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Cardiovascular Risk in South Asians Living in Canada: A Systematic Review

Journal:	*CMAJ*
Manuscript ID:	CMAJ-13-1139
Manuscript Type:	Research - Meta-analysis/systematic review
Date Submitted by the Author:	26-Jul-2013
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Keywords:	Cardiac Disease, Coronary, Diabetes, Systematic Review, Epidemiology, Endocrinology and Metabolism, Hypertension
More Detailed Keywords:	Ethnicity, South Asian, Cholesterol, Body fat, Cardiovascular risk
Abstract:	Background: Almost a million people of South Asian (SA) origin live in Canada, representing about 3% of the total Canadian population. Accumulating evidence demonstrates that SA immigrants living in Canada have a higher burden of certain cardiovascular risk factors and cardiovascular disease (CVD), compared to White Caucasians (WC). Objectives: To comprehensively review the body of literature describing the cardiovascular risk and management profile of adult SA living in Canada. Methods: We searched MEDLINE, EMBASE, Cochrane and CINAHL databases and reference list of articles from inception through May 31, 2012. English language studies of interventions, or direct or observational studies of biological or patho-physiological mechanisms underlying CVD risk in SA conducted in Canada were eligible for inclusion. Where appropriate, we used random-effects meta-analyses to pool the study results comparing the CVD risk profiles of SA and WC. Results: 52 articles were included in this review. Compared with WC, SA in Canada had higher prevalence and incidence rates of CVD, increased prevalence of diabetes [OR=2.00(95%CI: 1.91,2.09;p<0.001)] and hypertension [OR: 1.15(95%CI: 1.06, 1.26,p=0.001)], lower HDL-C levels [MD:-0.19 mmol/L(95%CI:-0.26,-0.12,p<0.001)] and a higher body fat % [Men:3.23%(95% CI:0.83%,5.62%;p=0.008); Women:4.09%(95%CI:3.46%,4.72%; p < 0.00001)]. SA were less likely to smoke tobacco [OR 0.33, (95% CI:0.25,0.44; p<0.001)] were more sedentary, and consumed higher carbohydrate diets than WC. No

	differences in access to diagnostic tests, outcomes following cardiovascular surgery, or utilization of cardiac rehabilitation programs were apparent. Interpretation: SA living in Canada have a higher prevalence and incidence of CVD and possess a unique cardiovascular risk profile.

Cardiovascular Risk in South Asians Living in Canada: A Systematic Review.

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Number of Figures: 23

Number of Tables: 1

Running Title: Cardiovascular risk in Canadian South Asians

Abstract Word Count: 438

Manuscript Word Count: 7501

Conflict of interest: None declared

ABSTRACT

Background: Almost a million people of South Asian origin live in Canada, representing about 3% of the total Canadian population. Accumulating evidence demonstrates that South Asian immigrants living in Canada have a higher burden of certain cardiovascular risk factors and cardiovascular disease (CVD), compared to White Caucasians living in Canada.

Objectives: To comprehensively review the body of literature describing the cardiovascular risk and management profile of adult South Asians living in Canada, and to highlight future areas of study.

Methods: We searched MEDLINE, EMBASE, Cochrane and CINAHL databases and reference list of articles from inception through May 31, 2012. Three authors independently assessed study quality and extracted data. Study authors were contacted for additional information. English language studies of interventions, or direct or observational studies of biological or patho-physiological mechanisms underlying CVD risk in South Asians conducted in Canada were eligible for inclusion. We used random-effects meta-analyses to pool the study results comparing the CVD risk profiles of South Asians and Caucasians. If three or more studies provided data, prevalence odds or mean differences were pooled using random-effects meta-analyses.

Results: 52 articles were included in this review. Compared with White Caucasians, South Asians in Canada had higher

prevalence and incidence rates of CVD, increased prevalence of diabetes [OR= 2.00 (95 % CI: 1.91,2.09; p<0.001)] and hypertension [OR: 1.15 (95% CI: 1.06, 1.26, p=0.001)], lower HDL-C levels [MD: −0.19 mmol/L (95% CI: −0.26, −0.12, p<0.001)] and a higher body fat percentage [Men: 3.23% (95% CI: 0.83%, 5.62%; p=0.008); Women: 4.09%, (95% CI: 3.46%, 4.72%; p < 0.00001)]. We found no differences in BMI [Men: −0.19 kg/m^2 (95 % CI: −1.94, 1.55; p=0.83); Women: −0.09 kg/m^2, (95 % CI: −1.74, 1.56, p=0.91)], LDL-C [MD: 0.08 mmol/L (95% CI: −0.17, 0.34, p=0.52)], waist circumference [Men: 0.14 cm, (95% CI: −3.59, 3.88; p=0.94); Women [MD: 0.48 cm, (95% CI: −3.21, 4.16; p=0.80)], diastolic blood pressure [MD: −1.05 (95% CI: −5.79, 3.68; p=0.66)] or systolic blood pressure [MD: −1.80 mmHg (95% CI: −4.19, 0.58; p=0.14)]. South Asians were less likely to smoke tobacco [OR 0.33, (95% CI: 0.25, 0.44; p<0.001)] were more sedentary, and consumed higher carbohydrate diets than White Caucasians. No clear differences in access to diagnostic tests (angiography or cardiac catheterization), outcomes following cardiovascular surgery, or utilization of cardiac rehabilitation programs were apparent.

Interpretation: South Asians living in Canada have a higher prevalence and incidence of CVD and possess a unique cardiovascular risk profile characterized by a propensity to diabetes, excess adiposity, low HDL cholesterol, higher sedentary behaviours, higher carbohydrate intake, and lower smoking compared to White Caucasians. Access to diagnostic tests for

coronary artery disease, and outcomes after myocardial infarction appear similar.

Abstract word count: 438

INTRODUCTION

South Asians (SA) are individuals whose ancestors originate from the Indian subcontinent, including India, Pakistan, Sri Lanka, Nepal, and Bangladesh. According to the 2006 Census Canada data, almost a million people of South Asian origin live in Canada, representing about 3% of the total Canadian population(1). Of this, approximately 70% were born outside Canada, 75% of whom immigrated to Canada in the last twenty years (1). SA immigrants living in Canada have higher cardiovascular disease (CVD) rates compared to the general population (2-4), and these differences appear to persist among the offspring of SA immigrants living in Canada(5). SA also have more severe CVD, present with disease at younger ages, and in some contexts have differential access to diagnostic and treatment services compared to non-SA(6-8).

In the last two decades, there have been numerous studies of CV risk factors or CVD conducted among SA living in Canada. The evidence to date suggests that CVD rates and health behaviours vary between ethnic groups in Canada, and that the adoption of some health behaviours typical of Western countries may promote the development of cardio-metabolic risk factors among SA. This paper will systematically review the literature comparing SA with White Caucasians (WC) living in Canada with respect to CVD risk factors, management, access to diagnostic testing, and adherence to cardiac rehabilitation programs.

METHODS

Search Strategy and Selection

In consultation with an information specialist, we developed search terms for MEDLINE, EMBASE, CINAHL and Cochrane Registry databases from inception through May 24, 2012 (**Appendix 1**). All studies were conducted in humans, and all study designs were eligible for inclusion as long as they described the association between South Asian ethnicity, established or novel CVD risk factors, or CVD. We included English language studies of interventions, or direct or observational studies of biological or patho-phyisological mechanisms underlying coronary heart disease (CHD) risk in SA, conducted in Canada. Three investigators (AR, RdS, and SSA) assessed appropriateness of each article for inclusion in this review. Disagreements were resolved by discussion and consensus. We excluded studies that were not published as full reports, such as conference abstracts and letters to the editors.

Data extraction

Three reviewers (AR, RdS, SK) extracted the following data from the studies: 1) study design (e.g. RCT, prospective cohort, cross-sectional, etc.); 2) location of conduct; 3) major research question(s); 4) sample size; 5) mean age of sample; 6) sex; 7) ethnicity; 8) anthropometry measures reported; 9) health status of participants (e.g. healthy, CVD, diabetes, etc.); 10) description and duration of intervention or exposure and follow-up; 11) primary outcomes 12) means and standard deviations for continuous outcomes and numbers of events, odds ratios (OR), and

95% confidence intervals for dichotomous outcomes. Missing variance measures were imputed using standard formulae(9).

Quality Assessment and Meta-analysis

Three reviewers (AR, RdS, SK) assessed the quality of the included studies using the modified Newcastle-Ottawa scale (NOS) that has been developed to assess the quality of non-randomized studies[8]. Each study could be assigned a maximum score of 7, 1 point for each of the following criteria: research design, recruitment strategy, sample representativeness, response rate, outcome measures, power calculation and statistical analyses.

Random-effects meta-analysis was conducted using Cochrane's Review Manager 5.2 for the following risk factors: systolic blood pressure (SBP), diastolic blood pressure (DBP), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C), triglycerides (TG), body mass index (BMI), physical inactivity, body fat %, waist to hip ratio (WHR), fasting insulin (fINS), fasting glucose (FG), Homeostasis Model of Assessment - Insulin Resistance (HOMA-IR), and prevalence odds of smoking, diabetes, hypertension and obesity. We qualitatively assessed the following outcomes: prevalence, incidence of CVD, prevalence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), lipoprotein (a), apolipoprotein B/ apolipoprotein A, C-reactive protein (CRP), plasminogen activator inhibitor-1 (PAI-1), diet intake, and management of CVD.

When more than three studies reported either mean differences or an odds ratio (OR) for a given outcome, we used the generic inverse variance method to pool effects and standard errors. Mean difference (MD) and 95% CI was the effect measure for continuous outcomes and the prevalence OR and 95% CIs was the effect measure for the dichotomous outcomes. A negative mean difference, or OR <1.0 indicates lower levels or prevalence in SA. Age- and sex adjusted means and OR were preferred, when available. Cochran's Q statistic was used to detect heterogeneity, and the I^2 statistic was used to estimate the percentage of variation across studies that arose from true heterogeneity rather than chance(9). If the original data were not amenable to meta-analysis, for example, in the case of non-normal data, or when less than three studies were available, we summarized the study results as percent prevalence, incidence rates, medians and interquartile range (IQR) or means ± SD.

We conducted pre-planned sensitivity analyses in which we included only high quality studies to test the robustness of the effect sizes and to evaluate heterogeneity. A high quality study was defined as one that had rigorous design and scored 5 or higher on the modified Newcastle-Ottawa scale(10). We also conducted post-hoc subgroup analyses by study type and sampling mechanism to identify the causes of heterogeneity in results.

RESULTS

Literature Flow

Our search of the electronic databases identified 18,057 potentially relevant articles. A total of 17,975 were excluded after abstract review leaving 82 retrieved for full text review. After full-text review, 52 articles were included (**Figure 1**).

Study Characteristics

The 52 included studies encompassed a wide range of accrual years (1979 to 2007) and various study designs. Twenty-seven were cross-sectional (52%), twenty-two were retrospective chart/database reviews (42%), one was a case-control study (2%) and two were qualitative studies (4%). The sample size ranged from 51 to 1276 in the cross-sectional studies, from 645 to 2,168,715 in the database reviews, and from 16 to 130 in other studies. A full description of study characteristics can be found in **Table 1**.

Summary of Findings

Prevalence and Incidence of Heart Disease

Three observational studies compared the prevalence and incidence of CVD in Canadian SA with WC, one used a random population based sampling technique (SHARE)(2) whereas the others used record linkage in existing databases(3,11,12).

The Study of Health Assessment and Risk in Ethnic groups (SHARE; n=946)(2), randomly sampled SA and WC from three cities in Canada between 1997-2000. The age and sex standardized prevalence of CVD [defined as a history of myocardial infarction (MI), angina,

silent MI, percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass grafting (CABG) or stroke] was 10.7 % in SA as compared to 5.4% in WC ($p<0.05$).

In a retrospective database analysis of National Population Health Survey (NPHS) and Canada Community Health Survey (CCHS) covering years 1996 to 2007, Chiu et al used record linkage (3) (n=163,797) restricted to the province of Ontario. The age and sex standardized self-reported prevalence of heart disease (SA: 5.2% vs. WC: 5.1%, $p>0.05$) or stroke (SA: 1.7 vs. WC:1.1, $p>0.05$) or combined heart disease or stroke (SA: 6.6 % vs. WC: 5.7 %, $p=0.22$) was higher but was not significantly different among SA compared to WC. This study scored lower on the NOS scale (NOS<5) and ethnicity and clinical outcomes were self-reported.

Using self-reported ethnicity, a retrospective cohort study of hospital administrative databases (1994 – 2003) in British Columbia (B.C.) (11) reported a higher age standardized incidence rate (/1000/year) of acute MI in SA men and women (SA Men: 4.97 vs. WC Men: 3.29, $p<0.001$; SA Women: 2.35 vs. WC Women: 1.53, $p=0.01$). Additionally, SA men had higher rates of acute MI at earlier ages than WC men. The age-specific incidence in 35-44 year old men was 0.89 (95% CI: 0.71,1.07) for SA and 0.48 (95% CI: 0.45, 0.51) for WC ($p<0.001$). In the 45-54 year age group, these rates were also higher 3.44 (95% CI: 3.04, 3.83) among SA men than WC men 1.77 (95% CI: 1.71, 1.83; $p<0.001$).

The mortality rates from CVD in SA and WC(12) were reported in a retrospective review of the Canadian mortality database (1979-1993). Here, SA were reported to have significantly higher age standardized proportional rates of mortality from CVD than WC (Men: 42% vs. 29%; p<0.001, Women: 29% vs. 19%; p<0.001).

Taken together the evidence suggests that SA in Canada have a higher prevalence and of CVD as compared to non-South Asians. Furthermore, between 1997-2003, SA appeared to have significantly higher rates of mortality from CHD.

BMI and Abdominal Obesity (Waist circumference and Waist-to-hip ratio)

Four cross-sectional studies(2,13-15) of 725 SA and 699 WC compared the sex specific body mass index (BMI) among SA and WC. Overall the mean difference for BMI was not significantly different in the two groups for men [MD: -0.19 kg/m^2 (95 % CI: -1.94, 1.55; p=0.83; I^2= 82%; P_{het} =0.001)] and women [MD: -0.09 kg/m^2 (95 % CI: -1.74, 1.56; p=0.91; I^2= 73%; P_{het} =0.01)]. When this analysis was limited to the two high quality studies(2,14), the mean difference in BMI was -1.11 kg/m^2 (95% CI: -3.66, 1.44; p= 0.39; I^2= 89% ; P_{het} =0.003) in men, and -0.52 kg/m^2 (95% CI: -1.51, 0.48; p= 0.31; I^2= 0% ; P_{het} =0.33) in women. When we conducted secondary subgroup analyses by sampling method used in the study (i.e. convenience versus random), heterogeneity was eliminated (I^2 •20%) within each subgroup, indicating that the high heterogeneity in the MD in BMI for men could be explained by

the variation in sampling techniques (p for test for subgroup differences < 0.0001; Fig 2).

Three low-quality studies(4,7,16) that used record linkage reported the prevalence of obesity (BMI • 30 kg/m^2) as determined by self-reported weight and height in 3,507 SA and 1,552 WC. The pooled OR was 0.62 (95% CI: 0.40, 0.96; p=0.03; I^2= 40%; P_{het} =0.19) indicating lower prevalence of obesity in SA, using the conventional BMI cut-off of • 30 kg/m^2.

Five cross-sectional studies(2,13-15,17) compared waist-to-hip ratio (WHR) among 812 SA and 753 WC. Overall, the mean difference for men was not significant [MD: 0.02 (95 % CI: -0.01, 0.04; p=0.15) I^2= 85%; P_{het} <0.001]; although there was substantially heterogeneity between studies. The mean difference for WHR in women was 0.02 (95% CI: 0.01, 0.04; p=0.005; I^2= 81%; P_{het} <0.001), which suggests that WHR is higher in SA women as compared to WC women. Again significant heterogeneity across studies is observed. When limited to three high quality studies(2,14,17), the difference remained non-significant for men [MD: 0.00 (95% CI: -0.01, 0.01; p=0.92; I^2 = 3%; P_{het} = 0.36)] and the mean WHR difference appeared marginally significant for women 0.03 (95% CI: 0.00, 0.05; p=0.04; I^2 =89%; P_{het} <0.001). When we conducted subgroup analyses by sampling mechanism (i.e. random vs. non-random; Fig 5) for WHR in women, heterogeneity was eliminated (I^2 • 21%) within each subgroup, suggesting that sampling mechanism was a source of heterogeneity (p for subgroup groups differences <0.0002).

Five studies(14,15,17-19) examined the differences in waist circumference in the two ethnic groups. These studies showed no significant differences in waist for men [MD: 0.14 cm, (95% CI: -3.59, 3.88; p=0.94) I^2= 89 %; P_{het} <0.001] or women [MD: 0.48 cm, (95% CI: -3.21, 4.16; p=0.80) I^2= 87%; P_{het} <0.001]. When limited to three high-quality studies(2,14,17), the difference remained non-significant in both men [MD: -2.18 cm, (95% CI: -5.89, 1.53; p=0.25) I^2= 89% ; P_{het} =0.0001] and women [MD: -1.08 cm, (95% CI: -4.55, 2.40; p=0.54) I^2= 86% ; P_{het} <0.001].

There were a total of three cross-sectional studies (13,14,17), which compared sex specific percent body fat in 346 SA and 337 WC. When compared to WC men and women, body fat was 3.23% higher in SA men (95% CI: 0.83, 5.62; p=0.008; I^2= 87%; P_{het} <0.001) and 4.09% higher in SA women (95% CI: 3.46, 4.72; p < 0.00001; I^2= 6%; P_{het} = 0.35). When limited to two high quality studies(14,17), the mean difference for men was 2.93% (95% CI: -0.29, 6.16; p =0.07; I^2= 91% ; P_{het} <0.001) and 4.05% in women (95% CI: 3.56, 4.54; p<0.0001; I^2= 0% ; P_{het} <0.45). Again, subgroup analyses for percent body fat in men showed that heterogeneity might be associated with the sampling mechanism used in the studies (I^2 within each subgroup < 10%; p-value for test for subgroup differences < 0.0001; Fig 8).

Hence, even with similar BMIs, SA have higher percent body fat and SA women have higher WHR when compared to White Caucasians. It is noteworthy that the mean waist circumference in SA men was higher in only one of the five studies[10], which may explain the

heterogeneity in the results for WC (men). The reasons for this may relate to difference in age ranges of the study sample. Smith, 2006 enrolled SA men that were much older than WC men. Three studies that showed no difference in the waist circumference for men recruited men with similar age ranges and BMIs between the two ethnic groups. Similarly, heterogeneity in the waist circumference in women may be explained by differences in age ranges of the sample. Two studies that showed no difference recruited men and women of similar age ranges and BMIs. One study that showed lower waist circumference in SA women had recruited a much younger cohort of participants as compared to the other four studies. One study that showed a higher waist in SA participants who were older than their WC counterparts.

Fat Distribution

Only two studies examined the differences in abdominal fat distribution using imaging between SA and WC, the Multicultural Community Health Assessment Trial (M-CHAT) (n= 408) and the Molecular Study of Health and Risk in Ethnic Groups(17) (mol-SHARE) (n=108). M-CHAT(20) compared total abdominal tissue (TAT, cm^2) in SA and WC. Overall, SA men had higher mean TAT than WC men (439.7 ±169.5 vs. 369.1±164.0; p=0.003). TAT was not significantly different in SA and WC women (454.3±162.9 vs. 438.4 ±184.7, p=0.420).

Visceral and Subcutaneous Abdominal Fat

In M-CHAT(20), compared to WC men, SA men had higher median visceral adipose tissue (VAT, cm^2) (140.3, IQR: 101.7, 177.2 vs. 104.9, IQR: 81.0, 144.5; p= 0.002). The differences in unadjusted median VAT for women in the two groups were not significant (101.8, IQR: 74.4, 126.8 vs. 98.0, IQR: 67.5, 136.2; p= 0.52). However, when adjusted for age, income, smoking status, menopausal status and BMI, SA women had significantly higher VAT than WC women (p=0.025). In this study SA men had higher median subcutaneous abdominal adipose tissue (SAT, cm^2) than WC men (283.2, IQR: 208.5, 363.1 vs. 221.5, IQR: 171.6, 296.3; p=0.006), although the difference in SAT were not significant in women (339.3, IQR: 238.3, 433.2 vs. 332.1, IQR: 214.1, 416.7; p=0.243). However, when the SAT values were adjusted for age, income, smoking status, menopausal status and BMI, SA women had higher SAT than WC women (p=0.01).

In mol-SHARE(17), in which SA and WC subjects were matched by BMI, no difference in VAT between SA and WC, overall (126.8± 6.1 vs. 117.5±7.0, p>0.05) or when stratified by sex [men: 153.5±8.8 vs. 134.5±12.1, p>0.05; women: 97.3±7.3 vs. 95.6±6.8, p>0.05] were observed. There were also no differences in sex-specific superficial subcutaneous fat (cm^2) between ethnicities (Men: 25.6±1.0 vs. 27.8±1.2, p>0.05; women: 42.2±1.4 vs. 38.6 ±0.9, p>0.05). However, when compared to WC, SA had relatively less superficial subcutaneous fat as a percentage of their total abdominal fat than WC [MD: -2.94 (95% CI: -5.56 to -0.32, p<

0.05)] and SA had 17% higher deep subcutaneous and visceral fat relative to superficial subcutaneous fat [MD: 0.34 (95% CI: 0.02 to 0.65; p<0.05]. Moreover, when compared to WC, SA had significantly greater adipocyte area [MD: 64.2 (95% CI: 24.3, 104.1; p<0.05)] and maximum adipocyte diameter [MD: 20.68 (95% CI: 7.86, 33.5; p<0.05)].

Liver Fat

Mol-Share(17) was the only study to compare liver fat % in SA and WC. Liver fat infiltration was significantly higher in SA [MD: 7.43% (95% CI: 2.30 to 12.55; p<0.05)].

Type 2 Diabetes and Impaired Glucose Tolerance

We identified 12 (2,3,6,8,21-28) (8 database and 4 cross-sectional) studies examining the prevalence of diabetes mellitus (DM) in 16,861 SA and 633,162 WC. In the database review studies, prevalence of DM was established using the International Classification of Disease (ICD)- 10 coding. The prevalence of DM in SA was twice of that of WC [OR= 2.00 (95 % CI: 1.91,2.09; p<0.001); I^2= 0 %; P_{het} =0.87]. When we limited our analysis to the 4 high quality studies(2,6,24,27), the OR was unchanged [OR: 2.00 (95% CI: 1.88, 2.11 , p<0.001); I^2= 0 % ; P_{het} =0.81]. Subgroup analyses showed that the type of study design (cross-sectional vs. database review) had no significant impact on the results (p for test for subgroup differences= 0.38) Consistent with this finding, in a chart review study, Khan, 2011(29)

reported that SA men and women (ages 35-65) had higher age-specific incidence rates of diagnosed diabetes when compared to WC men and women (p<0.001). Similarly, the administrative database study by Chiu et al.(30) reported that SA had a higher age adjusted crude incidence of diabetes rate/ 1000 per year when compared to WC patients (20.8 vs. 9.5). SA also developed diabetes 4.6 years sooner than their WC counterparts. The median age of diagnosis in SA was 49 years as compared to 58 years in WC. In addition, SA developed diabetes at lower BMI cut-offs. Incident rates of diabetes comparable to WC at a BMI of 30 kg/m^2, were seen at BMI of < 24 kg/m^2 for SA. In the random population-based SHARE(18,31), elevated fasting glucose values were observed above a BMI of 21 kg/m^2 in South Asians compared to a BMI •30 among WC.

Five cross-sectional studies(2,15,17,20,32) compared fasting glucose (FG) levels between 811 SA and 759 WC. Overall, the mean difference was not statistically significant (MD: 0.00 mmol/L, 95% CI: -0.29, 0.30; p=0.98; I^2= 96%; P_{het} <0.001). However, when limited to the three studies(2,17,20) with high quality, SA had 0.22 mmol/L higher FG than WC [(95% CI: 0.09, 0.34; p= 0.0006) I^2= 43 %; P_{het} =0.17].

Five cross-sectional studies(2,17,20,32,33) reported fasting insulin levels (fINS) in 792 SA and 755 WC groups. Fasting insulin levels were, on average, 19.88 pmol/L higher in SA than in WC (95% CI: 14.20, 25.55; p<0.001; I^2= 96 %; P_{het} <0.001). When limited to two high-quality studies(2,17,20), SA had 26.45 pmol/L

higher fINS than WC (95% CI: 24.37, 28.52; p<0.001; I^2= 42% ; P_{het} =0.18).

Four studies(17,32,34,35) compared HOMA-IR in 685 SA and 672 WC. The mean difference was 0.88 (95% CI: 0.73, 1.02; p<0.001; I^2= 18 %; P_{het} <0.30) indicating increased insulin resistance in SA. When limited to three high quality studies(17,34,35), the mean difference remained similar [MD: 0.88 (95% CI: 0.76, 1.00, p<0.001; I^2= 16 %; P_{het} =0.30)].

We identified two studies that compared IGT prevalence. Both studies showed a higher prevalence of IGT in SA when compared to WC. In the SHARE-pilot(21) (n=51), SA were more likely to have IGT than WC [34.5% vs. 9.5 % , p<0.04]. In the main study SHARE(2), 19% of South Asians had IGT as compared to 15% WC (p=0.03). Two studies reported the prevalence of IFG in SA and WC and showed no significant difference in the two groups. He, 2010(32) reported 13.3% prevalence of IFG in SA as compared to 12.6 % in WC (p>0.05), whereas in the random population based SHARE[2] the prevalence of IFG in SA trended higher than in WC 7.3% vs. 5.8% but the difference was not significant (7.3 % vs. 5.8 %, p=0.43).

Collectively, these studies suggest that SA have a higher prevalence of diabetes, higher levels of fating glucose and fINS, greater prevalence of IGT, and increased insulin resistance when compared to WC.

Blood Pressure, Hypertension

We identified five(2,15,17,20,32) cross-sectional studies which compared DBP in 759 SA and 811 WC. Overall no difference in DBP (mmHg) between SA and WC [MD: −1.05 (95% CI: −5.79, 3.68; p=0.66) I^2= 100 %; P_{het} <0.001] was identified. However, when we limited the analysis to three (2,17,20) high quality studies, SA had 1.70 mmHg higher DBP than WC (95% CI: 0.68, 2.71, p=0.001; I^2= 51% ; P_{het} =0.13].

We pooled five(2,15,17,20,32) cross-sectional studies that compared SBP in the two groups (778 SA and 811 WC). There was no significant difference in SBP among the two groups [MD: −1.80 mmHg (95% CI: −4.19, 0.58; p=0.14) I^2= 81 %; P_{het} <0.001], which was not altered when limited to three (2,17,20) high quality studies [MD: 0.39 (CI: −1.25, 2.03; p=0.64) I^2= 0 % ; P_{het} =0.59].

We identified 12 studies(2,3,6,8,21,23,25-28,32,36) that compared prevalence of hypertension in SA and WC, nine of these were database reviews that used ICD-10 codes to establish hypertension. SA were more likely to have hypertension than WC [OR: 1.15, 95% CI: 1.06, 1.26, p=0.001; I^2= 66%; P_{het} <0.001]. With the removal of low quality studies, the OR for the prevalence of hypertension was 1.18 and remained significant (95% CI: 1.11, 1.26; p<0.001; I^2= 8 %; P_{het} =0.36](2,6,21,27). Results were similar for both cross-sectional and database review studies (p for test for subgroup differences: 0.51).

Lipids

Five studies(2,15,20,22,32) reported the difference in total cholesterol (TC) (mmol/L) in 834 SA and 787 WC. There was a trend toward higher TC in SA compared with WC, but the MD was not significant [MD: 0.22, 95% CI: -0.14, 0.58; p=0.24; I^2= 89 %; P_{het} <0.001], although there was substantial heterogeneity. Limiting to high quality studies(2,20), there remained no difference in TC between the groups (MD: 0.33, 95% CI: -0.34,1.01, p=0.33, I^2= 91%; P_{het} <0.001). Again, significant heterogeneity was observed. A closer look at the studies reveals that the heterogeneity may be explained by differences in age ranges and body composition among the participants in the included studies. Three studies that showed a higher TC in SA enrolled men and women of similar ages. One study that showed lower TC levels in SA enrolled SA that were much older that the WC. Whereas a high quality study that showed no difference had recruited participants with similar sex ratios and BMIs between the two ethnic groups.

Four studies(2,15,20,32) measured LDL- C (mmol/L) in 755 SA and 707 WC. The mean difference was not significant [MD: 0.08 mmol/L (95% CI: -0.17, 0.34, p=0.52; I^2= 94%; P_{het} < 0.001)]. When the analysis was limited to two high-quality studies(2,20), the mean difference was 0.09 and approached significance (95% CI: -0.01, 0.19; p =0.09; I^2= 2 %; P_{het} =0.31).

Six studies(2,13,15,17,20,32) reported HDL- C (mmol/L) in 893 South Asians and 861 Caucasians. The mean difference was -0.19 mmol/L (95% CI: -0.26, -0.12, p<0.001; I^2= 70 % ; P_{het} <0.01)]. When limited to three high quality studies(2,17,20), South Asians

had significantly lower HDL levels when compared to WC [(MD: −0.15, 95% CI: −0.18, −0.11; p<0.01; I^2= 0 % ; P_{het} =0.96).

Four studies(13,17,18,20) directly compared the TC to HDL-C ratio in 763 SA and 723 WC. As predicted from the individual lipid results, SA had a higher TC:HDL-C ratio [MD: 0.72 (95% CI: 0.28, 1.17, p=0.002) I^2= 89%; P_{het} <0.001]. When limited to high quality studies(17,18,20), the difference in TC:HDL-C ratio was 0.41 and remained significant (95% CI: 0.16, 0.67; p=0.002; I^2= 50%; P_{het} =0.14].

Three studies(2,17,32) compared fasting triglyceride (TG, mmol/L) levels in 511 SA and 489 Caucasians. SA had significantly higher TG than WC [MD: 0.26 (95% CI: 0.09, 0.42, p=0.002) I^2= 48 % ; P_{het} 0.11]. When we limited the analyses to two studies of high quality(2,17), the mean difference was 0.21 mmol/L and remained significant (95% CI: 0.08, 0.35, p=0.002) I^2= 17 %; P_{het} =0.30).

Only one study looked at mean lipoprotein (a) in South Asians. In SHARE(2), SA had higher sex and age adjusted mean lipoprotein (a) concentrations compared to WC (34.1 v 17.3 mg/dL, p< .013). Moreover, the percentage of South Asians with abnormal Lp(a) values [>30 mg/dL] was 50% compared to 24% in WC [16].

One study compared the levels of apolipoprotein A-1 (Apo A1) in SA and WC. In SHARE(2), SA had lower levels of Apo A1 (g/L) than WC (1.30 ±0.25 vs. 1.42 ±0.28, p<0.0001). Two studies reported levels of apolipoprotein B (Apo B) in SA and WC. In SHARE, SA had higher levels of Apo B as compared to WC (1.08 ±0.26 vs. 1.00

±0.25, p=0.0002) although M-CHAT(37) reported that median differences in levels of Apo B were not significant. (SA men: 1.10, IQR: 0.97,1.23 vs WC men: 0.99 g/L, IQR: 0.85,1.20, p= 0.15; SA women: 0.95, IQR: 0.80,1.10 vs. WC women: 0.90, IQR: 0.74, 1.06, p=0.92). We identified one study that looked at the Apo B/ApoA ratio. In a study by Smith, 2006(13), ApoB/Apo A was higher in SA compared to WC men and women (Men: 0.85±0.04 vs. 0.54±0.66; p<0.001; Women: 0.74±0.04 vs. 0.52±0.03; p<0.001).

Collectively the evidence indicates that SA have lower HDL-C and Apo A-1 levels, and higher TC: HDL ratio, TG levels, lipoprotein (a) and Apo B levels levels when compared to WC.

Smoking:

We identified 14 (2,3,6-8,13,16,17,21,23,25,26,38,39) studies that reported the prevalence of current smoking in 10,264 SA and 511,460 WC in Canada. Collectively SA have a 67 to 76% lower prevalence of smoking than WC [OR 0.33, (95% CI: 0.25, 0.44; p<0.001) I^2= 89 %; P_{het} <0.001]. When the analysis was limited to high quality studies(2,17,20,38), the OR was 0.24 (95% CI: 0.18, 0.33; p < 0.001) I^2= 0 % ; P_{het} =0.46).

Novel Markers of Vascular Risk

A smaller evidence base is available for markers of inflammation and vascular endothelial function, plasminogen activator inhibitor-1 (PAI-1), homocysteine, and C-reactive protein (CRP). In SHARE(2), SA had elevated levels of PAI-1 (17.1±9.61 vs. 5.1±9.92 units/ml; p=0.02), homocysteine (11.22 ±3.76 vs.

10.0±3.78 µmol/L; p<0.001) when compared with WC. No significant differences were reported for fibrinogen levels(40) (3·07±0·85 vs. 2·93± 0·86 g/L, p=0.10).

Three cross-sectional studies compared levels of CRP between SA and WC. In SHARE(41), SA had significantly higher CRP levels (3.22 ±4.2 vs. 2.49±3.7 mg/L; p<0.001). In MCHAT(42), SA had higher median CRP levels (men: 1.7 vs. 0.9; p<0.001 and women: 2.7 vs. 1.4 ; p=0.04). However, in a small mechanistic study of relatively younger participants who were matched on BMI to WC, Mol- SHARE(17), sex specific CRP levels in SA were not significantly different than WC (Men: 1.66 ±0.33 vs. 2.22±0.95; women: 1.53±0.95 vs. 3.14 ±0.7).

Socioeconomic status and Psychosocial Stress

We identified only two studies that explored the influence of socioeconomic status and psychosocial stress on the relationship between acculturation and cardiovascular risk factors looked in SA and WC. Anand et al.(43) created a social disadvantage index based on income, income sources, job type, education, employment status, and marital status. In this study, SA scored higher on the social disadvantage index when compared to WC (Mean ± SE: 1.53±0.07 vs. 1.36 ±0.07; p<0.001). The study also showed that certain CV risk factors and CVD prevalence increased with increasing social disadvantage for both SA and WC (No Social disadvantage: 10 % ±2.55, low social disadvantage: 11 % ±3.25, moderate social disadvantage: 36 % ±4.36, high social disadvantage: 45% ±7.76, p<0.001)

Chiu et al.[3] reported that gender modified the association between ethnicity and psychosocial stress. In their study, 24.8% percent of Asian women reported experiencing stress “extremely” or “quite a bit” on most days, compared with only 20.8% of European women. However, there were no significant differences in the prevalence of self-reported stress between SA and WC men, with both reporting experiencing stress approximately 22% of the time. There was also evidence of an effect of time in Canada on this relationship, in women only; long-term Canadian residents were less likely to report psychosocial stress compared to recent immigrants (24.2 vs. 18.0, p=0.04).

Food Intake

We identified four studies which analyzed the diet of SA and WC. Using estimates derived from a validated culture-specific food-frequency questionnaire (FFQ) in SHARE(44), adult Canadian SA consumed more fibre (21±6 vs. 17±5 g/d; p<0.01) and carbohydrates (290±32 vs. 269±38 g, p<0.01) and slightly less total fat (59±11.14 vs. 62±13 g/d, p<0.01) and protein (70±10 vs. 78±14 g/d; p<0.01) relative to WC. Similar differences were also observed in M-CHAT(45) whereas as percentage of total energy intake, SA consumed more carbohydrates (55.5±8.7 vs. 47±8.8 %, p<0.001), less protein (16.3±3.7 vs. 17.3±4.2%, p<0.001) and total fat (27.6±7.8 vs. 33.7±7.9%, p<0.001) when compared to WC.

Other aspects of diet also differed between SA and WC. In two studies, SA were more likely to consume adequate amounts of

fruits and vegetables (3 or more times a day) compared to WC (1 77-90% vs. 65-82%)(4,16), although SA were more likely to frequently consume "junk food" (higher scores on a validated FFQ) (23% of SA vs. 16% of WC)(16). Moreover, Chiu et al.(4) noted diet quality, as measured by consumption of fruits and vegetables, was reported to worsen over time among SA. After 15 years of living in Canada, this difference between SA and WC had dissipated, and was no longer significant, with ~20% consuming inadequate servings of fruits and vegetables (less than 3 times a day).

Physical Activity

We identified five studies that assessed physical inactivity in SA and WC. In SHARE(46), SA had lower mean score on the physical activity index (physical exertion score estimated from reported type of occupation, time spent playing sports and type of leisure activities, where a higher score represents increased physical activity) than WC (7.5 ±1.7 vs. 8.3±1.6, $p<0.01$). For the participants in SHARE, Mente et al.(34) noted that SA spent fewer hours/wk on physical activity relative to WC (7.3±0.1 vs. 8.1±0.1, $p<0.001$). In Mol-SHARE, SA scored lower on a physical activity scale (0=low, 1=moderate, 2= high) than WC (Men: 1.5±0.1 vs. 1.9±0.1, women: 1.3 ±0.1 vs. 1.4±0.10). In M-CHAT(24), SA were physically active for almost 3 hours less per week than WC (Median mins/week: 166, IQR: 71,294 vs. 321, IQR: 148,151). In a study by Chiu et al.(4), SA were more likely to be physically

inactive (• 15 minutes/day of leisure time physical activity) than WC (72.8% vs. 62.7%).

In an effort to determine the reasons for this lack of physical activity, Khan, 2010(47), examined the scores on the perceived environments related to physical activity questionnaires, where higher scores indicate a more positive physical activity environment. In this study, SA reported lower availability of home environment (Mean score: 2.25±2.04 vs. 3.20±2.50; p<0.001) and lower convenience of physical activity facilities (Mean score: 3.94±4.39 vs. 5.88±4.87, p<0.001) when compared to WC[25]. In another study by Booth et al.(48), a greater number of recent immigrants (most often SA) resided in Greater Toronto Area neighbourhoods with low walkability as compared to long-term immigrants (20% vs. 18.3%). An interaction between low walkability and socioeconomic status (SES) was observed, putting low income recent immigrants in low walkability areas at threefold higher risk for diabetes (16.2 per 1,000) compared to those living in high-income, high walkability areas (5.1 per 1,000).

Diagnosis, management and outcomes

Access to testing

We identified four studies that examined symptom presentations and access to diagnostic tests in SA and WC. In a 2002 chart review study by Gupta et al.(8) of AMI patients in the Greater

Toronto Area, the median time from symptom onset to presentation to the hospital was longer for SA than WC (3.92 v. 3.08 hrs, p =0.04). Both groups received angiography (17% vs. 16.3%, p=0.8) at comparable rates, and the frequency of in-hospital major complications, median length of hospital days (six days for both) and frequency of procedures in hospital was similar. In a database review by King 2009(7), SA patients admitted with acute MI in Calgary health region (Alberta) were less likely to present with a classic symptom profile (midsternal pain and/or midsternal pressure with/without throat/ neck pain with/without shoulder pain with/without arm pain) as compared to WC (79% vs. 93% , p=0.016). In those patients who reported distinct time of onset of symptoms, a greater proportion of SA delayed presenting to the ER for more than 12 hours (47% vs. 27%). In this study, SA with acute MI in Calgary hospitals were also less likely to undergo cardiac catheterization/angiography in less than 3 hours from time of arrival to the Emergency Department as compared to WC (21% vs. 47%; p<0.01).

Khan 2010(6), in their retrospective cohort study of SA from British Columbia (BC) and Calgary Health Region (Alberta), noted that SA patients with acute MI were more likely to undergo cardiac catheterization at 30 d (OR:1.32, 95% CI:1.16-1.52, p<0.01) and at 1 yr (OR:1.44, 95% CI: 1.25-1.65), p<0.01) than WC. In an age-restricted retrospective chart review of incident acute MI cases by Albarak, 2012 (28)(n=3057; ages 20-55 yrs), overall, 44.1% SA in Alberta and BC underwent angiography as

compared to 42.7% WC patients. Furthermore there were no significant differences in utilization of cardiac catheterization in 24hrs following acute MI between SA and WC patients. However, in this study covering years 1995-2002, SA patients were more likely to undergo cardiac catheterization within 1 year of acute MI (ST-elevation and non-ST-elevation MI) compared with WC patients (88.8% vs 77.3%, $p < 0.01$).

Outcomes post- MI: Mortality rates and Recurrent AMI

We identified six studies that compared short- and long-term mortality rates in SA and WC patients with MI.

Short-term mortality

In Gupta 2002(8), risk-adjusted in hospital mortality rate in the Greater Toronto Area was similar for both groups (9.1% vs. 7.7%, p=0.20). In a chart review, Raghavan, 2008(25) noted that SA with acute coronary syndrome (ACS) in Montreal, Quebec had higher in hospital all-cause mortality (5% vs. 2%) when compared to non-South Asians. In a chart review in Toronto, Brister 2007(49) reported that as compared to WC, SA had increased in hospital operative mortality (2.5% vs. 1.1%, p=0.02) after admission for MI. South Asian ethnicity was also associated with higher post-CABG mortality (OR: 3.1, 95% CI: 1.4, 6.8) when compared to WC. However, Khan, 2010(6) reported lower 30-day mortality in SA acute MI patients (OR: 0.88, 95% CI: 0.75,1.03,

p=0.10) among SA in BC and Alberta. In a retrospective chart review of 7135 patients with AMI by Albarak, 2012(28), adjusted hazard ratios for short term mortality were not significantly different between SA and WC (HR: 0.90; 95% CI: 0.38 to 2.10) in BC and Alberta.

Long-term mortality

Raghavan 2008(25) reported that 1-year mortality was substantially higher in SA patients (6.1% vs. 1.5%) after MI in Montreal, Quebec. However, Quan 2010(27) showed that SA patients in BC and Alberta had better survival compared to other Canadians (aHR:0.76, 95% CI 0.61 to 0.95) in a follow-up of 10.5 years. Khan 2010(6) also noted that long-term mortality was lower in SA in BC and Alberta (HR:0.65, 95% CI: 0.57,0.72, p<0.001). Furthermore, Albarak, 2012(28) reported that 3.5 yr long-term mortality (HR: 0.81, 95% CI: 0.53,1.26) was not significantly different between SA and WC patients with acute MI in BC and Alberta.

Two studies described the frequency of recurrent AMI in patients with MI. In a retrospective cohort study by Khan, 2010(6) conducted in BC and Alberta, adjusted HR for survivors of MI only were non-significant among the two groups (aHR:1.07, 95% CI: 0.95-1.2, p=0.20). In Albarak 2012, 27.1 % of SA in B.C. and Alberta had recurrent AMI as compared to 24.4% of WC patients (HR: 1.07, 95% CI:0.89,1.29) and 2.9% had congestive heart

failure (CHF) vs. 2.7% of WC (HR: 0.90, 95% CI:0. 51,1.59). Although in a subgroup analysis of patients with diabetes, SA were significantly more likely to develop a recurrent AMI than WC (aHR: 1.48, 95% CI: 1.04, 2.11) over an 8-year follow-up period.

One study reported the health status after MI in SA and WC patients. In a database review by Bainey 2011(38), SA in Alberta were more likely to report poor health status, as measured by Seattle Angina Questionnaire (SAQ), at 1 year after angiography. SAQ is a self-reported measure of health status where lower scores indicate poor health. The mean scores for angina frequency (86±23 vs. 88±20, p<0.001), treatment satisfaction (86±19 vs. 89±16, p<0.001) and quality of life (QOL) (71±24 vs. 76±21, p<0.001) were significantly lower in SA. There were no significant differences in angina stability (77±28 vs. 77±27, p=0.627) and exertional capacity (75±23 vs. 80±23, p=0.11).

Revascularization procedures: Coronary artery bypass grafting (CABG) and Percutaneous coronary intervention (PCI)

In a retrospective chart review, Gupta 2002 reported that SA in the Greater Toronto Area were equally likely to undergo PCI (2.9 vs. 3.4, p=0.60) and CABG (4.2% vs. 2.2 %, p= 0.06). Similarly, in a chart review, Singh, 2005 reported that the revascularization procedure rates were comparable in SA and WC in the GTA (1% vs. 1 %). However, in the case control study by Raghavan 2008(25) (n=130), SA in Montreal were less likely to have PCI, (26% versus 34%) and more likely to undergo CABG (32%

versus 18%). This trend persisted at 1-year time point (PCI: 48% versus 62%, CABG: 35% versus 22%).

In a retrospective study by Quan 2010(27), SA with coronary artery disease (CAD) in BC and Alberta were less likely to undergo PCI (aOR: 0.86, 95% CI 0.79 to 0.93) within six months after coronary angiography when compared to WC. This was consistent after 10.5 years of follow-up after coronary angiography (aHR 0.95, 95% CI 0.90 to 1.00). However, the frequency of CABG was similar (aOR: 0.95 (95%CI: 0.87-1.04) in both groups. In a chart review study in BC and Alberta, Khan, 2010 noted that PCI [aOR: 1.06 (95% CI: 0.9, 1.24] or CABG frequency [aOR: 1.04 (95% CI: 0.82,1.32)] were not significantly different at 1 month after AMI. This trend was true for 1 year after AMI as well [PCI aOR: 1.06 (95% CI: 0.90,1.24 ; CABG aOR: 1.09 (95% CI: 0.90,1.33)].

Overall, SA appear to delay presentation to hospital, but once in hospital they appear to have a similar access to diagnostic procedure and interventions (PCI, CABG) compared to WC, however there is some practice and outcome variation between provinces. The outcomes after hospitalization for ACS suggest that SA may have higher short-term (< 1 yr) recurrent event rates including re-hospitalization, and recurrent angina. However short and long-term mortality post MI appears to be similar among SA and WC.

Cardiac Rehabilitation (CR)

We identified only one study that compared participation rates in CR programs between Canadian SA and WC patients. In a hospital cardiac rehabilitation record review by Banerjee, 2007(23), SA were less likely to complete the program than WC (43.3% vs. 50.8 %, p=0.04). However, at the end of 6-month program, from those who completed the program, SA were more likely to achieve target heart rate (41.8% vs. 54.7%, p=0.02) and achieved greater change in maximum metabolic equivalents during the exercise tolerance test (1.35±1.8 vs. 0.93±1.35, p=0.07). One qualitative study showed that South Asians respond differently to referral type for CR and may be more responsive to liaison referral, where the referral is facilitated through a discussion with a health care professional, as opposed to automatic referral via a computerized system(50).

Discussion:

In this review, we have assessed the CVD burden, risk factor profile, receipt of diagnostic and interventions and outcomes after ACS, and referral and outcomes after cardiac rehabilitation among South Asians in Canada.

CVD Burden: Our review of the literature shows that SA living in Canada have a higher prevalence and incidence of CVD as compared to WC. Moreover, a study of the Canadian National mortality database indicated that between 1979 and 1993 Canadian SA have significantly higher mortality rates from CHD than WC(12). However, some inter study variation in these results exists which we attribute to differences in the classification of ethnicity

(i.e. self report vs. direct assessment vs. surname classification) and classification of outcomes (self report vs. health administrative data). This variation emphasizes the need to develop a standardized surveillance system of non-communicable diseases (i.e. CVD, cancer, lung diseases) by ethnic group in Canada(51,52). Such a system will more efficiently shape health services policies and programs targeted toward particularly high-risk ethnic groups.

CV Risk Factors: Collectively our synthesized evidence shows that compared to WC, SA living in Canada are more likely to have an increased prevalence of hypertension, type 2 diabetes, dysglycemia, insulin resistance, higher percent body fat, increased visceral adiposity, lower HDL-C levels, elevated apo-B/apoA1 ratio, lower physical activity and higher carbohydrate intake, all of which play an important role in the etiology of CVD in SA. On the positive side, SA in Canada are less like to smoke cigarettes compared to WC. The sparse available data does not support differences in TC or LDL between SA and WC Canadians.

The studies to date suggest that, even at conventionally “normal” BMI ranges, Canadian SA, both male and females, have higher body fat %, increased visceral abdominal fat and greater insulin resistance(30,53) compared with WC. These findings are consistent with previous studies in the U.K(54) and the U.S.A.(55,56) of immigrant South Asian populations(30,53). The reasons for South Asians’ predisposition to this cardio-metabolic risk profile are

still not well characterized, and it may be a complex biological interaction between genetic predisposition and environmental factors exists. A comparative study showed that a greater proportion of babies in South India are born with central fat and increased cord blood insulin as compared to WC babies born in the U.K(57). This suggests that insulin resistance develops in South Asians in early infancy and carries an increased risk of diabetes and CVD in adulthood(58). Studies of Canadian SA adolescents noted that despite lower BMI, WC and weights, SA adolescents had substantially higher levels of TG and significantly lower levels of TC, indicating that the adverse SA risk factor profile develops in early ages(59). A study currently underway in Canada, START(60) (South Asian Birth Cohort), which aims to enroll 1000 SA babies born in Southern Ontario, will provide more insight into the developmental origins of CVD risk factors among SA infants in Canada.

Diagnostic and Therapeutic of CVD: Access to health care including diagnostic cardiac tests and interventions appear to be similar among SA and WC, although this is contextually dependent. For example, studies in Alberta and BC show SA are less likely to undergo angiography in less than three hours(7) after AMI but more likely to underdo angiography/cardiac catheterization at 30 day and 1 year after AMI(6). Whereas, a study in the Greater Toronto Area(8) showed that SA and WC were equally likely to undergo angiography. We did not find any notable differences in short or long-term mortality after MI, however more data are

required to understand the short-term clinical patterns after MI among SA in Canada, as again this appears to be contextually dependent and may reflect variations in health systems. Furthermore, studies in the U.K(61-63) have shown conflicting results where some studies show higher post-operative mortality while others show similar mortality rates between the two groups.

Cardiac Rehabilitation: Some data(64) in the UK suggest that SA are less adherent to rehabilitation programs than their WC counterparts. Studies in Canada suggest that the lack of knowledge of severity and risks of cardiovascular diseases(65,66) in SA population may make them less likely to continue CR. Grewal et al.(67) noted that SA in Canada may perceive illness differently than other ethnic groups, considering it as fate which may result in poor prognosis and recovery. Other issues could include language barriers(68), lack of social support and stress associated with migration.

Future Studies: Future research is required to understand the early origin and childhood risk factors prevalence among SA youth in Canada, to devise suitable screening and management strategies for SA youth in order to prevent early onset CHD.

Strengths and Limitations: In this review we statistically pooled the largest studies of CVD risk in Canadian South Asians, and where heterogeneity existed examined the causes. Most of our findings are consistent with literature in the U.K(61-63) and the U.S.A(54). However, this review is not without limitations.

Analysis of existing literature was difficult due to limited amount of studies in Canadian South Asians, diversity of study designs and sampling schema, and lack of standardized measures for race/ethnicity. Some studies measured ethnicity using self-report while others used an algorithm taking into account surnames and birthplace.

As with any systematic review of observational studies, we found much heterogeneity for most outcomes as the dataset encompassed a wide range of accrual years and various study types. The values for the I^2 statistic were frequently in the 75-90 % range, signifying considerable unexplained heterogeneity. We explored the causes of heterogeneity by conducting sensitivity analyses using high quality studies and subgroup analysis of study types and sampling mechanism. However, despite this high level of heterogeneity, we believe that some important consistencies were demonstrated—first, in the majority of individual studies, the point estimates were consistent with higher insulin, TG, HDL-C and TC: HDL-C in SA than in WC. Second, when we stratified our analyses by sampling mechanism, the unexplained heterogeneity in adiposity was reduced to almost 0%. Residual differences may be attributable to lack of standardized definitions of ethnicity and varying study designs.

Conclusion: Given the increased prevalence and mortality associated with CVD among SA living in Canada, intervention strategies to reduce risk factors and CVD in this group, and

research to understand the early life determinants of CV risk factors in this high risk population are needed.

ACKNOWLEDGEMENTS: We thank Arnav Agarwal and Sonia Ruparell for their assistance with extracting data for some of the articles. We also thank Dr. Katherine Cianflone and Dr. Aman Nijjar for sharing their data and additional information about the studies with us. Dr. Sonia Anand holds the Michael DeGroote Heart and Stroke Chair in Population Health, a Canada Research Chair in Ethnicity and Cardiovascular Disease and the Eli Lilly May Cohen Chair in Womens Health. Dr. Scott Lear holds the Pfizer/Heart and Stroke Foundation Chair in Cardiovascular Prevention Research at St. Paul's Hospital.

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Tables and Figures

Supplemental Appendix

Appendix 1. Search Strategy

	Main Study/ Database	City/ Province	Study Design	Study Duration	No. of Subjects	% Men/ Women	Mean Age	No. of SA	% SA	Outcomes Measured	Study Score
Albarak et al., 2012	Hospital Discharge Abstract Database (DAD)	British Columbia	Retrospective Cohort	8 years	7135	SA: 90/10, WC: 82/18	N/A	487	6.8	Diabetes prevalence, Hypertension prevalence, Thirty-day mortality after AMI, long-term mortality after AMI, Recurrent AMI	4
Anand et al., 2000	SHARE	Hamilton Toronto Edmonton	Cross-sectional Random Sampling	N/A	985	SA: 55/45, WC: 48/52	SA 49·4, WC: 51·2	342	34.7	CVD prevalence, Blood pressure, BMI, WHR,	6

										TC, LDL-C, HDL-C, TG, FG, Apo A1 and B levels, homocysteine, lipoprotein, fibrinogen	
Anand et al., 2003	SHARE	Hamilton Toronto Edmonton	Cross-sectional Random sample	N/A	936	N/A		315	33.7	Sensitivity, Specificity of the new diabetes cutoff	5
Anand et al., 2003	SHARE/ SHARE-AP	Hamilton Toronto Edmonton Oshweken	Cross-sectional Random Sample	N/A	1276	48.9/ 51.1	50.4	342	26.8	Prevalence of metabolic syndrome	5
Anand et al., 2004	SHARE/ SHARE-AP	Hamilton Toronto Edmonton	Cross-sectional Random sample	N/A	1250	48.9/ 51.1	50.4	323	25.9	Mean scores for C-reactive	5

		Oshweken								protein	
Anand et al., 2006	SHARE/ SHARE-AP	Toronto Edmonton Hamilton Oshweken	Cross-sectional Random Sampling	N/A	1227	WC: 48.2/ 51.8, SA: 55/45	WC: 51.3, SA: 49.4	342	27.9	Levels of social disadvantage	5
Anand et al., 2011	SHARE	Hamilton	Cross-sectional Random Sampling	2005-2009 (4 years)	108	49/51	35	56	52	Insulin, HDL cholesterol, adiponectin, adipocyte area, lean muscle mass, liver fat, visceral fat, superficial subcutaneous fat, deep subcutaneous fat	5
Anand et	SHARE-	Hamilton	Cross-	N/A	51	N/A	N/A	31	61.8	IGT, TC:HDL,	3

al., 1997	pilot		sectional Random Sampling						lipoprotein(a)	
Bainey et al., 2011	APPROACH	Alberta	Retrospective database review	1995-2006 (11 years)	19569	SA: 78/22, WC: 74/22	SA: 22.1, WC: 26.0	635	3.2	Health status outcomes	5
Banerjee et al., 2007	Hospital rehabilitation records	Toronto	Retrospective database review	2 years	1200	SA: 84.5/ 15.5, WC: 73.4/ 26.6	SA: 56.2, WC: 59.0	220	18.3	Maximum metabolic equivalents, Cardiac Rehab	3
Banerjee et al., 2010	N/A	Toronto	Qualitative study	N/A	16	81.2/ 18.8	57.4	16	100	Barriers to cardiac rehabilitation participation	2/4
Chiu et	NPHS 1996	Ontario	Retrospective	1996-	163797	49.1/	42.3	3364	2.1	Prevalence	3

al., 2010	& CCHS cycles 1.1 (2001), 2.1 (2003), and 3.1 (2005)		review	2007 (11 years)		50.9				of heart disease, psychosocial stress, diet, physical activity	
Chiu et al., 2011	NPHS 1996 & CCHS cycles 1.1 (2001), 2.1 (2003), and 3.1 (2005)	Ontario	Database review	12.8 years	59824	WC: 49.1/ 50.9, SA: 56.8/ 43.2	WC: 48.5, SA: 43.7	1001	1.7	Diabetes incidence rates, median age at diagnosis	3
Chiu et al., 2012	NPHS 1996 and CCHS Cycles 1.1 (2001), 2.1 (2003), 3.1	Ontario	Retrospective Cohort	N/A	163797	49.1/ 50.9	42	3364	2.1	Prevalence of CVD risk factors	3

	(2005), and 4.1 (2007)										
Gasevic et al., 2012	M-CHAT	Vancouver	Cross-sectional Targeted ethnic group Sampling	N/A	784	WC: 50/50, SA: 50/50	WC: 50, SA: 45	199	2500	TC, LDL, TG, BMI, FINS, FG, HOMA-IR	4
Graunau et al., 2008	N/A	Vancouver	Cross-sectional Random sampling	N/A	976	44/56	55.5	67	7	Perception of heart disease in Canada	2
Grewal et al., 2010	N/A	Ontario	Qualitative study	N/A	16	94/6	Men: 62.6	16	100	Cardiac Rehabilitation Referral	1/4
Grewal et al., 2010	N/A	Ontario	Cross-sectional Convenience sampling	N/A	562	N/A	61.9	53	9	Social support measures	5

Gupta et al., 2002	Hospital chart review	Brampton Scarborough	Retrospective chart review	1994-1999 (5 years)	1106	N/A	SA: 62.6, Non-SA: 63.0	553	50	Acute MI, Diabetes, Access to diagnostic testing	4
Kaul et al., 2011	Alberta Health and Wellness databases	Alberta	Retrospective cohort	1999-2005	54208	SA: 47.2/52.8, WC: 50/50	WC: 76.5, SA: 72.2	377	0.7	Diabetes, Hypertension, post-MI mortality rates	3
Khan et al., 2010	Hospital Administrative data	British Columbia and Alberta	Retrospective chart review	1994-2003	41615	67/33	N/A	2190	5.4	Diabetes, Heart failure, hypertension, revascularization	5
Khan,S. N. et al., 2010	N/A	11 acute care hospitals in Ontario	Retrospective Cohort	N/A	2472	SA: 78.4/21.6, WC:	SA: 61.7, WC: 64.4	171	6.7	Physical activity environment	3

						62.9/ 37.1					
Khan et al., 2011	Hospital discharge data and physician claims	B.C, Alberta, Canada	Database review	B.C.: 1993-1996 Alberta: 1994-2007	276237	N/A		15066	5.4	Diabetes incidence rates	5
King, 2009	DAD	Calgary	Chart review	2002-2006	406					BMI, Diabetes, smoking status	4
Kohli et al, 2010	M-CHAT	Vancouver	Cross-sectional Targeted ethnic group Sampling		408					BMI, Waist, body fat %, abdominal fat, smoking status	5
Lear et al., 2003	M-CHAT	B.C, Canada	Cross-sectional Targeted	N/A	69		WC: 36.5, SA:	34	49	BMI, WHR, TC, LDL-C, HDL-C,	2

			ethnic group Sampling			38.2			Triglycerides, glucose, insulin, S-BP, D-BP, C-reactive protein	
Lear et al., 2007	M-CHAT	Vancouver	Cross-sectional Targeted ethnic group Sampling	N/A	627	WC: 50.3, SA: 45.0	207	33	BMI, Waist, WHR, Body fat (%), abdominal fat, smoking(%), diabetes (%)	4
Lear et al., 2007	M-CHAT	Vancouver	Cross-sectional Targeted ethnic group Sampling	N/A	822	WC: 50.3, SA: 45.0	207	25.1	Diet, BMI, WHR, energy intake, physical activity	5
Lear et al.,	M-CHAT	B.C, Canada (as part of	Cross-sectional	N/A	828		208	25.1	BMI, WC, WHR, body fat %,	5

2009		MCHAT)	Targeted ethnic group Sampling							abdominal fat mass, current smoking	
Lear et al., 2012	M-CHAT	Vancouver	Cross-sectional Targeted ethnic group Sampling	N/A	408	50/50	WC Men: 49.8, WC Women :50.7, SA Men: 44.6, SA Women :45.4	207	51	Total fat, LDL-C, HDL-C, TC, TC:HDL, smoking	5
Liu et al., 2010	CCHS 2000, 2003 and 2005	Canada	Retrospective cohort	3 cycles of CCHS; 2000, 2003, 2005	37,154	SA: 52/48, WC: 48/52		4270	11	Diabetes, Hypertension, Smoking, BMI	4

He et al., 2010		Toronto London Cambridge	Cross-sectional Convenience sampling	2003-2006 (3 years)	354	SA: 43/57, WC: 49/51	N/A	113	32	BMI, waist, WHR, body fat %, SBP, DBP, TC, HDL-C, LDL-C, FG, FINS, TG, hypertension ,IFG, HOMO-IR,	4
Mente et al., 2010	SHARE/ SHARE-AP	Toronto EdmontonHamilton Oshweken	Cross-sectional Random Sampling	N/A	1176	N/A	50.3	317	27	Adiponectin, Leptin, HOMA- IR	6
Merchant et al., 2007	SHARE/SHARE-AP	Toronto, HamiltonEdmontonSix Nations	Cross-sectional Random Sampling	1996-1998	620	47/53		174	28.1	WHR, BMI, smoking status, physical activity score, diet	5

Merchant, 2005	SHARE	Hamilton	Cross-sectional Random Sampling	N/A	617	47/53	47.72	173	28	Diet	5
Nijjar et al., 2010	DAD	British Columbia Alberta	Retrospective cohort	1995-2002	41615			2190	5.2	Diabetes, hypertension	5
Nijjar et al., 2010	DAD	British Columbia	Retrospective chart review	1995-2002 (7 years)	2,168,715 (34848 AMI cases)	67/33	N/A	87,965	4.1	Acute MI hospitalization rates	4
O'Laughlin et al., 2007		Montreal	Retrospective	1993-1997 (4 years)	2033	42/58	39.7	42	3	Smoking, obesity, physical inactivity, poor diet	2
Prasad el al., 2011	Kidney transplant recipients	Toronto	Retrospective Cohort	1998-2009 (11 years)	864	SA: 106/11. WC: 346/204	SA: 48.4, WC: 47.1	139	16.1	Smoking Status	4

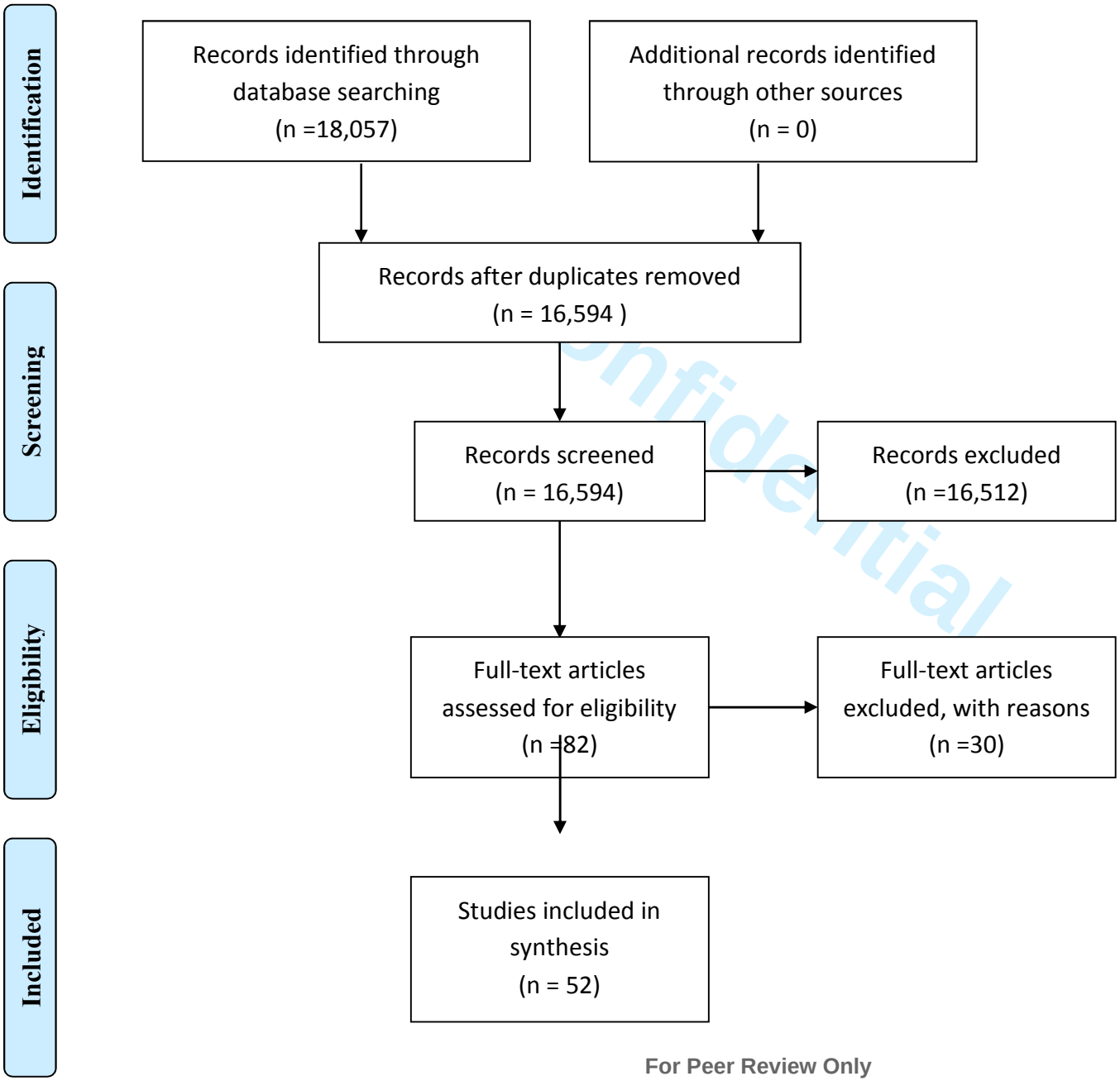
Quan et al., 2010	APPROACH and BCCR	Alberta British Columbia	Database review	1995-2004 (9 years)	81848	SA: 77.4/22.3, WC: 75/25	N/A	3061	3.7	Revascularization, 30-day mortality	5
Razak et al., 2007	SHARE	Toronto Edmonton Hamilton Oshweken	Cross-sectional Random Sampling	N/A	1078	SA: 55/45, WC: 48/52	SA: 49, WC: 51	289	27	BMI, waist, FG, HbA1c, HOMA-IR, LDL-C, HDL-C	6
Razak et al., 2005	SHARE	Toronto Edmonton Hamilton Oshweken	Cross-sectional Random Sampling	N/A	1251	SA: 54/46, WC: 48/52	SA: 49.3, WC: 51.3	328	59	FG, HbA1c, SBP,DBP, BMI, WHR, Waist	6
Raghavan et al., 2008		Montreal	Chart Review	1995-2000 (5 years)	130	92/8	59.7	65	50	All-cause mortality	4
Sheth et al., 1997	Canadian mortality database	Hamilton	Retrospective cohort	15 years	32537	N/A	N/A	10989	29.6	Mortality rates	5

Sheth et al., 1999	Canadian mortality database	Canada	Retrospective cohort	1979–1993	949859			6548	0.68	CVD mortality rates	5
Singh et al., 2005	Hospital chart review	Toronto	Retrospective cohort	1997–1999 (2 years)	887	SA: 51/49, Non-SA: 50/50	SA: 69.1, Non-SA: 75.1	90	12	Smoking, post-MI mortality rates	3
Smith et al., 2006		Montreal	Cross-sectional Convenience sampling	2004–2005 (1 year)	165	52/48		82	50	BMI, body fat %, WHR, Waist, TC, HDL-C, TC:HDL-C, ApoB/ApoA1, smoking status, FG	3
Smith et al., 2006		Montreal	Cross-sectional Convenience sampling	2004–2005 (1 year)	114	61/39		65	57	ApoB, ApoA1, diabetes	3

Smith et al., 2006		Quebec	Cross-sectional Convenience sampling	2004-2005 (1 year)	86	N/A	SA: 42.9 WC: 38.3	54	62.8	Body composition	3
Kayaniyil et al., 2009		Ontario	Cross-sectional Convenience Sampling	N/A	351	73/27				Cardiac knowledge	3
Booth et al., 2012	Administrative database	Toronto	Retrospective Cohort		1,239,262	50/50				Walkability score	4
Brister et al.,2007	Chart Review	Toronto	Retrospective Cohort	1994-2003	6,191	SA: 22/78, WC: 22/78	SA: 60.8, WC: 63.6	1163	19	CABG utilization, post CABG mortality	4

Table 1. Study Characteristics

Figure 1. CONSORT diagram of flow of studies through selection process.



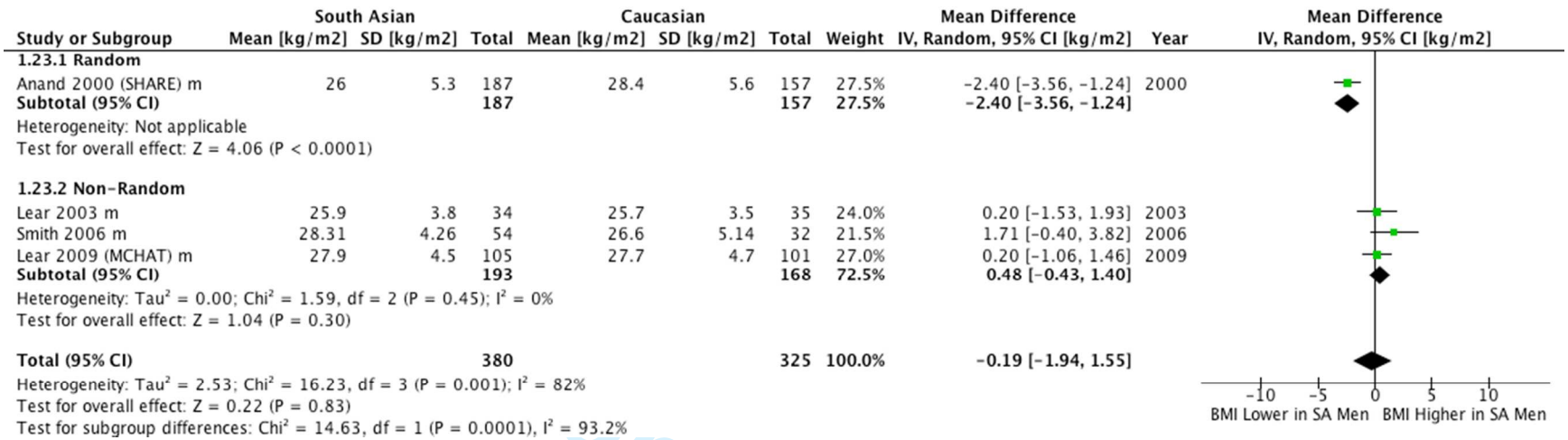


Figure 2. Forest plot of comparison: SA vs. WC, outcome: BMI [kg/m^2] men.

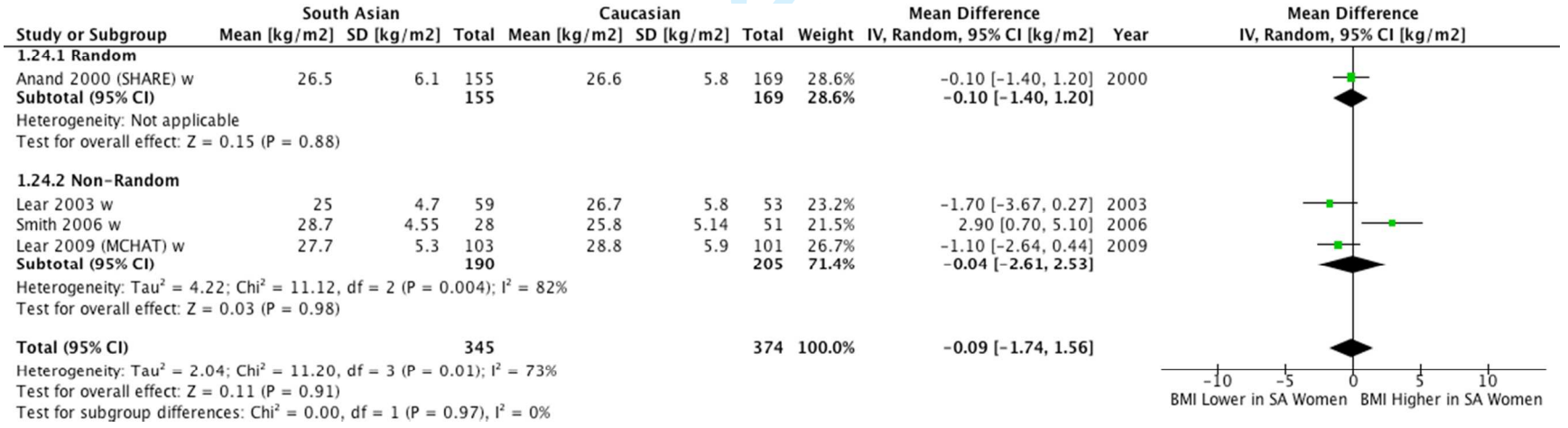
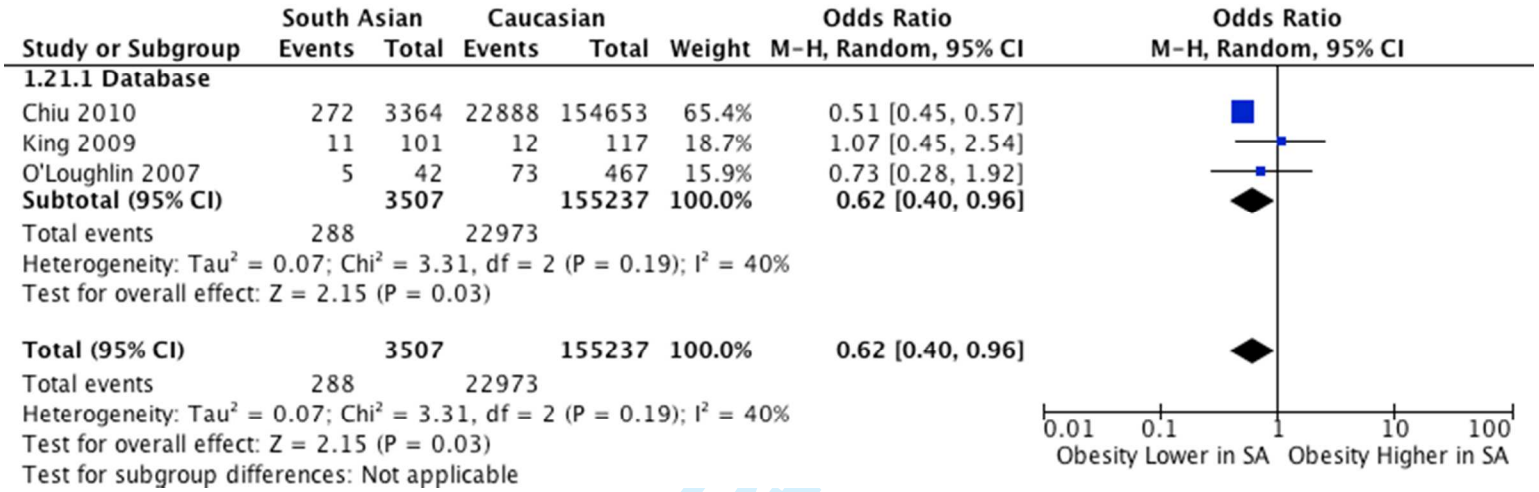


Figure 3. Forest plot of comparison: SA vs. WC, outcome: BMI [kg/m2] women.



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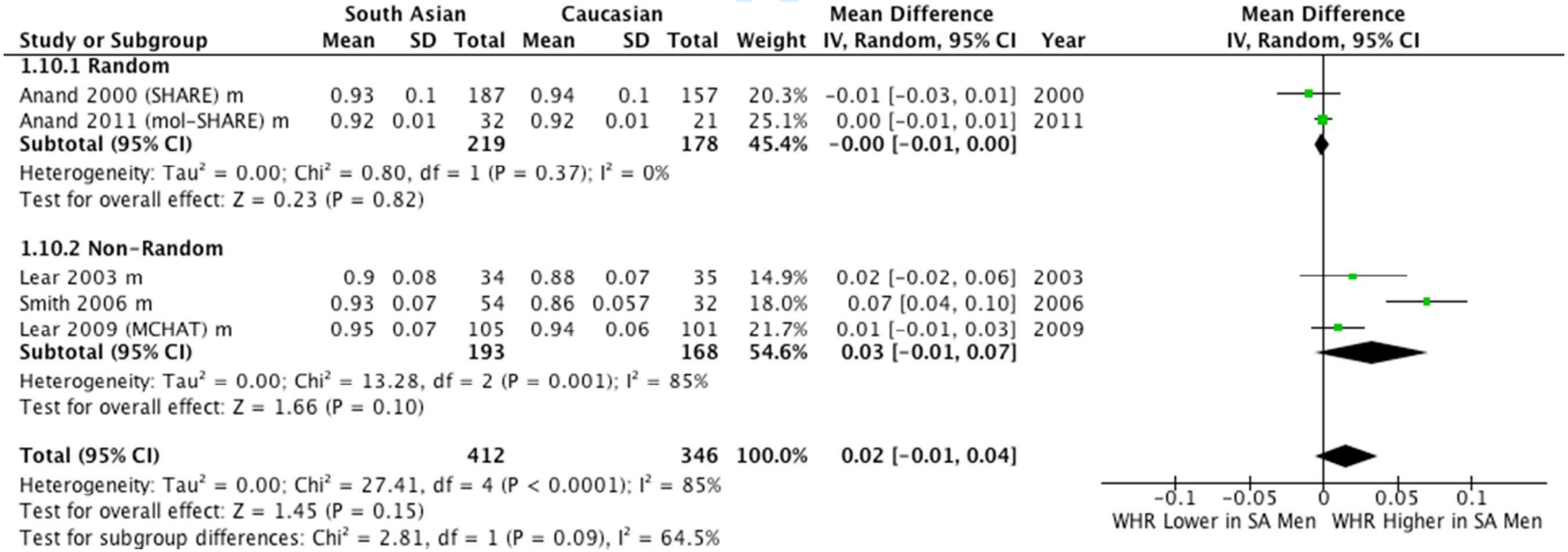

Figure 5. Forest plot of comparison: SA vs. WC, outcome: WHR men

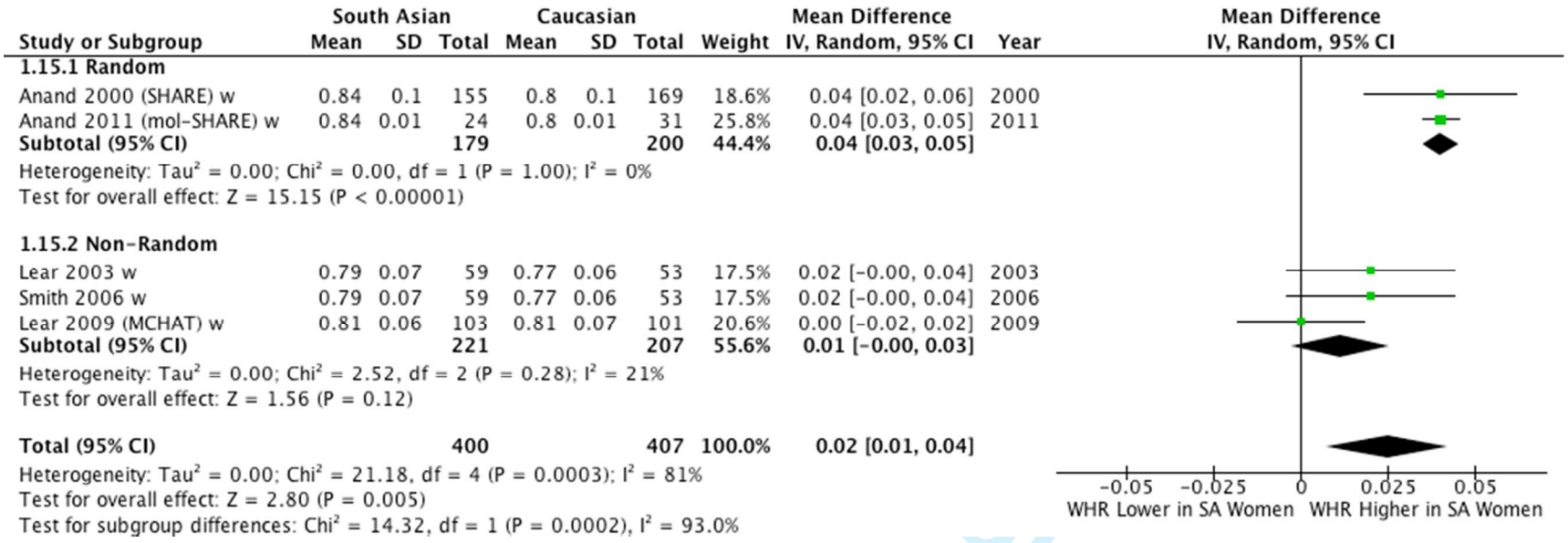

Figure 6. Forest plot of comparison: SA vs. WC, outcome: WHR women

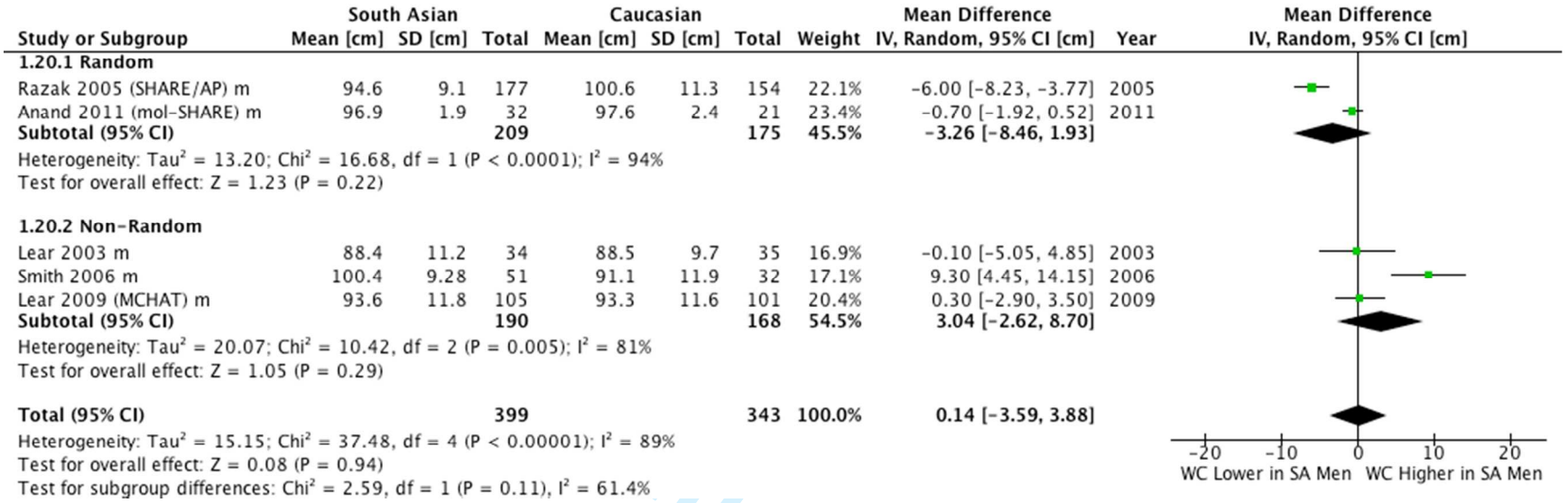

Figure 7. Forest plot of comparison: SA vs. WC, outcome: Waist Circumference [cm] men

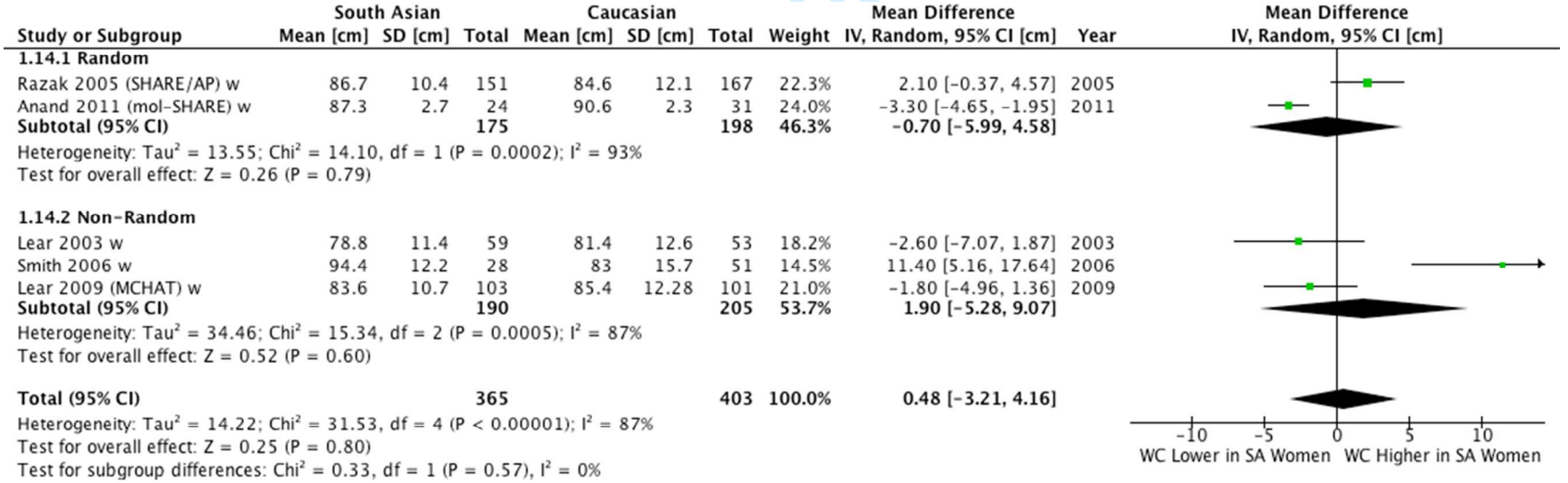

Figure 8. Forest plot of comparison: SA vs. WC, outcome: Waist Circumference [cm] women

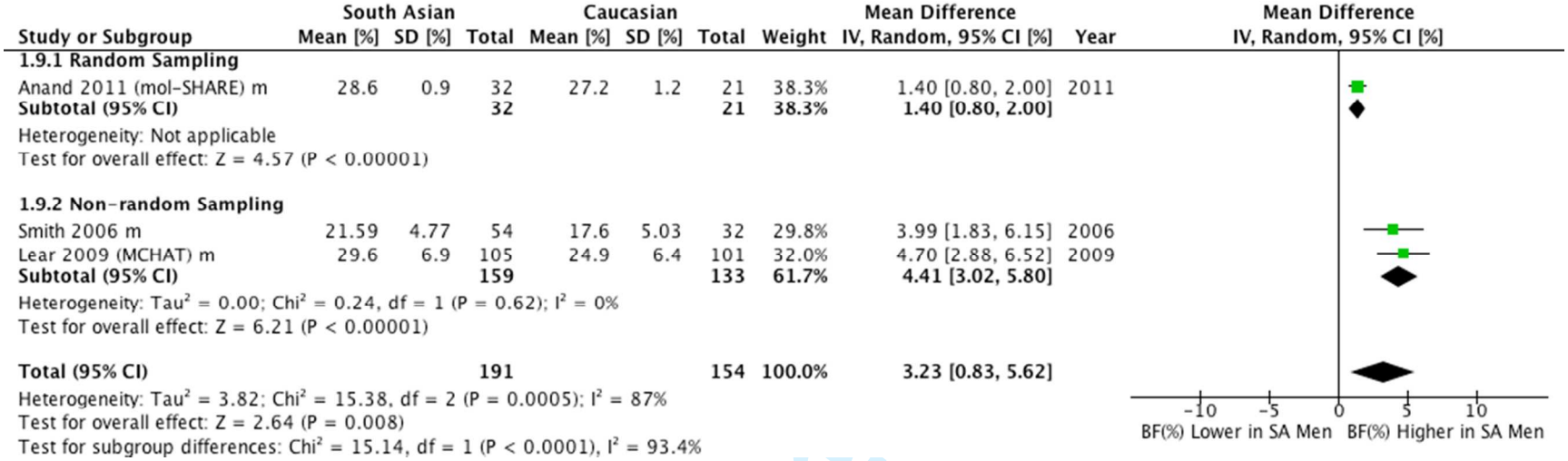

Figure 9. Forest plot of comparison: SA vs. WC, outcome: Body Fat [%] men

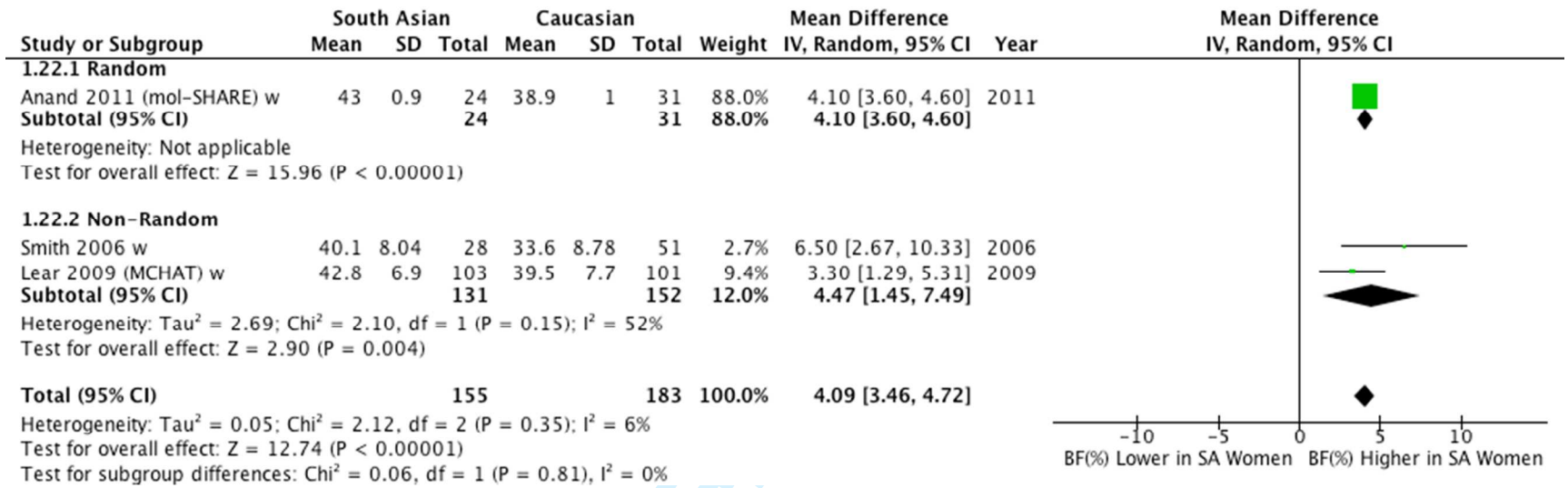

Figure 10. Forest plot of comparison: SA vs. WC, outcome: Body Fat [%] women

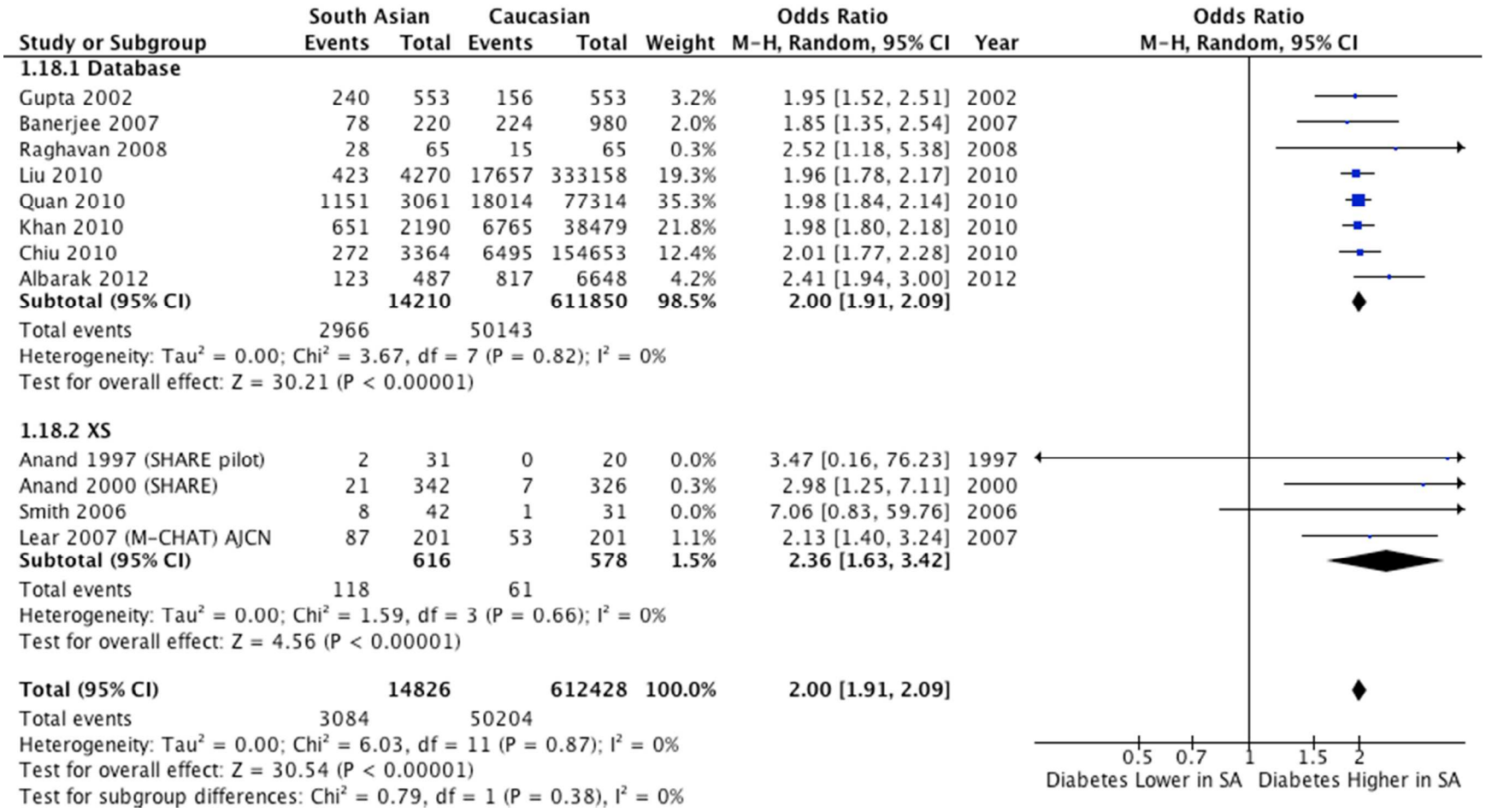

Figure 11. Forest plot of comparison: SA vs. WC, outcome: Diabetes

Study or Subgroup	South Asian Mean [mmol/L]	SD [mmol/L]	Total	Caucasian Mean [mmol/L]	SD [mmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Year
Anand 2000 (SHARE)	5.47	1.1	342	5.13	1.08	326	19.8%	0.34 [0.17, 0.51]	2000
Lear 2003	5.06	0.7	93	5.38	0.54	69	19.4%	-0.32 [-0.51, -0.13]	2003
He 2010	4.7	0.1	113	5	0.1	111	21.1%	-0.30 [-0.33, -0.27]	2010
Anand 2011	5.03	0.449	56	4.92	0.5048	52	19.6%	0.11 [-0.07, 0.29]	2011
Lear 2012	5.4	0.7	207	5.2	0.8	201	20.1%	0.20 [0.05, 0.35]	2012
Total (95% CI)			**811**			**759**	**100.0%**	**0.00 [-0.29, 0.30]**	

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 114.09$, df = 4 ($P < 0.00001$); $I^2 = 96\%$
Test for overall effect: Z = 0.02 (P = 0.98)

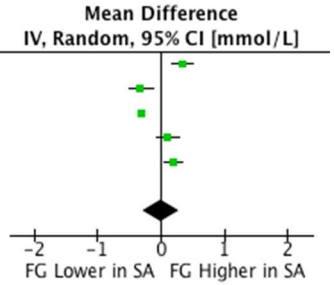

Figure 12. Forest plot of comparison: SA vs. WC, outcome: Fasting Blood Glucose [mmol/L].

Study or Subgroup	South Asian Mean [pmol/L]	SD [pmol/L]	Total	Caucasian Mean [pmol/L]	SD [pmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [pmol/L]	Year
Anand 2000 (SHARE)	99.7	3.23	323	72.5	3.24	322	24.8%	27.20 [26.70, 27.70]	2000
Lear 2003	66.6	39.1	93	66.3	26	69	14.0%	0.30 [-9.74, 10.34]	2003
He 2010	64.8	7.4411	113	46.2	7.375	111	24.1%	18.60 [16.66, 20.54]	2010
Anand 2011	70.8	8.082	56	45.1	7.8601	52	23.2%	25.70 [22.69, 28.71]	2011
Lear 2012	90	55	207	71	49	201	13.9%	19.00 [8.90, 29.10]	2012
Total (95% CI)			**792**			**755**	**100.0%**	**19.88 [14.20, 25.55]**	

Heterogeneity: $Tau^2 = 33.79$; $Chi^2 = 99.72$, df = 4 ($P < 0.00001$); $I^2 = 96\%$
Test for overall effect: Z = 6.86 ($P < 0.00001$)

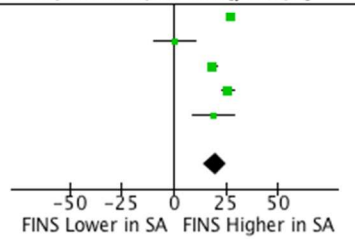

Figure 13. Forest plot of comparison: SA vs. WC, outcome: Fasting Insulin [pmol/L].

Study or Subgroup	South Asian Mean [index]	SD [index]	Total	Caucasian Mean [index]	SD [index]	Total	Weight	Mean Difference IV, Random, 95% CI [index]	Year
He 2010	2.4	0.2	113	0.7	7.37	111	1.1%	1.70 [0.33, 3.07]	2010
Mente 2010 (SHARE)	3.03	0.23	317	2.12	0.14	312	78.6%	0.91 [0.88, 0.94]	2010
Anand 2011	3.07	3.143	56	2	2.8844	52	1.6%	1.07 [-0.07, 2.21]	2011
Gasevic 2011 (MCHAT)	2.63	1.72	199	1.95	1.25	197	18.6%	0.68 [0.38, 0.98]	2011
Total (95% CI)			**685**			**672**	**100.0%**	**0.88 [0.73, 1.02]**	

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 3.66$, df = 3 (P = 0.30); $I^2 = 18\%$
Test for overall effect: Z = 11.83 (P < 0.00001)

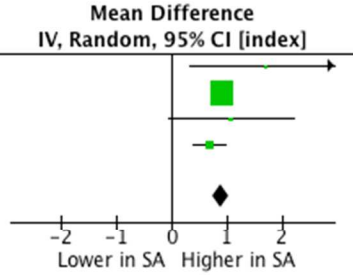

Figure 14. Forest plot of comparison: SA vs. WC, outcome: HOMA-IR

Study or Subgroup	South Asian Mean [mmHg]	SD [mmHg]	Total	Caucasian Mean [mmHg]	SD [mmHg]	Total	Weight	Mean Difference IV, Random, 95% CI [mmHg]	Year
Anand 2000 (SHARE)	76	10.3	342	73	10.6	326	20.1%	3.00 [1.41, 4.59]	2000
Lear 2003	68.73	9.8	93	73.16	9.78	69	18.9%	-4.43 [-7.48, -1.38]	2003
He 2010	72.1	1	113	78.4	0.9	111	20.6%	-6.30 [-6.55, -6.05]	2010
Anand 2011 (mol-SHARE)	75.22	0.96	56	73.86	1	52	20.5%	1.36 [0.99, 1.73]	2012
Lear 2012	78	11	207	77	9	201	19.9%	1.00 [-0.95, 2.95]	2012
Total (95% CI)			**811**			**759**	**100.0%**	**-1.05 [-5.79, 3.68]**	

Heterogeneity: $Tau^2 = 28.35$; $Chi^2 = 1227.00$, df = 4 (P < 0.00001); $I^2 = 100\%$
Test for overall effect: Z = 0.44 (P = 0.66)

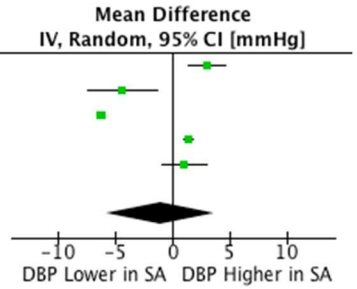

Figure 15. Forest plot of comparison: SA vs. WC, outcome: DBP [mmHg].

Study or Subgroup	South Asian Mean [mmHg]	SD [mmHg]	Total	Caucasian Mean [mmHg]	SD [mmHg]	Total	Weight	Mean Difference IV, Random, 95% CI [mmHg]	Year
Anand 2000 (SHARE)	119	15.7	342	118	15.8	326	21.3%	1.00 [-1.39, 3.39]	2000
Lear 2003	108.17	13.75	93	117.14	14.35	88	15.1%	-8.97 [-13.07, -4.87]	2003
He 2010	116.4	1.5	113	118.7	1.4	111	27.0%	-2.30 [-2.68, -1.92]	2010
Anand 2011 (mol-SHARE)	112.36	8.6058	56	111.59	8.5812	52	18.1%	0.77 [-2.47, 4.01]	2012
Lear 2012	119	15	207	120	17	201	18.6%	-1.00 [-4.11, 2.11]	2012
Total (95% CI)			**811**			**778**	**100.0%**	**-1.80 [-4.19, 0.58]**	

Heterogeneity: $Tau^2 = 5.44$; $Chi^2 = 21.42$, df = 4 (P = 0.0003); $I^2 = 81\%$
Test for overall effect: Z = 1.48 (P = 0.14)

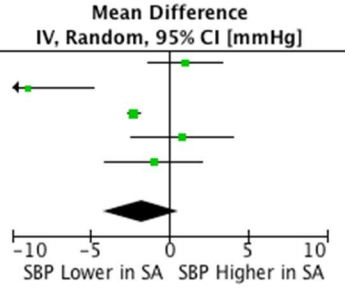

Figure 16. Forest plot of comparison: SA vs. WC, outcome: SBP [mmHg].

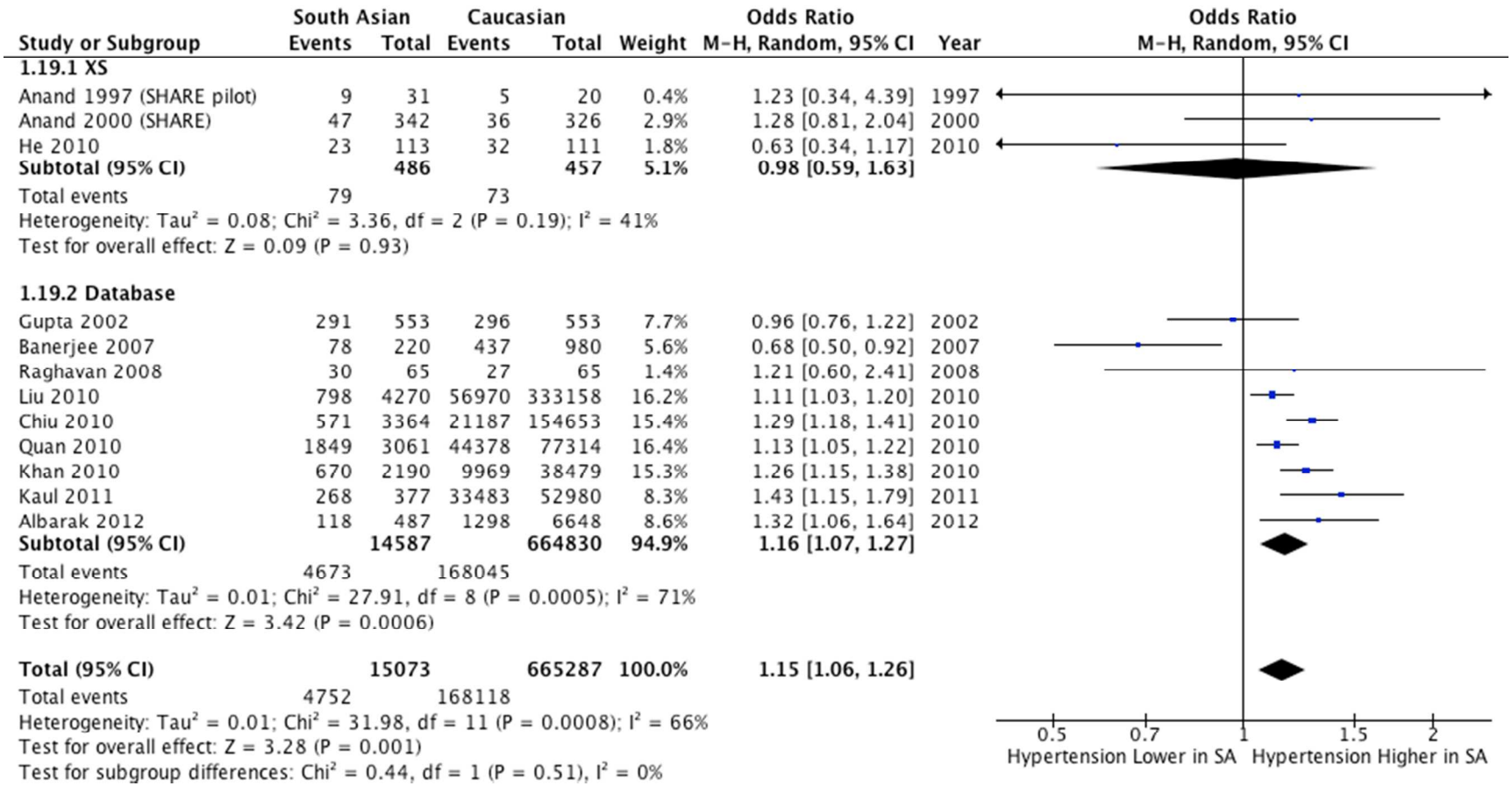

Figure 17. Forest plot of comparison: SA vs. WC, outcome: Hypertension

Study or Subgroup	South Asian Mean [mmol/L]	SD [mmol/L]	Total	Caucasian Mean [mmol/L]	SD [mmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Year
Anand 2000 (SHARE)	5.43	2.1	342	4.74	2.1	326	19.3%	0.69 [0.37, 1.01]	2000
Lear 2003	4.75	1.1	93	4.22	0.89	69	19.5%	0.53 [0.22, 0.84]	2003
Smith 2006	5.24	0.9	79	4.93	0.95	80	19.9%	0.31 [0.02, 0.60]	2006
He 2010	4.7	1.063	113	5.1	1.0536	111	20.0%	-0.40 [-0.68, -0.12]	2010
Lear 2012	5.28	0.97	207	5.28	1.04	201	21.3%	0.00 [-0.20, 0.20]	2012
Total (95% CI)			**834**			**787**	**100.0%**	**0.22 [-0.14, 0.58]**	

Heterogeneity: $Tau^2 = 0.15$; $Chi^2 = 35.51$, df = 4 ($P < 0.00001$); $I^2 = 89\%$
Test for overall effect: Z = 1.18 (P = 0.24)

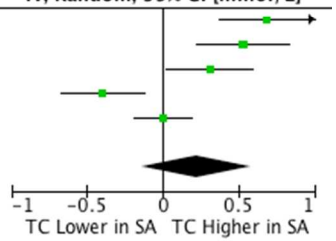

Figure 18. Forest plot of comparison: SA vs. WC, outcome: Total Cholesterol [mmol/L].

Study or Subgroup	South Asian Mean [mmol/L]	SD [mmol/L]	Total	Caucasian Mean [mmol/L]	SD [mmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Year
Anand 2000 (SHARE)	3.3	0.9	342	3.17	0.8	326	26.1%	0.13 [0.00, 0.26]	2000
Lear 2003	2.8	0.97	93	2.32	0.83	69	21.1%	0.48 [0.20, 0.76]	2003
He 2010	2.8	0.1	113	3	0.1	111	27.9%	-0.20 [-0.23, -0.17]	2010
Lear 2012	3.32	0.84	207	3.3	0.91	201	24.9%	0.02 [-0.15, 0.19]	2012
Total (95% CI)			**755**			**707**	**100.0%**	**0.08 [-0.17, 0.34]**	

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 51.35$, df = 3 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: Z = 0.64 (P = 0.52)

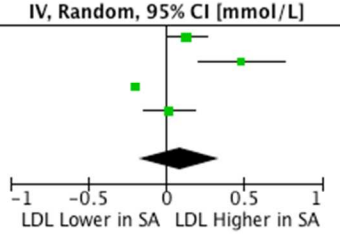

Figure 19. Forest plot of comparison: SA vs. WC, outcome: LDL-C [mmol/L].

Study or Subgroup	South Asian Mean [mmol/L]	SD [mmol/L]	Total	Caucasian Mean [mmol/L]	SD [mmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Year
Anand 2000 (SHARE)	1.04	0.3	342	1.19	0.3	326	25.3%	-0.15 [-0.20, -0.10]	2000
Lear 2003	1.28	0.34	93	1.46	0.35	69	17.1%	-0.18 [-0.29, -0.07]	2003
Smith 2006	1.03	0.25	79	1.4	0.39	80	17.8%	-0.37 [-0.47, -0.27]	2006
He 2010	1.3	4.2521	113	1.4	4.2143	111	0.4%	-0.10 [-1.21, 1.01]	2010
Anand 2011 (mol-SHARE)	1.24	0.2993	56	1.38	0.2884	52	16.7%	-0.14 [-0.25, -0.03]	2012
Lear 2012	1.18	0.29	207	1.32	0.38	201	22.7%	-0.14 [-0.21, -0.07]	2012
Total (95% CI)			**890**			**839**	**100.0%**	**-0.19 [-0.26, -0.12]**	

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 16.72$, df = 5 ($P = 0.005$); $I^2 = 70\%$
Test for overall effect: Z = 5.27 ($P < 0.00001$)

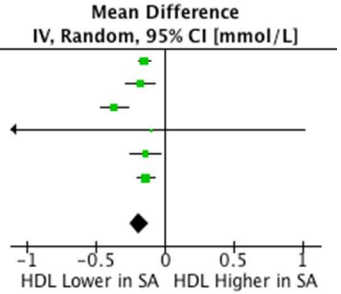

Figure 20. Forest plot of comparison: SA vs. WC, outcome: HDL-C [mmol/L].

Study or Subgroup	South Asian Mean	SD	Total	Caucasian Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Lear 2003	3.99	1.53	93	3.04	0.9	69	19.6%	0.95 [0.57, 1.33]	2003
Razak 2005 (SHARE/AP)	5.3	1.6	328	4.7	1.5	321	21.4%	0.60 [0.36, 0.84]	2005
Smith 2006	5.29	1.26	79	3.71	1.03	80	19.9%	1.58 [1.22, 1.94]	2006
Anand 2011 (mol-SHARE)	3.9	1.2722	56	3.81	1.2259	52	18.2%	0.09 [-0.38, 0.56]	2012
Lear 2012	4.73	1.33	207	4.35	1.58	201	20.9%	0.38 [0.10, 0.66]	2012
Total (95% CI)			**763**			**723**	**100.0%**	**0.72 [0.28, 1.17]**	

Heterogeneity: $Tau^2 = 0.23$; $Chi^2 = 36.90$, df = 4 ($P < 0.00001$); $I^2 = 89\%$
Test for overall effect: Z = 3.17 (P = 0.002)

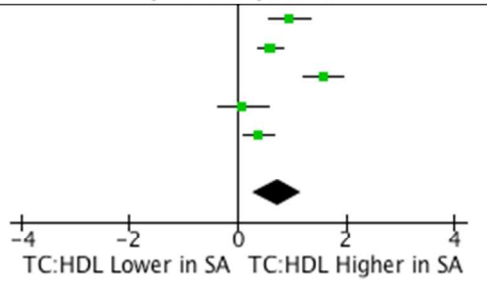

Figure 21. Forest plot of comparison: SA vs. WC, outcome: TC: HDL-C [mmol/L].

Study or Subgroup	South Asian Mean [mmol/L]	SD [mmol/L]	Total	Caucasian Mean [mmol/L]	SD [mmol/L]	Total	Weight	Mean Difference IV, Random, 95% CI [mmol/L]	Year
Anand 2000 (SHARE)	1.96	1.3	342	1.64	1.3	326	26.4%	0.32 [0.12, 0.52]	2000
Lear 2003	1.56	1.51	93	0.98	0.55	69	15.3%	0.58 [0.25, 0.91]	2003
He 2010	1.3	1.063	113	1.3	1.0536	111	19.1%	0.00 [-0.28, 0.28]	2010
Lear 2012	1.7	1.05	207	1.45	1.09	201	25.3%	0.25 [0.04, 0.46]	2012
Anand 2011 (mol-SHARE)	1.48	0.9728	56	1.33	0.9374	52	13.8%	0.15 [-0.21, 0.51]	2012
Total (95% CI)			**811**			**759**	**100.0%**	**0.26 [0.09, 0.42]**	

Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 7.65$, df = 4 (P = 0.11); $I^2 = 48\%$
Test for overall effect: Z = 3.10 (P = 0.002)

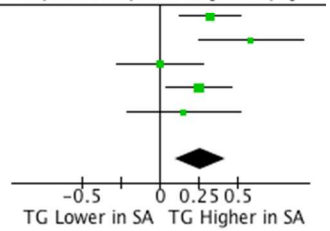

Figure 22. Forest plot of comparison: SA vs. WC, outcome: Triglycerides [mmol/L].

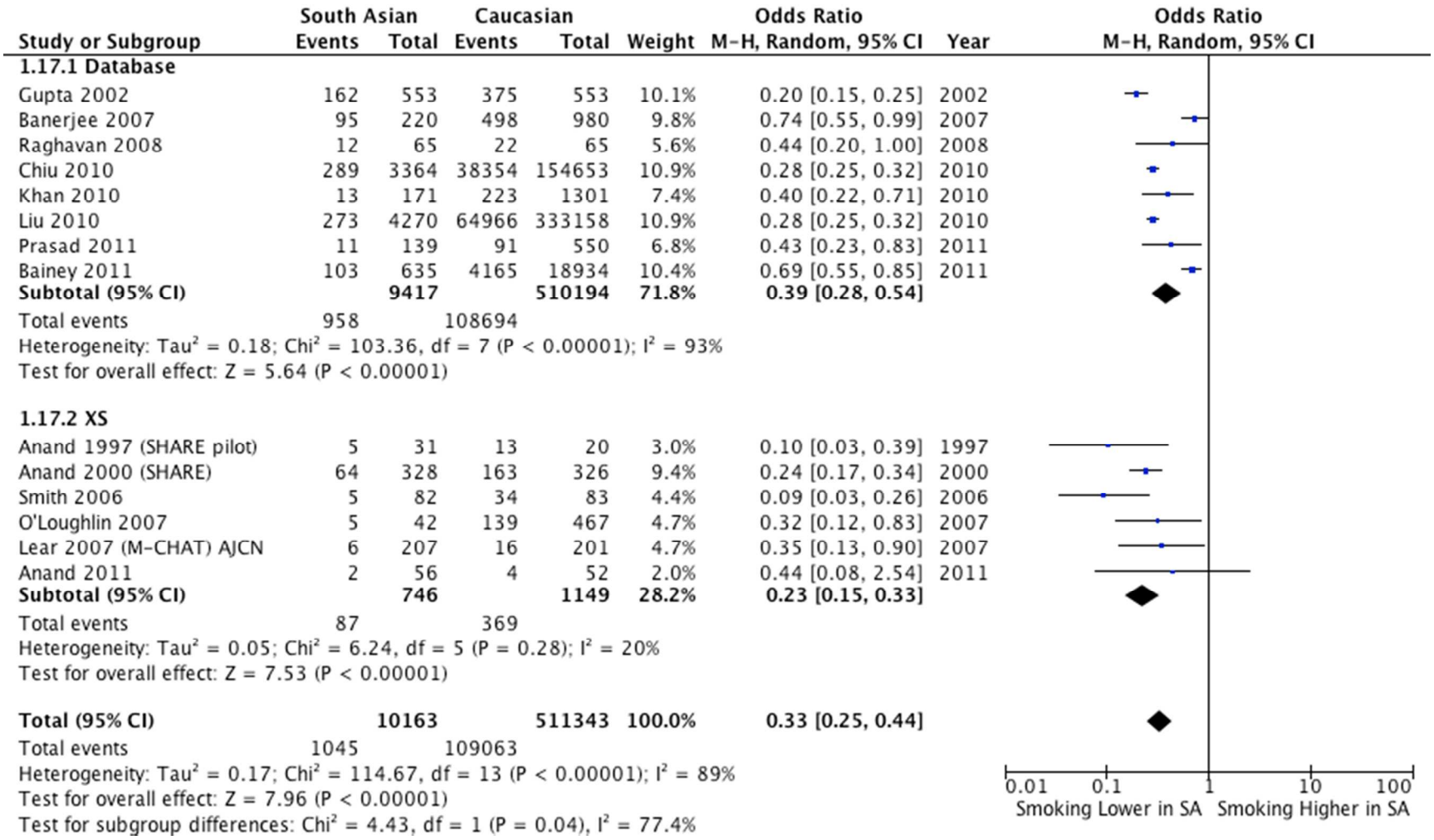

Figure 23. Forest plot of comparison: SA vs. WC, outcome: Smoking

Appendix 1

Search Strategy:

1 Cardiovascular disease.mp. or exp Cardiovascular Diseases/ (1734638)
2 cardio*.mp. (569398)
3 cardia*.mp. (495840)
4 heart*.mp. (918316)
5 coronory*.mp. (11)
6 angina*.mp. (58123)
7 ventric*.mp. (335032)
8 myocard*.mp. (422793)
9 pericard*.mp. (37376)
10 ischemi*.mp. (248980)
11 emboli*.mp. (110278)
12 arrhythmi*.mp. (100902)
13 thrombo*.mp. (312886)
14 atrial fibrillat*.mp. (39508)
15 tachycardi*.mp. (57832)
16 endocardi*.mp. (43527)
17 cardiomyopathy.mp. (47501)
18 vascul*.mp. (583854)
19 cerebrovasc*.mp. (102586)
20 sick sinus*.mp. (2945)
21 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 (2893189)
22 south asian*.mp. (2379)
23 exp Asian Continental Ancestry Group/ (31766)
24 exp India/ or india*.mp. (125658)
25 indian*.mp. (60002)
26 exp bangladesh/ or exp india/ or exp nepal/ or exp pakistan/ or exp sri lanka/ (86935)
27 pakistan*.mp. (12324)
28 pakistani*.mp. (2486)
29 bangladesh*.mp. (7970)
30 bengali*.mp. (229)
31 nepal*.mp. (5363)
32 Srilanka*.mp. (7)
33 indo*.mp. (146235)
34 ethnic groups/ or asian americans/ (42900)
35 indo canadian.mp. (13)
36 indo asian.mp. (98)
37 asian canad*.mp. (47)
38 22 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 (333775)
39 cholesterol*.mp. or exp Cholesterol/ (203403)
40 lipid*.mp. (375922)
41 apolipoprotein B.mp. or exp Apolipoproteins B/ (12242)
42 hyperlipid*.mp. or exp Hyperlipidemias/ (61618)
43 lipaemia.mp. (403)

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44     blood pressure.mp. or exp Blood Pressure/ (340494)
45     BP.mp. (105093)
46     SBP.mp. (10707)
47     DBP.mp. (8568)
48     mean arterial pressure.mp. (22707)
49     hypertensi*.mp. (345936)
50     exp Hypertension/ (195670)
51     exp Acute-Phase Proteins/ (139403)
52     body weight.mp. or exp Body Weight/ (392043)
53     body fat.mp. or exp Adipose Tissue/ (75928)
54     Body Mass Index/ or BMI.mp. (92077)
55     waist circumference.mp. or exp Waist Circumference/
(10470)
56     Body Constitution/ or waist to hip.mp. or Waist-Hip
Ratio/ (16792)
57     exp Triglycerides/ (58028)
58     hyperglycemia/ or glucose intolerance/ or
hyperinsulinism/ or exp insulin resistance/ or exp metabolic
syndrome x/ (68481)
59     exp Hypercholesterolemia/ or hypercholesterol*.mp.
(34480)
60     39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or
48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or
58 or 59 (1675739)
61     38 and 60 (32676)
62     21 and 38 (40412)
63     21 and 23 (5073)

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