SHARE: STUDY OF HEART ASSESSMENT
AND RISK IN ETHNIC GROUPS

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By

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A Thesis Submitted to the School of Graduate Studies

in Partial Fulfilment of the Requirements

for the Degree

Master of Science

McMaster University

MASTER OF SCIENCE (1996) McMaster University

Clinical Epidemiology & Biostatistics Hamilton, Ontario

TITLE: Share: Study of Heart Assessment and Risk in Ethnic Groups

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NUMBER OF PAGES: xxi, 132

Abstract:

Cardiovascular disease (CVD) is the major cause of death in Canada and most developed countries. One of the next major advances in reducing CVD morbidity and mortality will likely occur when the epidemiology and the pathophysiology of specific risk factors for atherosclerosis across diverse populations are better understood. It is now apparent that different ethnic groups have different risks of CVD mortality that cannot be accounted for by differences in risk factors like smoking, hypertension, hypercholesterolemia, and diabetes. Therefore, both from global and national perspectives, studies that explore reasons for ethnic differences in CVD rates are of major public health importance.

The Study of Heart Assessment and Risk in Ethnic groups (SHARE) is a unique initiative designed to determine the prevalence of subclinical atherosclerosis and cardiovascular risk factors in South Asians and European Canadians. South Asians in Canada and in several countries have the highest rates of coronary heart disease (CHD) compared to any other ethnic groups in the world, and present a unique opportunity to test research hypotheses to discover emerging risk factors for atherosclerosis. SHARE builds upon previous cross-sectional studies that have examined the traditional CHD risk factor profile of South Asians, and extends this investigation to determine the prevalence of subclinical atherosclerosis in South Asians, and the contribution to its development from metabolic, fibrinolytic,

nutritional, and psychosocial factors.

This thesis represents a carefully designed research proposal to study CVD risk factors and subclinical atherosclerosis in South Asians and White Canadians. A pilot study to test the feasibility of this design was conducted over the past one year. The information obtained from this experience has led to further pilot studies and modification of the final proposal, which has recently been funded by the Medical Research Council of Canada.

This cross-sectional study proses to use a stratified random sampling to identify potential South Asian and White Canadian participants in Canada. Ethnic specific sampling frames were created, in conjunction with Statistics Canada, by using a compact disc programme of public telephone directories. South Asian Canadians were identified by using a comprehensive list of last names, a method which is highly sensitive and specific to South Asian ethnicity. A sampling frame of Canadians of European origin matched by postal code to the South Asian sampling frame was also created. In the pilot study we recruited participants by mail and multiple telephone calls, and our results are comparable to other population-based studies who utilized similar methods of recruitment. However, it is likely that our contact rates may be improved and after seeking the advice of the York Institute for Social Research in Toronto we have modified our recruitment protocol to maximize contact rates.

Both traditional and emerging risk factors will be identified utilizing a combination of existing and new measurement instruments. The primary outcome measurement is subclinical atherosclerosis as measured by the carotid B-Mode

ultrasound. This technology allows precise quantitation of atherosclerosis and is desirable for use in population-based studies as it is not subject to reporting bias by study participants. As well, it is a continuous measurement and decreases sample size requirements. Furthermore it allows the study of the relationship of risk factors and disease across a continuum.

Interesting demographic and laboratory differences were identified between the South Asians and White Canadian populations during the pilot study. Lifestyle differences in smoking and alcohol consumption, as well as socio-economic status and education were identified between the groups. As well, intriguing differences in glucose and lipid abnormalities were identified, as were differences in emerging CVD risk factors such as Lp(a) and urine microalbumin. Although extensive measures of fibrinolysis were not incorporated into the pilot study they are planned for the large study.

Few instruments to measure nutritional and psychosocial factors in non-white populations have been developed. The development of these instruments is outlined in this thesis proposal and. preliminary validation of these instruments has been completed as part of the SHARE pilot study. In both of these areas no "gold standard" exists against which surrogate measures may be validated and this posed unique methodologic challenges. After careful consideration of nutritional hypothesis and discussion with experts in the field of nutritional epidemiology, it was decided that a food frequency questionnaire (FFQ) would be the most appropriate instrument to identify significant qualitative differences in macronutrient consumption between ethnic populations. As no FFQ exists for South Asians,

nutrient data collected from the SHARE pilot study were used to create a South Asian specific FFQ. With the initiation of the large SHARE project this FFQ will be validated against multiple 24 hour recalls taken at random.

Although psychosocial factors have been repeatedly demonstrated to be associated with the development of CVD, it is extremely difficult to study these relationships precisely. There are many instruments which have be validated to measure stress and associated factors such as hostility, coping strategies and depression, yet no validation of these instruments had been conducted in the South Asian population. Therefore a SHARE Life Stress and Satisfaction Questionnaire was created after careful consideration of which stress factors may be unique to South Asians immigrants. Previously validated subscales were compiled to create this questionnaire which was completed by a subset of the SHARE pilot study participants. Validation of this questionnaire was performed on three levels content, criterion and construct. As well, reliability testing using tests of internal consistency and test-re-test reliability were conducted. Although this satisfies the criteria of validation and reliability testing of psychosocial instruments, whether or not we were attempting to measure the relevant stress factors of South Asian Canadians is questionable. In our attempt to confirm what we believed were important stressors, and to discover new factors, a qualitative substudy was designed. Using focus groups a subsample of South Asian and White Canadians will be studied and the emergent themes generated from this study will be used to develop an explanatory model of the dominant psychosocial factors and their potential relationship with health behaviours and disease status. This substudy will be run

concurrently with the initiation of the SHARE project, and based on these results the Life Stress and Satisfaction questionnaire will be modified.

In summary, this thesis outlines a proposal to document the prevalence of traditional and emerging risk factors and sub-clinical atherosclerosis in South Asians and White Canadians in Canada. It is our intention to follow the group identified in this cross-sectional study (Phase 1) for the progression of atherosclerosis and clinical events over time in a national cohort study (Phase 2).

Acknowledgements:

This thesis represents sixteen months of concentrated effort towards designing a research protocol to advance our knowledge of cardiovascular disease risk factors in South Asians. It has formed the basis of my current Heart and Stroke Foundation of Canada Research Fellowship, has recently been funded by the Medical Research Council of Canada, and has served as my initial training in cardiovascular epidemiology. I would like to thank Drs' D. Cook, H. Gerstein, and G. Dagenais for their advise and encouragement. I credit the early success and quality of this research endeavour in large part to the experience and skill of my research supervisor Dr. Salim Yusuf, with whom it is a privilege to work. Finally, I thank my family for their continued support, and dedicate this dissertation to my parents who have been my greatest teachers.

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September 1996

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Chapter 1: Background

1.1 Introduction

There is compelling evidence that South Asian (SA) men and women (people who originate from India, Sri Lanka, Bangladesh, and Pakistan) have a high mortality from coronary heart disease (CHD) both within their countries of origin and abroad[1,2]. It is believed, but not proven, that this excess of CHD morbidity and mortality occurs as a result of increased premature atherosclerosis (ATH), which is unaccounted for by traditionally accepted risk factors for CHD. SA possess a unique risk factor profile which includes impaired glucose tolerance (IGT), insulin resistance, elevated Lp(a) and impaired fibrinolysis, and SA suffer premature CHD mortality when they adopt urban lifestyles as they appear extremely susceptible to environmental factors such as over nourishment, physical inactivity and psychosocial stressors associated with migration. This leads to an increased prevalence of abdominal obesity, diabetes, and dyslipidemia known as Syndrome X. The adverse effects of these environmental factors associated with urbanization, along with the genetic predisposition of SA, are thought to accelerate ATH and contribute to an increased risk of subsequent clinical events

1.2 Hypothesis

The underlying hypothesis of this research proposal is that the excess rate of CHD in SA is due to a genetic predisposition to IGT, insulin resistance, impaired fibrinolysis, and increased Lp(a), which is unmasked with SA adoption of an urban lifestyle (increased total energy and fat content of the diet, decreased physical activity, and psychosocial stressors associated with migration) and results in increased abdominal obesity, DM and dyslipidemia; the overt markers of these two sets of factors (nature and nurture) (Figure 1).

1.3 Importance of determining risk factors for ATH in South Asians

CHD is the major cause of death in Canada and most developed countries[3]. Globally CHD accounts for 25% of all deaths. Several developing countries have experienced substantial gains in longevity chiefly through the control of pretransitional (eg. infectious and diarrheal) diseases which has resulted in the control of childhood deaths. The World Bank and World Health Organization project that CHD will account for an increasing proportion of deaths worldwide as developing countries move into a post-transitional period[4,5] and by the year 2020 over half of all CHD deaths will occur in these countries, especially in the Indian subcontinent (Table 1,2)[6]. There are three reasons why determining risk factors for CHD in SA is important:

1) **SA constitute a significant proportion of the world's population**[6], as 20% originate from South Asia, 25% from China, and 10% from Subsaharan Africa . Worldwide, there are 1.2 billion SA, (1.8 million live in North America, and 0.5 million SA in Canada[7]) . Together SA and Chinese represent the two largest non-white ethnic groups (defined by ancestral origin) in Canada.

2) **SA experience one of the highest rates of CHD within Canada and in the world** [8] **and the rates are increasing.**

3) **SA have a different susceptibility for CHD risks factors** which cannot be accounted for by differences in the traditional risk factors like smoking, hypertension, hypercholesterolemia, and diabetes[1]. Therefore, both from global and national perspectives, studies that explore reasons for the differences in CVD rates in SA are of major public health importance. The majority of our current knowledge of risk factors for CHD is derived from studies that have included predominantly white males, and the most influential risk factors for CHD in SA remain unconfirmed. This high risk group requires an in-depth study as they face large burdens of disease and present special challenges for prevention

1.4 High rates of CHD among SA compared to other groups

The impression that CHD was not a significant medical problem in SA persisted

until reports appeared from studies of SA migrants to other countries, which showed a higher mortality from CHD in SA compared to other ethnic groups; this sparked epidemiologic research within India and abroad [2,8-10]

● *High rates of CHD among Migrant SA*

Despite cultural and geographic diversity, migrant SA, to many countries including Canada, have an excess mortality from CHD in their adopted countries. The standardized mortality rates in SA for CHD are higher relative to the remaining population in many countries. CHD deaths among SA were 4 times that of the Chinese in Singapore, 3 times that of the Melanese in Fiji, 2.6 times that of the Blacks in Trinidad, 1.5 times that of the Whites in the United Kingdom, 1.4 times that of South African whites [2] (Table 3). We have recently completed an analysis of the Canadian mortality data from the period 1979 to 1993 which indicates an age (35-74) standardized CHD mortality rate of 368 among SA, 306 among WC, and 152 among Chinese per 100,000. Furthermore, the proportional mortality rate for CHD among those 35-74 years was 45% in SA males compared to 30% in other Canadian males, 32% in SA females compared to 20% in other Canadian females[11,12]. Severe premature ATH has been observed (5-8 years earlier) in SA compared with other ethnic groups as demonstrated by the younger age of myocardial infarction (MI) [13-15]. In a study we conducted, the mean age of first MI was 47 years in an Indian tertiary care hospital compared to 54 years in Canada [16]. CHD death rates are also increasing among SA in Western countries such as the UK, whereas declines have been observed in other ethnic groups. Balarajan et al

reported that while death rates from CHD declined among most immigrant groups and those born in the UK between 1970-72 and 1979-83, persons born in India showed an increase in mortality of 6% among men and 13% among women during the same period [17].

● *High and increasing rates of CHD in urban India*:

In urban India, CHD rates are as high as in Indians overseas, whereas in rural India a much lower prevalence of disease has been reported [18-21]. An urban population survey in 1990 reported a CHD prevalence based on clinical diagnosis of 39.5 per 1000 males and 25.3 per 1000 females [22], which appears to be higher than that reported from the Framingham Offspring Study (25 per 1000 in males and 11 per 1000 in females) despite some potential differences in methodology [23]. Recently an observational study in India examined urban and rural differences and found a prevalence of CHD (based on history and ECG) of 107 per 1000 in urban males, and 102 per 1000 in urban females, compared to 55 per 1000 in rural males and 64 per 1000 in rural females [21]. **This striking urban-rural difference in CHD rates observed among SA within India, and high rates observed when SA migrate to other countries, supports our hypothesis of a genetic predisposition to ATH which is unmasked after migration to urban environments.** Concomitant with urbanization and the control of pretransitional disease, it is projected that deaths due to CHD will double in India over the period 1985-2015 (Table 2).

● *CHD among SA Women*

Although gender differences in risk factor prevalence, and the subsequent risk of CHD in Whites are understood [24], there are limited data in SA women. The impact of diabetes mellitus (DM) on CHD appears to be greater in women compared to men in data largely derived from white populations. The Framingham Heart study reported a relative risk for CHD mortality of 1.7 in diabetic men relative to non-diabetic men and 3.3 in diabetic women compared to their non-diabetic counterparts [25]. Mortality statistics, including Canadian data, suggest that SA women are at higher risk of developing premature CHD than their white female counterparts. As abnormal glucose metabolism appears to be closely associated with increased CHD rates in SA, it is important to consider ethnic and gender specific differences as SA men and women have high rates of DM and IGT. Other important differences in risk factors between SA females and white females have been suggested; fewer SA women smoke, more lead sedentary lives, and may have different psychosocial stressors (eg. increased social isolation in SA women). The risk factor profile differs substantially from WC women. Therefore we propose to examine separately among women and men the role of ethnicity in developing CHD, and as a corollary within each ethnic group, gender differences in prevalence of risk factors, disease (ATH), and their associations.

1.5 Traditional Risk Factors do not fully explain CHD risk in SA

Although CHD mortality in SA is higher than in other ethnic groups, this excess

is not fully explained by our traditional concepts of CHD risk factors. Studies have repeatedly demonstrated a lower prevalence of risk factors such as hypertension, elevated LDL cholesterol, and smoking, and an increased prevalence of DM in SA[1,21,22]. Despite this a recent study of 200 cases and 200 controls that was conducted in India indicated an increased relative odds for MI of 5.0 among cigarette smokers, and 3.3 among hypertensives [26]. Furthermore, there were no differences in total cholesterol, or its subfractions between cases and controls [26]. These data suggest that some (eg. cholesterol) but not all of the traditional risk factors continue to be important in SA, while others less studied risk factors may be more important in this group. For example, an increased prevalence of late onset DM, IGT, insulin resistance, increased triglycerides, low HDL cholesterol (HDL-C), elevated Lp(a) and abdominal obesity is observed in urban SA[1,13,21,27], and appears to place them at an increased risk of developing CHD. **Although this clustering of multiple CHD risk factors has been described previously, the precise interplay in which a proatherogenic milieu is created remains unknown, and no study has explored a clear link between these markers and ATH in SA.**

● *Thrifty Gene Hypothesis*

SA predilection to disorders of glucose metabolism and the phenomenon of urban-rural differences in SA may be partially explained by the **thrifty gene hypothesis** which provides an anthropologic explanation as to why DM increases in prevalence in migrant populations who change from a rural to urban lifestyle. In

1962 Neel proposed that individuals subjected to harsh environments (starvation) developed insulin resistance as a protective mechanism, utilizing the least energy expending mechanism to store energy as fat rather than as glycogen in muscle during times of food abundance. This would enhance the probability of survival under adverse circumstances. However, migration to an urban (affluent) society where energy was in excess neutralized the protective effect of this gene and resulted in increased abdominal obesity and DM [28]. It has been hypothesized that a similar anthropologic and biologic mechanism may explain the higher prevalence of Syndrome X in several populations (i.e. SA, Hispanics, First Nations Canadians, aboriginal groups in other countries) who adopt a 'Westernized' lifestyle. Of these groups SA appear to be at the highest risk of developing CHD. The reasons why some individuals with Syndrome X develop CHD whereas others do not is unclear.

● *Diabetes and abnormalities of glucose*

IGT and DM are strong independent risk factors for CHD in SA and European populations. People with IGT are at increased risk of developing DM as well as CHD [29-31]. Emerging data suggest that people with moderately elevated glucose concentrations in the non-diabetic range may also be at higher risk for CHD [26,32]. SA have a predisposition to altered glucose metabolism with earlier progression from mild hyperglycemia, to IGT, to overt DM and appear especially susceptible to IGT and DM when compared to other populations [33,34]. In India the prevalence of IGT is similar in urban and rural environments (8.7% and 7.8%) yet a fourfold increased prevalence of DM is observed in the urban environments (8.2% vs 2.4%)[35]. Two

studies of SA and their risk factors found approximately a 10% prevalence of IGT and hyperinsulinemia [13,26] . This pattern is also observed outside of India in SA where the prevalence of late onset DM is 5 times higher in SA than in Europeans by the age of 55 (20% versus 4 %)[8]. The exact link between elevated glucose levels, insulin, and ATH is not known[36]. Insulin is released in response to elevated glucose levels and insulin resistance is a characteristic feature of abdominal obesity, IGT, and DM. While three population studies have demonstrated high fasting and 2-hr plasma insulin levels to be independent predictors of CHD risk in non-diabetic subjects[32,37,38], these results are not consistent across all studies. Insulin resistance is associated with high triglycerides and low HDL cholesterol, and is also associated with an increased concentration of plasminogen activator inhibitor-1 (PAI-1) which links it to impaired fibrinolysis[39]. The observation that SA have higher rates of moderate elevations in glucose, IGT and DM, and that this is associated with urbanization provides further support for the hypothesis that the increased susceptibilities to factors that increase the risk of diabetes, such as high fat diets, physical inactivity, and obesity are likely to be very important in SA.

● *Lipids*

Although elevated total cholesterol and LDL cholesterol are powerful risk factors for CHD in White Caucasians, this lipid abnormality has not been consistently associated with CHD in SA[2,13]. The lipid abnormalities tat have been observed, however , include elevated triglycerides and low HDL cholesterol - a pattern associated with insulin resistance [2,8,40-45]. The relationship of this

dyslipidemia and the development of ATH is not clear.

● *Abdominal Obesity*

Abdominal obesity is a marker of an increased risk of CHD, abnormal glucose-insulin metabolism, hypertension, low HDL-C and increased triglycerides[46-50]. Intra-abdominal fat, independent of BMI is more closely associated with blood glucose and insulin concentrations than is total body fat[51]. Although abdominal visceral fat is most accurately measured by abdominal CT scan[52-53], it is difficult to use this measure in epidemiologic studies, whereas simple measurements of the waist and hip diameter are reliable surrogates, and are closely related to clinical outcomes [36-37]. At any given level of waist to hip ratio (WHR), the prevalence of DM and insulin resistance are double in SA compared to whites [39-45], and both WHR and DM are independently related to CHD among SA [13,26,34].

● *Microalbuminuria*

Microalbuminuria has been demonstrated to be a predictor of CHD in both diabetics and nondiabetics [54,55] and may represent a subclinical marker of renal vascular damage. It is associated with hyperinsulinemia and increased fibrinogen, platelet adhesiveness and PAI -1 levels. [51-57]. No studies to date are available linking microalbuminuria and CHD in SA. Given the increased prevalence of IGT, DM and CHD in SA, microalbuminuria may represent a valuable and simple screening tool in identifying high risk individuals in this ethnic group who already have vascular damage.

● *Sedentary Lifestyle*

Observational studies indicate that physical inactivity is an independent risk factor for CHD[58]. Cross-sectional survey data from the UK indicate that physical activity levels in SA are low compared to Europeans[59] Although a high proportion of Canadians are sedentary (39%), no ethnic group specific data are available[60]. A sedentary lifestyle predisposes to obesity, hypertension, glucose intolerance, hypertriglyceridemia, and low HDL levels. The influences of physical activity on weight control, glucose tolerance, insulin sensitivity, blood pressure and HDL-C are favorable, and may reduce CHD future risk[58].

● *Dietary Factors*

The contribution of diet to the excess risk of CHD among migrant SA has not been studied extensively[61-63]. Urbanization in India and abroad has led to a transition from consumption of the traditional foods to a more refined, high fat, low fiber diet. The increased availability of carbohydrates and fats in the diet, along with the decreased dietary fibre and a more sedentary lifestyle likely leads to abdominal obesity and glucose metabolic abnormalities [64].Vegetarianism is much more common among SA than non-Asians and studies in India among SA and in the USA among whites show a significant negative correlation between vegetarianism and CHD. This suggests that **vegetarianism may offer protection to SA** [22.26,61]. Reduced vegetarianism, and adoption of diets high in saturated fats may help explain the higher rates of CHD in urban India and among SA abroad. Any comprehensive assessment of ATH predictors must include a valid assessment

of dietary intake to quantify total energy intake, total fat intake, and the percent of saturated fat. In SA, an accurate quantitation of the carbohydrate intake as part of the total energy intake is essential. **No study of SA immigrants has examined diet as a risk factor for ATH. Therefore, improved dietary assessment protocols exploring vegetarianism, total and saturated fat content, fibre, antioxidants, and the glycemic index of food.**

Emerging Risk Factors

● *Lipoprotein (a)*

Lipoprotein (a) (Lp(a)) is a genetically determined plasminogen-like apolipoprotein that may be related to both atherogenesis and thrombogenesis. Lp(a) has been demonstrated to be a powerful independent risk factor for premature ATH including CHD, stroke and peripheral vascular disease among whites in several, but not all studies[65-68]. Preliminary data from cross-sectional studies indicate that Lp(a) may vary significantly between ethnic groups yet the significance of this is not known. Cross-sectional studies indicate that Lp(a) is significantly higher in SA compared to whites or Hispanics, although the impact of this on the development of ATH or thrombosis remains unclear[69] A recent migration study confirmed that urban SA in the UK when compared to their siblings in rural India had similarly elevated levels of Lp(a) despite major differences in their glucose and lipid profiles, which lends support to the hypothesis that Lp(a) is not influenced by migration[27], but is a consequence of genetics.

● *Impaired Fibrinolysis*

Recent studies in whites indicate that impaired fibrinolysis predicts future myocardial infarction[70-72]. Based upon the results of studies to date, it is reasonable to hypothesize that SA have a higher prevalence of impaired fibrinolysis which makes them susceptible to CHD. Lp(a) is homologous to plasminogen and competes with it for binding to endothelial cells and possibly to fibrin, and therefore has the potential to decrease fibrinolytic activity both at cell surfaces and on clots. In view of the observation that SA have elevated levels of Lp(a), this could result in impaired fibrinolysis. In addition, two cross-sectional studies have reported PAI-1 levels to be higher in SA compared to Europeans[73.74]. Although no "global" tests of fibrinolysis were performed, these elevated PAI-1 levels have the potential to cause impaired fibrinolysis. *It is likely that impaired fibrinolysis in SA may occur by two potential mechanisms i) excess Lp(a) may compete with plasminogen and impairs its conversion to plasmin and ii) increased levels of plasminogen activator inhibitor -1 (PAI-1) inhibit the activity of endogenous tissue plasminogen activator and inhibit the formation of plasmin. Both mechanisms could increase the likelihood of arterial thrombosis.*

● *Socioeconomic Status and Psychosocial Factors*

Several studies including one that we conducted in India, have reported an inverse relationship between markers of low socioeconomic (SES) (i.e. income, education, poor housing) and cardiovascular mortality[26.75] . Lower SES may also be associated with less knowledge about disease prevention and unhealthy

lifestyles[76] . To understand the inverse relationship between SES and cardiovascular disease, the role of psychosocial factors must be considered. There has been little research into the effect of migration and acculturation on SA and the potential stresses this may cause. In a qualitative study on health beliefs and attitudes among first generation SA migrants to the UK, the two sources of stress that were identified included long working hours, and the divergence of children's behavior from their parents expectations. In a survey from Glasgow, Scotland of SA, stress was attributed to long working hours, low income, crowded housing, and perceived lack of social support of women[59]. Lack of social support has been shown to be an independent risk factor for CHD and all-cause mortality in several epidemiologic studies [77]. While it is uncertain how these stressors relate to CHD, the process of migration along with social isolation may increase the levels of depression which has been implicated with CHD. Recent studies among whites indicate that measures of hostility (a component of Type A behavior) relate to CHD[77–80]. Higher levels of hostility, as measured by the Cook-Medley Hostility Scale have been positively associated with health behaviors that can increase the risk of CHD, including smoking, lack of exercise and consumption of animal fat, sugar and alcohol. The stressors associated with migration to a new social and cultural environment, and the process of acculturation in Canada impact on the health of migrants. Little is known of the relationship between these stressors and the development of CHD. **This study will be the first to systematically address this question in this population.**

● *Other Factors*

The role of low birth weight, and relative poverty at infancy followed by affluence in later years[81], the Barker Hypothesis has been proposed as an explanation for SA high rates of CHD. As well, angiotensin converting enzyme (ACE) gene polymorphism[82] , and hyper-homocysteinemia[83] have not been extensively studied in SA populations. Recently evidence suggests that obese carriers of the codon 972 insulin receptor substrate -1 gene possess a clustering of metabolic cardiovascular risk factors associated with insulin resistance [84], and an association between the DNA variation of chromosome 1q with the WHR has been demonstrated in a homogeneous North American population [85]. **Both the Barker hypothesis and these genetic markers have the potential to be valuable links in our understanding of SA unique propensity to develop IGT and DM.**

Table 1-1: Disability-adjusted life year (DALY) lost (hundreds of thousands) from ischemic heart disease in 1990[4,5] (Projected data from the World Bank)

Country	Male	Female
India	49.5	31.9
Africa	6.7	5.4
China	24.8	17.6
Market Economies	56.4	37.2
Total World	249.6	175.0

Note that DALY lost from IHD in India is only slightly lower than all the market economies combined.

Table 1-2: Estimated and projected mortality rates (per 100,000) by sex, for major causes of death in India

	1985		2000		2015	
	Male	**Female**	**Male**	**Female**	**Male**	**Female**
All causes	1158	1165	879	790	846	745
Infectious	478	476	215	239	152	175
Neoplasms	43	51	88	74	108	91
Circulatory	**145**	**126**	**253**	**204**	**295**	**239**
Pregnancy	0	22	0	12	0	10
Perinatal	168	132	60	48	40	30
Other	239	293	260	285	167	171

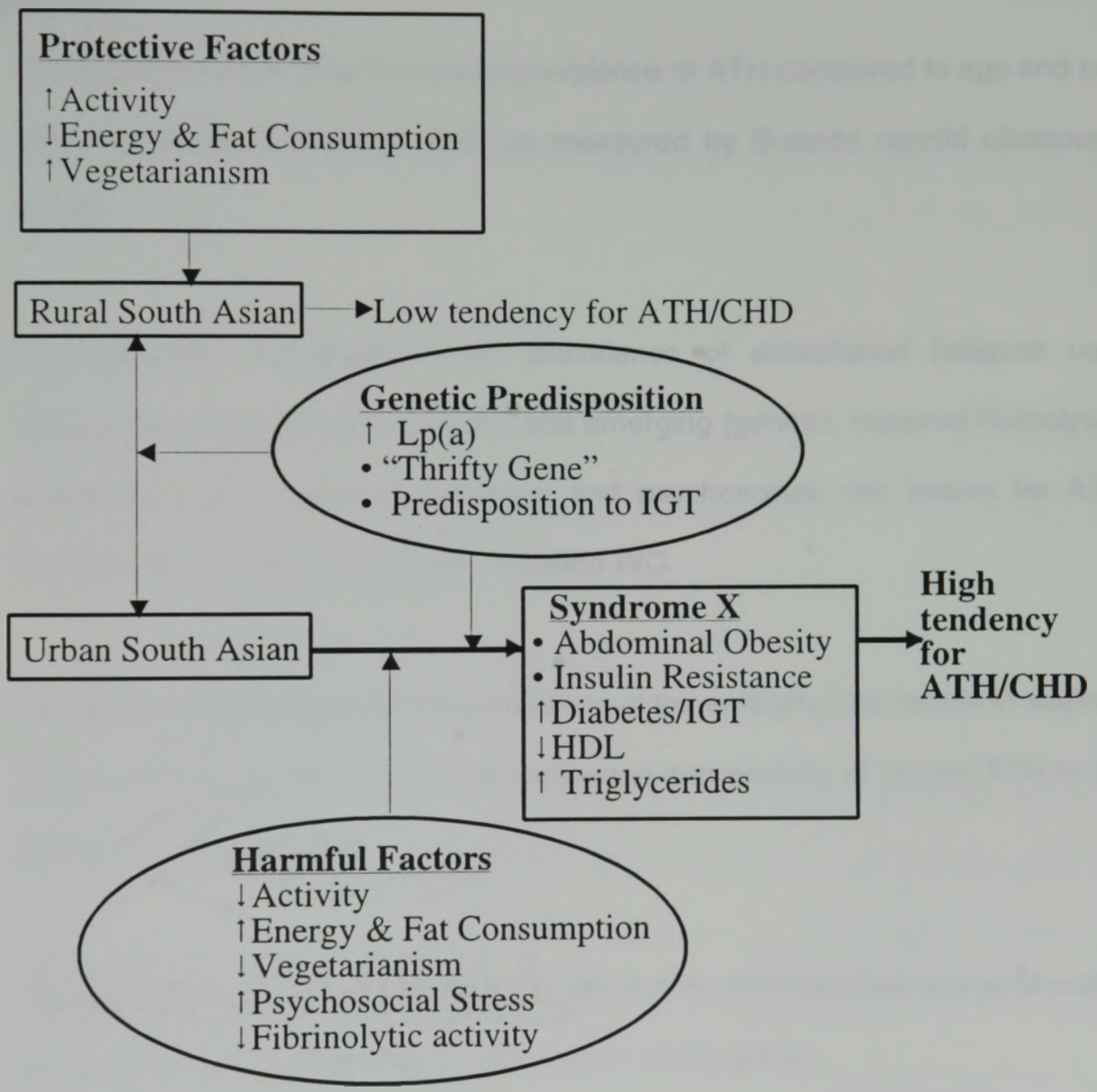
Note that mortality rates from circulatory causes are projected to double in 30 years in India. This contrasts with a decline in CVD in many western countries, including Canada.

Table 1-3: Coronary Artery Disease Mortality Among South Asians Overseas[2,17]

COUNTRY - GROUP	PERIOD OF SURVEY	STANDARDIZED MORTALITY
Singapore	1954-1957	400
South Africa - Women	1955-1957	149
Singapore	1957-1978	300
South Africa - Men	1968-1977	145
Fiji	1971-1980	300
Trinidad - compared with Africans	1977-1984	260
Trinidad - compared with mixed descents	1977-1984	820
London	1979-1983	150
England & Wales - Women	1979-1983	146
England & Wales - Men	1979-1983	136
England & Wales - Men aged 20-29 years	1979-1983	313

* Standardized mortality in the reference indigenous population is 100

Figure 1-1: Hypothesis for Premature CHD in South Asians



Chapter 2 - Study Objectives, Design, and Outcomes

Objectives:

i) To determine if SA have increased prevalence of ATH compared to age and sex matched White Canadians (WC) as measured by B-mode carotid ultrasound (CUS).

ii) To determine differences in the prevalence of established (tobacco use, lipoproteins, hypertension, glucose) and emerging (genetic, impaired fibrinolysis, metabolic factors, detailed nutritional and psychosocial) risk factors for ATH between SA and age and gender matched WC.

iii) To determine the independent contributions of the emerging risk factors in addition to the established risk factor to the presence and severity of carotid ATH in SA compared with WC and

iv) To determine if important differences in risk factors, ATH and their interrelationship exist between men and women within each ethnic group.

2.1 Study Design:

The design of this study encompasses two major components

i) Cross-sectional prevalence study of risk factors for ATH, in two randomly identified populations in Ontario.

ii) An integrated retrospective longitudinal assessment of the impact of these risk factors on ATH over time.

2.2 Target Population and eligibility

i) People of SA origin defined as individuals whose ancestors originate from India, Pakistan, Bangladesh, or Sri Lanka. All grandparents and parents must be of SA origin. Only participants between the age 35 and 75 years who have lived in Canada for at least 5 years will be included.

ii) The reference population will include WC whose country of origin is Canada, USA or European countries, excluding First Nations individuals. All grandparents and parents must be of Canadian or European descent. Only people between the ages of 35 and 75 years who have lived in Canada for more than 5 years will be included. Volunteers are not accepted into the study to minimize the healthy volunteer bias.

Exclusion Criteria

People with severe debilitating chronic illnesses (cancer, renal or hepatic failure) will be excluded as their diseases may change lifestyle or alter the risk factors for vascular

disease. Individuals of Chinese, Japanese, other South East Asian countries and Black Africans will be excluded. Individuals with clinical vascular disease are not excluded.

2.3 Sampling Frame

The sampling frame will be created by extracting all individuals with SA surnames in the Hamilton, Toronto, and surrounding regions from a compact disc (CD) program, CD Canada 96. CD 96 is a comprehensive commercial telephone directory database developed by ProPhone Canada[102] created from all public telephone directories in Canada. The CD allows one to search a specific geographic area in Canada by province or city. To search the CD for specific surnames, the names must be keyed into the computer and matches will provide lists of names in that specified geographic area. We have generated a comprehensive list of SA surnames from the East-West directory a local SA unrestricted cultural community directory [103] and from lists obtained from the Council of Indo-Canadian Communities (CICC) membership list of community organizations. SA surnames are 96% sensitive and 95% specific for SA ethnicity[12], which enables classification of individuals living Canada by SA ethnicity by using public telephone directories. This method was validated in the SHARE pilot study, and in studies we conducted utilizing the Canadian Mortality Database. Probability systematic random sampling will be used to identify SA households from the sampling frame.

2.4 Recruitment of WC

As each postal code generally identifies a cluster of dwellings in a similar geographic region, WC households will be identified by the list of households generated

from the identical postal code as the SA respondent. Prior to sampling, this list will be scanned and unique SA and Chinese names will be removed from the list. The remaining households will be representative of non-Asian surnames. Potential subjects will then be sampled randomly and approached in the same manner in which the SA were approached. If no respondents are located through this method, the last digit of the SA postal code will be changed at random to generate a new list of possible reference households. As non-Asian surnames may not be representative of the eligible reference population they will be screened at the time of telephone contact for ethnic origin, and individuals who are not part of our target population will be excluded. The method of choosing which subject to approach from the list of names identified from the postal code match will be based on a random selection. The selected household will be matched by gender to the SA respondent (Figure 2).

2.5 Sampling

A letter tailored to the gender of the individual identified will be mailed to each selected household (Appendix 1) and follow up telephone calls will be placed 4 days after the original letter is sent. If more than one eligible subject lives within the household, the member with the earliest birthday in the calendar year will be selected. Up to twelve attempts will be made to contact the subject by telephone, and at least three calls will be placed during the evening hours, and three calls on weekends, to ensure the greatest likelihood of subjects being at home. Subjects who are not reached are classified as non contacted. Subjects who are contacted will be screened for eligibility. Those who are not eligible will be excluded. Those who are eligible but do not

choose to join the study are classified as non-responders. Basic demographic, socio-economic and linguistic information from the respondents and nonrespondents will be collected to better characterize this group and assess non-responder bias. Eligible and consenting subjects will be invited to an appointment at the study centre in each city (Hamilton General Hospital, McMaster University, Hamilton and St. Michael's Hospital, University of Toronto, Ontario). Non-diabetics will be asked to fast overnight.

2.6 Hospital Visit

Ethnic origin will be further confirmed by the interviewer at the time of the hospital visit on the basis of name, country of birth, and appearance. After written informed consent (with additional consent for DNA analysis) the following will be performed:

i) Obtain fasting blood samples, and cuff-occlusion samples for fibrinolytic parameters*, collect random urine sample for microalbuminuria

ii) Administration of an oral glucose load: 75 grams (non-diabetics only)

iii) Self administered questionnaire to collect information on demographics (age, sex, religion, employment status, educational level), lifestyle (tobacco including brand to estimate tar content, alcohol, physical activity, measures of SES, and psychosocial factors), medical and family history (diabetes, hypertension, hypercholesterolemia, cardiovascular disease) and subjects knowledge about risk factors

iv) Physical measurements: Weight, height, waist and hip circumference, blood pressure in the right arm and ankle, and heart rate recorded by standardized methods (Table 2-1).

v) B-mode CUS for presence of plaque and quantitative IMT (see below) and lumen diameter.

vi) Resting 12 lead electrocardiogram (ECG) blindly coded for significant Q waves (Minnesota Code 1-1 and 1-2) [104] and left ventricular hypertrophy[105].

vii) Formal dietary and psychosocial assessments.

Study Outcomes:

2.7 Ultrasonography

Rationale for the use of the carotid ultrasound to measure subclinical ATH

The CUS can be used to detect non-invasively the presence of both very early and advanced ATH. Pathological and epidemiological data support the use of CUS to detect early-stage carotid ATH. There are several reasons why CUS is a valid and important surrogate marker for the development of clinical outcomes and appropriate for use in South Asians.

i) a strong relation exists between ATH in the carotid and the coronary arteries, as demonstrated by autopsy [86-87], and angiographic studies [88-91]

ii) asymptomatic carotid artery disease measured by increased intimal medial thickness (IMT), detected by CUS, has been shown to be a good predictor of CHD, and stroke independent of classical risk factors [92]. For each mm increase in IMT the risk for MI increases 2.14 fold (95% CI=1.08-4.26) [93];

iii) risk factors that predict clinical CHD also correlate with carotid ATH [94]

iv) interventions that prevent CHD e.g. lipid lowering, have also been shown to simultaneously reduce clinical events and carotid and coronary ATH [95,96], and

v) reduced insulin sensitivity (insulin resistance which is prevalent amongst South Asians) has recently been demonstrated to be an independent predictor of ATH [97].

Thus, IMT measured by the CUS is a valid surrogate for clinical events. It identifies subclinical ATH, therefore it is useful in studying early disease changes thereby increasing the sensitivity of epidemiologic studies. CUS is now being used in several large studies such as ARIC [98,99] in 16,000 subjects, CHS [100] with 4500 subjects, IRAS with 1400 subjects [97], and several randomized trials including the Canadian SECURE trial[101] , an MRC funded study of 735 subjects. In our studies the reproducibility is comparable to the published experienced from Bowman-Gray, a world leader in this methodology. It can also be used as a qualitative variable identifying those with and without specific abnormalities (plaques of specific size, lumen diameter). Therefore the B-mode CUS is a sensitive and efficient approach to conducting epidemiologic studies

linking risk factors to both *early* and *late* ATH.

ATH will be assessed by standardized B-mode CUS. The scanning protocol is similar to that used and validated in several other large studies[96,100,101,108]

i) Instrumentation: High resolution ACUSON/ACOUSTIC RESPONSE TECHNOLOGY ART 1 colour flow imaging system, equipped with a 7.5 MHz broad band width frequency carotid probe, Panasonic Super VHS will be used in Hamilton and Toronto.

ii) Scanning protocol: A standardized imaging protocol will be used. The CUS will be performed by trained technicians who will scan the near and far wall of the extracranial carotid arteries bilaterally during the hospital visit. Each carotid artery will be divided into 3 segments: the common carotid artery, the carotid bifurcation, and the internal carotid artery (6 segments/artery and 12 segments/subject). The arteries will also be examined for compliance according to standardized methods [98]. We intend to develop a program to measure lumen size, by standardizing anatomic landmarks, as there is coronary angiographic evidence to suggest that SA may have "small arteries" [109].

iii) Reading Protocol: A standardized reading protocol will be used. Reading and measurements will be performed by trained sonographers. The sonographers will be blinded to the ethnic origin of the subject at the time of the reading to minimize

measurement bias. The complete videotaped US examination for each patient will be initially reviewed qualitatively. The frames from each arterial segment showing the thickest plaques, will be digitized and measurements will be obtained. **The primary outcome measurement is the plaque (defined as an atherosclerotic lesion with an IMT>1.5 mm) prevalence and the secondary measurement is mean of the maximal IMT averaged from measurements at 12 preselected segments in the carotid arteries.** Scanning and reading techniques are based on methods developed from studies in the US National Heart, Lung and Blood Institute's Multicenter B-mode Ultrasound Assessment Trial [110-112] and further validation and improvements of this technique in the MIDAS [113], ARIC [96], ACAPS[114], CHS [100] and SECURE studies [101].

iv) Experience of Sonographers and Reproducibility: Study sonographers require intensive training and certification. Our technicians have received this training at the Division of Vascular Ultrasound Research, Bowman Gray School of Medicine, Winston-Salem, North Carolina and a customized reading station has been developed locally, to reflect specific equipment and patient characteristics in this study.

2.8 Methodology for Laboratory Tests

Each centre will be provided with the necessary materials including sample tubes, transfer vials, needles and vacutainer tube holders, labels, plastic bags, and absorbent

strips. Coagulation and insulin samples must be frozen and shipped on dry ice. Fasting blood samples: include **total cholesterol, triglycerides, HDL, LDL, glucose, insulin, euglobulin lysis time, non-esterified fatty acids** (NEFA), **TPA antigen** and **PAI-1**. A random urine for **microalbumin** and **creatinine** will be collected. After cuff occlusion for 10 minutes a repeat PAI-1 sample will be drawn. By using a methodology that stresses the fibrinolytic system (cuff occlusion of the arm for 10 minutes), and performing assays that reflect both global fibrinolytic capacity (euglobulin lysis time (ELT) plasmin alpha antiplasmin (PAP) complexes and components of the fibrinolytic system (PAI-1, TPA antigen) we will be able to test the relationship between levels of Lp(a), PAI-1, and fibrinolytic activity.Post 75 g glucose load: blood will be drawn for **glucose, triglycerides, insulin** and **NEFA**. At this time blood is also drawn for **complete blood count, glycosylated hemoglobin, albumin, Lp(a), fibrinogen, homocysteine and Factor VIIc** (Figure 3). Blood will also be stored at - 70 degrees Celsius for other future analyses of DNA, and other analysis relating the antioxidant hypothesis (T-BARS and Vit E levels) to CHD. All blood measurements will be analysed blindly in a central laboratory in Hamilton. **A random 10% from each ethnic group will be requested to undergo repeat blood analyses, 6-12 months after their initial assessment to statistically correct for regression to the mean of all risk factors**, thus minimizing dilution in estimating the strength of the relationship between a given risk factor and ATH (regression-dilution bias).

2.9 Dietary Assessment

Food frequency questionnaires (FFQ) are currently the instrument of choice for dietary assessment in large epidemiologic investigations. However, the use of existing FFQ's and nutrient composition tables, designed for the general Canadian population, are inadequate for assessing diets in a SA population. There are considerable differences in recipes and ethnic foods between the two groups. It is proposed that dietary information for this study be collected using two methods:

i) Three 24 hour recalls: The participants will be asked to complete three separate 24-hour recalls, one at the clinic and two subsequently in a predetermined random manner, over the telephone. All interviews will be conducted by trained interviewers, the data collection forms and manuals for which have already been developed for the pilot study. This method of dietary assessment is the "gold standard" and is the most cost efficient design for a diet validation study [106].

ii) Self administered FFQ

All participants will be asked to complete a self-administered FFQ. The WC subjects will complete a standard self-administered FFQ, developed by Jain et al[107] , which is being used by the Canadian Cohort Study of Diet, Lifestyle and Health. The SA will complete a FFQ developed by our group for SA food items based on the information obtained from the pilot study where four day food records were collected from a random sample of 30 SA (Chapter 5) . These data will form the basis for developing a FFQ suitable for this population, representing the main

contributors of energy, total and saturated fats, total sugar, fiber etc. The SA FFQ will be validated against the three 24 hour recalls collected from the same subjects. Nutrient analysis will be based on values from the Canadian Nutrient File, expanded for SA foods by the study nutritionist. This will be the first SA specific FFQ to be validated and could have widespread epidemiologic use in future studies (See Chapter 5).

2.10 Psychosocial Assessment

A detailed assessment of psychosocial factors tapping the domains of self-esteem, hostility, depression, job stress, racism, and social support will be undertaken in the form of a "Life Stress and Satisfaction" questionnaire which has been developed and validated in 29 randomly sampled SA and WC from the SHARE pilot study (See Chapter 6). The identification and impact of these stressors will be examined in the context of their relationship to the development of premature ATH, and other unhealthy lifestyle behaviors. The steps of validation and reliability testing of the instrument are found in Tables 6-8. Concurrent to the administration of this questionnaire to all study participants, a qualitative susbstudy will be conducted in a subset of the SHARE population to identify issues concerning acculturative stress (Chapter 7). The data from this substudy will be used to revise the Life Stress and Satisfaction Questionnaire.

2.11 Translation of Study Instruments:

During the telephone interview, subjects will be asked if they are able to read and write English. If unable, their "first" language will be ascertained. Apart from English,

the questionnaire will be available in the three most common SA languages (Punjabi, Gujarati, Tamil) spoken in Canada based on the 1991 Census data (the questionnaire will be translated into the 3 most common SA languages, and back translated to ensure its validity). The 1991 Census indicated only 9% of the all SA living in Canada were illiterate in English, and this increased with increasing age[7]. If necessary a translator or an English speaking family member will be sought. It is expected that only a minority of subjects will require translation; every attempt shall be made to include them in the study to minimize potential biases.

2.12 Physical Examination:

The physical assessment section of the study evaluates indicators of current health status and takes approximately 10 minutes to complete. Standard yet simple measurements will be performed in duplicate by the same preceptor on each participant. Both the intra-and inter-observer levels of agreement for these measures will be assessed by a kappa score. The specific details of the physical measures are found in Table 2-1.

2.13 Follow-up

After the clinic visit all participants are given a brochure outlining the major risk factors for cardiovascular disease, and SA are given the SA specific heart health pamphlet. The participants will be informed of all clinically important results and general recommendations will be made, if necessary subjects will be advised to see their family

doctor. Participants will also be asked to consent to using their health card number for future long term follow up by record linkage and repeat studies.

2.14 Feasibility and Logistics

During June /July 1995 (summer months), we conducted a feasibility study in Hamilton. The results of which may be found in Chapter 8. This data from our feasibility study are being used to further refine our sampling and recruitment process, to refine and further validate our questionnaires, and has been used to develop estimates of staffing requirements for the proposed study. We have also obtained the collaboration of various divisions of Statistics Canada (in developing the sampling methodology, forms designs and nutritional analyses) and **have conducted preliminary validation of the nutritional and psychosocial instruments.**

Figure 2-2: Probability Sampling Methodology

Creation of Frames of SA and Non-Asian Canadians:

Create a file from the East-West directory and the community membership lists of distinct SA names and enter them into the CD Programme (file I).

⇓

Create a file from the CD-Canada 95 of all names which fall in the Toronto, Hamilton and surrounding communities to be included in the study (file ii).

⇓

Match the files in I with ii on last names to separate records on file ii that have the same last names as on file I.

⇓

Sampling frame of SA population and the remaining records will form the Non-SA population.

Selection of a sample of SA and WC by Systematic Random Sampling:

Sort the SA frame by postal codes -implicit stratification by geographic areas

⇓

Count the number of records on the frame, Let it be "N"

⇓

Let "n" be the size of the sample we desire to select of SA. This number is greater than the number of responses wanted for the study to account for the possible non-contacted, non-eligible, and non-responders. The sample size also is augmented to adjust for screened out non SA and non Canadian/European white households.

⇓

Calculate d=(N/n - ratio of number of records in the frame divided by the size of the SA sample we desire to select)

⇓

Select a random number between 1 and d, let it be R.

⇓

Select the Rth, (R+d) th, (R+2d)th... records from the sampling frame until the end

⇓

Records of non-SA generated by the identical postal codes as the SA selected above will give the reference sample

Selection of Non-Asian Households:

Scan the list of names generated from the SA postal codes and remove unique SA and Chinese names (Step a)

⇓

Use a random number table to determine the exact household to be selected

⇓

Send introductory letter, followed by telephone contact 4 days later using the same procedure as for SA

⇓

Match the White household for gender to the identified SA respondent. Screen for eligibility and response

⇓

If not contacted after 6 attempts, non-eligible, or non-responder, randomly select another household from the list in step a.

⇓

If no respondents are yielded from this postal code matching, change the last digit of the original SA postal code to generate a new list of potential non-SA households.

Figure 2-3: Specific Assays

Laboratory Test	Method
PAI-1	Chromogenic Assay kit for PAI-1: Spectrolyse/PL PAI-1 is a two-stage indirect enzymatic assay.
Lp(a)	Quantitative determination performed by automated immunoprecipitin analysis.
Fibrinogen	Clauss method
Euglobulin Clot Lysis Time	Lysis of a plasma clot that has had inhibitors reduced
TPA-antigen	Enzyme immunoassay (ELISA): Asserachrom tPA (Wellmark Diagnostics)
Plasmin-antiplasmin complexes (PAP)	Enzyme immunoassay for plasmin/alpha antiplamin enzyanost PAP mices (Behring Diagnositics)
Complete blood count:	Automated cell counter.
HBA1c	765 Glycomat determination uses low pressure cation exchange chromatography in conjunction with gradient elution to separate human hemoglobin subtypes
Insulin	I^{125}-labelled insulin competes with the subjects insulin for sites on the insulin specific antibody immobilized to the wall of a polypropylene tube. The antibody fraction is isolated by decanting the supernatant, the gamma counts being inversely related to the amount of insulin present.
Glucose	Glucose oxidation is catalyzed by glucose oxidase to form hydrogen peroxide and gluconate. Oxidative coupling catalyzed by peroxidase in the presence of chromogens produces a dye, measured by reflected light.
Cholesterol	Cholesterol esters in the presence of cholesterol ester hydrolase and cholesterol oxidase form cholesterol and hydrogen peroxidase, in proportion to the original cholesterol concentration.
HDL-C	Precipitated with dextran sulphate and a calcium salt, then measured the same as cholesterol.
Triglycerides	Hydrolysed by lipase to glycerol and fatty acids. Glycerol is phophorylated by glucose kinase, and is oxidized forming hydrogen peroxide which is measured by production of a dye at 540 nanometers (nm).
Non-esterified fatty acid	Treated with acyl CoA synthetase, ATP, magnesium cations and CoA, produces Acyl CoA. which is oxidized by Acyl CoA oxidase to hydrogen peroxide, while in the presence of peroxide forms a coloured adduct measured at 550 nm.
Albumin	Addition of bromcresol green forms a complex measured at 630 nm.
Homocysteine	High-pressure liquid chromatography

Table 2-1: Physical Measurement Methods

Test	Description
Blood Pressure	A standard mercury sphygmometer will be used. BP will be recorded from the right upper arm with the subject seated quietly for at least 5 minutes. The cuff should be applied with its lower border 2-3 cm above the antecubital space. Systolic pressure is determined by the first heard sound (Korotkoff phase I). Diastolic pressure is recorded at the level when the sound just disappears (Korotkoff phase V). Two readings should be recorded - one at the beginning and one at the end of the interview. The average of the 2 readings to the nearest whole number will be taken as the BP.
Height	Standing height will be measured with the subject in bare feet, back square against a wall and eyes looking straight ahead. A set square resting on the scalp and a tape measurement from the wall will be used to measure height to the nearest 0.5 cm.
Weight	Weight will be measured in undergarments using a platform scale, to the nearest 200gm. The scale will be standardized to 0 before each use.
BMI	BMI will be calculated by dividing weight in Kg and by height in metres.
Waist Circumference	Waist circumference will be measured to the nearest cm, using a standard tape measure. It will be measured over the unclothed abdomen at the smallest diameter between the costal margin and iliac crest. The tape measure must be kept horizontal and just tight enough to allow the little finger to be inserted between the tape and the subject's skin.

Chapter 3: Statistical Issues

The primary objectives of this study proposal are:

i) To determine if South Asians (SA) have increased prevalence of ATH compared to age and sex matched White Canadians (WC) as measured by B-mode carotid ultrasound (CUS).

ii) To determine differences in the prevalence of established (tobacco use, lipoproteins, hypertension, glucose) and emerging (genetic, impaired fibrinolysis, metabolic factors, detailed nutritional and psychosocial) risk factors for ATH between SA and age and gender matched WC.

iii) To determine the independent contributions of the emerging risk factors in addition to the established risk factor to the presence and severity of carotid ATH in SA compared with WC and

iv) To determine if important differences in risk factors, ATH and their interrelationship exist between men and women within each ethnic group.

3.1 Differences in the prevalence of atherosclerosis between SA and WC men and women

The B-mode carotid ultrasound as a surrogate measure of CHD is a sensitive and efficient method of linking risk factors to both early and late ATH. In addition to being a useful measurement of ATH, utilizing B-mode CUS decreases sample size as it is a continuous variable that is available in all subjects.

Based on the Atherosclerosis Risk in Community (ARIC) study of 10,214 [99] individuals aged 45-64 years reported that the prevalence of carotid plaque was 34.4 % in whites and a mean IMT of 0.79 mm (+/- 0.20). There are no data on plaque prevalence or IMT in SA. Given that SA have 1.4 times the relative risk of CHD compared to whites [14], we assumed a similar excess of plaque prevalence. With 400 subjects in each ethnic group, there will be 90% power to detect a 1.32 relative increase and 80% power to detect a 1.28 relative increase in plaque prevalence. Plaque prevalence in ARIC was 40.1% in men and 28.3% in women. Similar differences (relative risk of 1.32) could be detected at 90% power in the overall group of 400 women versus 400 men. Assuming a 1.4 higher plaque prevalence rates among both SA men and women (49% and 35% respectively) compared to WC men and women (40% and 28%), we can detect differences in relative risk of 1.35 between SA males versus females and 1.47 in WC men versus females with 80% power (Table 3-1). In the ARIC study the differences in mean IMT between White men and women was 0.1 mm. Differences of 0.05 mm (about a 6.3% relative difference) could be detected between

SA and WC at 90% power in the overall group of 400 versus 400 subjects and 0.04 mm at 80% power. Similar differences at the same power can be detected between men and women. Differences in IMT of 0.058 mm or 0.068 could be detected at 80% or 90% power respectively comparing women and men within each ethnic group. Similar differences could also be detected between ethnic groups in each gender (Table 3-2). The differences in prevalence of plaque between SA and WC will be examined utilizing logistic regression controlling for age and gender.

3.2 Differences in the prevalence of risk factors between and within SA and WC

400 subjects in each group also provides high power (80%) to detect plausible differences in risk factors such as diabetes (prevalence of DM and IGT is 10% in WC), between ethnic groups: 80% power to detect a 1.67 fold excess in diabetes and 90% to detect a 1.79 fold excess. Within ethnic groups gender differences (200 males versus 200 females) in risk factor prevalence (i.e.10% prevalence) relative differences of 1.99 at 80% power and 2.17 at 90% power could also be detected. Prior to statistical analyses of the data, the distributions of variables will be plotted to check the assumption of normality. If the variables are not normally distributed (eg triglycerides or Lp(a)), they will be appropriately transformed (eg natural log) before conducting statistical analyses. Categorical variables will be examined using logistic regression , and continuous variables will be assessed using multiple linear regression controlling for age and gender.

3.3 The relationship of emerging risk factors to ATH

We expect that several "emerging" (fasting glucose, Lp(a), waist/hip ratio, HDL-cholesterol) risk factors will predict ATH by IMT over "traditional" (hypertension, smoking, cholesterol) risk factors in SA. A hierarchical linear regression model will be fit predicting IMT on "traditional " and "emerging" risk factors and their interactions with ethnic group. We will test for collinearity amongst these risk factors before fitting this model. The order of testing in the model will be *emerging risk factors by ethnic group*, *traditional risk factors by ethnic group*, and the *main effects of emerging risk factors*, while controlling for traditional risk factors. A random effects model will be used given the random sampling of subjects. The methods of Gatsonis and Sampson [115] uses a series expansion to determine the exact power required to identify independent predictors assuming a multivariate linear model to show a minimal desirable level of the partial multiple R^2. Using this method a total sample size of 800, will provide 90% power to detect a partial R of 0.16 ($R^2 = 0.03$) testing the independent predictive value of the emerging risk factors and their interactions, controlling for traditional risk factors and their interactions (Full Model). Secondary analyses will be performed to determine the relationship of key dietary, and psychosocial factors to ATH to examine if these relationships are linked through the above emerging and traditional risk factors or are independent predictors.

Table 3-1: Relative Risk of Plaque Prevalence that can be detected in SA at 80% and 90% power

Plaque Prevalence in the group with the lower rate	Comparison	Power	Number of Subjects per group	
			200	400
28%	WC women vs SA women	80%	1.47	-
34%	All WC vs All SA or All women vs All men	80%*	-	1.28
		90%*	-	1.32
39%	SA women vs SA men	80%	1.35	-
40%	WC men vs SA men	80%	1.35	-

* Main Comparisons

Table 3-2: Mean Difference in Imt (Mm) That Can Be Detected Between WC and SA Or Men Versus Women Overall and in Subgroups

Power*	Number of Subjects per group	
	Subgroups	Main Groups
	200	400
80%	0.058	0.040
90%	0.068	0.050

* assuming a standard deviation of 0.20 mm at 80% and 90% power using a 2alpha = 0.05

Chapter 4 - Development of Study Instruments - General Questionnaire:

The SHARE questionnaire was created to acquire information on participants risk factors for cardiovascular disease. Information on ethnic background, socio-economic status, education, lifestyle factors such as physical activity, alcohol consumption and smoking, as well as traditional cardiovascular risk factors including a history of hypertension, diabetes, and hypercholesterolemia is collected in a self-reported format. A nutrition and medication use section is also incorporated into the questionnaire. A section at the end of the questionnaire inquires about difficulties participants may have encountered with the readability or clarity of the questions (Appendix 2).

The General Questionnaire was compiled utilizing previously validated sections from other questionnaires which have been used in prior longitudinal studies of cardiovascular risk factors. As no one previously validated questionnaire was deemed to be appropriate for the multiethnic population of SHARE, a new questionnaire was designed. Utilizing sections from existing instruments appears to be an acceptable approach in the creation of a new measurement instrument. The SHARE questionnaire included unique questions pertaining to ethnicity, religion and SA specific diet, and smoking habits.

In Table 4-1 the source of the questions compiled in the SHARE questionnaire are shown. The questions were chosen for their appropriateness of content, and past use in large population-based studies.

Table 4-1: SHARE Questionnaire*

Domain	Method	Source
Ethnic Group	Unique Name Self-Report Country of Origin Ancestors origin	Mortality Data Base, Statistics Canada[12], 1996 CHD in South Asians in UK[13], 1991 Hypertension in Afro-Caribbeans[116], UK 1993 Survey Chinese Canadians[117], 1993
Physical Activity	Seven day recall of habitual physical activity	Five-City Project[118] Canadian Study Diet, Lifestyle, and Health[119]
Alcohol	Seven day recall	Canadian Study Diet, Lifestyle, and Health[119]
Smoking	Type of tobacco Frequency Years Filter/Nonfilter	Epidemiology Standardization Project[120] European Prospective Investigation of Cancer (EPIC)[121]
Medical History	Rose Questionnaire - Angina - Claudication	MRFIT[122,123]
Diet	Food Frequency	Canadian Study of Diet, Lifestyle and Health[119]
Menopause	Premature menopause Hormone replacement therapy	Nurses' Health Study[123] Canadian Study Diet, Lifestyle, and Health[119]

The format of the questionnaire was based on Frame maker, an integrated publishing software program. A copy of the questionnaire is provided in Appendix 2.

This was reviewed by the Survey and Methodology group, and the Questionnaire Design Resource Centre at Statistics Canada, and subsequently modified to improve its clarity and readability.

This self-administered questionnaire was pretested in 51 randomly sampled SA and WC. The mean time to completion was approximately 15 minutes. A study monitor was available to assist with any difficulties encountered during its completion. This is usually a standard practice when key measurements are self0administered as opposed to interviewer-based. This was felt to be extremely important in the SA population of SHARE as potential issues of comprehension, and regular use of the English language exist. Therefore at the end of each questionnaire participants were asked:

- Were any questions difficult to understand?
- Were the instructions helpful?
- Was the length appropriate?
- Do you have any suggestions to improve this questionnaire?

The responses are shown in Table 4-2. Although the majority of participants from each group did not report difficulties with the questionnaire, a substantial number of South Asians did not complete this section of the questionnaire. This may reflect a lack of comprehension of the questions, a reluctance to criticize the questionnaire, or responder burden due to the length of the questionnaire. However all participants responses were checked at the time of data entry for face validity and consistency of

responses. Furthermore, all participants were asked by the study monitor if they had encountered any difficulties with the questionnaire - it is hoped that most major difficulties would have been identified at this time.

Table 4-2: SHARE Questionnaire Comments

Responses	SA n=31	WC n=20
No difficulties with the questionnaire	21 (68%)	16 (80%)
No responses entered	7 (23%)	1 (5%)
Comments provided	3 (10%)	3 (15%)

- Participants suggestions to improve the questionnaire included requests for: additional questions regarding physical exertion at the work place, expansion of the job description section to include more options, addition of former job categories for those who had retired, use of more specific terminology instead of 'heart disease', explanation of the term 'angioplasty' , expansion of the parental heart disease section, and addition of more South Asian foods to the nutrition section.

- *Language*

For the pilot study, the questionnaire was available in English only. No difficulties with literacy were encountered. Data from the 1986 Census indicates that approximately 9% of the South Asian immigrant population in Canada cannot read English or French. Of these people, 82% are over the age of 35, and 39% are between the ages of 50 and 64. However, over 85% of South Asians over the age of 40, including 70% of those over the age of 65, have completed more than 5 years of schooling, indicating the ability to

at least read their native language.

● A breakdown of South Asians in Canada by frequency of spoken language is shown in Table 4-3 based on the 1991 Census Data. The three most commonly spoken languages of South Asians in Ontario are Punjabi, Tamil, and Gujarati [7] (Note: Urdu and Hindi are very similar).

Table 4-3: Commonly Spoken South Asian Languages in Ontario

Language	Ontario Population
Punjabi	46,945
Tamil	24,325
Gujarati	23, 580
Urdu	18,890
Hindi	17,420
Bengali	4,650
Marathi	900
Telugu	600

Translation: Although the instruments used in the pilot study were only available in English, prior to its use in the full scale study, translation and back translation of the questionnaire into the three most common South Asian languages Punjabi, Tamil, Gujarati, and Hindi is required. The *translation* process will include translation of the individual items or questions into the other languages. Ideally, this should be performed by an individual who is fluent in both English and the target tongue, and who is knowledgable about the content area, and aware of the intent of each item. This is

necessary because the literal translation of certain phrases may convey very different meanings in different languages. *Back-translation* is the process by which another bilingual person, one who was not associated with the initial translation phase and preferably knowledgable in the content area, translates the new version back into English. If the meaning seems to have been lost or altered, then that particular set of items requires alteration in the translation process to ensure the prime intent of the questions is conveyed [123].

Chapter 5 - Development of Study Instruments - Nutritional Assessment

The objective of the SHARE nutritional assessment is to attempt to link specific dietary exposures to the development of insulin resistance and atherosclerosis by determining the macronutrient and micronutrient breakdown of the reported dietary intake by ethnic group.

Rationale

Nutrition is a major determinant of health and chronic disease, and specific dietary components have been implicated in the development of obesity, diabetes, hypertension, vascular disease and cancer. Because of the complex way in which diet and nutrition may affect the risk of disease, it is important to have as detailed and reliable information on dietary patterns as possible [124] . Furthermore, as no reliable external validation standards exist (i.e. blood markers), it is difficult to validate dietary assessment instruments. Most population-based studies have relied upon a *single dietary assessment at baseline* as the sole measure of dietary intake, the validity and reliability of which may be questioned (See 24-hour recall Table 5-1). Furthermore, potential lifestyle confounders are not measured or considered in the analysis of the data which weakens the interpretation of associations between dietary factors and disease.

The influence of diet on chronic disease in migrants

Dietary patterns are established by ethno-cultural tradition, socioeconomic status, and a move in urban societies toward efficiency. There is evidence that migrant populations adopt the dietary customs of the new location to which they migrate. An observational study of the migration of Japanese from Japan to Hawaii and San Francisco (Ni-Ho-San) provided the ideal opportunity to study this process [125]. Dietary fat consumption was observed to increase steadily with migration of the Japanese towards the West. The fat consumption in Japan was averaged at 7%, compared to 23% in Hawaii and 26% in San Francisco. These changes in dietary composition were parallelled by increases in BMI, and age-adjusted CHD incidence rates.

Unfortunately such an ideal natural experiment is not possible to perform in SA migrants. Despite this, there is similar evidence that changes in diet, anthropometric indices, and disease rates occur when rural SA migrate to urban environments [126]. Observational studies indicate that an increase in fat and sugar consumption occurs with migration to urban areas, and urban diets tend to contain more animal products, fats, and sugars, and less fibre compared to that of rural communities. Singh [127] et al reported that urban SA consumed lower complex carbohydrates, greater refined carbohydrates, and more total and saturated fat, cholesterol and caffeine when compared with rural SA. This has been observed both within India and when SA migrate to countries outside of India [128]. Furthermore,

the rates of vegetarianism are declining as SA move from rural to urban areas. Data from a case-control study of patients with acute myocardial infarction which was conducted in India demonstrated that vegetarians had a more favourable glucose and lipid profile than non-vegetarians[26]. The prevalence of CHD appears to parallel these increases in dietary fats, simple sugars, BMI, and loss of vegetarianism. An examination of data across studies indicates that the CHD prevalence of SA migrants to the UK is twice that of Indians in urban India and four times that of Indians from rural India.

Nutritional Hypotheses

Protective dietary components such as high fibre, consumption of fruits and vegetables, and vegetarianism exist against vascular disease, specific dietary factors such as excessive intake of fat, total energy, simple carbohydrates, processed and refined foods may increase CHD. **As these changes appear to dominate the changes observed in migrant populations, a study of the dietary patterns of SA in comparison to WC and the association of five key areas of nutrition and the development of ATH is proposed.**

5 key aspects of dietary intake which appear to be associated with the development of insulin resistance and atherosclerosis will be studied in SHARE, and include :

i) *Total energy consumption (% kcal/day):* Increases in total energy content leads to increases in body weight. Obesity and abdominal fat distribution are associated with an increased prevalence of chronic disease.

ii) *Total dietary fat intake and percent saturated fat*: Increased dietary saturated fatty acids are strongly associated with increased serum cholesterol, increased LDL cholesterol, and increased risk of CHD. Sources of visible fat intake in the Indian diet are mustard oil, hydrogenated fat, butter, ghee (clarified butter high in cholesterol oxides), coconut oil and refined oil.

iii) *Dairy products:* There is evidence to suggest that excess dairy products consumption is associated with an increased CHD risk. It has been hypothesized that milk consumption may be linked to the development of CHD.

iv) *Fruit and fibre intake:* Increased intake of antioxidants have been associated with a reduction of coronary heart disease and cancer [129]. As well, experimental studies suggest that fibre (soluble) may reduce the risk of CHD through cholesterol reduction, slowing absorption of macronutrients leading to increased insulin sensitivity, lowered PAI-1 and Factor VII activity, and increased satiety leading to overall decreased energy consumption [130].

v) *Glycemic Index:* The glycemic index is a way of ranking foods based on the glycemic response they elicit when compared to a standard carbohydrate. The

rise of blood glucose in individuals after a meal is extremely variable and dependent on the source of carbohydrate, the method of preparation, and the composition of the total meal. This classification of food consumption is useful, particularly in populations who are at high risk for developing impaired glucose tolerance (IGT) and diabetes mellitus (DM).

Methods of Dietary Assessment

Currently there is no gold standard measurement of dietary intake for use in population-based epidemiologic studies. Therefore dietary instruments must be validated against the accepted standards which have some recognized limitations. To be valid, a dietary instrument should be able to determine an individual's "usual" intake based on their long term dietary intake. To be reliable the data must be reproducible.

Due to variability in reporting, variable intake according to current life events, and seasonal availability of food, the more assessments of an individuals dietary intake which are performed, the less variability of intake there will be over time. However, the ideal number of assessments to perform remains unclear and this is a decision left to the research team. In SHARE we have decided to use the food frequency questionnaire (FFQ) to measure our populations usual dietary intake. Below the features of other commonly used dietary assessment instruments are described, and justify why the FFQ was chosen.

1. In-depth dietary interview

Each participant must be interviewed by a trained nutritionist who uses models and pictures to assist in the participants description and quantitation of dietary intake. It allows for greater assessment of individual food items and is more precise at determining nutrient intake. However it is not usually feasible due to its time requirements and expense in population-based studies.

2. Food Records

This method utilizes records of daily intake completed by subject at home prospectively for 4 or 7 days, and attempts to give an accurate recording of volumes and portion sizes. The advantage of this method is there is no reliance on memory, and therefore the chance of recall bias is minimized. In the past this method has been used as a gold standard against which other dietary questionnaires are validated. However, it requires the population under study to be highly literate and motivated, as they must prospectively measure, weigh and record their dietary intake for a period of 4 to 7 days. As well the assessment of an individuals "usual" intake is based on this 4 - 7 days of their food consumption. There is a concern that the social desirability bias may be operating, in which subjects are aware their reports will be scrutinized by the dietician or physician such that their reported intake and preparation habits may not reflect their usual practices.

3. 24 hour recall

In this assessment subjects are asked to define and quantify what they

consumed over the preceding 24 hours. Its success depends on the memory, recall and cooperation of the subject. This represents an efficient method, which minimizes the potential for recall bias because of the short time frame used. Also as the assessment is relatively open-ended, it is useful for assessing mean nutrient intake within groups over time. However, it is subject to extreme variability in dietary intake as it reflects the food consumed in only one day. Surprisingly, the 24 hour recall is often used as the sole measurement tool in the assessment of dietary intake in longitudinal studies.

4. Multiple 24 hour recalls

On the other hand, with the use of multiple 24 hr recalls, subjects are asked to recall what they consumed over the preceding 24 hours on multiple occasions chosen at random. The advantages of this approach is that the extreme variability of a single recall is limited, and this method appears to account for variability in food intake due to season and day of the week. In fact, multiple 24 hour recalls are used as the gold standard of nutrient intake if taken at random occasions over time. Although, the optimal number of recalls to perform is unknown, 3-4 appear to produce statistically similar results as 7 [129].

5. Food frequency questionnaire

A food frequency questionnaire (FFQ) is a pre-coded dietary form which is composed of a food-list and a frequency response section. It is self-administered and appears to be the most desirable dietary assessment instrument from an

efficiency and feasibility standpoint for use in population-based epidemiologic studies. The use of FFQ's are conditioned upon the following: the coding of core foods, use of average nutrient composition of each food group as its nutrient data base, and limited objectives with respect to the nutrients or food components to be assessed. The likelihood of recall bias is minimized with this method as it does not ask for specific recall in one week but asks for the average over one year, and has less potential to be influenced by recent dietary changes and fads.

However, to ensure the validity of any FFQ, a gold-standard must be constructed against which the FFQ can be tested. To validate a FFQ one must add commonly eaten items (identified by the food records or 24 hour recalls) to an existing FFQ, develop a coding system, and develop estimates of nutrient conversion. This particularly challenging in ethnic populations as the key food groups may not be the same. Most nutritional epidemiologists conclude that the optimal study validation technique for FFQ are multiple 24 hour recalls taken at random.

Table 5-1: Choice of Gold Standard for Validation of SA Food Frequency Questionnaire

Method	Definition	Pros	Cons
In-Depth Interviews	Performed by a nutritionist using models and pictures.	Allows for greater assessment of individual food items. More precise at determining nutrient intake.	Not feasible and expensive in population-based studies.
Food Records	Records of daily intake completed by subject at home prospectively for 4 or 7 days, and attempts to give accurate recording of volumes and portion size.	Gold Standard If the population is highly literate and motivated. Do not rely on memory.	The assessment of an individuals "usual" intake is based on only 4 or 7 days of their food consumption Social desirability bias in recording foods prospectively.
Single 24-Hour Recall	Subjects are asked to recall what they consumed over the preceding 24 hours.	Efficient Potential for recall bias is limited and likely reasonable.	Extreme variability in diet as it reflects only one day.
Multiple 24 Hour Recalls*	Subjects are asked to recall what they consumed over the preceding 24 hours on multiple occasions chosen at random	Multiple 24 hour recalls as gold standard of nutrient intake if taken over time. Two or 3 recalls per subject is sufficient. Takes into account variability due to season and day of the week.	The optimal number of recalls to perform is unknown, although 3-4 produce statistically similar results as 7.

*Choice of "gold" standard for SHARE: 3 randomly selected 24 hour recalls over 6 months.

Approach to Validation of SA Food Frequency Questionnaire:

The proposed method of dietary assessment in the SHARE project is to use the FFQ. The white Canadian population will use the Canadian Cohort Study of Diet, Lifestyle and Health developed by Jain et al. This is a short self-administered questionnaire developed in 1981. The original version contained 86 food items and

has now been modified and expanded. This was validated against seven day food records and was found to be able to distinguish individuals based on distribution of energy, and 18 different nutrients. The SA FFQ is currently being developed based on the data collected from the pilot study of commonly reported SA specific foods, and will be validated in the upcoming study of 400 SA and 400 WC by the SHARE project group. The gold standard of an individuals "usual" dietary intake will be multiple 24 hr recalls. A nutrient data base will be based on an expanded version of the Canadian Nutrient file, expanded for foods of SA origin by the study nutritionists.

Chapter 6 - Validation of the Psychosocial Instrument

The impact of psychosocial factors on the development of cardiovascular disease, has not been fully elucidated. However, there is substantial evidence to suggest that cardiovascular disease (CVD) is inversely related to stress, hostility, depression, poor coping responses, and social isolation [77]. No previously validated questionnaire measuring stress migrant SA existed, therefore a psychosocial instrument was created for SHARE with the intent of identifying differences in psycho-social stressors between South Asian (SA) Canadians and White Canadians. However as it is likely that immigrants who must adapt to a new socio-cultural atmosphere face unique stressors, an in-depth study to determine these factors is required. Therefore a qualitative substudy has been designed and will be conducted concurrently during the initial months of the SHARE project (Chapter 7). The Life Stress and Satisfaction questionnaire was designed as an interim measure of stress factors in the SHARE population until the results of the qualitative susbstudy are available and can be used to modify the existing questionnaire. It is the ultimate intent of the SHARE project to determine the contribution of these factors to the development of unhealthy lifestyle behaviours and CVD in ethnic populations. Below the creation and validity of the SHARE Life Stress & Satisfaction questionnaire is presented.

- Object of Measurement: South Asians as a group vs White Canadians as the control

A careful review of the literature of SA migrants to the UK revealed that social isolation, depression, worry about ones children, loss of traditional values, and racism were the major contributors to their perceived level of stress. The SHARE pilot study conducted in July-Aug 1995, identified depression, financial security, and job stress as the most important perceived stressors amongst migrant SA Canadians. Based upon this information, the SHARE Life Stress and Satisfaction (LS+S) Questionnaire was created (Appendix 3) and the major domains included were Job Stress, Self-esteem, Depression, and Social Support. The sources for these subscales which were chosen to measure each domain are discussed below.

Source of Subscales

The subscales of the SHARE LS+S questionnaire were derived from different sources of previously validated questionnaire and included the National Population Health Survey (NPHS) questionnaire, and the Social Relationship Scale [130]. The NPHS (1994-1995) was a Canadian initiative in which the psychosocial determinants of health was evaluated in 22,000 Canadians households. Ethnicity was coded as part of the NPHS, therefore it was decided that use of some identical subscales would allow correlation of our sub-population in SHARE with the National Cohort. The NPHS subscales for job stress, self-esteem and depression

were incorporated into the SHARE LS+S questionnaire. The measure of social support used was the Social Relationship scale which was developed by McFarlane et al in 1981[130]. This measures the extent of an individual's network of social relationships and its 'helpfulness' in dealing with the effects of life stresses on health. This scale is a self-administered scale in which the respondent is asked to identify the people who supported him/her in each of six areas in which s/he had experienced life changes. The test-re-test reliability of this scale ranges from 0.62 to 0.99. The validity was assessed by content and by its ability to discriminate between groups of people with known marital discord and those without.

Table 6-1: SHARE: Life Stress and Satisfaction Questionnaire

- Job Stress
- Social Support
- Depression
- Self-Esteem

Validation of the Instrument

The SHARE LS+S instrument was validated on three levels: content, criterion, and construct validity. The LS+S instrument was assessed by content experts and it was pre-tested by volunteer South Asian immigrants. Minor modifications were made to the questionnaire after these assessments. The criterion validity was assessed by the concurrent administration of a well used instrument to assess general well-being and health, called the General Well Being Schedule (GWBS) [131]. The construct validation was performed by testing a specific attribute or construct against another to observe if the measurements operated in the hypothesized

direction. In SHARE, job stress was ranked by South Asians as a major perceived life stressor. Therefore, it was hypothesized that higher job stress would be linked to increased depression. This construct was tested in the SHARE validation and the results are presented below Table 6-3).

Choice of the GWBS as the Criterion Standard

Criterion Validity refers to the correlation of a scale with some other previously validated measurement of the same trait. Concurrent validity refers to the correlation of the new scale with the criterion measure given at the same time and is tested by the Pearson Correlation Coefficient. The General Health and Well-Being Schedule (GWBS) scale created by Dupuy 1977 offers a brief but broad-ranging indicator of subjective feelings and psychological well-being for use in community surveys. It covers six domains Anxiety, Depression, General Health, Positive Well-being, Self-Control, and Vitality [131]. It is a self-administered questionnaire developed for the US Health and Nutrition Examination Survey (HANES I). It consists of 18 items and each item uses a time frame 'during the last month'. It is excellent as a general population indicator of subjective well-being, as it incorporates questions regarding depression and self-esteem. Because the SHARE population is relatively healthy, a questionnaire which does not make continual reference to the physical symptoms of emotional distress is preferred. Furthermore, data from the NHANES study indicated that the instrument had acceptable validity and reliability. From the NHANES data, Monk reported a test re-test reliability coefficients (after 3 months) of 0.68 and 0.85 for 2 different groups [132], and the internal consistency of the

GWBS was reported to be 0.93 in 6,913 subjects in the NHANES study [132]. The validity of the GWBS was assessed in relation to other established instruments to measure depression. The average correlation of the GWBS and six independent depression scales was 0.69, and the average correlation with three anxiety scales was 0.64 [132].

Methods

After the SHARE LS+S instrument was compiled, it was mailed in Mid-February 1996 to the 51 participants in the SHARE pilot study. They were asked to complete the LS+S instrument, and mail it back to the SHARE project office. A self-addressed, stamped envelope was provided. Reminder telephone calls were placed approximately 7 days after the initial mailing. Of those who returned the initial questionnaire, a second questionnaire was mailed to them to test the reliability of the instrument.

Figure 6-1: Methods of Validation: LS+S

- Created Instrument / Content Validity
- Pre-tested instrument in South Asian Canadians
- Mailed LS+S instrument to 29 SA and 21 WC from former pilot study
- First Mailing early February
- Second Mailing late February
- Initial Data analysis
- Second Analysis (Test-Re-test)

Table 6-2: Response to Mailed Questionnaire

Group	First Mailing	Second Mailing
South Asian	14/29 48%	8/14 57%
White Canadian	15/21 71%	7/15 47%

Validation Results:

Criterion Validity or Concurrent Validity

The depression subscale of the new LS+S instrument was correlated with the GWBS for agreement between the parallel constructs. The correlation coefficient was 0.77 between the two instruments which provides support to the validity of the new subscale to measure general well being.

Construct

A multiple linear regression was performed using depression as the dependent variable and the subscales from the new instrument as the independent variables. These subscales accounted for 67% in the variation of depression subscale (R-0.82). Specifically the construct of job stress was identified as an independent predictor of depression (P=0.001)

Table 6-3: Methods of Validation

Type	Definition	Application
Face Validity	Content judged by experts in the field	The proposed instrument was assessed for face validity by examination by experts in anthropology and questionnaire design as well as SA migrants who confirmed that the proposed instrument was measuring the pre-specified domains.
Criterion Validity	Testing the validity of the new instrument against existing scales	The General Well-Being (GWB) schedule covers six dimensions: anxiety, depression, general health, positive well-being, self-control, and vitality. The depression subscale of the new instrument (measures similar constructs) was correlated with the GWB schedule for agreement between scales on parallel constructs. The correlation coefficient between the scales was 0.77 which supports the validity of the new instrument.
Construct Validity	Testing a specific attribute against another to observe if the measurements operate in the same manner.	A multiple linear regression was performed using depression as the dependent variable and the subscales from the new instrument as the independent variables. These subscales accounted for 67% of the variation in the depression subscale (R=0.82). Specifically, the construct of job stress was identified as a significant independent predictor of depression (p=0.001).

Reliability

The reliability of the instrument was assessed for internal consistency of the subscale, and test-re-test reliability. The internal consistency of the LS+S subscales was assessed using the item-total correlation, or Cronbach's alpha which

is a method used to assess the homogeneity of a scale. Generally an item should correlate with the total score above 0.20. Items with lower scores should be discarded. The alpha is dependent on the magnitude of the correlations among the items and on the number of items in a scale. Therefore a scale can be made to look homogeneous simply by increasing the number of items. Furthermore an alpha which is too high suggests that items may be redundant. Therefore it is usually accepted that the α should be above 0.70 but probably not higher than 0.90 [123] The Cronbach alpha's for the LS+S subscales are shown below and are acceptable.

Cronbach's Alpha

$\alpha = n/n\text{-}1\ (1 - \Sigma\sigma_1 / \Sigma\sigma_{T2})$

n = number of items in the scale

σ_1 = standard deviation for each item

σ_{T2} = standard deviation for the total score

Table 6-5: Reliability Testing: Internal Consistency of Subscales

Sub- scale	Cronbach's alpha*
Job-Stress	0.53
Self-esteem	0.74
Depression	0.77
General Well Being Scale	0.64

* A measure of the internal consistency of items in each subscale.

Test re-test reliability is a measure of the ratio of the between subject variance and the total variance (comprised of the subject variance and the error of measurement associated with the instrument). The greater the error associated with the instrument, the poorer the test-re-test reliability. A score of zero indicates no reliability and one indicates perfect reliability. A simple assessment of reliability may be made by a simple correlation of the mean scale scores, taken at different time points. The formal reliability assessment involves performing an ANOVA comparing the scores at time one and time two. In the table below both the simple correlations and the formal calculation are provided.

Table 6-6: Test-Re test: Calculated per subscale N=14

Subscale	Mean Score Time 1	Mean Score Time 2	Simple Correlation	Reliability
Job stress	41.36 (6.67)	43.07 (5.29)	0.49	0.47
Self-esteem	42.76 (3.88)	41.29 (5.47)	0.73	0.69
Depression	46.69 (17.12)	55.19 (6.92)	0.41	0.50
GWBS	69.41 (7.16)	71.12 (8.05)	0.71	0.71
Health	16.35 (6.10)	15.82 (6.03)	0.71	0.71

Interpretation: The time between assessments was approximately 2 weeks. The job stress and depression subscales demonstrated poorer test-re-test reliability compared to the other scales. Although it is not surprising that job stress and depression may vary from time point to time point, the same variations are not reflected in the GWBS measurement. This implies that although these attributes may be extremely variable and difficult to measure the GWBS appears to be more reliable and will be used as the major subscale to measure general well-being in the large study.

Chapter 7 - SHARE: A Qualitative Substudy of the Immigration Experience of South Asians in Canada

I. Description of the Study

There is evidence to suggest that coronary heart disease (CHD) is negatively influenced by factors such as poor psychological well being, social isolation and stress. Immigrants are faced with a unique set of psychological stressors when they settle in a foreign land. South Asians are at high risk for developing premature CHD when they migrate to urban environments, and the explanatory factors for this have not yet been elucidated. This study is designed to explore the psychological effects of the acculturation process on immigrant South Asians in Canada to generate explanatory models which facilitate future studies of the impact of acculturation on the health of immigrant South Asians.

II. Hypothesis

Men and women originating from India, Pakistan, Bangladesh and Sri Lanks have an increased susceptibility to develop CHD due to a combination of genetic and environmental factors. These genetic factors are magnified when South Asians adopt urban lifestyles both within their countries of origin and abroad. We hypothesize that South Asians encounter unique environmental stressors which

impact on their adoption of unhealthy lifestyle behaviours and health.

III. Objectives

An examination of the obstacles faced by South Asian immigrants in Canada toward social integration, and the associated psychological stressors is proposed to identify sources of stress associated with acculturation. This may partially account for the excess of CHD observed in migrant South Asians.

Using qualitative methods we will examine:

i. The pre-migratory factors which lead South Asians to immigrate to Canada
ii. The role of South Asian men and women, as parents, and spouses in the family, the workplace, and in the community
iii. The differences in acculturative patterns between South Asian children and their parents
iv. The major social support structures of South Asian immigrants in Canada
v. The self-perception of immigrants as equal members in Canadian society, their degree of acceptance of the host culture practices and the degrees to which they are reluctant to relinquish their traditional beliefs from the heritage culture.

It is the ultimate intent of this study to incorporate the attitudes, experiences, and behaviours which emerge into a formalized instrument designed to measure the impact of acculturation on the adoption of certain lifestyle habits and health of South Asian immigrants in Canada

IV. Background

The process of migration from one extreme culture to another is one of the most radical transitions which can be experienced in an individual's lifetime. The immigrant population and the host population are heterogenous groups, and upon interaction a mutual adaptation occurs and new social patterns emerge which are determined by the complex interplay of the technological, demographic, economic, and cultural forces [133]. As the number of South Asian migrants in Canada continues to increase, furthering our understanding of the associated acculturative stressors experienced by South Asians is necessary to increase our understanding of the social concerns of this sector of the Canadian population [134].

Unique stressors of migrant South Asians

Most immigrants to Canada attempt to achieve financial security, adopt similar cultural traits of the host country, and attain adequate professional skills, which they believe will lead to successful integration within Canadian society [135] . There has been little research of the effects of migration on South Asians beliefs , attitudes, and lifestyle practices, and the potential internal, and external conflicts this may cause. In a qualitative study on health beliefs and attitudes among first generation South Asians migrants to the UK, two sources of stress were identified and included long working hours, and the divergence of children's behaviour from their parents expectations. In a survey from Glasgow, Scotland of South Asians, stress was attributed to long working hours, low income, crowded housing, and perceived lack of social support of women [74]. In the SHARE pilot study of 31

randomly sampled South Asians from Southern Ontario, the three most important sources of stress identified by South Asians included concerns about financial security, job stress, and the future of their children [136].

South Asians in Canada

The immigration policy of the Canadian government in the 1960's encouraged the maintenance and development of various ethnic groups within the framework of Canadian society. This policy was intended to reduce the pressures felt by ethnic groups to assimilate within mainstream Canadian society (with resultant culture loss), yet at the same time reduce the separation of multiple ethnic groups (with resultant social fragmentation) [137]. Most South Asians in Canada immigrated for professional opportunities and for the educational opportunities of their children. However, increasingly more South Asians from Sri Lanka, and other conflict torn states in India are immigrating because of political reasons. In the early 1960's there was an influx of South Asian professionals into Canada , as there was a tremendous opportunity for South Asian immigrants to advance professionally and economically [138]. At that time the acceptance of visible minorities was still limited within Canadian society, which made the immigrant experience of South Asians different from the experience of immigrants who come to Canada today. However, despite the opportunities for upward social mobility, the Canadian lifestyle and social values remain vastly different from the first generation of South Asians Canadians. Adaptive challenges faced by this group included social isolation, religious, linguistic, and other customary differences [138].

South Asian Family Roles

The concept of a strong and supportive extended family is a dominant feature of the South Asian heritage culture [139]. The roles of males and females in the family, marriage and Indian society are vastly different from contemporary Canadians norms. In traditional Indian society, the male is expected to be the dominant figure in the household, and the wife is granted as much independence within the family as the husband or in-laws will allow. Furthermore, it is expected from one's children, that family-cultural practices will be adopted without question, as the family plays a large role in determining the future of the children. South Asian immigrants to this country no longer have extensive social networks or extended families as they had in their native countries, and must rely more upon the nuclear family for support. In Canada, as South Asian women often take up employment outside of the home they gain independence which leads to changes in their traditional household roles. The children of South Asian immigrant families in Canada, the so called 'second generation' grow up more integrated within Canadian society than their parents, and often serve as the bridge between the heritage culture and the host culture for their families. Often, South Asian parents continue to be authoritarian and emphasize the practice of traditional cultural values. The degree to which traditional practices are maintained by the immigrant family is usually proportional to the degree of conflict which arises between parents and children. This conflict has been identified as a major source of stress for both parents and their children [139].

Women and Social Isolation

Community surveys in Ontario report diminished family support in migrant groups [140]. The social isolation of South Asians in Canada compared to life in their native country is a dominant issue for most South Asians who immigrate without a family or for South Asian women who do not work outside the home, and remain as the household managers. Men who enter the workplace and interact socially with colleagues, gain greater insight and apparent acceptance into Canadian society. However South Asian women must adapt to a new country and ensure their children have a hopeful future, despite often remaining out of the work force and isolated from their new community. The immigrant experience of South Asian women is likely much different from that of men as they are double minorities - being both visibly different and female [141]. Most Indian women accompanied their husbands to Canada, and therefore often continue to have a dependent status, although many of them have strong educational backgrounds. A cross-sectional survey of South Asian women conducted in 1979 revealed that Indian women face common problems in terms of social and economic adaptation in Canadian society due to their ethnicity and culture [142]. These women who are representative of middle-class families who immigrated during the 1960's, reported that factors such as understanding social etiquette, social interaction with a wide range of people, and mastery of English greatly influenced their quality of life experiences in Canada. The acculturative stress which is associated with migration is likely to be felt more deeply by South Asian women, as they are usually the custodians of the

religious and cultural convictions for the entire family. Most women continue to visit the Indian place of worship or establish a small 'temple' in the home, cook Indian food, and continue to be vegetarian. Areas of changes or adoption of the Canadian way of life are recognized initially when traditional patterns are perceived as resulting in negative consequences. Patterns of dress, and food are adapted easily. Sarees are no longer worn on a continual basis by most South Asian women, as they attract attention and are usually only worn on special occasions. Many women are expected to forgo career aspirations to concentrate their time toward raising a family and supporting their husbands. Many are under-employed. and take on part-time jobs [138].

Discrimination

Social identity theory is rooted in the assumption that individuals have a fundamental need for a positive sense of self, and that an important part of ones identity is derived from social group membership (i.e. social identity) [143]. For first generation immigrants, ethnic differences from the host culture has a profound impact on their social identification. Immigrants are more likely to experience prejudice and discrimination and feel unaccepted by the host society than others. [144]. Previous qualitative studies have observed that South Asians like other ethnic groups do experience discrimination both in their communities and in the workplace [139]. Although it is often subtle, first generation South Asians who have imperfect English and unique clothing do not feel equal or accepted in Canadian society. Racist discrimination in employment is complex and subtle therefore difficult to

quantify. In a study in Toronto of South Asians, West Indian, and Europeans, Head reports that almost 68% of South Asians had experienced personal discrimination, and 47% had experienced employment discrimination compared to only 27% of Europeans [145].

Parents and Children

Integration of immigrant parents into Canadian society is often more difficult than that of their children. For children who have no difficulty integrating into Canadian society, the relinquishing of traditional heritage cultural practices is often a source of conflict for both parents and children. Given that ties to the heritage culture tend to become weaker over time, immigrant parents are more likely than their children to maintain a maintain a strong ethnic identification and a collective acculturation orientation. It follows therefore that immigrant children would possess a more favourable attitude toward multiculturalism than their parents. These attitudes represent the normative beliefs taught by the host culture. School also creates a widening gap between children and their parents beliefs. Parents often have a great deal of uneasiness about how "Candianized" their children will become. In a study of South Asians in Saskatoon, almost two-thirds of South Asian parents believed that typical Canadian youth have too much freedom, and showed a great deal of reluctance in giving the same amount of freedom to their own children [146]. The concept of westernization is threatening to South Asian parents, as their lifestyles drift away from traditional South Asian cultural norms. A schism exists between advancing with Canadian society both socially and professionally

and expecting their children to retain traditional Indian values. Therefore the maintenance of cultural identity is extremely important for these families, as is their desire to preserve cultural traditions. Most of the social customs of the dominant culture like Halloween, Thanksgiving, Sunday School, Valentines day, Christmas and Easter which are new to Indian immigrant families have been adopted by their children. Parents encourage this, and children enjoy these activities because it leads to greater acceptance by their peer group [146].

Although undoubtedly children are influenced by what their parents say, there is a strong desire as with all children to gain acceptance from their peer group. South Asian parents appear to be more authoritarian toward female children compared to male children and are more willing to grant more freedom to boys than girls. There is a definite standard for females, such as no dating or contact with men prior to marriage, while no set standard exists for males [138]. Inter-religious marriages are gaining more acceptance yet inter-racial marriages still remain problematic. However, there are many examples of South Asian parents arranging marriages for their Canadian born and raised children which have been successful, and there are others for whom this arrangement has failed. On the other hand the same may be said for inter-ethnic marriages. **The acceptance of Western values, and traditions by South Asian parents appears to be proportional to the degree of acculturation of the South Asian family.** Therefore the more traditional a family is in its day to day cultural practices, the more likely the expectations of the parents will be for their children to maintain these traditions, whereas the more acculturated

to the family, the more accepting they will be toward adoption of Western marriage partners, and cultural traditions.

What is acculturation?

Acculturation is a cultural change which results from the continuous first hand contact between two distinct cultural groups [147]. Acculturative changes include everything from physical changes in environment, biological changes (eg new nutritional status, new diseases) and at the heart of acculturation: political, economic, technical, linguistic, religious, and social integration. Acculturation can occur at both a group and at an individual level. At the individual level changes in the individual behaviour and internal characteristics may occur. Some individuals adapt very well to this transformation while others experience a great deal of difficulty. Psychological consequents of acculturation include a behavioural change towards new norms, and acculturative stress may accompany these cultural changes. Whether identification with both cultures can be maintained or whether giving up identification with one culture is necessary, has not been the subject of in-depth research.

Theoretical Models of acculturation:

Unidirectional Models

The earlier explanatory models of the changes that individuals experience upon migration have been unidirectional in the sense that they equate the process

of acculturation with assimilation. Assimilation differs from acculturation in that it presupposes a unidirectional process in which the immigrant is absorbed into the host society [148]. In a unidirectional model developed in an immigrant study conducted in Montreal, researchers distinguished between the processes of acculturation and assimilation and concluded that assimilation requires a change in values to occur in the host society and an internal change in the individual immigrant, whereas acculturation resulted in the maintenance of some aspects of cultural heritage [149].

Bidirectional Models of Acculturation

These models propose acculturation as a bi-dimensional process in which an immigrant group's identification with both the host and heritage culture is assessed on two separate dimensions, and the degree of change is measured along each dimension. In 1980, Berry developed and validated a bi-dimensional model of acculturation, assessing both identification and behaviour toward the heritage and host cultures [150]. According to Berry, acculturation attitudes form the central variable which helps us to understand individual differences in the way people orient themselves during the process of acculturation. His models taps into the degree of desirability of inter-ethnic contact, deciding whether positive relations between the heritage and host cultures are of value and should be sought. This two dimensional model allows for a fourfold classification of acculturation outcomes. The four categories include

i. *Integration:* maintenance of the cultural integrity of the group, and the

movement of the group to become an integral part of the larger framework

ii. *Assimilation:* relinquishing one's cultural identity and moving into larger society,

iii. *Separation:* there are no positive relations with the larger society, and the group seeks only to maintain unique cultural traditions,

iv. *Marginalization:* cultural and psychological contact with both cultures is lost. In this model one dimension tests attitude and the second assesses behaviour. The validity of this model was tested in nine samples of various native and ethnic groups in Canada [151]. Strong support of its validity was observed across four ethnic groups (Koreans, Vietnamese, Malaysian, Native Canadians). *This model and its subsequent validation underscores the importance of both heritage culture maintenance and intergroup relations within Canadian society.*

Orthogonal Models of acculturation

Zak [152] was the first to propose that the heritage and host culture identities should not be placed at either extreme of one bipolar dimension, but rather are orthogonal and independent of each other. The two identities of heritage and host culture are conceived as being distinct, and uncorrelated processes. This model has been validated in four studies with different immigrant groups [152-155] . In 1992 Sayegh and Lasry presented an orthogonal model based upon Zak's original model, in which the identification towards heritage and host cultures occurs on two orthogonal dimensions, and also includes Berry's four categories as described above [155]. This represents the most advanced model of acculturation to date. The first dimension represents identification towards the heritage culture, the second

represents identification towards the host culture. Change occurs along each dimension independently of the other. Two identification scores (heritage culture and host culture) serve as coordinates for each subject and allows for four acculturation classifications. *Integration, marginalization, assimilation, and ethnocentrism.* This orthogonal model has been validated by Lasry and Sayegh 1992 in a population of Lebanese immigrants in Montreal (Figure 2) [155].

How is the process of acculturation associated with stress?

Stress is defined as a generalized physiological and psychological state of a person which is brought on by environmental stressors, requires coping mechanisms, and persists until some satisfactory adaptation to the new situation is achieved [156]. The stress associated with this attempt at adaptation is known as **acculturative stress** and is defined as a reduction in health status (including psychological, somatic, and social aspects) of individuals who are undergoing acculturation, and for which there is evidence that these health phenomenon are related systematically to the acculturation phenomena [150]. In review of the literature by Berry and Kim in 1987, cultural and psychological factors were identified which governed the relationship between acculturation and mental health [151]. They concluded that although mental health problems often arise during acculturation, they are not inevitable, and depend on a variety of group and individual characteristics which enter into the acculturation process. They concluded that each individual is uniquely affected by the variables that govern the relationship between acculturation and stress. Acculturative stress has its source of stress in the

process of acculturation, and certain stress behaviours often occur during acculturation such as lowered mental health status (confusion, anxiety, depression), feelings of marginality and alienation, psychomotor symptoms increase, and identity confusion occurs. Results from a survey of 1,197 people in Canada which used an instrument to measure acculturative stress, indicated substantial differences in stress phenomena across types of acculturating groups. *Therefore, we hypothesize that acculturative stress which includes physical, psychological and social components, leads to impaired health of immigrants individuals.*

How is psychologic stress linked to the development of CHD?

Perturbations in ones psychological state may lead to physiologic changes and disease. The stress response is the neural and endocrine systems adaptations to the stressful stimuli which help re-establish an individuals homeostasis [156]. It has been shown repeatedly that the more effectively people deal with forces that affect their life and living circumstances, the better is their health and well-being. Acculturative stress may alter prior learned coping mechanisms such as one's sense of control over destiny, locus of control, sense of control, and powerlessness [157]. A positive association between the degree of powerlessness and all-cause mortality was observed in the Whitehall Study of British Civil servants which began in 1967. This observational study of individuals (with an overall high socio-economic status), demonstrated that a steep inverse association exists between social class, (as assessed by grade of employment) and mortality across a wide range of diseases. In 1985-88 a second cohort of British civil servants was studied, and this

revealed an inverse association between employment grade and prevalence of angina, and a lower self-perceived health status. There were clear employment differences in health risk behaviours including smoking, diet and exercise and type of work by employment grade [158]. **There have been no studies which have assessed the stressors associated with acculturation and the relationship of these factors to the development of CHD.** Lack of social support has been shown to be an independent risk factor for CHD and all-cause mortality in several epidemiologic studies. While it is uncertain how these stressors relate to CHD, they are likely to be important and integral to any study of risks and risk behaviour among migrant populations.

V. Research Design and Methods:

Recruitment

Participants will be recruited from an on-going study to assess cardiovascular risk factors in South Asians and White Canadians in Canada. The eligibility requirements for this study require that participants be between the ages of 21 and 75 years, originate from India, Pakistan, Sri Lanka, and Bangladesh, and have lived in Canada for at least 10 years. Individuals with concurrent chronic diseases such as cancer, renal, or hepatic failure will be excluded.

Sampling characteristics

The overall study population will be recruited by utilizing computerized public

telephone directories and stratified random sampling. South Asians are identifiable by their unique surnames which have a sensitivity and specificity of approximately 96% for South Asian ethnicity. A subset of 30 South Asians will be recruited from this sample for the qualitative component of the study. An equal representation of South Asian participants by religious affiliation will be sought: i.e Hindu, Sikh, Christian, and Moslems. Each participant will be approached for consent and the consent of their offspring and spouse to participate in the study

Methods

The primary method of data collection will be through focus groups. These will be conducted on three levels i. individual immigrants, of mixed age, and gender, ii. immigrants and their spouses, and iii. the children of immigrants born in Canada. A group session of no more than 7 participants will be conducted on one occasion. All groups will be comprised of heterogenous strangers representing different religious and educational backgrounds (determined from initial study). Each session will be conducted for 2 hours. These sessions will be audio taped and transcribed in conjunction with the researchers field notes. (See focus group schema outlining key probe questions-Figure 3). The goal for the focus group is to be small enough to provide everyone the opportunity to participate, yet large enough to provide a wide diversity of opinions. The role of the researcher will be to moderate, listen, and observe. Probe questions will be developed to guide the interviews to elucidate the reasons for migration, differences in current lifestyle compared to former lifestyle, positive and negative attributes of their host country, issues around self-identity and

social support, interactions with local ethno-cultural groups, discrimination, job stress, family dynamics, and concerns about the acculturation of their children. These probe questions will be pre-tested on other SA migrants and modified prior to the interview, and will be re-evaluated and modified on an on-going basis based on feedback after each session. The interviewer will remain flexible and may allow the interview to stray from the content and order of the probe questions [159]. However responses to all probe questions are encouraged over the period of interview time. Responses are encouraged to be open-ended, and the interviewer must not appear to rush the respondent through a list of questions. Furthermore the interviewing style used during the focus group is designed to be open-ended and free-flowing as possible to encourage the emergence of un-anticipated themes, attitudes and beliefs regarding acculturation and its associated stressors [160]. If it is observed by the interviewers that there has not been enough time allotted to cover pre-specified areas, the study team will re-asses the interviewing time and probe questions. The interview will be tape-recorded (consent from the participant obtained) and transcribed together with the interviewers field notes.

Each participant in the focus group will have completed a study questionnaire in which data is collected to assess health characteristics related to the development of CHD, in-depth dietary, life stress and satisfaction assessments, and completion of Sayegh's orthogonal model of acculturation assessment described above (Figure 2). This information will be used to test emerging constructs and triangulate the data collected in Phase I and II. Construct validation

will be conducted by correlating individual self-perception (i.e. integrated, assimilated, marginalized or ethnocentric) with responses to lifestyle questions, social support networks, and reported participation in local cultural organizations.

VI. Analysis and Interpretation

Data Preparation

The data acquired in this study will be primarily in the form of transcribed texts and field notes, the traditional data gathering approach in qualitative research [161]. The data, after being transcribed, will be cleaned which will include minor editing, correction of spelling mistakes, and formatting.

Data Identification

A considerable effort will be spent on coding the transcribed texts by a core group of three researchers. Each reviewer will receive the identical transcriptions and will meet on bi-weekly basis for a period of 4 weeks to code and interpret the texts. *The focus will be to extract the major exploratory themes which deal with acculturation and stressors associated with this process.* Two independent researchers skilled in qualitative research techniques will also receive the unabridged texts and will be asked to code emergent themes and issues related to the process of acculturation and the impact of this on individual immigrants. This will then be compared to the coding system developed above. Finally all people involved in the development of the coding system will meet to finalize it. An iterative process of developing the coding system will be undertaken which will

include continual recoding and reorganization of data as new analytic concepts emerge. The transcribed text will then be coded formally. A computer program will be developed to allow accurate identification of particular lines and sentences to which the codes apply [162] .

Data Manipulation

The NUDIST (Nonnumerical Unstructured Data Indexing, Searching and Theorizing) software will be used to mange the derived data [162] . Specifically it will assist in coding discrete units of text based on the coding system developed as described above. This is essentially a computerized tool for facilitation of hypothesis testing. The codes developed and validated by the researcher will allow for the determination of the major emergent themes and to assess if any correlation between acculturative stressors and unique lifestyle characteristics exists. Furthermore quantitation of emergent themes may be conducted. NUDIST automatically numbers text units as they are entered and is able to insert identifiers for the current speaker and contextual comments will appear with the comments to which they refer. Other functions include automatic text formatting, line numbering, rather than chunking for coding, retrieval of properly identified required text, and removal of size constraints on files. A summary of all codes from each focus group will be provided.

Data Analysis

The analysis process will be systematic and reproducible. It will follow a

prescribed, sequential process such that another independent researcher would be able to arrive at similar conclusions using the available documents and raw data. Personal opinions not related to the intent of the research will be minimized to minimize the noise. The goals of interpretation of the focus group texts include description of participant characteristics, descriptive phrases or words used by the participants, themes in the responses to key questions, subthemes indicating the point of view held by participants with common characteristics, and description of the group interaction. Simple descriptive statistics reflecting the frequency of which reference was made to dominant themes, and word usage will be used. Consistency between the participants comments (from the focus groups) and the more formalized assessment of life stressors and health characteristics from the questionnaire, will be examined to determine if collectively these data provide support for emerging constructs. Internal consistency within focus groups, and discrepancies within important emerging themes will be considered carefully and cautiously at the time of analysis.

Data Conclusions and Verification

Patterns and themes will be coded and compiled into the creation of a hypothetical model of acculturation and the associated stressors experienced by South Asian immigrants in Canada. The data will be verified through triangulation methods and an audit trail. Triangulation entails checking for biases that will lead to misleading conclusions or unsubstantiated conclusions about the data [163]. Use of confirmatory tactics such as theoretical triangulation whereby independent

interpreters make the same conclusions about the data independently, and the researchers observations regarding emergent themes and beliefs correlate with other measures of attitudes and beliefs such as the response from the questionnaire. Triangulation also refers to the agreement between researchers i.e. similar observations are made when in the same field, and convergence along theories from those who interpret the data. There are different ways one can triangulate the data to minimize different biases and strengths [164]. Specifically the data will be checked for representativeness. The external reviewer must be able to replicate key findings. This feedback from informants is an ongoing process and technically triangulation of the data should be built into the actual data collection to add in checks of the data collection, as biased data collection can only lead to bias conclusions [163] . Auditing implies a systematic review of a given study by an external examiner. The external reviewer will determine whether the sampling measurement and analyses leading to the main conclusions and explanations stand up to the most common sources of bias and error. This will allow us to determine if our findings are grounded in data, if our inferences are logical, and that the data are weighed correctly.

VII. Conclusion:

This qualitative substudy will provide new insights into the stressors associated with the acculturation process of South Asian Canadians. This data will be incorporated into the SHARE Life stress & Satisfaction questionnaire to augment

our measurement of psychosocial stressors, and enable us to study the relationship of these factors to the development of unhealthy lifestyle behaviour and cardiovascular disease.

Figure 7-1: Study Summary

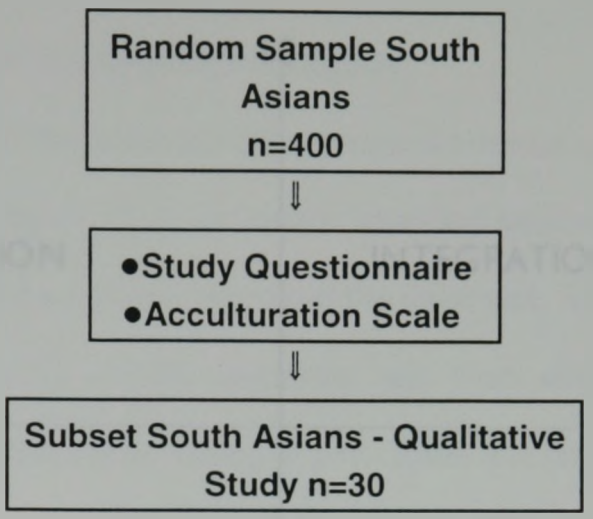


Figure 7-2: Orthogonal Model of Acculturation

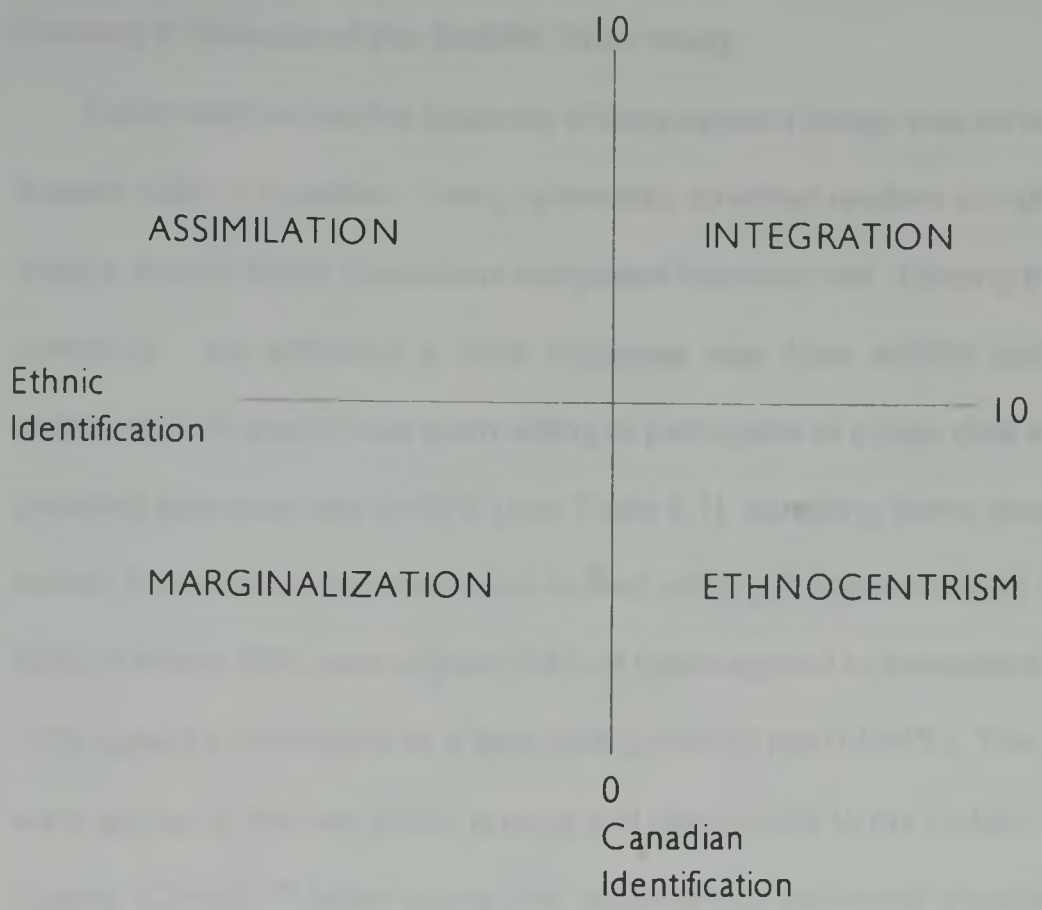


Figure 7-3: Focus Group Summary

- Factors which led individuals to immigrate to Canada
- Perception of South Asians as equal members in Canadian society in Canada, their degree of acceptance of the host culture practices and the degrees to which they are reluctant to relinquish their traditional beliefs from the heritage culture.
- Explore the major social support structures of South Asian immigrants (both parents and children) in Canada i.e. involvement with local cultural groups, extended family, friends
- Personal experiences of discrimination in general and in the workplace

Chapter 8: Results of the SHARE Pilot Study:

A pilot study to test the feasibility of the proposed design was carried in July and August 1995 in Hamilton. Using systematic stratified random sampling 31 South Asians, and 20 White Canadians completed the clinic visit. Utilizing this method of sampling, we achieved a 59% response rate from eligible participants. An additional 10% would have been willing to participate at a later date increasing the potential response rate to 69% (see Table 8.1). sampling frame was created and tested, 310 letters of invitation were mailed; utilizing 3 telephone calls we contacted 59%; of whom 60% were eligible; 54% of these agreed to participate, and another 10% agreed to participate at a later date (potential total of 64%). The contact rates were similar in the two ethnic groups and also similar to the Ontario Heart Health Survey (OHHS) [60] (after taking into account our additional eligibility criteria for ethnicity, age, and other disease) (Table 8.2).

Table 8-1: Sampling and Recruitment

Group	# Letters Mailed	# Contact	# Eligible	# Response
SA	160	97 (61%)	59 (61%)	35 (59%)
WC	150	86 (57%)	50 (58%)	24 (48%)
Total	310	183 (59%)	109 (60%)	59 (54%)*

* An additional 10% have agreed to come at a later date.

In the proposed study of 400 SA and 400 WC, all attempts will be made to contact subjects who have moved (within the target geographic region).The contact rate of potential participants may be increased from that of our pilot study (60%) (Table 8.1), by using trained interviewers, and by increasing the number of telephone calls (12), and varying the timing of (evening and weekends) telephone calls to each household.

Table 8-2: Recruitment Rates Other Population-Based Studies

Study	Sample Size*	Method of Recruitment	Response Rate (Clinic Visit)
OHHS[60]	2583	Mail Telephone	56%
ARIC[165]	16000	Mail Telephone	61%
Framingham[166]	4469	Mail	69%*
Cardiovascular Health Study[167]	4500	Mail Telephone	61%

* Included volunteers. Note that the response rates in these major studies were only slightly higher than that observed in our unfunded pilot.

Concerns regarding Sampling Procedure:

Non-responders:

Three key variables (smoking, education, family history of CHD) were collected over the telephone from all persons contacted to characterize the non-responders (NR). The pilot study data indicated that 27% of NR and 30 % responders (R) had a family history of CHD, 27% of NR and 33% R were smokers, 45% of NR and 52 % of R had a university education, and 100% of NR and R had lived in Canada

longer than a year. This suggested that there were no major systematic differences existed between non-responders and the responders.

Selection Bias

Using our sampling method, SA women married to non SA who have changed their last name will not be identified. We recognise this limitation; however data from the 1991 Census, indicates this proportion is less than 1%.

Undercoverage bias may operate when different proportions of the target population are missing from the sampling frame and may occur if a disproportionate number from an ethnic group has no telephones or unlisted numbers. To reduce the potential of undercoverage bias we developed a supplementary mechanism that identifies the unlisted SA numbers with the addition of community based SA membership lists and added these to the CD generated list. Telephone coverage data from the 1994 Household Surveys Division of Statistics Canada indicates that 99.4% of Ontarians had a household telephone (96.3% in the lowest income group to 99.9 % in the highest income group) indicating very little potential bias for this methodology [168].

Completed Visits

Of those participants who completed clinic visits, the geographic distribution of their residences by postal code is shown in Table 8.3. No differences in the geographic representation of SA and WC participants were identified. Half of the

participants came from Burlington and Oakville which may raise the concern that the SHARE pilot sample was overrepresented by higher socioeconomic participants, however this was balanced by the remaining 50% of the sample originating from within the city of Hamilton.

Table 8-3: Geographic Distribution of Study Participants

Location	Attempted	Completed	Percent Yield
Hamilton	158	23	14.5%
Burlington	52	9	17.3%
Dundas	13	-	-
Oakville	74	17	23%
Ancaster	5	2	40%
Stoney Creek + Other	8	-	-
Total	310	51	16%

Demographic Data

Key demographic data are displayed below in Table 8.4 and represent a mixture of categorical and continuous variables. Tests of significance using the Chi square test and the t-test of independent samples were performed to identify differences between the groups. The distribution of continuous variables was checked for normality and transformed if a non-normal distribution was observed.

Table 8-4: Demographic Characteristics of SHARE

Variable	SA (n=31)	WC (n=20)	P value
Mean Age (year)	48	49	NS
Female (%)	40	57	NS
Mean Years in Canada	18	48	0.001
Married (%)	97	71	0.009
Ever Smoked (%)	18	66.6	0.0005
Current Smoker	3.7	29	0.01
Drink Any Alcohol (%)	46.7	81	0.01
Vigorous Exercise (%)	30	20	NS
Vegetarian (%)	10	0	NS
Some University Education (%)	66	43	0.09
Currently Employed (%)	76.6	71.4	NS
History of Diabetes (%)	7	0	NS
History of Hypertension (%)	29	23	NS

Interpretation of results

The mean age of participants from both ethnic groups was 48 years, which support our method of community random sampling to achieve similar groups based on age. On average SA had lived in Canada for approximately 18 years compared to a lifetime for WC. All SA were married compared to 71% of WC in which there were increased reported divorce and separation rates. More SA reported being currently employed, although more WC were retired. Furthermore, more SA had reported having some prior university education compared to WC. These differences may reflect a healthy immigrant effect [137].

Not surprisingly, 94% of WC reported being Christian compared to 7% of SA. Of the SA, 24% were Hindu, 14% Muslim, and 48% Sikh. Religious affiliation in SA is often correlated with important lifestyle characteristics such as diet, alcohol, and smoking differences. The large proportion of Sikh's in this sample was likely due to a over sampling of individuals with the last name Singh, which is a common Sikh surname. All of the WC first language was English compared to 3% of SA. The most common mother tongues reported amongst SA included Punjabi in 55%, and Hindi in 13%, followed by Tamil, Urdu, and Sinhalese.

Other lifestyle differences were identified between the groups. SA were more likely to be abstainers from alcohol, and less likely to be cigarette smokers compared to the WC. No differences were observed in regular vigorous exercise between the groups. Not surprisingly SA were more likely to be vegetarian compared to WC.

No differences in rates of hypertension, and a slight trend towards an increased prevalence of diabetes were observed in SA.

Laboratory Measurements

In all participants blood, urine, and carotid ultrasound testing was performed. Repeat blood samples of key metabolic parameters were drawn at 2 hours after ingestion of a 75 gram glucose load. All of these measurements were examined for non-normality and transformed appropriately. Presented below are the mean values

of the laboratory measurements for all 51 participants, and the reported value of each ethnic group adjusted for age and sex by the method ANOVA using age and sex as co-variates. Significance testing was also performed by ANOVA.

Table 8-5: Pilot Study - Laboratory Results*

VARIABLE	SA (n=31)	WC (n=20)	P value
Fasting Glucose	5.3	5.0	0.07
Fasting insulin	4.7	4.3	0.06
Fasting Triglycerides (ln)	0.6	0.3	NS
Fasting FFA (ln)	5.9	5.6	0.09
2 hr glucose	7.1	5.6	0.01
2 hr insulin	6.3	5.4	0.005
2 hr Triglycerides (ln)	0.7	0.5	NS
2 hr FFA	4.5	4.3	0.13
FIRI	40	16	0.06
HbA1C	7.4	7.2	NS
IGT %	34.5	9.5	0.04
ln Lp(a)	5.5	4.6	0.02
Total Cholesterol	5.1	5.0	NS
HDL Cholesterol	1.0	1.2	0.01
Total Chol/HDL	5.1	4.2	0.05
Microalbumin	21	8.5	0.09
Systolic BP	119	116	NS
IMT (mm)	0.65 +/- 0.19	0.72*+/- 0.17	NS
Body Mass Index (BMI)	27.3	26.5	NS
Waist/Hip Ratio	0.92	0.96	NS

*age and sex adjusted
Legend: 2 Hr: 2 hours post glucose load, FIRI: Fasting insulin resistance index, Tchol:Total cholesterol, Ln: natural log, FFA: Free fatty acids, IGT: Impaired glucose tolerance (2 hr Glucose > 7.8), IMT: Intimal Medial Thickness,

Interpretation

These laboratory data demonstrate that there is a higher prevalence of

Syndrome X among SA, which is characterized by glucose metabolic abnormalities (impaired glucose tolerance), and dyslipidemia (low HDL cholesterol and increased triglycerides). Strikingly, 34.5% of asymptomatic SA had evidence of impaired glucose tolerance compared to 9% of WC. This prediabetic state is associated with a 1.5 increased risk for developing diabetes [29-31]. Urine microalbumin tended to be higher in SA, which suggests that early vascular endothelial damage may be present. Given SA preponderance to glucose-metabolic abnormalities one may expect that they would have an increased prevalence of abdominal obesity as measured by the waist-hip ratio. However no difference in waist to hip ratio between SA and WC was noted, which may be due to the small sample size. Furthermore, SA were found to have elevated levels of Lp(a), an atherogenic apoprotein which is genetically determined. A possible explanation for the increased rates of CHD in SA maybe due to an interaction between Lp(a) and Syndrome X whether this is due to greater atherosclerosis will be studied in greater detail in the proposed study.

No significant differences in intimal medial thickness (IMT) were observed between the groups when adjusted for age and sex. However given the very small number of subjects studied substantial differences may still become apparent in larger studies. The technicians who performed the carotid studies observed that SA appeared to have a smaller carotid artery diameter. We have not yet formally measured the lumen diameter. If this suggestion is true, adjustment of the IMT for artery diameter may be important, and this will be pursued in the large study.

Simple Logistic Regression

Impaired glucose tolerance (IGT) is defined as a 2 hours glucose of > 7.8 mmol/L. Overall 13 individuals were found to have impaired glucose tolerance 11 (34.5%) in the SA group and 2 (9.5%) in the WC group ($p<0.04$). Logistic regression was used to identify independent predictors of IGT in all 51 participants. Initially univariate analysis was done to identify potentially important predictors of IGT. Those which were significant in the univariate analysis and others which were biologically plausible potential predictors were included in the model. The goodness of fit statistic was significant which indicated that the data used did not fit the model which was created. The lack of fit may be explained by a biologically implausible model, failure to include of measure important predictors of IGT, or because of the very small sample size which could alter the approximation of the X^2 of the test-statistic distribution. Despite the lack of fit, certain independent predictors of IGT were revealed. Fasting glucose, ethnicity, and microalbumin were identified as independent predictors of IGT.

The Model Equation:

$\text{Log} < y/ 1-y> = \alpha + \beta x$ where y = prob (IGT)

Univariate Predictors of IGT:

Variable:	Odds Ratio:	P Value†:
1. Age	1.04	0.24
2. BMI	1.08	0.30
3. Ethnicity	2.41	0.03
4. Fasting Glucose	9.18	0.008
5. Fasting Insulin	2.42	0.06*
6. Tchol/HDL	1.39	0.11
7. Microalbumin	1.06	0.02
8. Waist/Hip	2.11	0.69
9. Smoking	0.81	0.52
10. Gender	1.63	0.15

† Testing the significance of individual variables

* Fasting Glucose and fasting insulin simple correlation in 0.31 ($P<0.03$)

Multiple Logistic Regression:

$$\text{Log} < y/ 1-y> = \alpha + \beta x_1 + \beta x_2 + \beta x_3 + \beta x_4$$

Variables entered:

Variable:	Beta	SE	Sig	EXP(B)
1. Age	0.05	.05	0.38	1.04
2. Ethnic group (1)	0.69	.50	0.16	2.00
3. Fasting Glucose (G)	1.62	0.83	0.05	5.03
4. Microalbumin (MA)	0.05	0.03	0.05	1.05
5. Gender (1)	0.04	0.44	0.93	1.03
CONSTANT	-12.84			

Final Equation:

Logist (y) = -12.84 + 0.05 AGE +0.69 Ethnic + 1.62 Fasting G + 0.05 MA + 0.04 Gender

Goodness of Fit: Significant by the Chi-Square statistic which indicates there is a lack of fit of the data to the proposed model: reasons include

i) A non-linear model may exist to explain the data or

ii) A better model may exist to predict IGT

4. Multiple Regression

Asymptomatic carotid artery disease measured by increased intimal medial thickness (IMT) has been shown to a be a reliable surrogate measure of CHD, and stroke independent of classical risk factors. For each mm increase in IMT the risk of MI increases 2.14 fold (95% CI+1.08-4.26). Based on the Atherosclerosis Risk

in Community (ARIC) study of 10,214 individuals aged 45-64 years, a mean IMT of 0.79 mm (+/- 0.20) was reported and the differences in mean IMT between white men and women was 0.1 mm. Using the IMT as the dependent variable, a model of multiple regression was created to identify independent predictors of IMT in the 51 participants. Simple correlation using the Pearson correlation coefficient testing the significance of r compared to 0 of potential independent predictors of IMT was performed prior to the testing of the model to determine the degree of correlation between the independent and dependent variables. Also other important cardiovascular risk factors (i.e. smoking) were entered into the model. It was hypothesized at the initiation of this study that SA may suffer increased atherosclerosis compared to WC, and therefore ethnic group was included in the model. Log transformations of non-linear plots was performed to achieve linearity.

Simple Correlations of Continuous variable with IMT:

Variable:	**r**	**P Value**
Age	0.51	0.001
2 hr Glucose	0.009	0.95
Fasting Glucose	0.07	0.62
Sys BP	0.33	0.03
BMI	0.13	0.39
W/H	0.06	0.70
Tchol/HDL	0.23	0.11
Ln Lp(a)	0.07	0.64
Microalbumin	0.18	0.22

Variables entered into the model by Stepwise regression:

Model: IMT = $\beta_0 + \beta_{1\ AGE} + \beta_{2\ SYS\ BP} + \beta_{3Ethnic} + \beta_{4Smoking} + \beta_{5\ Tchol/HDL}$

Variable 1. Age

R Square = 0.28

Standard Error =0.19

ANOVA:	DF	Sum of Squares	Mean Square:	Sig F
Regression	1	0.684	0.684	0.0001
Residual	47	1.77	0.037	

Variable in the Equation:

IMT = 0.03 +0.0133 AGE

Variables not in the equation:

- SYS BP
- TChol/HDL
- Ethnicity
- Smoking

Comment: Using Stepwise multiple regression AGE was the only significant independent predictor of IMT in the model, using this equation for a 48 year person, the predicted IMT value is 0.03 + (0.0133x48) or 0.67 which approximated the overall mean. , although blood pressure and serum lipids are plausible predictors

and likely would be significant with an increased number of subjects studied. A note of caution to avoid overinterpretation of these preliminary results, as the sample size is small and we appreciate the limitations of a B-error.

Qualitative Dietary Analysis

A qualitative review of self-reported dietary intake revealed interesting dietary differences between SA and WC. SA tend to consume a *usual* Canadian diet at breakfast and lunch including cereals, sandwiches, and pasta while continuing to consume their traditional foods for the main meal of the day. Specifically, SA reported a greater consumption of high fat dairy products, increased use of salt, and increased consumption of fried foods on a weekly basis.

Table 8-6: Pilot Study Results of Dietary Intake

Food	SA (n=31)	WC (n=20)	P-value
High Fat Dairy Products	100%	61%	0.001
Regular Use of Salt	66%	9%	0.001
Fried Foods	24%	4.7%	0.02
Fish (2-3 servings/week)	25%	10%	NS
Vegetarianism	10%	0%	NS

Currently the most commonly reported SA foods and WC foods reported in the multiple 24 hour recalls and 4 day food records are being incorporated into food frequency questionnaire for validation in a large study.

SHARE Life Stress and Satisfaction Questionnaire Results

Data from 14 SA and 15 WC who participated were collected from the LS+S questionnaire which measured psychosocial stressors (Chapter 6). Although the numbers are small, interesting trends were observed when the groups were compared (Table 8.7). SA appeared to experience more job stress, more depression, and worse overall emotional health compared to WC. Although by the GWBS mean scores relative to the previously published data, both SA and WC scores did not reflect positive well being. These subtle differences will be examined in greater detail in the full-scale study. In Table 8.8 the results of the Social Relationship Scale are presented. No differences in the number or quality of social supports between SA and WC are identified. This is contrary to what has been reported in the literature concerning immigrant families experiencing social isolation and a lack of social support.

Table 8-7: Comparison of Subscales (Mean Score) by Ethnic Group

Sub-scale	SA n=13	WC n=11	P-value
Job-stress*	38.9	42.9	0.32
Self-esteem	55.1	54.4	0.85
Depression**	55.1	61.7	0.11
General Well Being***	56.0	61.0	0.13

* Higher score indicates lower job stress, ** higher score indicates less depression, *** higher score indicates better overall emotional health. (A total score indicates more severe distress: 0-60 = Severe Distress, 61-72: Moderate Distress, 73-110: Positive Well-being)

Table 8-8: Social Relationship Scale

Ethnic Group	Extent of Network (Mean)	Helpfulness Score	Confidant
South Asian n=14	2.8 +/- 0.89 Median = 3	5.3 +/- 1.5	0.73
White Canadian n=15	3.1 +/- 1.58 Median = 3	5.7 +/- 0.72	1

Three scores may be derived, the extent of the network by the average number of supports listed, the quality of the network estimated by the 7-point helpfulness ratings, and a score reflecting the degree of reciprocity in which the respondent has these people confiding in him/her.

Conclusions

The SHARE pilot study was an unfunded study conducted during 6 weeks of the summer of 1995, to test the feasibility of our sampling methods and learn about difficulties in the conduct of the study. Although the method of stratified random sampling from the community was successful, the contact rate may be improved by utilizing specific strategies such as increased numbers of telephone calls at varying times of the day. We were able to contact 60% of those selected using a single letter and only 3 telephone calls. Of those contacted, 60% were eligible, and 54% of them completed a 2 hour clinical assessment. Therefore, although our response rate (of those eligible) is comparable to other population-based studies (see Table 8.2) our contact rates can be improved.

Although we studied only a small number of participants, this pilot data revealed striking differences in specific demographic characteristics, prevalence of IGT, glucose metabolic abnormalities, dyslipidemia, and elevated Lp(a) in SA

compared to WC.

Use of the carotid ultrasound suggested a qualitative difference in the width of the arteries in SA compared to WC, as reported by our technicians (not confirmed). Therefore in the upcoming study we are developing methods to standardize the measurements of IMT for artery width, and the participants height. Although significant differences in IMT were not observed in the pilot, age, blood pressure, and a trend with serum lipids were confirmed as independent predictors of IMT in both SA and WC, which strengthens our plan to match for age and gender up front during our sampling procedure. Furthermore, the independent predictors of atherosclerosis, both classical (smoking, blood pressure, and emerging (glucose, Lp(a), ethnicity) must be studied in greater detail in the full-scale study to elucidate with confidence the independent contribution of the proposed variables.

Our dietary analysis revealed interesting qualitative differences between SA and WC. These data from the pilot study provided information we are now using to create a SA specific food frequency questionnaire. Furthermore we were able to test the feasibility of performing 24 recalls by telephone after participants had completed their clinic visit. This is an important step as it serves as the primary method of validation of the SA specific FFQ.

Even though data concerning SA immigrant dominant psychosocial concerns are limited, we created and performed preliminary validation of a Life Stress and

Satisfaction Questionnaire. Although the numbers were small, a subset of the initially selected sample of SA and WC completed this questionnaire and we observed interesting trends. It appeared that SA may suffer from more depression, experience less general well-being, and experience more job stress than WC. These hypotheses will be studied in more detail in the main study.

Overall, the pilot study demonstrated the proposed sampling method is feasible, and the instruments planned for outcome measures are valid. Further validation of the psychosocial instrument will be conducted after the Qualitative substudy (Chapter 7) has been completed.

Chapter 9: Conclusions:

South Asians represent one of the largest ethnic groups in Canada and worldwide constitute about 2 billion people. They have an increased mortality from premature CHD which is not fully explained by traditional cardiac risk factors. This proposal is designed to add to our understanding of the link between emerging risk factors such as abdominal obesity, IGT, insulin resistance, elevated Lp(a), impaired fibrinolysis, key dietary factors, psychosocial factors and premature vascular disease in SA men and women.

Potential New Discoveries

SHARE is the first study which will document the presence and severity of ATH in SA. Previous studies of SA used insensitive measures of vascular disease (eg. Q waves on ECG) which required large sample sizes, and only allowed for indirect associations between risk factors and disease. The new information provided by this study includes: i. confirmation that the pathologic basis of high CHD rates is ATH ii. identification of emerging risk factors in addition to and traditional ones of ATH iii. determination of the relationship between Lp(a) and and impaired fibrinolysis in SA iv. elucidation of the interrelationship of Syndrome X and the presence of ATH v. validation of a SA-specific FFQ to study the relationship of key

dietary factors and ATH in SA vii. development (using qualitative methods) and validation of a psychosocial assessment instrument to measure stressors experienced by SA migrants in Canada and the relationship of these to unhealthy lifestyle behaviours and ATH.

Potential Relevance

The results of this study will not only be relevant to the health needs of SA in Canada but also SA resident in other countries and to individuals with Syndrome X. Many of the lessons learned from this study may be applicable to populations other than SA who suffer from Syndrome X (i.e. First Nations, Hispanics). This study will also assist in the resolution of fundamental questions about the relationship of IGT, hyperinsulinemia, Lp(a), the fibrinolytic system, increased triglycerides and low HDL and their inter relationship to the development of ATH in both men and women. It is expected that while some strategies of prevention (eg. smoking cessation, or blood pressure lowering) in SA will be similar to Whites, others (eg. decreasing abdominal obesity, lowering glucose, modifying fibrinolytic activity) may have to be specifically developed and targeted at this group. This study is an important step towards this goal.

Future

Although this proposal involves the identification and study SA and WC in a cross sectional study (Phase 1), long term follow is explicitly planned (Phase 2). However, even the current study will provide useful information on etiological

factors because the B-mode carotid ultrasound (CUS) measures subclinical ATH. These lesions have developed over decades, and as such this study represents an *integrated index of the impact of risk factors over time.* Since the lesions are subclinical, it is unlikely that subjects would have changed their lifestyle in response to this. Therefore our approach utilizes a retrospective-longitudinal design that provides much more information than the usual cross sectional study.

Summary

This proposal represents a cross-sectional study in which the prevalence of traditional and emerging risk factors in South Asians and White Canadians in Canada will be determined, and the relationship of these factors to subclinical ATH using the CUS within each group will be explored. The measurement of ATH represents *an integrated measure of the impact of risk factors over decades* - providing a retrospective longitudinal perspective. This thesis outlines Phase 1 of this program and represents how studying subclinical ATH represents an *efficient* strategy that will yield results *quickly* in order to help better facilitate the efforts of larger and long term epidemiologic studies of relating risk factors to clinical outcomes, and assist in the development of preventive strategies to reduce CHD in SA.This study examines the role of both emerging and traditional risk factors in SA who are uniquely at high risk of CHD and will form the basis of a prospective cohort study to document the development of subsequent clinical events (Phase 2)

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Appendices

Appendix 1: Introductory Letter

Dear Family,

Heart disease is Canada's number one killer. We at McMaster University and at the University of Toronto are looking into how heart disease varies between Canadians of different backgrounds by examining people like you. We would like to invite you to help us by participating in a research study.

How you were chosen
We have selected your family randomly from among all of the households in the Hamilton/Wentworth area. In a few days, we will be contacting you by telephone. We will wish to speak to either a male or a female member of your family who is between the ages of 35 and 65. On the phone, we will assess your eligibility to participate, and if eligible, invite you to join our study.

What is expected of you
If you are eligible and willing to join our study, we will ask you a few questions on the telephone and make an appointment for you to come to our teaching hospital, the Hamilton General Hospital. There, you will be requested to fill out a brief questionnaire about your health, diet, and lifestyle habits. You will then have a simple blood test, brief physical examination, and an ultrasound examination of your neck. We will forward the results of the tests to you. All information will be kept strictly confidential and used for scientific analysis only in groups. Your participation is completely voluntary and you may withdraw from the study at any time.

Time commitment
We realize that your time is very valuable. When we contact you by telephone, we will arrange a time for your tests that is convenient for you. The total time commitment is about two hours.

Benefit to you
All of your individual results from the study will be mailed to you and, if needed, explained to you by a professional health care worker. Participants will also be entered in a draw for one of four possible pairs of Blue Jay Baseball tickets at the Skydome in Toronto.

Benefits to the Community
Most of us have a friend or a relative who has been affected by heart disease. This research project may benefit many of these people. The information obtained from you and other study participants will teach doctors more about how people of different backgrounds develop heart disease and allow them to develop strategies to prevent heart disease. This will improve the health of all Canadians, including our children.

We believe that this study is a very important one and hope that you will join us in the fight against Canada's number one killer. If you have any questions we would be happy to answer them when we contact you by telephone. Thank you in advance for your cooperation.

Sincerely,

Dr. Sonia Anand, MD
Study Investigator

Dr. Salim Yusuf, MBBS, FRCP, D Phil
Study Investigator
Director of Cardiology, McMaster University

Appendix 2: SHARE General Questionnaire

SHARE

Study of **H**eart **A**ssessment and **R**isk in **E**thnic Groups

This questionnaire asks for some background information about you. Please answer every question. If you are uncertain about how to answer a question, please ask the monitor for help.

INSTRUCTIONS

Please answer EACH question by checking ONE box on each line:

☑

or, by writing number(s) in the spaces provided:

[0|2]

or, by specifying the answer on the line(s) provided

OFFICE USE: **Subject ID#** ☐ ☐☐☐ *Case No.* **Subject Initials** ☐☐☐ *F M L* **Monitor Check:** ☐

Visit Date ☐☐ ☐☐ ☐☐
year month day

1. Your Name: *(please print)* _____ *Last Name* _____ *Given Names*

_____ *Apt. No.* _____ *Street* ☐☐☐-☐☐☐ *Postal/Zip Code*

_____ *Town/City* _____ *Province*

2. Your Date of Birth ☐☐ ☐☐ ☐☐
year month day

3. Your Gender *(check one)* ☐ Male ☐ Female

4. Tel.: Home ☐☐☐-☐☐☐-☐☐☐☐ *(Area Code)* Work ☐☐☐-☐☐☐-☐☐☐☐ *(Area Code)*

Check only the box to the left of your response

South Asian= India, Pakistan, Bangladesh, Sri Lanka

5. Your Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations

☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

6. Your Mother's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations

☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

7. Your Father's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations

☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

Subject ID# ☐ ☐☐☐ **Subject Initials** ☐☐☐

Check box to the left of your response

8. Your Maternal Grandmother's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations ☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

9. Your Maternal Grandfather's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations ☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

10. Your Paternal Grandmother's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations ☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

11. Your Paternal Grandfather's Ethnicity: ☐ White Caucasian ☐ South Asian ☐ Black ☐ First Nations ☐ Hispanic ☐ Japanese ☐ Chinese ☐ Other (specify) _____

12. Your country of origin *(specify)*: _____

13. If you have lived in another country, in which country did you live? _____

14. How many years have you lived in Canada: All my life ☐ *or* ☐☐ *yrs.*

15. Your first language or mother tongue *(specify)*: _____

16. a) Your Fathers first language *(specify)*: _____

b) Your Mother's first language *(specify)*: _____

17. Your Religion *(check)*: ☐ Christian ☐ Hindu ☐ Muslim ☐ Sikh ☐ Jewish ☐ Other *(specify)* _____

Subject ID# ☐ ☐☐☐ **Subject Initials** ☐☐☐

18.What is you current Marital Status *(check)*: ☐ Married ☐ Common-law ☐ Living with partner

☐ Never married ☐ Widower ☐ Separated ☐ Divorced

19. Your highest level of education obtained *(check one)*:

☐ No formal education

☐ Completed junior high school (grade 9 or equivalent)

☐ Completed high school (secondary school)

☐ Some university

☐ Diploma or certificate from trade, technical or vocational school, or business college

☐ Diploma or certificate from community college, CEGEP, or nursing school

☐ Bachelor's or undergraduate degree or teacher's college (eg. B. Sc., B.A.)

☐ Professional degree (eg. M.D., D.D.S.,D.V.M.)

☐ Master's (eg. M.A., M. Sc., M. Ed.)

☐ Doctorate (eg. Ph. D.. D.Sc.)

☐ Other (*specify*): _____

20. Are you currently employed outside the home *(check)*? ☐ Yes ☐ No ☐ Retired

If no or retired go to "leisure" (question 25)

21. What is your usual occupation *(specify)*? _____

22. Which category below best fits your job *(check one)*:

- ☐ Professional
- ☐ Business
- ☐ Clerical Worker
- ☐ Sales Worker
- ☐ Skilled / Foreman
- ☐ Manager, Official Proprietor
- ☐ General Labour
- ☐ Self employed

23. For statistical purposes only, we need to know the range of your total gross household income last year. Please indicate the income range of your household.

- ☐ < 12 000
- ☐ 12 000 - 24 999
- ☐ 25 000 - 49 999
- ☐ 50 000 and over
- ☐ No response

24. Thinking back over the past 3 months, which of the following best describes your usual daily activities or work habits? *(check one)*

- ☐ Usually sit during the day and do not walk around very much
- ☐ Stand or walk a lot during the day, but do not have the energy to carry or lift things very often
- ☐ Usually lift or carry light loads or climb stairs or hills often
- ☐ Do heavy work or carry very heavy loads

LEISURE and EXERCISE

25. Do you regularly engage in physical activity during your leisure time? By regularly,we mean at least once a week during the past month.

☐ Yes ☐ No ☐ Can't remember

# of times X 1 week = _____ If no, go to question 28

26. How much of this activity is strenuous enough to cause sweating or heavy breathing?

- ☐ Most of it
- ☐ Some of it
- ☐ None of it

27. How long do you usually exercise?

- ☐ < than 15 minutes
- ☐ 15 -30 minutes
- ☐ 31-60 minutes
- ☐ more than 60 minutes
- ☐ don't know

ALCOHOL

28. Have you ever taken a drink of beer, wine, liquor, or any other alcoholic beverage? *(check)*

☐ Yes ☐ No → Go to "smoking" (question 31)

29. Last week, on how many days did you consume alcoholic beverages of any type *(check one)*?

- ☐ No days → Go to "smoking" (question 31)
- ☐ One day
- ☐ Two days
- ☐ Three days
- ☐ Four days
- ☐ Five days
- ☐ Six days
- ☐ Seven days

30. About how many drinks did you have last week *(check one)*?

- ☐ 0 drinks
- ☐ 1-5 drinks
- ☐ 6-10 drinks
- ☐ 11-15 drinks
- ☐ More than 15 drinks

CIGARETTE SMOKING

31. Which of the following best describes you *(check one)*?

☐ I currently smoke cigarettes regularly

☐ I don't currently smoke cigarettes regularly, but I used to

☐ I have never smoked cigarettes regularly → Go to question 40

32. If you are or have smoked, how many years have you been a regular smoker? ☐☐ years

33. At the present time, if you smoke cigarettes, do you smoke regularly (every day) or occasionally (not every day)?

☐ Regularly ☐ Occasionally

34. How many cigarettes do you smoke per day? ☐☐ cigarettes

35. If you have smoked cigarettes in the past, when did you quit? ☐☐ years ago

36. Does anybody else in your home smoke regularly *(check)*? ☐ Yes ☐ No

37. When you smoke(d) cigarettes, how deeply do/did you inhale *(check one)*?

☐ Deeply into my lungs

☐ Moderately into my lungs

☐ I do not inhale into my lungs

38. Do/did you usually smoke(d) FILTER cigarettes *(check one)*?

☐ All, or nearly all FILTER

☐ Mixed

☐ All, or nearly all NON-FILTER

39. If you smoke cigarettes, what is your brand *(specify)*? _____

OTHER TOBACCO PRODUCTS

40. Do you now, or have you ever smoked pipes or cigars *(check)*? ☐ Yes ☐ No

41. Do you now, or have you ever smoked beedies (a South Asian cigarette)? ☐ Yes ☐ No

42. Do you now, or have you ever used chewing tobacco *(check)*? ☐ Yes ☐ No

43. Do you now, or have you ever chewed paan (A South Asian condiment) with tobacco *(check)*? ☐ Yes ☐ No

PAST MEDICAL HISTORY

44. In general, would you say your health is *(check one)*:

☐ Excellent ☐ Good ☐ Poor

☐ Very Good ☐ Fair

45. Has a doctor ever told you that you have high blood /urine sugar *(check)*? ☐ Yes ☐ No

If no go to question 49

46. Has a doctor ever told you that you have diabetes*(check)*? ☐ Yes ☐ No

47. At what age was this diabetes diagnosed? ☐☐ years of age

48. Are you on any treatment for your diabetes? Check all that apply.

☐ No current treatment ☐ Diet

☐ Insulin ☐ Weight

☐ Pills to control blood sugar ☐ Other _____

49. Has a doctor ever told you that you have high blood pressure *(check)*? ☐ Yes ☐ No

50. How long ago did you last have you blood pressure checked?

☐ < 6 months ago ☐ 6-12 months ago ☐ > 1 yr. ☐ don't know

51. Do you take blood pressure pills*(check)*? ☐ Yes ☐ No

52. Have you ever had pain or discomfort in your chest on exertion*(check)*? ☐ Yes ☐ No

If no, go to question 54

53.How do you relieve this discomfort*(check)*?

☐ I usually rest

☐ I take medication under my tongue (nitroglycerin)

☐ Other _____

54. Have you ever had a heart attack*(check)*? ☐ Yes ☐ No ☐ don't know

55. Have you ever had angioplasty or coronary bypass surgery*(check)*? ☐ Yes ☐ No

56. Have you ever been diagnosed with other heart disease *besides* angina or a heart attack *(check)*? ☐ Yes ☐ No

If yes, please specify_____

57. Do you get pain or cramps in your calves when walking*(check)*? ☐ Yes ☐ No

58. Have you ever had your cholesterol measured? ☐ Yes ☐ No ☐ not sure

59. Have you ever been told by a doctor, nurse or other health professional that your blood cholesterol was high?
☐ Yes ☐ No ☐ can't remember

60. Are you presently on a special diet or drug which was recommended by a doctor to lower your blood cholesterol?

☐ Yes Drug ☐ Yes Diet ☐ Both ☐ Neither

61. Have you ever had a stroke or warning stroke *(check)*? ☐ Yes ☐ No ☐ don't know

62. Have you ever tried to lose weight? ☐ Yes ☐ No

63. Are you presently trying to lose weight, gain weight, or neither?

☐ Gain Weight ☐ Lose Weight ☐ Neither

64. Have you ever been hospitalized before (except for pregnancy) *(check)*? ☐ Yes ☐ No

65. If "yes", please specify why: _____

_____

_____

66. Have you ever been diagnosed with any other major illness *(specify)*?_____

☐ Cancer ☐ Liver disease _____

☐ Kidney disease _____

FAMILY HISTORY

67. Have the members of your immediate family ever had any of the following diseases *(check)*?

(a) Heart attack before age 65 years?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(b) Other heart trouble?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(c) Heart surgery?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(d) Angioplasty?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(e) Diabetes?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(f) High blood pressure?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A
(g) Stroke?	☐ Father	☐ Mother	☐ Brother(s)	☐ Sister(s)	☐ N/A

"Brothers" and "sisters" Includes half-brothers and half-sisters

DIET AND NUTRITION

68.

Are you a vegan (eats NO animal products including milk)*(check)*? ☐

OR

Are you a lacto-vegetarian (eats milk and milk products) *(check)*? ☐

OR

Are you a lacto-ovo vegetarian (eats eggs + and milk, but no meat) *(check)*? ☐

OR

Are you predominantly vegetarian (eats meat rarely) *(check)*? ☐

OR

Are you a vegetarian who eats fish*(check)*? ☐

OR

Are you a non-vegetarian(eats meats regularly)? ☐

If you EVER eat fish or meat, please answer the following

69.

(a) How many 3 oz. servings (approximately the size of a deck of cards) of meat do you eat per week? (meat = chicken, lamb, pork and beef) *(check one)*

- ☐ 0 servings per week
- ☐ 1 serving per week
- ☐ 2-3 servings per week
- ☐ 4-7 servings per week
- ☐ 8-15 servings per week
- ☐ 16-25 servings per week
- ☐ More than 25 servings per week

(b) How often do you eat the skin on chicken *(check one)*?

- ☐ Always
- ☐ Sometimes
- ☐ Never

(c) How many servings of fish do you eat per week *(check one)*?

- ☐ Never
- ☐ Less than 1 serving per week
- ☐ 1 serving per week
- ☐ 2-3 servings per week
- ☐ 4-7 servings per week
- ☐ 8-15 servings per week
- ☐ 16-25 servings per week
- ☐ More than 25 servings per week

(d) How much of the visible fat on your meat do you eat *(check one)*?

- ☐ Most of it
- ☐ Some of it
- ☐ As little as possible

70. What kind of milk do you use most often at home *(check one)*?

- ☐ Homogenized (Whole)
- ☐ 2%
- ☐ 1%
- ☐ Skim/fat free
- ☐ Soya
- ☐ Powdered
- ☐ None
- ☐ Other *(specify)* _____

71. How much milk do you use each DAY , including with coffee, tea, cereal, etc. *(check one)*?

- ☐ None
- ☐ Quarter of a litre (250 m, 8oz)
- ☐ Half a litre (500 ml, 16 oz)
- ☐ Three quarters of a litre (750 ml, 24oz)
- ☐ One litre
- ☐ More than one litre

72. How much cheese do you eat per week *(grams or ounces)*?
(1 gram = 1 slice)
☐☐ g/0z

73. What sort of cheese do you eat most often *(check as many as apply)*?

- ☐ Mainly cheddar
- ☐ Mainly mozzarella
- ☐ Swiss cheese
- ☐ Feta cheese
- ☐ Farmer's cheese or paneer (A South Asian cheese)
- ☐ Low fat cheddar or mozzarella
- ☐ None
- ☐ Other *(specify)* _____

74. What sort of oil or fat do you use most often for frying *(check one)*?

- ☐ Vegetable oil → *Go to question 75*
- ☐ Butter
- ☐ Ghee (South Asian clarified butter)
- ☐ Vegetable fat
- ☐ Lard
- ☐ Margarine
- ☐ None
- ☐ Other *(specify)* _____

75. If you use vegetable oil, what kind *(check one)*?

- ☐ Sunflower oil
- ☐ Corn oil
- ☐ Canola oil
- ☐ Coconut oil
- ☐ Olive oil
- ☐ Other *(specify)* _____

76. How often do you eat fried foods at home *(check one)*?

- ☐ Daily
- ☐ 4-6 times per week
- ☐ 1-3 times per week
- ☐ Less than once a week

77. How often do you eat fast foods away from home *(check)*?

- ☐ Daily
- ☐ 1-3 times per week
- ☐ 4-6 times per week
- ☐ Less than once a week

78. How often would you say salt is added to your food when cooking*(check)*?

- ☐ Often/ Always
- ☐ Almost never/never
- ☐ Sometimes
- ☐ Don't know
- ☐ Occasionally

79. How often do you add salt to any food at the table*(check)*?

- ☐ Often/ Always
- ☐ Occasionally
- ☐ Sometimes
- ☐ Almost Never/ Never

80. During the last month did you take any of the following supplements/medication *(check)*?

	Yes	No		Yes	No
Aspirin	☐	☐	Beta-carotene	☐	☐
Multiple vitamins	☐	☐	Cod liver oil	☐	☐
Multiple plus iron	☐	☐	Iron	☐	☐
Multiple plus minerals	☐	☐	Calcium	☐	☐
B complex	☐	☐	Selenium	☐	☐
Vitamin C	☐	☐	Zinc	☐	☐
Vitamin E	☐	☐	Ginseng	☐	☐
Vitamin A	☐	☐	Garlic pills	☐	☐

Other vitamins *(specify)* _____

Other minerals *(specify)* _____

81. Do you take these supplements everyday? ☐ Yes ☐ No

MEDICATIONS

82. Please list your current regular medications

Drug Name	Drug Name	Drug Name	Drug Name

FOR FEMALE RESPONDENTS ONLY

83. At what age did your periods first start? ☐☐ years old

84. Do you still have regular periods *(check)*? ☐ Yes ☐ No

85. If you no longer have periods, how old were you when they stopped? ☐☐ years old

86.Has your uterus been removed (hysterectomy) ☐ Yes ☐ No

87.Have your ovaries been removed (oophorectomy) ☐ Yes ☐ No

88. After your periods stopped, did you go on hormone therapy *(check)*? ☐ Yes ☐ No

89. If "yes", how long have you been on hormone replacement therapy? ☐☐ years

90. Have you ever tried to become pregnant but couldn't *(check)*? ☐ Yes ☐ No

91. How many live births have you had? ☐☐ (number)

Thank you for your time!

You can help us to make this questionnaire better by answering the following questions

Please write your responses on the lines provided

1. Why did you decide to join the study? _____

2. Were any of the questions hard to understand? _____

If so, WHICH ones and WHY? _____

3. Were the instructions helpful? _____

If not, WHY? _____

3. Was the length appropriate? _____

WHY or WHY NOT? _____

4. HOW else do you think we could make this questionnaire better? _____

_____

_____

5. Would it be alright if we contacted you in 3 to 5 years as a follow up call? _____

_____

_____

Subject ID# ☐ ☐☐☐ *Case No*

Subject Initials ☐☐☐ *F M L*

Appendix 3: SHARE Life Stress and Satisfaction Questionnaire

SHARE

Life Stress and Satisfaction Questionnaire

This questionnaire asks for some information about your life stressors. Please answer each question as best as possible.

INSTRUCTIONS

Please answer EACH question by checking ONE box on each line:

OR

By writing numbers(s) in the spaces provided:

0	4	2

OR

By specifying the answer on the line(s) provided.

For office use only

Subject ID# ☐☐☐☐ Subject Initials ☐☐☐ Monitor Check ☐

1. **Do you work at a job or business?**

☐ Permanently unable to work.

☐ No → go to question 2

☐ Yes → go to question 3

2. **What is the reason that you are currently not working for pay or profit?**

☐ Own illness or disability

☐ Pregnancy

☐ Caring for own children

☐ Caring for elder relative(s)

☐ Other personal or family responsibilities

☐ School or educational leave

☐ Labour dispute

☐ Temporary layoff due to seasonal conditions

☐ Temporary layoff, non-seasonal

☐ Permanent layoff

☐ Unpaid or partially paid vacation

☐ Other (please specify)

_____

3. **How many hours per week do you usually work?**

___ ___ ___ hours

4. **The following series of statements might describe your job situation. Please indicate if you STRONGLY AGREE, AGREE, DISAGREE, or STRONGLY DISAGREE with each of the following.**

a) Your job requires that you learn new things.

Strongly Agree Agree Disagree Strongly Disagree

b) Your job requires a high level of skill.

Strongly Agree Agree Disagree Strongly Disagree

c) Your job allows you freedom to decide how you do your job

Strongly Agree Agree Disagree Strongly Disagree

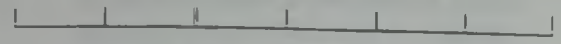
d) Your job requires that you do things over and over.

Strongly Agree Agree Disagree Strongly Disagree

For office use only

Subject ID# ☐☐☐☐ Subject Initials ☐☐☐ Monitor Check ☐

e) Your job is very hectic.

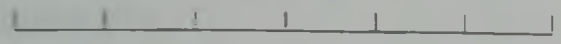


Strongly Agree Agree Disagree Strongly Disagree

f) You are free from conflicting demands that others make.

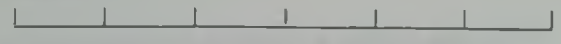
Strongly Agree Agree Disagree Strongly Disagree

g) Your job security is good.



Strongly Agree Agree Disagree Strongly Disagree

h) Your job requires a lot of physical effort



Strongly Agree Agree Disagree Strongly Disagree

I) You have a lot to say about what happens in your job.

Strongly Agree Agree Disagree Strongly Disagree

j) You are exposed to hostility or conflict from the people you work with.

Strongly Agree Agree Disagree Strongly Disagree

k) Your supervisor is helpful in getting the job done.

Strongly Agree Agree Disagree Strongly Disagree

l) The people you work with are helpful in getting the job done.

Strongly Agree Agree Disagree Strongly Disagree

5. **How satisfied are you with your job? (check one)**

- ❑ Very Satisfied
- ❑ Somewhat Satisfied
- ❑ Not too Satisfied
- ❑ Not at all Satisfied

6. **In the past 12 months, did you (or your partner) experience a change of job for a worse one, or were either of you demoted at work or take a cut in pay?**

❑ Yes ❑ No

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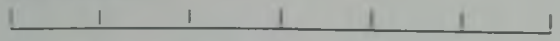
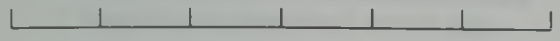
7. **In the next series of statements, please indicate if you STRONGLY AGREE, AGREE, DISAGREE, or STRONGLY DISAGREE with each of the following.**

a) You feel that you have a number of good qualities.



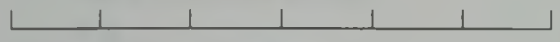
Strongly Agree Agree Disagree Strongly Disagree

b) You feel that you are a person of worth at least equal to others.



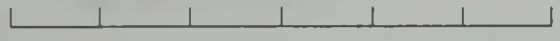
Strongly Agree Agree Disagree Strongly Disagree

c) You are able to do things as well as most other people.



Strongly Agree Agree Disagree Strongly Disagree

d) You take a positive attitude toward yourself



Strongly Agree Agree Disagree Strongly Disagree

e) On the whole you are satisfied with yourself.

Strongly Agree Agree Disagree Strongly Disagree

f) All in all, you are inclined to feel you are a failure.

Strongly Agree Agree Disagree Strongly Disagree

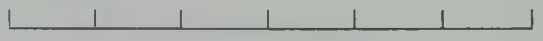
8. a) You have little control over the things that happen to you.

Strongly Agree Agree Disagree Strongly Disagree

b) There is really no way you can solve some of the problems you have.

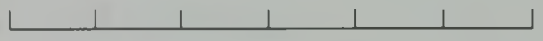
Strongly Agree Agree Disagree Strongly Disagree

c) There is little you can do to change many of the important things in your life.



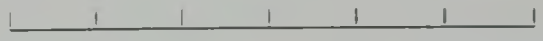
Strongly Agree Agree Disagree Strongly Disagree

d) You often feel helpless in dealing with problems of life



Strongly Agree Agree Disagree Strongly Disagree

e) Sometimes you feel that you are being pushed around in life



Strongly Agree Agree Disagree Strongly Disagree

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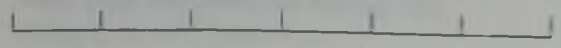
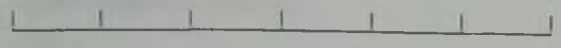
f) What happens to you in the future mostly depends on you.



Strongly Agree Agree Disagree Strongly Disagree

g) You can do just about anything you really set your mind to.



Strongly Agree Agree Disagree Strongly Disagree

9 **During the past month, how much of the time have you felt that the future looks hopeful and promising? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

10. **How much of the time, during the past month, has your daily life been full of things that were interesting to you? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

11. **How much of the time, during the past month, did you feel relaxed and free of tension? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

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12. **During the past month, how much of the time have you generally enjoyed the things you do? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

13. **How much of the time, during the past month, have you been a very nervous person? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

14. **When you got up in the morning, this past month, about how often did you expect to have an interesting day? (check one)**

- ☐ Always
- ☐ Very often
- ☐ Fairly often
- ☐ Sometimes
- ☐ Almost never
- ☐ Never

15. **During the past month, how much of the time have you felt tense or "high strung" ? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

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16. **During the past month, have you been in firm control of your behaviour, thoughts, emotions, and feelings? (check one)**

- ❑ Yes, very definitely
- ❑ Yes, for the most part
- ❑ Yes, I guess so
- ❑ No, not too well
- ❑ No, and I am somewhat disturbed
- ❑ No, and I am very disturbed

17. **During the past month, how often did you feel that you had nothing to look forward to? (check one)**

- ❑ Always
- ❑ Very often
- ❑ Fairly often
- ❑ Sometimes
- ❑ Almost never
- ❑ Never

18. **How much of the time, during the past month, have you felt calm and peaceful? (check one)**

- ❑ All of the time
- ❑ Most of the time
- ❑ A good bit of the time
- ❑ Some of the time
- ❑ A little of the time
- ❑ None of the time

19. **How much of the time, during the past month, have you felt emotionally stable? (check one)**

- ❑ All of the time
- ❑ Most of the time
- ❑ A good bit of the time
- ❑ Some of the time
- ❑ A little of the time
- ❑ None of the time

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20. **How much of the time, during the past month, have you felt downhearted and blue? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

21. **In choosing your friends, how important to you are things like their race, their religion, or their political beliefs? (check one)**

- ☐ Always very important
- ☐ Almost always important
- ☐ Usually important
- ☐ Not too important
- ☐ Hardly ever important
- ☐ Not important at all

22. **During the past month, have you been anxious or worried? (check one)**

- ☐ Yes, extremely so, to the point of being sick or almost sick.
- ☐ Yes, very much so
- ☐ Yes, quite a bit
- ☐ Yes, some, enough to bother me
- ☐ Yes, a little bit
- ☐ No, not at all

23. **During the past month, how much of the time were you a happy person? (check one)**

- ☐ All of the time
- ☐ Most of the time
- ☐ A good bit of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

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24. **How often, during the past month, have you been waking up feeling fresh and rested? (check one)**

- ❑ Always, every day
- ❑ Almost every day
- ❑ Most days
- ❑ Some days, but usually not
- ❑ Hardly ever
- ❑ Never wake up feeling rested

25 **During the past month, have you been under or felt you were under any stain, stress or pressure? (check one)**

- ❑ Yes, almost more than I could stand to bear
- ❑ Yes, quite a bit of pressure
- ❑ Yes, some, more than usual
- ❑ Yes, some, but about normal
- ❑ Yes a little bit
- ❑ No, not at all

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Appendix 4: Published Abstracts

Glucose metabolic abnormalities in South Asians in Canada study of heart assessment and risk in ethnic groups (SHARE): pilot study results

S. Anand, H. Gerstein, S. Yusuf

McMaster University, Hamilton, Canada

South Asians (SA) have a higher prevalence of impaired glucose tolerance (IGT), overt diabetes (DM), and premature coronary heart disease (CHD) than other populations. Moreover SA living in North America have not been systematically assessed for the presence of these diseases. We designed a cross-sectional population based study in Canada of SA and people of European origin (EC) to study risk factors for CHD utilizing carotid B-mode ultrasound to measure the intimal medial thickness (IMT) a measure of subclinical atherosclerosis. Preliminary data collected in a pilot study to test the feasibility of this approach for a large study are presented.

We randomly sampled 30 SA and 21 EC in a cross-sectional study using stratified random sampling with computerized phone directories. All participants completed a health questionnaire, underwent physical testing, a dietary assessment, laboratory tests and a carotid ultrasound.

Despite the small numbers studied, age and sex adjusted analyses of these asymptomatic individuals, revealed a higher prevalence of IGT and DM in SA compared to EC (34.5% v 9.5%, $p < 0.04$). Although the groups' fasting glucose and insulin levels were similar ($p < 0.07$, $p < 0.06$ respectively), 2 hours after a 75 g oral glucose load the SA group had higher glucose (7.12 mmol/L v 5.63 mmol/L, $p < 0.01$), and insulin levels (6.32 pmol/L v 5.45 pmol/L, $p < 0.005$). SA also had a higher total cholesterol/HDL ratio (5.14 v 4.25, $p < 0.05$). Fasting triglycerides, free fatty acids, waist/hip ratio and BMI did not differ. There was a trend towards a higher urinary microalbumin concentration in SA (21.00 mg/L v 8.47 mg/L, $p < 0.09$). The mean IMT was 0.65 ± 0.19 mm in SA and 0.72 ± 0.17 mm in EC (P = NS).

This pilot data from a randomly sampled Canadian population revealed striking differences in the prevalence of glucose metabolic abnormalities in SA compared to EC. Although the exact relationship between glucose dysregulation and CHD is unclear, this study is designed to elucidate it.

Other epidemiology/prevention
Diabetes

Society of General Internal Medicine
19th Annual Meeting
Washington, DC
May 2-4, 1996

STUDY OF HEART ASSESSMENT AND RISK IN ETHNIC GROUPS (SHARE): PILOT STUDY RESULTS. S Anand, S Yusuf. Department of Medicine, McMaster University, Hamilton, Ontario.

Purpose: South Asians (SA), people who originate from India, Pakistan, Bangladesh and Sri Lanka have an increased susceptibility to develop coronary heart disease (CHD) compared with whites. There are little data on lifestyle factors of migrant SA in North America. In preparation for a large cross-sectional population-based study of risk factors for CHD in SA, the feasibility of our design was tested in a pilot study and preliminary results are presented below.

Methods: Fifty-one Canadians of SA and European (EC) origin were randomly sampled from a sampling frame created from a compact disc program of public telephone directories in Canada. All participants visited the hospital and completed a health questionnaire, dietary, physical and laboratory assessments.

Results: The average duration of residency in Canada was 18 years in the SA and 48 years in the EC group ($p<0.001$). The mean age of all participants was 48 years. An increased prevalence of impaired glucose tolerance and diabetes in response to an oral glucose tolerance test was observed in the SA as compared to the EC (34.5% v 9.5%, $p<0.04$). After adjusting for differences in age and sex, a significant difference in the lipoprotein (a) concentration (log) (SA: 5.50mg/L v EC: 4.57 mg/L, $p<0.02$), and HDL (SA: 1.04 mmol/L v EC: 1.25 mmol/L, $p<0.01$) was observed. SA were found to have significantly lower rate of smoking (18% v 67%, $p<0.0005$) and alcohol use (47% v 81%, $p<0.01$), were more likely to be married (97% v 71%, $p<0.009$), and were more likely to be university educated (66% v 43%, $p<0.09$) compared to EC. No differences in amount of regular exercise was noted. A self-administered dietary questionnaire revealed a trend toward increased vegetarianism in the SA population (10% v 0%). No differences in fast foods or fish consumption per week were observed. SA (100%) consumed higher fat milk (homo or 2%) compared to EC (61%), who were more likely to use skim or 1% ($p<0.001$). SA reported regularly adding salt to their food when cooking (66% v 9%, $p<0.001$) compared to EC. No significant differences in the blood pressure, waist to hip ratio or body mass index were observed.

Conclusions: These representative data re-enforce that key metabolic and lifestyle differences exist between asymptomatic migrant SA compared to EC, and may help explain differences in CHD rates between the groups.

Journal of General Internal Medicine 1996; 11 (supp. 1): 42.

49th Annual meeting of the Canadian Cardiovascular Society
October 29 - November 2, 1996
Montreal, Quebec

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METABOLIC ABNORMALITIES AND DIETARY DIFFERENCES IN SOUTH ASIAN CANADIANS COMPARED TO EUROPEAN CANADIANS -STUDY OF HEART ASSESSMENT AND RISK IN ETHNIC GROUPS (SHARE)

S. Anand*, H. Gerstein*, S. Yusuf McMaster University, Hamilton, Canada.

Mortality statistics from Canada indicate South Asians (SA), people who originate from India, Pakistan, Bangladesh, and Sri Lanka have an increased mortality from CHD compared to other Canadians. In preparation for a large cross-sectional population-based study of CHD risk factors in SA, a pilot study was conducted and preliminary results are presented. We randomly sampled 30 SA and 21 Canadians of European origin (EC) using a compact disc program of public telephone directories in Canada. All participants completed a health questionnaire, dietary assessment, physical and laboratory testing. The mean age of each group was 48 years. The average duration of residency in Canada for SA was 18 years and 48 years for EC ($p<0.001$). Age and sex adjusted analysis revealed a higher prevalence of impaired glucose tolerance and diabetes mellitus in SA compared to EC (34.5% vs 9.5%, $P<0.04$), and a trend to higher fasting glucose and insulin levels ($P<0.07$, $P<0.06$ respectively). Two hours after a 75 gram oral glucose tolerance load SA had a higher glucose (7.12 mmol/L vs 5.63 mmol/L, $p<0.01$), and insulin levels (6.32 pmol/L vs 4 45 pmol/L, $P<0.005$). A trend towards higher urine microalbumin in SA (21.00 mg/L vs 8.47 mg/L, $P<0.09$) was observed, indicating early vascular damage. SA also had a higher total cholesterol /HDL ratio 5 14 vs 4.25, $P<0.05$), and Lp(a) concentration (In 5.50 vs 4.57, $P<0.02$) compared to EC. Dietary analysis revealed that although more SA were vegetarians, (10% vs 0 %), they consumed more fried foods (>3 servings/week) (24% vs 4.7%, $p<0.02$), used salt regularly with cooking (66% vs 9%, $p<0.001$), and consumed higher fat dairy products (100% vs 61%, $p<0.001$) more often. These pilot data from a randomly sampled Canadian population revealed striking differences in the prevalence of glucose and lipid abnormalities between SA and EC and a higher prevalence of microalbuminuria. These abnormalities in SA may be partly related to dietary changes associated with migration superimposed upon an inherent tendency for abnormal glucose and lipid metabolism.