CARDIOVASCULAR DISEASE AND DIABETES

Social disadvantage and cardiovascular disease: development of an index and analysis of age, sex, and ethnicity effects

Sonia S Anand,1,2* Fahad Razak,2 AD Davis,3 Ruby Jacobs,3 Vlad Vuksan,4 Koon Teo1,2 and Salim Yusuf1,2

Accepted 4 July 2006

Background Social disadvantage is defined by adverse socio-economic characteristics and is distributed unequally by age, sex, and ethnicity. We studied the relationship between social disadvantage, cardiovascular risk factors, and cardiovascular disease (CVD) among men and women from diverse ethno-racial backgrounds.

Methods A total of 1227 men and women of South Asian, Chinese, Aboriginal, and European ancestry were randomly selected from four communities in Canada to undergo a health assessment. Socio-economic factors, conventional and novel CV risk factors, atherosclerosis, and CVD were measured. A social disadvantage index was generated and included employment status, income, and marital status. Social disadvantage was examined in relation to risk factors for CVD, atherosclerosis, and prevalent CVD.

Results Social disadvantage was higher among older people, women, and non-white ethnic groups. Cigarette smoking, glucose, overweight, abdominal obesity, and CRP were higher among individuals with higher social disadvantage, whereas systolic blood pressure, lipids, norepinephrine, and atherosclerosis were not. Social disadvantage is an independent predictor of CVD after adjustment for conventional and novel risk markers for CVD (OR for 1 point increase = 1.25; 95% CI 1.06–1.47).

Conclusion The social disadvantage index combines social and economic exposures into a single continuous measure. Significant variation in social disadvantage by age, sex, and ethnic group exists. Increased social disadvantage is associated with an increased burden of some CV risk factors, and is an independently associated with CVD.

Keywords Social disadvantage, cardiovascular disease, social and economic status, ethnicity, variations in health status

Understanding the determinants of common diseases using only biologic factors is limited and may be enhanced by examining biologic and social factors, and their interactions.1,2 Cardiovascular disease (CVD) is the leading cause of death and disability in developed countries, and will reach epidemic proportions in developing countries by the year 2020.3 Prior studies have demonstrated that social and economic factors are associated with CVD,4–10 and because these factors are distributed unequally by sex and ethnicity,11–15 they may help to explain ‘apparent’ sex and ethnic differences in CVD distribution. It is challenging to quantify the effect of social disadvantage on health outcomes because social and economic factors are surrogates for the latent construct of social
disadvantage. However, it is important to determine the impact of social disadvantage on CVD to further our understanding of the pathogenesis of CVD, to understand apparent sex and ethnic differences, and to aid us in identifying high-risk populations so that appropriate interventions may be developed and tested. To address some of these issues, this paper (i) presents the development of an index to quantify social disadvantage, (ii) examines how social disadvantage varies by age, sex, and ethnic group, and (iii) investigates the relationship between social disadvantage, cardiovascular risk factors, and CVD.

Design and methods

Study design and sample

Between 1998 and 2000, 1285 men and women of European, Chinese, South Asian, and Aboriginal origin were randomly selected from four communities in Canada (Hamilton, Toronto, Edmonton), and the Six Nations Reservation (Ohsweken, Ontario), and completed a 3 h health assessment.10–12 Households of South Asian and Chinese ethnicity were identified using a validated method of unique surname identification13,14 from regional telephone directories. Respondents of European descent were matched by postal code to South Asian or Chinese respondents. Aboriginal households were identified by randomly selecting households from the community list of the Six Nations. Selected households were mailed a letter of introduction followed by telephone contact to assess eligibility. To be eligible, individuals must have lived in Canada for at least 5 years, and be between the ages of 35 and 75 years. Individuals with chronic debilitating illnesses such as terminal cancer and renal failure were excluded. The response rates were 62% in Europeans, 59% in South Asians, 69% in Chinese, and 79% in Aboriginals. After written informed consent was obtained, all participants completed a health questionnaire which elicited information on employment, income, education, and marital status. Given the multi-ethnic nature of the sample, questionnaire development included translation into some South Asian languages and Chinese, and back-translation to English to ensure that the validity of questionnaire was preserved.12 All participants had physical measurements recorded including blood pressure, height and weight, fasting blood samples, a 12-lead electrocardiogram, and a carotid B-mode ultrasound examination.10 The reliability of questionnaire responses was checked in 85 individuals who had a repeat examination 1 month after their first. Biomarkers were analysed using a standardized protocol.10,11 Norepinephrine was drawn after participants had rested quietly for 15 min on a stretcher with a butterfly catheter in place. Blood was drawn into a pre-chilled 5 ml EDTA tube. All tubes were placed on crushed ice until they were centrifuged. Blood was processed within 60 min, and centrifuged at 3000 rpm for 15 min, and 1 ml of plasma was stored frozen at −70°C. The 25 l-norepinephrine radioimmunoassay for the quantitative determination of norepinephrine in plasma was used (Immuno-Biological Laboratories, Hamburg Germany). The intra-assay coefficient of variation (CV) in our lab is 9.3%, and the inter-assay C.V. is 8.9%. All data were transferred and stored at the central coordination center and core laboratory at McMaster University in Hamilton, Ontario, Canada as described previously.10,11

Creation of the social disadvantage index

Social and economic variables collected from participants included income, income sources, job type, education, employment status, and marital status based on questions used in the National Population Health Survey in Canada.15 These variables were included in the SHARE general health questionnaire because previous studies confirmed that they are valid and reliable proxies of social and economic status in most populations.1–9,16,17 Specifically we considered that being married as a proxy for social support compared with being single, separated, or widowed. This appears to be an appropriate assumption based on Canadian perceptions and trends regarding marriage.18 To generate the social disadvantage index, these variables were entered into a logistic regression model with prevalent CVD as the dependent variable. Using backward elimination four variables emerged [annual household income <20 000 dollars (OR = 2.21, P = 0.03); annual household income between 20 and 60 000 dollars (OR = 1.79, P = 0.048), unemployment (3.09, P = 0.0001), and being unmarried (1.60, P = 0.04)]. The beta coefficients of these variables were rounded to the closest 0.5 and then doubled to make each value into an integer (Table 1). Income <20 000/year equaled a score of +2, income between 20 and 60 000 dollars per year = +1, unemployment was equal to a score of +2, and being unmarried was equal to a score of +1. The maximum social disadvantage score was 5, and the lowest possible score was 0, reflecting the least social disadvantage. The intraclass correlation among 85 participants whose score was retested was 0.92 (0.88–0.95).

Selected biologic outcomes

The biological determinants of CVD explored in relationship to social disadvantage included known determinants of CVD [cigarette smoking, blood pressure (BP), total cholesterol to HDL ratio, body mass index (BMI), abdominal obesity (measured using the waist to hip ratio), and HbA1c], as well as novel risk markers such as high sensitivity CRP (hs-CRP), and plasma norepinephrine.19 Norepinephrine is a catecholamine which is secreted into the circulation in response to sympathetic stimu-

<table>
<thead>
<tr>
<th>Variable entered</th>
<th>Beta coefficient (SE)</th>
<th>Significance</th>
<th>Odds ratio</th>
<th>Integer score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Income 20–60 000</td>
<td>0.58 (0.29)</td>
<td>0.048</td>
<td>1.79</td>
<td>+1</td>
</tr>
<tr>
<td>Income &lt;20 000</td>
<td>0.79 (0.35)</td>
<td>0.03</td>
<td>2.21</td>
<td>+2</td>
</tr>
<tr>
<td>Unemployment</td>
<td>1.13 (0.24)</td>
<td>0.0001</td>
<td>3.09</td>
<td>+2</td>
</tr>
<tr>
<td>Unmarried</td>
<td>0.47 (0.23)</td>
<td>0.04</td>
<td>1.60</td>
<td>+1</td>
</tr>
</tbody>
</table>

Minimum Score = 0 and Maximum Score = 5. CVD = cardiovascular disease; SE = standard error.
lation secondary to physical and emotional stress, and has been identified in previous studies to be an independent predictor of CVD.20,21 Atherosclerosis was measured using the standardized quantitative B-mode carotid ultrasound scanning method which consisted of a transverse scan followed by a full-circumferential longitudinal scan in which images from six well-defined carotid artery segments for the right and left carotid arteries (12 segments/patient) were obtained. The maximal intimal medial thickness (IMT) for each segment was identified, and the mean of the maximum IMT readings for the 12 segments was calculated for each participant.10,11 Using this technique the intraclass correlation coefficients for between and within ultrasonographer (0.91, 0.90) and reader (0.88, 0.92) reliability were high. Prevalent CVD was classified as (i) coronary artery disease, defined as angina (Rose questionnaire), a self-reported hospitalization for a MI, silent MI (major Q waves by Minnesota criteria), percutaneous coronary angioplasty (PTCA), or coronary artery bypass graft (CABG) surgery; or (ii) cerebrovascular disease, defined by self-report of a prior stroke confirmed by a physician.10,11

Statistical considerations
All analyses were conducted using SPSS (version 10.1). Means, standard deviations, and proportions are presented. Social disadvantage scores were grouped as being ‘no’ for scores of 0, low for scores of 1, moderate for scores of 2–3, and high for scores >4. Between group comparisons of continuous variables were made using ANCOVA with adjustment for age, sex, and ethnicity where indicated. Post hoc between group comparisons were made used Tukeys test to adjust the level of significance for multiple testing. For between group comparisons of categorical variables, logistic regression with age, sex, and ethnicity adjustment was used. To determine the direct relationship of social disadvantage on CVD independent of age, sex, and ethnicity, and other factors associated with CVD, and to study the possible interaction of social disadvantage with sex and ethnicity, a multivariate logistic regression analysis was performed.22

Results
Data were complete on 1227 of the 1285 participants, 614 women and 613 men. The demographic characteristics by ethnic group are shown in Table 2. Briefly, the average age of the population was 50 years, and 51% were women. The social disadvantage index varied by age, sex, and ethnicity. Increasing social disadvantage was associated with older age and was higher among women compared with men [mean score, 2.02; (SE = 0.05) vs 1.42 (0.06), P < 0.0001], after adjustment for age and ethnicity. People of European origin had the least social disadvantage [mean score, 1.36 (0.07)] compared with Aboriginal people who had the most social disadvantage [mean score, 2.44 (SE, 0.08)], with Chinese 1.66 (0.08), and South Asians [1.53 (0.07)] having intermediate levels, overall P < 0.0001. Figure 1 depicts social disadvantage by sex and ethnic group.

Risk factors and social disadvantage groups
Individuals with high social disadvantage (score > 4) were more likely to be older, women, smokers, and have higher body weight, abdominal obesity, glucose, and inflammatory marker elevation compared with individuals with lower degrees of social disadvantage (Table 3). Crude associations between social disadvantage and systolic BP, total cholesterol/HDL ratio, norepinephrine, and atherosclerosis were present, but became non-significant after adjustment for age. However, norepinephrine was higher in the 210 individuals with high social disadvantage compared with the 1076 individuals classified as having either no, low, or moderate social disadvantage [1.82 (0.07) vs 1.66 (0.03); P = 0.03].

Disease outcomes and social disadvantage
The prevalence of CVD increased with rising social disadvantage, and this gradient was present in each ethnic group. To determine the independent predictive value of social disadvantage on CVD, a multivariate logistic regression analysis was performed. Independent variables including age, sex, ethnicity, BMI, smoking status, HbA1C, systolic BP, treatment with BP or cholesterol lowering medications, norepinephrine, CRP, total cholesterol to HDL ratio, waist to hip ratio, and social disadvantage were entered simultaneously into the model. Significant determinants of CVD included age, sex, ethnicity, use of blood or cholesterol lowering medications, and social disadvantage (Table 4). The odds ratio and 95% CI for social disadvantage was 1.25 (95% CI 1.06–1.47) suggesting that for every one point increase in the social disadvantage index, the relative increase in CVD is likely 25% (range 6–47%). Compared with the Europeans, the Chinese had a lower probability of CVD, whereas Aboriginal people had a higher probability of CVD, and South Asians trended toward a higher probability of CVD. As expected, female sex was associated with a lower probability of CVD as protective factor against CVD. [Odds ratio = 0.54 (95% CI 0.29–0.98)] No interaction between social disadvantage and ethnicity or social disadvantage and sex was observed. Using the predicted probability of CVD equation derived from the logistic regression model, the ethnic-sex differences of social disadvantage are shown graphically to demonstrate that when ethnicity and sex

<table>
<thead>
<tr>
<th>Table 2 Demographic characteristics by ethnic group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>European</strong></td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
</tr>
<tr>
<td>Female, N (%)</td>
</tr>
<tr>
<td>Years lived in Canada</td>
</tr>
</tbody>
</table>

* Overall test for significance between ethnic groups.
Figure 1: Comparisons of Social disadvantage by Sex and Ethnic Group (*Age-adjusted). Note: Although overall women have more social disadvantage than men, when stratified by ethnic group, Native Indian men had significantly higher social disadvantage compared with women from all other ethnic groups. EU = Europeans, SA = South Asians, CH = Chinese, AP = Aboriginal People

Table 3: CVD Risk factors and social disadvantage index

<table>
<thead>
<tr>
<th>Social disadvantage</th>
<th>0 (No)</th>
<th>1 (Low)</th>
<th>2–3 (Moderate)</th>
<th>4-5 (High)</th>
<th>P for linear trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>N/Group</td>
<td>376</td>
<td>308</td>
<td>392</td>
<td>210</td>
<td></td>
</tr>
<tr>
<td>Age (SE)a</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Women (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Total cholesterol/HDLb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.97</td>
</tr>
<tr>
<td>Systolic BPb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.40</td>
</tr>
<tr>
<td>Hemoglobin A1c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Body mass indexb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Waist to hip ratiob</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>C-Reactive proteinb</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.0001</td>
</tr>
<tr>
<td>Norepinephrineb,c</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.39</td>
</tr>
<tr>
<td>Atherosclerosis b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.11</td>
</tr>
<tr>
<td>CVD (%)b</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

SE = Standard Error; BP = Blood Pressure; mmIMT: Mean maximal IMT.

a Adjusted for sex and ethnicity.
b Adjusted for age, sex, and ethnicity.
c Comparing individuals with high social disadvantage (n = 210) to individuals with no, low, or moderate social disadvantage (n = 1076), norepinephrine is significantly higher [1.82 (0.07) vs 1.66 (0.03); P = 0.03] adjusted for age, sex, and ethnicity.
characteristics are considered, increasing social disadvantage is associated with a greater predicted probability of CVD in some of the female subgroups (i.e. Aboriginal and South Asian) compared with some male subgroups (i.e. European and Chinese) (Figure 2).

Discussion

The social disadvantage index is a summary measure of social and economic factors which are associated with CVD. We have demonstrated that social disadvantage increases with age, is higher among women than men, and varies significantly by ethnic group. Further, independent of age, social disadvantage is associated with an increase in some, but not all, CV risk factors, and is a significant determinant of CVD. This suggests that the mechanisms by which social disadvantage is associated with CVD are largely independent of classical CV risk factors, sex, and ethnic origin.

The majority of the social disadvantage components represent later life-course influences (e.g. employment, income, and marital status), although it is likely that the determinants of unemployment and low income reflect patterns of social and economic hardship which have accumulated over time, as opposed to circumstances which were created because CVD developed. The effect of social disadvantage on CVD was independent of CV risk factors, sex, and ethnicity. Norepinephrine, one biologic marker of physical and emotional stress, was not associated with social disadvantage in a linear fashion, although individuals with the highest social disadvantage had elevated norepinephrine compared with those with no, low, or moderate social disadvantage. Further, in the multivariate analysis, rising norepinephrine was associated with CVD, although the association did not reach conventional levels of statistical significance. Previous studies have demonstrated that long-term elevation of norepinephrine is associated with elevated blood pressure, abnormal lipids, and atherosclerosis—all factors which are known determinants of CVD. Therefore the direct association of norepinephrine to CVD is likely attenuated by its association with other cardiovascular risk factors.

The unique make-up of our sample allowed us to explore social disadvantage by age, ethnicity, and sex subgroups. Older people had more social disadvantage as some of the components of the index such as marital status and income are correlated with age. Members of non-European ethnic groups also had higher social disadvantage compared with Europeans. Ethnicity was associated with CVD, and compared with Europeans, Aboriginal people and South Asians (trend) had an increased probability of CVD, whereas the Chinese had a lower probability of CVD even after accounting for differences in social disadvantage and other known risk factors. This suggests that the construct of ‘Ethnicity’ reflects unmeasured or unaccounted for cultural (e.g. dietary factors) or genetic differences (i.e. varying frequency of single nucleotide polymorphisms associated with CVD), which may increase or decrease the risk of CVD independent of differences in social disadvantage.

Women had more social disadvantage compared with their male counterparts of similar age. This was observed across ethnic groups. Furthermore a greater proportion of individuals in the moderate and high social disadvantage categories in which the risk factor burden is the highest were women. Accounting for differences in social disadvantage between women and men in the prediction of CVD, likely balances differences in risk factors for CVD between women and men and once this occurred, female status was associated with a lower predicted probability of CVD. Although women experienced more social disadvantage than men, men from the most socially disadvantaged group (e.g. Aboriginals) had higher absolute scores compared with women from groups of higher social advantage.
position. In the overall dataset, women had a lower probability of CVD, although considering sex-ethnic differences, Aboriginal and South Asian women had a higher predicted probability of CVD compared with European and Chinese men. This emphasizes the importance of considering ethnic-sex differences when assessing the impact of social disadvantage on CVD.

Our study has several strengths. First, the components of the social disadvantage index have face validity. Second, the index is weighted to account for differences in the strength of association between various factors and CVD and considers their independent effects of these factors on CVD. Third, its test–retest reliability is high, and fourth because detailed measures of CV risk factors, and atherosclerosis were made, we were able to explore the pathways by which social disadvantage influences risk factor development and disease outcomes including atherosclerosis. However, the cross-sectional nature of our sampling strategy has some limitations as the highest risk individuals who died from CVD (and who likely had more atherosclerosis) would not have been included in our analysis. This is consistent with the results of a recent study of acute MI mortality and socio-economic status from Canada in which the 30 days post mortality rate was highest among the individuals with the lowest socio-economic status.26 Therefore our estimates of risk factors, atherosclerosis and CVD with social disadvantage likely represent underestimates of the true associations. In addition, the sample size of our cohort is modest. Furthermore, biomarkers were measured once at baseline, and therefore we could not account for regression dilution bias.27 These factors could also lead to underestimation of the association between risk factors and disease, and may account for some of the borderline associations (i.e. norepinephrine) in this study.

Since social disadvantage is associated with biological factors that cause CVD, quantifying social disadvantage has an important role in research, clinical, and public health settings. This may assist health care professionals in determining which individuals require extra assistance from the health care system during an illness, or could be used to assess the effectiveness of interventions aimed to decrease ‘social disadvantage’ among high-risk individuals or communities (e.g. by development programs to increase employment and income, or create community services and supports to prevent marital separation and divorce).

Conclusions
The social disadvantage index combines social and economic exposures into a single continuous measure. Significant variation in social disadvantage by age, sex, and ethnic group exists. Increased social disadvantage is associated with an increased
burden of some CV risk factors, and is independently associated with CVD.

Acknowledgements
Dr S.S.A. is a recipient of a Canadian Institutes of Health Research Clinician Scientist Award. Mr F.R. is a recipient of an Ontario Graduate Scholarship. Dr S.Y. is a recipient of Research Clinician Scientist Award. Mr F.R. is a recipient of an Dr S.S.A. is a recipient of a Canadian Institutes of Health Research Clinician Scientist Award and holds a Heart and Stroke Foundation of Ontario Research Chair.

References
14 Statistics Canada. Healthy today, healthy tomorrow? Findings from the national population health survey. 2004. Cat # 82-618-MWE.
15 Statistics Canada. Healthy today, healthy tomorrow? Findings from the national population health survey. 2004. Cat # 82-618-MWE.
18 Statistics Canada: Canadian Statistics on Marriage. Available at: http://www40.statcan.ca/l01/cst01/famil01.htm.