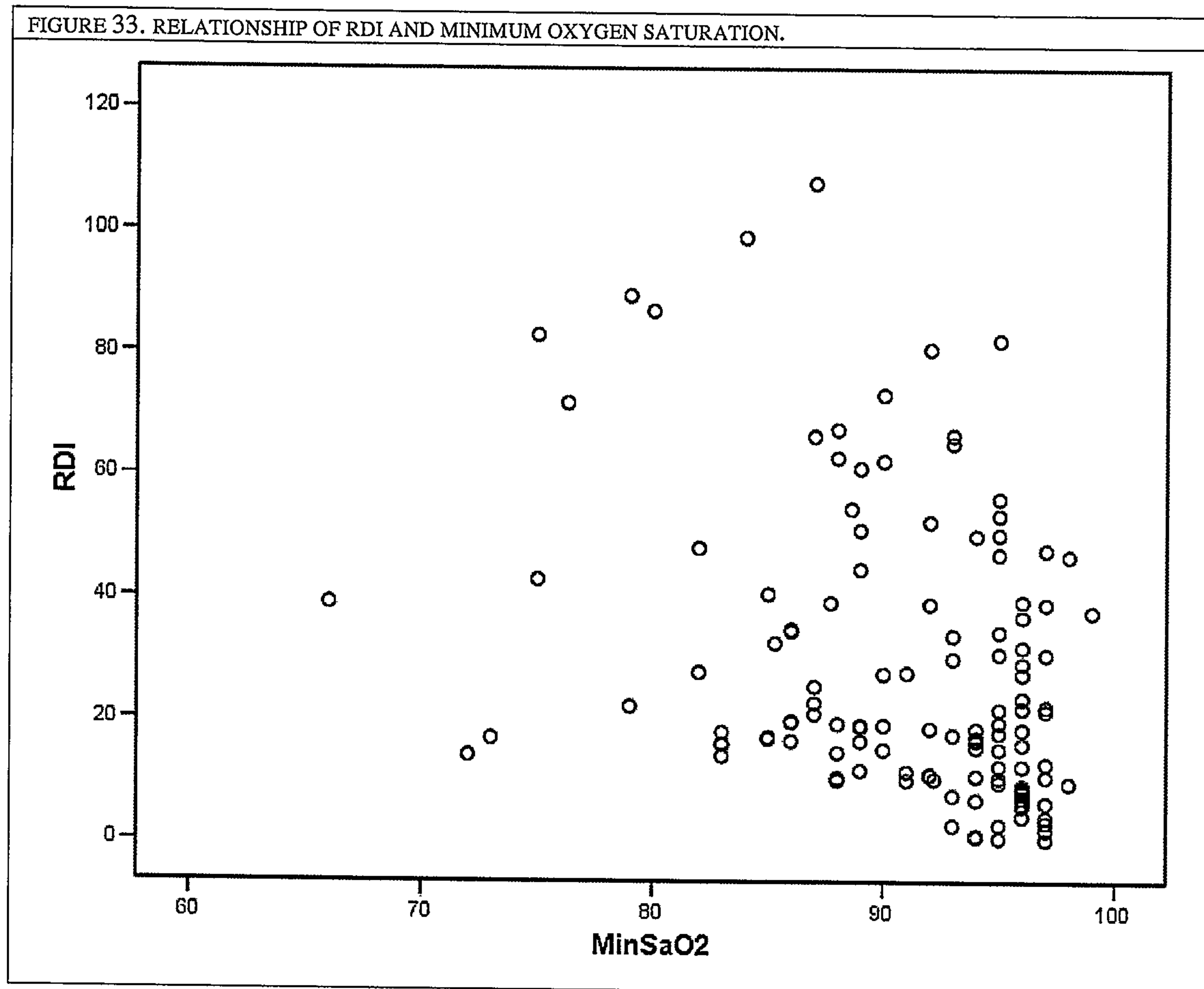
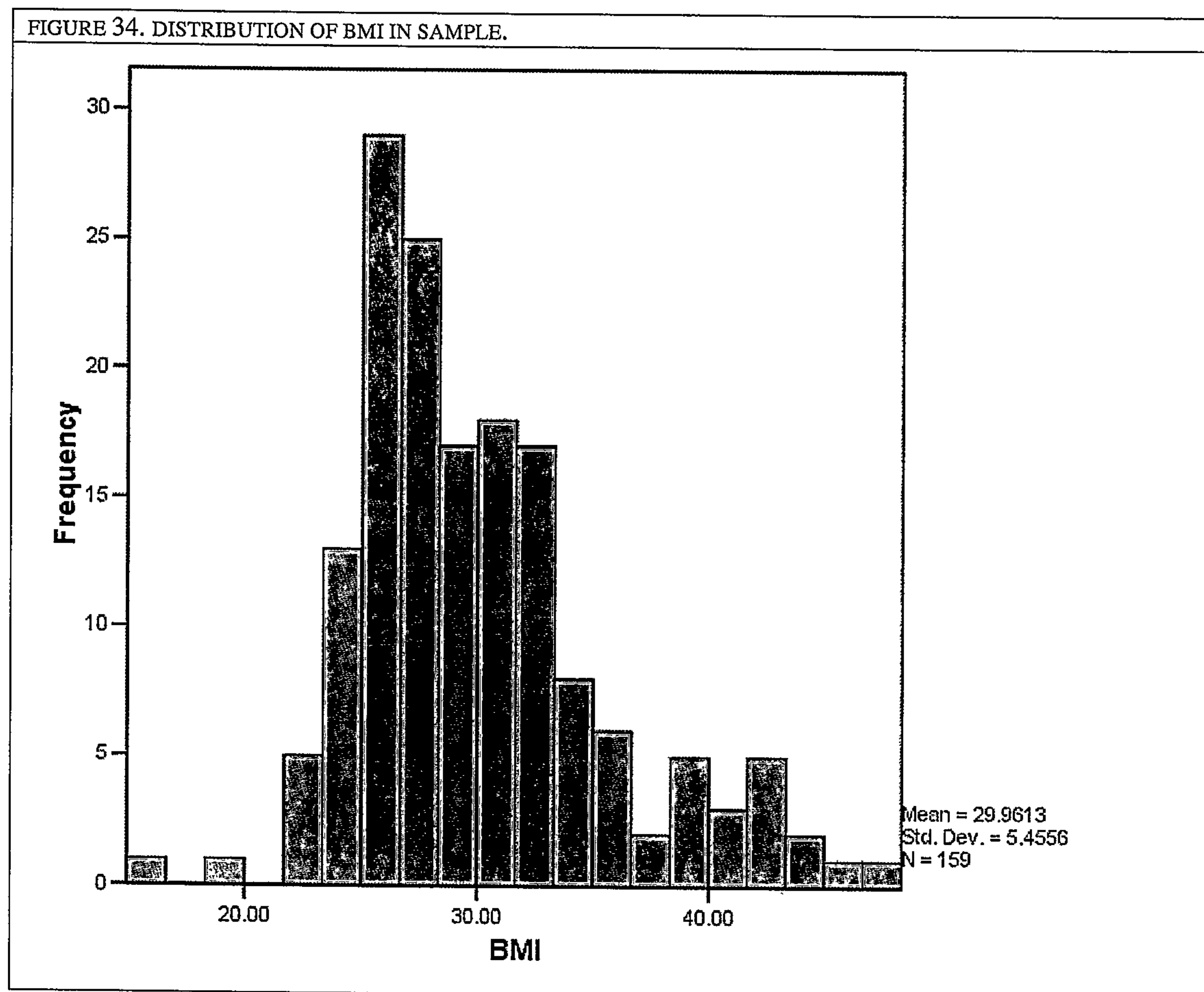


FIGURE 34. DISTRIBUTION OF BMI IN SAMPLE.



CAUCASIAN

Factor Analysis

Total Variance Explained									
Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	1.890	31.508	31.508	1.890	31.508	31.508	1.642	27.374	27.374
2	1.264	21.068	52.576	1.264	21.068	52.576	1.512	25.202	52.576
3	.972	16.206	68.782						
4	.780	13.002	81.784						
5	.616	10.261	92.045						
6	.477	7.955	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix^a

	Component	
	1	2
PAS	.267	.780
PNSP	.738	-.090
MxSfPI	.590	.130
Phwspt	.313	.569
TL	.680	.226
THt	.344	-.710

Extraction Method: Principal Component Analysis.

Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 3 iterations.

Factor Analysis

Total Variance Explained									
Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	5.458	54.582	54.582	5.458	54.582	54.582	5.398	53.976	53.976
2	1.631	16.307	70.889	1.631	16.307	70.889	1.691	16.913	70.899
3	.974	9.737	80.625						
4	.506	5.056	85.681						
5	.471	4.706	90.387						
6	.399	3.987	94.374						
7	.308	3.083	97.456						
8	.157	1.568	99.025						
9	.096	.956	99.981						
10	.002	.019	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix ^a		
	Component	
	1	2
PFH	.803	-.067
UFH	.793	-.148
LAFH	.638	-.445
AFH	.839	-.387
GoMe	.795	-.189
SN	.919	.069
ANSPNS	.796	.242
CoA	.926	.147
OJ	-.132	.651
OB	.167	.879

Extraction Method: Principal Component Analysis.
 Rotation Method: Varimax with Kaiser Normalization.
 a. Rotation converged in 3 iterations.

Factor Analysis

Total Variance Explained									
Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	4.640	42.180	42.180	4.640	42.180	42.180	2.855	25.953	25.953
2	1.857	16.879	59.059	1.857	16.879	59.059	2.776	25.240	51.194
3	1.389	12.630	71.689	1.389	12.630	71.689	2.255	20.496	71.689
4	.944	8.585	80.274						
5	.866	7.870	88.144						
6	.516	4.688	92.832						
7	.471	4.278	97.110						
8	.254	2.305	99.415						
9	.058	.527	99.942						
10	.006	.057	100.000						
11	5.081E-05	.000	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix^a

	Component		
	1	2	3
SNA	-.372	.059	-.753
SNB	-.331	-.756	-.386
ANB	-.001	.884	-.316
Yaxis	.555	.732	.252
SNPP	-.067	.305	.767
SNOP	.450	.110	.262
SNMP	.793	.513	.204
PPMP	.866	.364	-.232
ArGoMe	.833	-.051	.077
SNBa	.033	.043	.710
CVTSN	.131	.615	.339

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
^a. Rotation converged in 5 iterations.

Canonical Correlation Analysis

Run MATRIX procedure:

Correlations for Set-1
RDI MinSaO2
RDI 1.0000 -.3273
MinSaO2 -.3273 1.0000

Correlations for Set-2
Columns 1 - 8
pc1soft pc2soft pc1hardl pc2hardl pc1harda pc2harda pc3harda MPH
pc1soft 1.0000 .4051 .4161 -.1575 -.2015 -.1208 -.0356 .3418
pc2soft .4051 1.0000 .1343 .0836 -.1050 -.0582 .1673 .0227
pc1hardl .4161 .1343 1.0000 -.7009 -.0684 -.1334 .1043 .2510
pc2hardl -.1575 .0836 -.7009 1.0000 -.3720 -.2215 -.2800 -.1141
pc1harda -.2015 -.1050 -.0684 -.3720 1.0000 .8421 .5666 .0262
pc2harda -.1208 -.0582 -.1334 -.2215 .8421 1.0000 .6398 .0819
pc3harda -.0356 .1673 .1043 -.2800 .5666 .6398 1.0000 -.1180
MPH .3418 .0227 .2510 -.1141 .0262 .0819 -.1180 1.0000
BMI .2596 .1895 -.0416 -.0173 -.1077 -.0569 .2232 .1266
Neck .6096 .2195 .3803 -.2069 -.2464 -.1631 .0045 .3034
Columns 9 - 10
BMI Neck
pc1soft .2596 .6096
pc2soft .1895 .2195
pc1hardl -.0416 .3803
pc2hardl -.0173 -.2069
pc1harda -.1077 -.2464
pc2harda -.0569 -.1631
pc3harda .2232 .0045
MPH .1266 .3034
BMI 1.0000 .4306
Neck .4306 1.0000

Correlations Between Set-1 and Set-2

Columns	1	-	8						
		pc1soft	pc2soft	pc1hard1	pc2hard1	pc1harda	pc2harda	pc3harda	MPH
RDI		.1255	-.1167	.0882	-.2098	.2027	.1034	-.2095	.2940
MinSaO2		-.0905	-.1496	.1148	-.0278	.0526	.0152	.1147	-.0449
Columns	9	-	10						
		BMI	Neck						
RDI		.0527	.1871						
MinSaO2		-.2360	-.1043						

Canonical Correlations

-

1	.581
2	.384

Test that remaining correlations are zero:

	Wilk's	Chi-SQ	DF	Sig.
1	.565	36.280	20.000	.014
2	.853	10.129	9.000	.340

Standardized Canonical Coefficients for Set-1

	1	2
RDI	-1.036	.216
MinSaO2	-.134	1.050

Raw Canonical Coefficients for Set-1

	1	2
RDI	-.064	.013
MinSaO2	-.025	.198

Standardized Canonical Coefficients for Set-2

	1	2
pc1soft	-.002	.029
pc2soft	.115	-.604
pc1hard1	-.136	.645
pc2hard1	.078	.597
pc1harda	-.947	.636
pc2harda	-.052	-.683
pc3harda	.958	.630
MPH	-.194	.119
BMI	-.201	-.638
Neck	-.366	.095

Raw Canonical Coefficients for Set-2

	1	2
pc1soft	.000	.004
pc2soft	.016	-.084
pc1hard1	-.003	.015
pc2hard1	.007	.054
pc1harda	-.047	.032
pc2harda	-.003	-.042
pc3harda	.085	.056
MPH	-.028	.017
BMI	-.035	-.112
Neck	-.107	.028

Canonical Loadings for Set-1

	1	2
RDI	-.992	-.127

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MinSaO2	.205	.979
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Cross Loadings for Set-1

	1	2
RDI	-.576	-.049
MinSaO2	.119	.376

Canonical Loadings for Set-2

	1	2
pc1soft	-.203	-.177
pc2soft	.243	-.475
pc1hard1	-.184	.363
pc2hard1	.381	-.194
pc1harda	-.374	.258
pc2harda	-.188	.100
pc3harda	.347	.195
MPH	-.514	.043
BMI	-.039	-.616
Neck	-.309	-.180

Cross Loadings for Set-2

	1	2
pc1soft	-.118	-.068
pc2soft	.141	-.182
pc1hard1	-.107	.140
pc2hard1	.221	-.075
pc1harda	-.217	.099
pc2harda	-.109	.038
pc3harda	.202	.075
MPH	-.299	.017
BMI	-.023	-.236
Neck	-.180	-.069

Redundancy Analysis:

Proportion of Variance of Set-1 Explained by Its Own Can. Var.

	Prop Var
CV1-1	.513
CV1-2	.487

Proportion of Variance of Set-1 Explained by Opposite Can.Var.

	Prop Var
CV2-1	.173
CV2-2	.072

Proportion of Variance of Set-2 Explained by Its Own Can. Var.

—

	Prop Var
CV2-1	.094
CV2-2	.095

Proportion of Variance of Set-2 Explained by Opposite Can. Var.

	Prop Var
CV1-1	.032
CV1-2	.014

CHINESE

Factor Analysis

Total Variance Explained									
Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	2.581	43.009	43.009	2.581	43.009	43.009	2.561	42.686	42.686
2	1.199	19.981	62.990	1.199	19.981	62.990	1.218	20.304	62.990
3	.732	12.204	75.194						
4	.663	11.047	86.241						
5	.448	7.471	93.712						
6	.377	6.288	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix^a

	Component	
	1	2
PAS	.593	.345
PNSP	.807	.054
MxSfPI	.677	-.403
Phwspt	.008	.879
TL	.836	-.082
THt	.634	.392

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
a. Rotation converged in 3 iterations.

Factor Analysis

Total Variance Explained									
Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %
1	3.193	31.933	31.933	3.193	31.933	31.933	2.963	29.628	29.628
2	2.015	20.148	52.081	2.015	20.148	52.081	2.096	20.955	50.583
3	1.131	11.312	63.393	1.131	11.312	63.393	1.281	12.810	63.393
4	.938	9.384	72.777						
5	.826	8.260	81.037						
6	.640	6.398	87.435						
7	.555	5.553	92.989						
8	.388	3.881	96.870						
9	.305	3.046	99.916						
10	.008	.084	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix^a

	Component		
	1	2	3
PFH	.381	-.034	.646
UFH	.574	.277	.182
LAFH	.084	.904	-.023
AFH	.389	.858	.150
GoMe	.612	-.079	.327
SN	.712	.267	-.173
ANSPNS	.742	-.086	.007
CoA	.848	.021	.007
OJ	.200	-.252	-.797
OB	.371	-.561	-.186

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.

a. Rotation converged in 6 iterations.

Factor Analysis

Total Variance Explained

Component	Initial Eigenvalues			Extraction Sums of Squared Loadings			Rotation Sums of Squared Loadings		
	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative %	Total	% of Variance	Cumulative
1	5.328	48.434	48.434	5.328	48.434	48.434	4.084	37.124	37.1
2	1.681	15.281	63.715	1.681	15.281	63.715	2.819	25.627	62.7
3	1.243	11.301	75.017	1.243	11.301	75.017	1.349	12.267	75.0
4	.891	8.102	83.118						
5	.706	6.416	89.534						
6	.593	5.391	94.925						
7	.379	3.446	98.371						
8	.124	1.124	99.495						
9	.050	.459	99.954						
10	.005	.046	100.000						
11	4.270E-05	.000	100.000						

Extraction Method: Principal Component Analysis.

Rotated Component Matrix^a

	Component		
	1	2	3
SNA	-.719	-.224	.608
SNB	-.860	-.385	-.014
ANB	.234	.248	.890
Yaxis	.850	.437	.085
SNPP	.814	-.109	.225
SNOP	.457	.369	.029
SNMP	.600	.759	.127
PPMP	.129	.956	-.023
ArGoMe	.051	.842	.125
SNBa	.611	.115	-.259
CVTSN	.653	.091	.169

Extraction Method: Principal Component Analysis.
Rotation Method: Varimax with Kaiser Normalization.
a. Rotation converged in 5 iterations.

Canonical Correlation Analysis

Run MATRIX procedure:

Correlations for Set-1
RDI MinSaO2
RDI 1.0000 -.6716
MinSaO2 -.6716 1.0000

Correlations for Set-2
Columns 1 - 8
pc1soft pc2soft pc1hard1 pc2hard1 pc3hard1 pc1harda pc2harda pc3harda
pc1soft 1.0000 .2805 .2650 .2496 .2077 .1902 -.0028 -.0199
pc2soft .2805 1.0000 .2017 .1931 .0112 .1958 .1672 -.0278
pc1hard1 .2650 .2017 1.0000 .4952 .5917 .0680 -.1069 .0231
pc2hard1 .2496 .1931 .4952 1.0000 .4301 .6083 .5828 .1454
pc3hard1 .2077 .0112 .5917 .4301 1.0000 -.1736 -.4008 -.3081
pc1harda .1902 .1958 .0680 .6083 -.1736 1.0000 .8169 .2779
pc2harda -.0028 .1672 -.1069 .5828 -.4008 .8169 1.0000 .4074
pc3harda -.0199 -.0278 .0231 .1454 -.3081 .2779 .4074 1.0000
MPH .3356 .0226 .0518 .1421 -.0210 .3172 .1921 .1004
BMI .2679 .1997 -.0026 .0580 .0242 .1696 .0766 -.1254
Neck .4934 .1684 .2295 .1271 .2198 .1033 -.0195 -.0961
Columns 9 - 11
MPH BMI Neck
pc1soft .3356 .2679 .4934
pc2soft .0226 .1997 .1684
pc1hard1 .0518 -.0026 .2295
pc2hard1 .1421 .0580 .1271
pc3hard1 -.0210 .0242 .2198
pc1harda .3172 .1696 .1033
pc2harda .1921 .0766 -.0195
pc3harda .1004 -.1254 -.0961
MPH 1.0000 .2838 .3971
BMI .2838 1.0000 .6472
Neck .3971 .6472 1.0000

Correlations Between Set-1 and Set-2

Columns	1	-	8						
	pc1soft	pc2soft	pc1hard1	pc2hard1	pc3hard1	pc1harda	pc2harda	pc3harda	
RDI	.3319	.1191	.0051	.2433	.2109	.1879	.0934	-.1133	
MinSaO2	-.4243	-.1164	-.0152	-.2031	-.1323	-.2009	-.1040	.1065	
Columns	9	-	11						
	MPH	BMI	Neck						
RDI	.3717	.5835	.5612						
MinSaO2	-.2098	-.4396	-.4845						

Canonical Correlations

1	.726
2	.345

Test that remaining correlations are zero:

	Wilk's	Chi-SQ	DF	Sig.
1	.416	66.670	22.000	.000
2	.881	9.658	10.000	.471

Standardized Canonical Coefficients for Set-1

	1	2
RDI	-.849	-1.049
MinSaO2	.208	-1.334

Raw Canonical Coefficients for Set-1

	1	2
RDI	-.031	-.039
MinSaO2	.044	-.281

Standardized Canonical Coefficients for Set-2

	1	2
pc1soft	-.101	.940
pc2soft	-.013	-.210
pc1hard1	.477	.151
pc2hard1	-.515	-.471
pc3hard1	-.140	-.124
pc1harda	-.013	.328
pc2harda	.223	.387
pc3harda	.017	-.219
MPH	-.173	-.735
BMI	-.460	-.311
Neck	-.381	.236

Raw Canonical Coefficients for Set-2

	1	2
pc1soft	-.007	.064
pc2soft	-.004	-.063
pc1hard1	.036	.011
pc2hard1	-.044	-.040
pc3hard1	-.023	-.020
pc1harda	.000	.013
pc2harda	.010	.017
pc3harda	.003	-.038
MPH	-.028	-.120
BMI	-.088	-.059
Neck	-.110	.068

Canonical Loadings for Set-1

	1	2
RDI	-.988	-.154
MinSaO2	.778	-.629

Cross Loadings for Set-1

	1	2
RDI	-.718	-.053
MinSaO2	.565	-.217

Canonical Loadings for Set-2

	1	2
pc1soft	-.509	.630
pc2soft	-.172	.087
pc1hard1	-.010	.043
pc2hard1	-.342	.045
pc3hard1	-.284	-.130
pc1harda	-.277	.205
pc2harda	-.139	.118
pc3harda	.163	-.067
MPH	-.494	-.319
BMI	-.807	-.075
Neck	-.794	.166

Cross Loadings for Set-2

	1	2
pc1soft	-.370	.218
pc2soft	-.125	.030
pc1hard1	-.007	.015
pc2hard1	-.249	.016
pc3hard1	-.206	-.045
pc1harda	-.201	.071
pc2harda	-.101	.041
pc3harda	.118	-.023
MPH	-.359	-.110
BMI	-.586	-.026
Neck	-.577	.057

Redundancy Analysis:

Proportion of Variance of Set-1 Explained by Its Own Can. Var.

	Prop Var
CV1-1	.790
CV1-2	.210

Proportion of Variance of Set-1 Explained by Opposite Can.Var.

	Prop Var
CV2-1	.417
CV2-2	.025

Proportion of Variance of Set-2 Explained by Its Own Can. Var.

	Prop Var
CV2-1	.194
CV2-2	.056

Proportion of Variance of Set-2 Explained by Opposite Can. Var.

	Prop Var
CV1-1	.102
CV1-2	.007