ANALYSING THE SOCIOECONOMIC DETERMINANTS OF HYPERTENSION IN SOUTH AFRICA: A STRUCTURAL EQUATION MODELLING APPROACH

by

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To the memory of my father Spartaco

and my aunt Maria.

Dissertation

Epidemiological research has long since observed that the prevalence of hypertension varies across populations' socioeconomic strata. Higher socioeconomic status (SES) has been consistently associated with lower levels of blood pressure in most studies from Europe and North America, while research in low- and middle-income countries at an earlier stage of the epidemiological transition revealed mixed patterns.

The causal mechanisms underlying these varying relationships are largely unknown. Only in recent years the pathways through which SES impacts the cardiovascular system have been explored in large-scale studies, with results suggesting that body mass index, heart rate, and — to a lesser extent — physical exercise, alcohol use and smoking, may play a role in mediating these associations. However, these results refer to high-income countries, while similar research in low- and middle-income countries, and sub-Saharan Africa in particular, is lacking.

In 2008, the National Income Dynamics Study (NIDS) collected a broad range of information on a representative sample of the population of South Africa, a medium-income country undergoing rapid epidemiological transition. Among other topics, information was gathered on blood pressure, biologic and behavioural risk factors, education, income and other indicators of socioeconomic position.

The present study took advantage of this dataset to describe the relationships between SES dimensions (namely education, income, wealth and employment status) and blood pressure in the South African adult population, and to explore causal pathways and bio-behavioural mediators which may explain the observed associations.

Part A of this dissertation (**Protocol**) describes the characteristics of the NIDS dataset, gives details on sampling and data collection in the original study, and delineates the methodology of the secondary analysis which forms the object of the present study.

Part B (**Literature review**) illustrates the main findings of the conflicting epidemiological literature on the socioeconomic determinants of hypertension in sub-Saharan Africa,

and presents a summary of the major biological and behavioural factors associated with blood pressure levels in individuals and prevalence of hypertension in populations.

Part C (**Article**) presents methodological details, results, and possible interpretations of the analyses carried out on the NIDS dataset.

The estimated prevalence of hypertension in the South African population aged 15 years and over was 33.4% among women (95%CI: 31.5 to 35.4), and 28.0% among men (95%CI: 26.0 to 30.0), both remarkably higher than the corresponding estimates form the first South African Demographic and Health Survey carried out in 1998. Multivariate linear models showed that higher education and income were independently associated with higher blood pressure in men and with lower blood pressure in women.

Analysis through structural equation modelling showed a direct, strong relationship between SES and body mass index in both genders and suggested that the latter is an important mediator of a harmful effect of increasing socioeconomic status on blood pressure, explaining a sizable proportion of the overall association in men, and contributing to reduction of the overall protective effect found in women.

Data also suggested that other biological and behavioural factors, and especially heart rate, are involved in the causal pathway, but they seem to play a more modest role.

The results reinforce previous evidence that the pattern of association between socioeconomic status and blood pressure in low- and middle-income countries undergoing epidemiological transition do not replicate those found in Europe and the US.

Acknowledgements

First, I would like to thank my supervisor, *Prof. Rodney Ehrlich*, who suggested the subject of this dissertation and guided me throughout the process of transforming a set of broad and, possibly, confused ideas in a readable piece of research. I will not forget his timely, discreet, and stimulating comments on my work — always respectful of my personal ideas and approach to problems — and his patience in reviewing the manuscript well beyond his supervisor's duties.

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Prof. Francesca Little, Associate Professor at the Department of Statistical Science of the University of Cape Town, for giving much-needed hints and suggestions on the statistical analyses in this dissertation, and for accepting to do that notwithstanding the very short time available.

Declaration

I, Annibale Cois (CSXANN001), hereby declare that the work in this dissertation is based on my original work (except where acknowledgements indicate otherwise) and has not, in whole or in part, been submitted towards another degree, at this University or elsewhere.

The University is empowered to reproduce either the whole or any portion of the contents for the purposes of research.

Signature

University of Cape Town, 09/11/12

Acronyms and abbreviatons

ADF asymptotic distribution free.

BMI body mass index.

DALY disability adjusted life year.

DBP diastolic blood pressure.

DPS digit preference score.

GNP Gross National Product.

HR heart rate.

IQR interquartile range.

JNC-7 Seventh Joint National Committee report.

LMIC low- and middle-income country.

ML maximum likelihood.

NIDS National Income Dynamics Study.

OR odds ratio.

PIR proportion of identical readings.

PSU primary sampling unit.

SADHS South African Demographic and Health Survey.

SALDRU Southern Africa Labour and Development Research Unit.

SBP systolic blood pressure.

SEM Structural Equation Modelling.

SES socioeconomic status.

sSA sub-Saharan Africa.

US United States of America.

Part A: Protocol

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1 Protocol Summary

This protocol presents a study aimed at investigating the association between socioeconomic status (SES) and hypertension in the South African adult population.

The study consists in a secondary analysis of blood pressure and anthropometric measurements, health-related and socioeconomic status indicators, and demographic characteristics, collected in 2008 during the first wave of the National Income Dynamics Study (NIDS), on a cross-sectional sample of 15 574 individuals (9 314 women and 6 260 men), representative of the South African population.

The lack of knowledge on the causal mechanisms underlying the observed association between SES and blood pressure represents the main justification of this study. Despite the evidence that SES and prevalence of hypertension are epidemiologically related, in fact, the nature of the relationship and the possible biologic and/or behavioural mediators are largely unknown. This is especially true in low- and middle-income countries (LMICs), in which the simple direct relationships between socioeconomic position as a whole and blood pressure levels, consistently found in studies in high-income countries, cannot account adequately for the inter- and intra-population heterogeneity repeatedly observed in these contexts. Therefore, consensus exists that the relationships between sub-components of the composite construct defining the individual's position in the society and blood pressure need to be analysed deeper in order to explain the seemingly inconsistent research findings in countries characterised by ongoing epidemiological transition.

In this study, a structural equation modelling approach is proposed to identify possible causal pathways through which different sub-elements defining individual's SES — namely education, income, wealth and employment status — affect mean blood pressure levels in the South African adult population; and the extent to which the variations in the bio-behavioural factors involved in these pathways may account for the observed variability of hypertension risk among different population strata.

2 Background

Hypertension is a leading component of cardiovascular disease worldwide, and epidemiological data soundly support the existence of a direct relationship between increasing levels of both systolic and diastolic blood pressure and the risk of ischaemic heart disease, stroke and renal failure.[1]

The pathogenetic mechanism leading to hypertension at the individual level involves the complex interaction of several genetic, hormonal and environmental factors. Beside genetic characteristics of the individuals, strong epidemiological and experimental evidence supports a causal link between hypertension, body mass index (BMI) and a series of lifestyle risk factors, especially low physical activity, malnutrition (high intake of salt, fats, high-energy processed food and low vegetable and fruit consumption) and elevated alcohol consumption.[2–5]

A growing literature supports, moreover, the association between blood pressure levels and education, income, type of employment and other characteristics defining the individuals position in the social structure, often summarised in the multidimensional concept of socioeconomic status.[6] In high-income countries, the protective impact of higher SES on the cardiovascular risk factor profile in general, and hypertension in particular, is well-established. A systematic review of 50 studies reporting on SES differences in blood pressure after adjusting for age,[7] shows that the large majority found a significant negative association between SES and blood pressure (usually stronger in women than in men), and more recent studies, reviewed by Grotto and colleagues,[8] confirm substantially the results.

In low- and middle-income countries a relationship between SES and hypertension has also been repeatedly found, but the direction and pattern of the association are less consistent. Some studies, coherently with the findings in high-income countries, show a negative association between SES and blood pressure; some have found a significant positive association, and other a U-shaped gradient in which either high or low incomes are associated with higher blood pressures than intermediate incomes.[7–10]

Methodological differences, heterogeneity of samples and differences in the degree of eco-

nomic development have been advanced as possible explanations of the conflicting results, as well as inconsistencies in SES measurements and, particularly, the use of indicators which perform differently in different context (like household monthly income).[9, 11] The difficulty of taking into account a plethora of possible confounding or mediating factors, which can make spurious relationships appear or mask real associations, is also likely to account for part of the inconsistencies.

Overall, the fact that socioeconomic factors influence blood pressure — and, consequently, prevalence of hypertension varies in populations according to SES — can be considered acquired. Nevertheless, significant evidence indicates that a simple relationship between the composite (and theoretical) construct of SES and blood pressure levels or prevalence of hypertension is not sufficient to account for the inter- and intra-population heterogeneity which observational studies have repeatedly found across countries, populations and time. Therefore, as reported by Colhoun, at present "*there is little need for further reports depicting SES differences in BP without exploration of the specific effects of other potential mediating factors*".[7, p 107] A finer understanding of the possible causal pathways involved in the association between the sub-components of SES (income, education and occupation are the elements most often considered) and blood pressure, as well as the relationship with other known risk factors, is needed to understand this heterogeneity.

These relationships and causal pathways have been explored largely in high-income countries. For example, there is little doubt that the variations in BMI and alcohol consumption across SES categories (no matter if these are defined in terms of education, income or occupation) are the main, albeit not unique, mediators of the observed association with prevalence of hypertension, while differences in access to diagnosis and treatment seem to have only a marginal role.[7] The same associations are, in contrast, inconsistent in LMICs: for example, preliminary univariate analyses of recent national survey data in South Africa seem to indicate a protective effect of education on hypertension, while other commonly used SES indicators (income and count of household assets) show no significant effect or, possibly, a harmful one.[12]

In sub-Saharan Africa (sSA), the high burden of mortality and morbidity associated with hypertension is well documented, and so is the considerable lack of awareness and widespread under-diagnosis and treatment. It is largely agreed that hypertension repre-

sents, as elsewhere, a major public health issue, for various reasons: the huge human and economic cost; adding to the burden on the health systems of perinatal/maternal and infectious diseases; substantial evidence that prevalence is on the rise following the same path of many high-income countries in the past decades; and the fact that it is largely preventable.[2, 13–16]

Addressing the problem of hypertension from a public health perspective especially in a context of over-burdened health systems requires a careful identification of suitable intervention targets to ensure effective and efficient resource allocation. This, in turn, calls for a sufficient understanding of the main drivers of the epidemic, their socio-economic correlates, and their inter-relationship at the population level.

This essential requirement contrasts with the scarce and inconclusive evidence provided by specific research, mostly coming from small-scale studies and non-representative samples, and the uncertain applicability of the results found in other contexts, namely in high-income countries. It calls for further research able to unravel the complex pathways leading to hypertension in sSA.

In this situation of limited data, the availability of the results of a large-scale survey of good methodological quality collecting information on blood pressure, hypertension prevalence, known risk factors (especially BMI, alcohol and tobacco use) together with multiple indicators of SES, represents an important opportunity to explore specific relationships and gain a better understanding of the phenomenon.

The National Income Dynamics Study,[17] carried out in South Africa in 2008 gathered information on health and SES in a representative sample of the South African population, with sample sizes large enough to produce reliable estimates of the various parameters of interest at the level of each of the 53 district councils. A deeper analysis of the NIDS data — beyond the already published estimates of average blood pressure levels, hypertension prevalence and univariate association with main risk factors (which indicate a striking increase in prevalence compared to 1998 data across all population groups [12])— is an opportunity to clarify the nature of the relationship between blood pressure and SES. A better understanding through which pathways SES influences blood pressure could have significant implication for public health. It could lead to the identification of suitable targets for large-scale interventions aimed at reducing the burden of hypertension and

related problems by lowering the average blood pressure of the whole population (*whole-population* or *low-risk strategy*), rather than focusing on hypertensive or pre-hypertensive subjects, offering them suitable treatment (*high-risk strategy*).[18] In some cases, in fact, the former, preventive, *upstream*, approach has been proven more effective than the latter, and it is of particular interest in the specific case of hypertension control, also considering the low level of awareness and treatment availability in LMICs.[18, 19]

3 Rationale

Despite the evidence of a significant correlation between SES and hypertension, the causal mechanisms underlying this association are largely unknown. Growing evidence indicates that simple direct relationships between socioeconomic position as a whole and blood pressure levels, consistently found in studies in high-income countries, cannot account adequately for the inter- and intra-population heterogeneity repeatedly observed in LMICs. A consensus exists that the relationships between sub-components of the composite construct defining the individual's position in the society and blood pressure need to be analysed specifically in order to explain seemingly inconsistent research findings in contexts characterised by an earlier stage of epidemiological transition than high-income countries.

The rationale of this study is to take advantage of the availability of a large dataset on blood pressure levels, related known risk factors and multiple indicators of socioeconomic position in the South African population, to improve the understanding of the relationships between SES and hypertension prevalence in LMICs during epidemiological transition.

4 Objectives

The study aims to identify possible causal pathways through which different sub-elements defining individuals' SES — namely education, income, wealth and employment status – affect mean blood pressure levels in the South African adult population; and the extent to which the variations in the bio-behavioural factors involved in these pathways may account for the observed variability of hypertension risk among different population strata.

Specific objectives of the study are:

- to describe the basic patterns of association between SES dimensions (education, income, wealth and employment status) and blood pressure in the South African adult population, as they emerge from the NIDS survey results;
- to specify a set of causal hypotheses linking SES sub-elements and blood pressure through possible mediators, and to test their compatibility with the observed data, taking into account measurement error and uncertainties;
- to interpret and discuss the results of the analyses in light of the finding of other studies on SES and hypertension in sSA.

5 Methods

A secondary analysis of the data collected in the first wave of the NIDS study will be performed.

The main characteristics of the NIDS study (design, sampling strategies and measurements) are described in section 5.1, while the specific approach proposed for the secondary analysis which forms the object of this protocol, are reported in section 5.2.

5.1 The National Income Dynamics Study

NIDS is a nationally representative panel survey of 28 255 individuals who were resident in 7 305 households in South Africa in 2008. The study, still ongoing, is conducted by the Southern Africa Labour and Development Research Unit (SALDRU) based at the University of Cape Towns School of Economics, in a collaborative effort with various other research institutions.[17]

The data collected include a broad range of information, and despite the name of the survey, the emphasis is not on income but on a range of measures of well-being. Among other topics, information is gathered on:

- expenditures, assets owned and access to services;

- level of education and occupation;
- wages, social grants and other income;
- health status, alcohol and tobacco use, physical exercise;
- height, weight, waist circumference, heart rate, systolic and diastolic blood pressure.

The NIDS datasets, in which information is recorded in such a manner that subjects cannot be identified, are publicly available for research purposes, and can be downloaded from the NIDS website, on acceptance of the terms of use.[20]

5.1.1 Population

The South African resident population in 2008.

5.1.2 Sampling

The target population for NIDS is private households and residents in workers' hostels, convents and monasteries. The frame excluded other collective living quarters such as student hostels, old age homes, hospitals, prisons and military barracks.

A stratified, two-stage cluster sample design was employed in sampling the dwelling units to be included in the study. In the first stage, a random sample of 400 primary sampling units (PSUs) was drawn from Statistics South Africa's 2003 Master Sample, consisting of 3 000 PSUs.[21] The sample was stratified using as stratification units the 53 district councils, and PSUs were selected within each stratum with probability proportional to size. In the second stage, households were systematically selected in each PSU with a procedure described in detail by Woolard *et al.*[17] They also report on the procedure used to deal with problems arising from the discrepancies between the master sample and the situation in the field and from the low response rate in some racial groups. All resident household members at selected dwelling units were included in the survey, and asked to participate.

5.1.3 Sample size

The final NIDS dataset includes 7 305 households with 28 255 individuals. Household response rates for the baseline survey ranged from 60% to 81% across provinces, from 36% to 76% by racial group (with the lowest level among whites), and from 59% to 83% by residential location and type (rural/urban, formal/informal). The overall response rate was 69%.[17]

5.1.4 Measurements

A household questionnaire as well as an individual adult questionnaire were utilised to gather data. A copy of both questionnaires and the accompanying metadata are freely available from *DataFirst* (*http://www.datafirst.uct.ac.za/catalogue3/index.php/catalog/175*) at the University of Cape Town.

The questionnaires were designed, piloted, modified and pre-tested in various contexts before being applied in the field, to ensure adequate reliability, acceptability and validity in capturing the variables of interest. The final version of the questionnaires, and the relevant accompanying documentation, were translated into all 11 official languages.[17]

In addition, a stadiometer, a measuring tape, an electronic scale and an automatic blood pressure monitor were used to measure height, waist circumference, weight, and blood pressure and heart rate, respectively. Details on measurement procedures are reported in the fieldworkers' manual.[22]

Both questionnaire administration and anthropometric measurements were carried out by about 150 fieldworkers, trained under the direct supervision of the NIDS scientific team. Special training was provided by a qualified nurse on the correct methods on performing anthropometric measurements.

Strict supervision by the NIDS team was provided during data collection.

5.1.5 Data capturing, handling and quality control

Data capture was done partly by the NIDS team at SALDRU, and partly by an external specialist company. Data storage, protection, cleaning, pre-elaboration and de-identification before public release were carried out by the NIDS team. The Department of Economics at the University of Cape Town calculated various sets of sampling weights to take into account the complex sampling design and the biasing effect of non-response at household and individual level.[23]

Strict procedures for quality control were put in place. These included:

- Repeated and summary items in the questionnaire, to reduce incomplete filling and help reconcile inconsistent data;
- In-field and telephonic call-backs, to verify that the fieldworkers were administering the questionnaires in a professional manner, that the correct households were being interviewed and to obtain feedback from the respondents on the questionnaire and the fieldworkers;
- A specific procedure to check reasons for non-response at household level, including repetition of visits;
- Regular comparative analyses of the questionnaires returned by each fieldworker, to identify repeated errors and possible cheating;
- Double capture and random cross-checking of data dumps received from the data capture company against hard copies of the questionnaires, to ensure a low rate of mistakes;
- Secure and redundant storage of data, and separate storage of full datasets and confidential data allowing identification of single respondent.

A detailed description of the procedure to ensure reliability of data is reported by Woolard *et al.*[17]

5.2 The present study[†]

5.2.1 Study design

Secondary analysis of cross-sectional raw data on blood pressure, heart rate, anthropometric measures, health-related variables, SES indicators and demographic characteristics as recorded in the wave 1 dataset of the NIDS survey.[24]

5.2.2 Population

The South African adult population (15 years and over) in 2008.

5.2.3 Sampling

From the original NIDS wave 1 dataset, a sub-set consisting of all records referring to adult subjects who were administered the adult questionnaire will be extracted.

5.2.4 Sample size

The NIDS adult sample consists of 16 819 individuals, of which 1 245 refused to participate, and no information about them was collected beyond basic demographic characteristics and the fact that they belonged to a specific household. The number of subject included in this study is, therefore, 15 574 (9 314 women and 6 260 men).

The main analytical technique that will be applied to answer the research question – Structural Equation Modelling (SEM), described in section 5.2.6 – has quite stringent requirements regarding minimum sample sizes ensuring the proper convergence of the model fitting algorithms and the reliability of the estimates.[25, 26] No universally agreed rules exist to this regard, and various "*rules of thumb*" scarcely supported by scientific evidence are commonly used. The most widely applied rules require: [27]

[†]Future tense is used as the protocol approval precedeed the analysis.

(a) a minimum sample size which is 10 times the number of variables involved in the model. This rule is largely satisfied in this study. Given the objective of including 25 variables in the analysis among those listed in table 1, of conducting separate calculations for males and females, and supposing to have 20% of missing data, the required minimum number of observations $n = 25 \cdot 10 = 250$ is largely below the available sample ($6\,260 \cdot 0.80 = 5\,008$ men and $9\,314 \cdot 0.80 = 7\,452$ women);

(b) a minimum sample size which is 5 times the number of parameters to be estimated (correlation coefficients, error variances and covariances between variables). In this case the limit is also largely respected by the sample. In the worst case scenario in which the estimation involves all variances and covariances between the 25 variables, the number of parameters would be $(25 \cdot 26)/2 = 325$, which gives a minimum sample size of $325 \cdot 5 = 1\,625$, again largely below the available sample size for both men and women.

A more precise and justified approach to sample size calculation has been recently proposed by Westland,[27] who provides an algorithm to calculate the minimum required sample size as a function (other than of the number of observed variables and latent constructs) of the expected effect size of the relationships (δ), the significance level (α) and the desired power (β) of the statistical analyses. The results of the application of the algorithm (in the implementation by Daniel Soper, on his Statistical Calculator Website[28]) leads to a much more stringent requirements ($n = 3\,288$, for 25 observed variables, 2 latent variables, $\delta = 0.1$, $\alpha = 0.05$ and 80% power), but still largely below the available number of observations.

5.2.5 Variables

No additional measurement will be done for the present analysis. All analysed data will come from the measurements taken in the NIDS survey. The analyses will consider a subset of the indicators provided by the full NIDS dataset, partially recoded for the specific purpose. A summary of the chosen variables is shown in table 1.

Table 1: Variables considered in the present study

Code	Name	Scale	Units	Possible Values
	Demographic			
Age	Age	Continuous	*years*	15+
Gender	Gender	Binary	-	Male, female
Race	Population group	Nominal	-	Black, Coloured, Asian, White
Prov	Province of residence	Nominal	-	WC, EC, NC, FS, KZN NW, G, MP, LI
Dis	District council of residence	Nominal	-	1-53
Geotype	Type of place of residence	Nominal	-	Urban formal, urban informal, rural formal, rural informal
Edu	Education	Continuous	*years*	0-24
	SES Indicators			
Inc	Individual monthly income	Continuous	*ZAR*	0+
Assets	Number of household assets	Discrete	-	0-25
Employ	Employment status	Nominal	-	Economically inactive, unemployed, employed
Fatheduc	Father's education	Continuous	*years*	0-24
Motheduc	Mother's education	Continuous	*years*	0-24
	Expenditure			
Foodex	Household monthly food expenditure	Continuous	*ZAR*	0+
Othex	Household monthly non-food expenditure	Continuous	*ZAR*	0+
F1 - F15	Household monthly food expenditure per food type	Continuous	*ZAR*	0+
	Health			
Htn	Previous diagnosis of hypertension	Binary	-	Yes, no
Htnmed	Current medication for hypertension	Binary	-	Yes, no
	Smoking and alcohol			
Currsmok	Current regular smoking	Binary	-	Yes, no
Eversmok	Any regular smoking	Binary	-	Yes, no
Curralc	Current alcohol use	Binary	-	Yes, no
Everalc	Any alcohol use	Binary	-	Yes, no
Alcfreq	Frequency of current alcohol use	Ordinal	-	0-6
Alcq	Average quantity of current alcohol use	Ordinal	-	0-6
	Anthropometric			
Sys1 - Sys2	Systolic BP - Readings 1 & 2	Continuous	*mmHg*	80+
Dia1 - Dia2	Diastolic BP - Readings 1& 2	Continuous	*mmHg*	30+
HR1 - HR2	Heart Rate - Readings 1 & 2	Continuous	*bpm*	15-200
Height1 - Height3	Height - Readings 1 to 3	Continuous	*cm*	45-210
Weight1 - Weigh3	Weight - Readings 1 to 3	Continuous	*kg*	40-150
Waist1 - Waist3	Waist Circumference - Readings 1 to 3	Continuous	*cm*	40-200

WC=Western Cape, EC=Eastern Cape, NC=Northern Cape, FS=Free State, KZN=Kwazulu-Natal, NW=North West, G=Gauteng, MP=Mpumalanga, L=Limpopo, *bpm*=beats per minute.

5.2.6 Data analysis

After a preliminary process of data cleaning, the characteristics of the distribution of the variables of interest will be analysed in order to assess the validity of the assumptions for

the following statistical procedures. The overall quality of the blood pressure measurements in the dataset will be estimated through the calculation of suitable indices allowing comparisons with other studies in literature. Basic descriptive statistics of the sample will be reported (see Table 2).

Table 2: Sample descriptive statistics (dummy table)

Variable	N	Median or %	Range	IQR or frequency
Age				
Men				
Education				
Tertiary				
Secondary				
Primary				
None				
Income Quintile				
I				
II				
.....				
.....				

Survey adjusted estimates of population parameters will be calculated to describe the prevalence of hypertension in the South African population.

Linear regression models will be used to describe the association between SES components and blood pressure, taking into account the effect of age, gender and other possible confounders, and the multi-stage sampling scheme of NIDS, and the relevant results reported as in Table 3.

Table 3: Association between systolic blood pressure and SES indicators (dummy table)

	Models adjusted for age and ***		**Full Models (adjusted for all significant SES predictors)**	
Factor	β	95%CI	β	95%CI
Income Quintile				
Ref: V				
I				
II				
III				
IV				
Education				
.....				
.....				

A structural equation modelling approach will be then applied to test the compatibility of the data with alternative causal pathways linking SES sub-elements to blood pressure levels, taking into account measurement reliability. The proportion of the global effect of the different SES indicators mediated through various biologic and behavioural factors will be estimated following the approach of Ditlevsen and colleagues.[29] Figure 1 and 2 show how the global models and the results of the mediation analysis will be graphically depicted.

The SEM approach, is chosen for the core analyses of the present study for two main reasons:[26, 30]

(a) Its ability to explore complex mediation pathways involving multiple determinants and multiple outcomes at the same time, explicitly modelling alternative causal hypotheses and testing them against observational data;

(b) the possibility of modelling relationships between variables which are measured with error, adjusting the analysis for the reliability of the measures and potentially providing less biased estimates of the regression coefficients.

    This characteristic is of special interest for the present analysis, because it can help one to take advantage of the presence in the dataset of multiple measurements of systolic and diastolic blood pressure – notoriously affected by a high degree of random variability from physiologic and measurement sources – to estimate their reliability and adjust the analyses accordingly.

Statistical analyses will be performed using Stata® Statistical Software Version 12 for Windows.[31]

The software offers a broad implementation of SEM, including the specific techniques of interest for this study, i.e. measurement and structural model building, calculation of a wide range of global fit and modification indices, and multiple-indicators / multiple-sample models. It also allows one to select estimation procedures robust to deviation from normality in the distribution of the variables, and can calculate results which are corrected for sampling procedures different from simple random sampling (in our case, multi-stage stratified random sampling with non-uniform weights).

Figure 1: Possible causal pathways for blood pressure: Structural equation model (dummy graph)

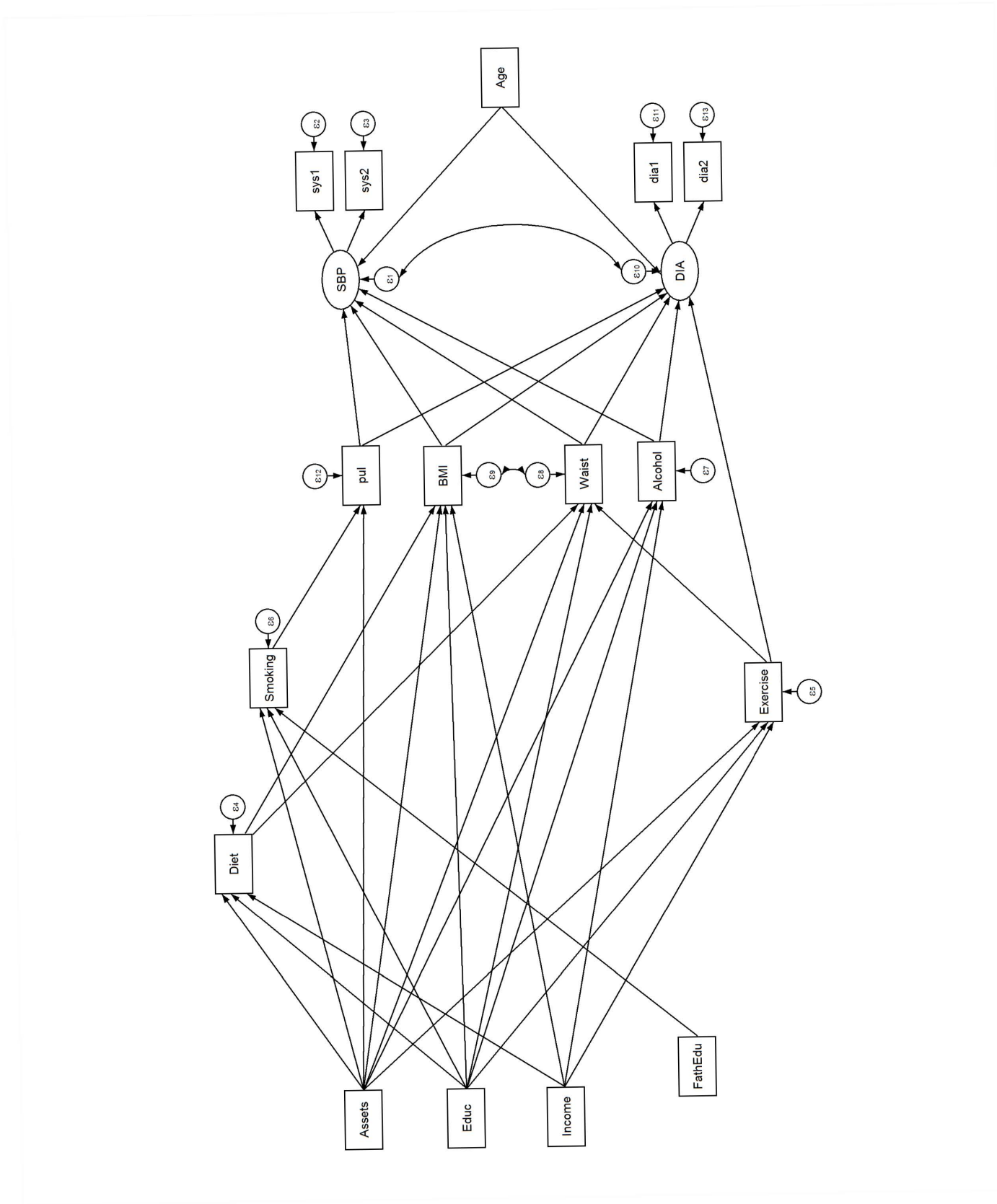
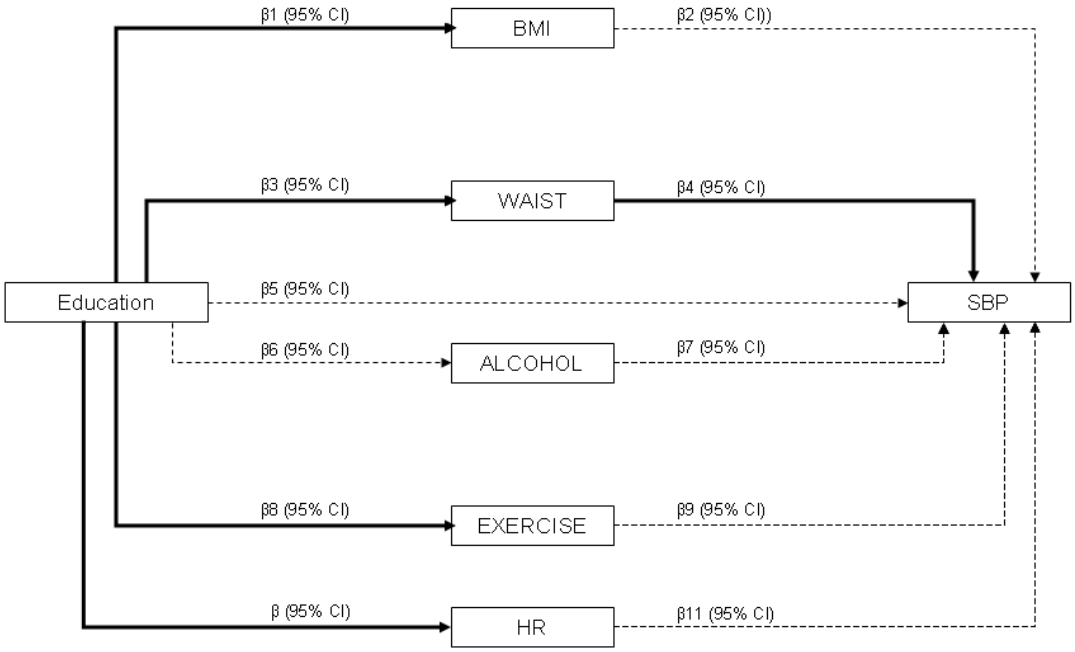


Figure 2: Bio-behavioural mediators between education and systolic blood pressure (dummy graph)



5.2.7 Ethics

The study only involves secondary analyses of previously collected data.

The Commerce Faculty Ethics Committee at the University of Cape Town assessed the informed consent forms and procedures, the questionnaires, the proposed fieldwork procedures and confidentiality plans and granted ethical approval for the NIDS study. A copy of the approval letter is appended in A.

The dataset that will be used for the analyses has been cleaned of all direct or indirect identifying information, and records cannot be linked back to the subjects from whom data were originally collected. The dataset will be obtained from the official holders, on acceptance of the terms and conditions of use, including the agreement not to attempt to identify specific individuals from the data and not to redistribute the data to other users without explicit consent by the data holder.

In fulfilment of the ethical obligation to make publicly available the results of scientific research, especially when human subjects are involved, though indirectly,[32] the finding

of this analysis will be made available in the Health Science library of the University of Cape Town, and submitted for publication in peer-reviewed scientific journals in the field of epidemiology.

A copy of the dissertation will be also sent in electronic format to the SALDRU, as required by the condition of use of NIDS datasets.

5.2.8 Timeline

The analyses required by this study will be carried out during the months of July and August 2012.

5.2.9 Budget

No direct cost, other than the author's time commitment is involved in this study, for the following reasons:

- the data object of the analyses are already collected and the dataset is publicly available, free of charge for research purposes;
- access to bibliographic references and software for statistical analysis, as well as scientific supervision and support, are provided by the University of Cape Town, as a part of the Master of Public Health of which this study constitutes the final dissertation.

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Part B: Literature Review

Contents

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1 Introduction

An inverse relationship between socioeconomic status (SES) and mortality from coronary heart disease, stroke and renal failure, and a pattern of increasing mortality with decreasing SES have been long since observed in high-income countries.[1] These associations have been shown consistently across different measures of SES, and partly explained by the inverse relationship between SES and blood pressure.[2]

More recently, a series of studies have analysed in greater detail these relationships and the extent to what a set of well-known lifestyle related factors — especially body mass index (BMI), waist circumference, heart rate, physical exercise, alcohol use and smoking — mediate this observed effects of socioeconomic variables on blood pressure. The findings of a growing number of these studies support this general hypothesis, but particularly that of BMI and waist circumference (or other measures of central obesity) as major components, albeit not solely, of the causal pathways linking SES to blood pressure levels and prevalence of hypertension.[3–6]

In contrast, epidemiological research in low- and middle-income countries (LMICs) at an earlier stage of the epidemiological transition than high-income populations, does not show the same consistent results. A review of the literature on the relationships between socioeconomic status and blood pressure published in 1998 by Colhoun *et al*, found a consistent inverse association between SES and average level of blood pressure in high-income countries, but a mixed pattern in the 13 studies from developing countries, where a direct association was often shown.[2] Subsequent studies confirm this somewhat incoherent pattern, showing a mix of direct, inverse and U-shaped gradients in the relationship between various indicators of socioeconomic status and blood pressure in LMICs, unlikely to be explained purely by methodological differences and heterogeneity of samples.[7–9]

The objective of this chapter it to review the main findings of the conflicting epidemiological literature on the socioeconomic determinants of hypertension in sub-Saharan Africa (sSA) and South Africa in particular. In addition, it will present a summary of the major biological and behavioural factors associated with average blood pressure levels in individuals and prevalence of hypertension in populations worldwide, which must be taken into account as possible confounders and/or mediators of the relationships of interest.

The review is limited to studies involving adult, or predominantly adult, subjects.

The initial search of the literature — which is not meant to be comprehensive — was conducted on the electronic database *PubMed* (*http://www.ncbi.nlm.nih.gov/pubmed*), searching for the articles published in the last decade on hypertension in adults in developing countries (the search string is reported in Appendix B). The articles deemed relevant for the objectives of this review (according to a first screening based on the title, and then on the abstracts) were read in full, and their reference list examined to find other relevant papers on the relationship between SES and hypertension in LMICs. Further papers were also included based on the advice of the supervisor of this dissertation and on previous knowledge.

A series of articles on the worldwide epidemiology of hypertension, collected in a single volume edited by Hall & Lip,[10] constituted the basis for the review of major biological and behavioural risk factors for hypertension, together with their reference list. Further electronic searches have been done for single risk factors, predominantly in *PubMed*, *Google Scholar* (*http://scholar.google.com*) and on the Internet as a whole through *Google search* (*http://www.google.com*).

2 Hypertension

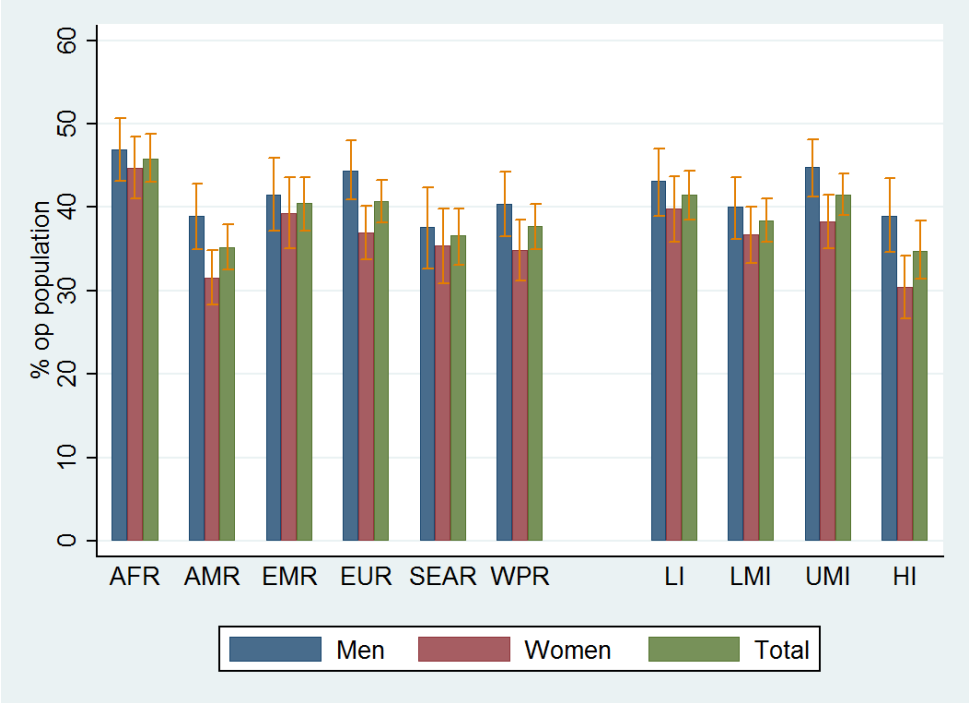
Hypertension is an important cause of mortality and morbidity worldwide. Raised blood pressure — currently defined for epidemiological purposes as systolic blood pressure (SBP)$\geq$ 140 mmHg and/or diastolic blood pressure (DBP)$\geq$ 90 mmHg, and/or taking medication to lower blood pressure — is estimated to cause 7.5 million deaths annually, about 12.8% of the total of all deaths. This accounts for 57 million disability adjusted life years (DALYs) lost or 3.7% of total DALYs lost in 2004.[11]

Hypertension is a major risk factor for coronary heart disease and stroke, and sound epidemiological evidence supports the existence of a direct relationship between systolic and diastolic blood pressure levels and the risk of these diseases. The association has been observed in men and women of all ages, race/ethnic groups, and countries, independently of other risk factors for cardiovascular disease. A strong dose-response pattern characterises this relationship, continuous across levels of blood pressure. In some age groups, the risk

of cardiovascular disease doubles for each increment of 20 mmHg of systolic or 10 mmHg in diastolic blood pressure, starting as low as 115/75 mmHg.[12, 13] Other than coronary heart diseases and stroke, consequences of raised blood pressure include cardiac failure, peripheral arterial disease, renal failure, retinopathy and visual impairment.[13]

The World Health Organization's estimates of the age-standardised prevalence of hypertension in adults aged 25 years and over indicate a global average around 40% in 2008, corresponding to a nearly 1 billion people, with large differences across countries, geographical regions and World Bank groups based on Gross National Product (GNP) per capita. The highest values by geographical region were recorded in Africa (46%), and the lowest in the Americas (35%). In all regions, the prevalence is slightly higher among men than among women, but the difference is only minimally significant in the Americas and in Europe. Average age-standardised prevalences are higher in LMICs than in high-income countries. Figure 1 summarises these geo-economic disparities. [13–15]

Figure 1: Age-standardized prevalence of raised blood pressure in adults aged 25+ years, by WHO Region and World Bank income groups. Estimates 2008 and 95% confidence intervals.



Note: AFR=African Region, AMR=Region of the Americas, EMR= Eastern Mediterranean Region, EUR= European Region, SEAR=South-East Asia Region, WPR=Western Pacific Region, LI=Low Income Countries, LMI=Lower Middle Income Countries, UMI=Upper Middle Income Countries, HI=High Income Countries.

Source: Data from World Health Organization Data Repository, http://www.who.int/gho/database, accessed 01/08/2012.

Global trend estimates show a slight decrease in age-adjusted prevalence of hypertension in the last three decades, but because of population growth and ageing, the estimated number of people with hypertension increased by 400 000 in the same period. The percentage reduction is substantially driven by the decrease in north America and Europe (with some recent data suggesting an inversion of this positive trend), while Oceania, southern Asia and sSA continue to show increases, at least among women.[14, 16]

The following section 3 will present a summary of the main bio-behavioural factors associated with blood pressure in the international literature. The subsequent section 4 will focus on sSA and South Africa in particular, and will review the main findings of the epidemiological literature on the relationships between SES, blood pressure and its potential mediators.

3 Hypertension and bio-behavioural risk factors

3.1 Age

A number of cross-sectional surveys in countries with divergent cultures and at different stages of economic development, — and, more recently, some longitudinal studies — have documented a consistent relation between age and blood pressure. Almost the totality of the studies demonstrated a general tendency of both systolic and diastolic blood pressure to rise during childhood and adulthood, with a rate consistently greater for the former than for the latter. Systolic pressure maintains this trend until the eighth or ninth decade, albeit with a lower gradient after the sixth decade. Diastolic pressure tends, by contrast, to remain constant or decline after the age of 55/60 years.[12]

Nevertheless, this pattern of association is not universal. In contrast to the experience of most countries, in various isolated populations whose dietary habits are characterised, among other aspects, by extremely low sodium intake, there is no evidence of an age-related change in blood pressure, and both systolic and diastolic blood pressure remain low until old ages.[17] This fact, adding to the results of migration studies which consistently show the tendency of migrants to assume the blood pressure pattern of the country of arrival, supports the hypothesis that age-related changes in blood pressure are not a

biological necessity, and environmental/lifestyles factors play a major role in shaping this relationship.[12, 17, 18]

3.2 Gender

Early in life there is little evidence of a difference in pressure between genders, but beginning in adolescence men tend to display a higher average level. Discrepancies are most evident in young and middle-aged adults. Later in life the difference narrows and the pattern often reverses, because of the steeper gradient in the increase in blood pressure with age in women and of the higher rate of premature death of men with high blood pressure in middle-age.[17, 19]

The incidence and the progression rate of hypertension reflect the same trend: both are markedly higher in men than in age-matched, premenopausal women. After menopause, this gender relationship no longer exists, and the incidence as well as the rate of progression of hypertension and other cardiovascular diseases are very similar in both sexes. [20, 21]

These gender-modified differences in the relationship between blood pressure and age have been shown consistently across many populations. Specific evidence for sSA is less strong but it does not contradict the global findings, as shown in a review of 25 studies carried out between 1992 and 2004 in 10 different countries of the region, where the pattern is substantially confirmed, even though most of the observed differences do not reach statistical significance.[22]

3.3 Race/ethnicity

Many studies have examined racial and ethnic differences in blood pressure and prevalence of hypertension and other cardiovascular disease risk factors, most of which have been carried out in the United States.[12] Prevalences of hypertension differ by race and these disparities are large and significant, with African Americans of both sexes showing higher levels than whites in all age classes. Difference between "non-Hispanic whites" and Mexican Americans are also significant, but the differences are not consistent across gender and ages.[12, 23]

Similar results regarding the higher predisposition of people of African ancestry to hypertension have been found in other countries, including sSA, and various explanations — involving differences in genetic predisposition, autonomic nervous system and cardiac function, and environmental factors — have been proposed.[24, 25] The relative contribution of these factors is, nevertheless, unclear, and current literature tends increasingly to emphasise environmental rather than genetic factors to explain the higher incidence of hypertension in black subjects.[25]

In South Africa, the distribution of hypertension by racially defined population groups was analysed by Steyn *et al* in the results of the first South African Demographic and Health Survey (SADHS), on a sample of 13 802 subjects, representative of the South African population in 2008. Using multiple logistic regression, the authors estimated the odds ratios (ORs) for hypertension in the different population groups. They showed that racial differences were large and significant in the crude data, with the African rural population at the lowest level of risk and whites at the highest. Nevertheless, after adjusting for age, gender and basic socioeconomic variables, the differences in the odds of hypertension among the different population groups became smaller and, except in the rural African group, not statistically significant.[26] These results suggest that the effect of race on blood pressure and hypertension is mediated predominantly by lifestyle and environmental factors, rather than determined by population level genetic differences.

3.4 Diet

Among environmental factors, diet and nutrition have been studied extensively, and some association between blood pressure and eating habits have long since established. The major findings can be summarised as follows:[27–29]

- reduced sodium intake lowers blood pressure in hypertensive and, to a lesser extent, in normotensive individuals. Evidence of this relationship has been found in observational and experimental studies, and it is consistent across different geographical and socioeconomic contexts.[30] In South Africa, a randomised study in a natural urban environment confirmed the positive effect of a low-sodium diet in lowering blood pressure in drug- treated mild-to-moderate hypertensive subjects;[31]

- increased dietary potassium intake seems also to reduce the risk of hypertension, but results are controversial;
- increased protein, fiber, monounsaturated fat and fish oil appear to be beneficial, even though the effect in normotensive patients is less established;
- A diet high in fats is strongly associated with raised blood pressure, but conflicting results have been found when the increase in body weight, usually associated with high-fat diet, has been taken into account.

3.5 Physical activity

Observational and experimental studies have shown a consistent inverse relationship between physical activity and blood pressure. The association persists after adjustment for the body weight reduction associated with increased activity, suggesting that exercise may reduce blood pressure through a mechanism independent on body weight, for example reducing resting heart rate which some epidemiological studies show to be correlated with blood pressure. [32, 33]

The protective effect of physical exercise on the development of hypertension has also been confirmed in some studies carried out in sSA.[34–36]

3.6 Body weight and obesity

The link between obesity (defined, in adults, as a BMI $\geq 30\ kg/m^2$) and hypertension — and, more generally, between BMI and blood pressure — has been documented in many large epidemiological studies, and the burden of hypertension attributable to obesity has been found high in both men and women. Some studies have also documented an effect of waist circumference, independently of BMI.[37]

Population-based studies consistently demonstrate an increased risk of hypertension among overweight and obese people. Compared with normal weight cohorts (BMI < 25), obese individuals have a 2- to 3-fold risk for developing high blood pressure. The mean systolic and diastolic blood pressure values were estimated to be 9 and 7 mm Hg higher in obese men and 11 and 6 mmHg higher in obese women than in a cohort with normal BMI.[38]

A meta-analysis of the results of 25 randomised controlled trials on weight reduction in subjects with different ethnic origins, published between 1978 and 2002 and reviewed by Neter *et al* in 2003, showed an average reduction of 4.4/3.6 mmHg for an average 5 kg weight loss by means of energy restriction, physical activity, or both. Larger reductions were achieved in populations that included subjects taking antihypertensive drugs.[39]

In sSA, various studies have confirmed this general finding of a positive association between body weight/obesity and hypertension. Among these the studies of Poulter *et al* in Kenya,[40], Mollentze *et al* in the Free State,[41] Steyn *et al* in the Cape Peninsula,[42] and, more recently, the THUSA study in the North West Province.[43]

A pooled analysis of thirteen studies on the relationship between BMI and blood pressure in populations of African descent, shows a direct, but not linear, relationship between BMI and both systolic and diastolic blood pressure. In particular, the study found that the strength of the relationship tends to decrease as BMI increases.[44]

3.7 Alcohol

Observational studies have demonstrated a positive and independent association between alcohol consumption and elevated blood pressure. Various clinical trials have also investigated the relationship, but the low power of most of them is the likely cause of their inconsistent results.[29] However, meta analyses carried out to overcome this statistical weakness, as in the study by Xin *et al*, confirm substantially the results of the observational studies.[45]

The dose-response relationship between alcohol consumption and hypertension has also been analysed repeatedly. In their recent meta-analysis, Taylor *et al* found evidence for a linear dose-response relationship in men, with a relative risk of 1.57 at 50 g pure alcohol per day (equivalent to 3.5 glasses of wine) and 2.47 at 100 g per day, compared to non drinkers. Among women, they found a modest protective effect for consumptions below 5 g per day, and a linear dose-response relationship thereafter, with a relative risk of 1.81 at 50 g per day and of 2.81 at an average consumption of 100 g per day.[46]

Analogous results of increased risk of hypertension with increased used of alcohol have been found in various studies in sSA. In South Africa, a significant relationship between

problem drinking (measured by the CAGE questionnaire)[47] and increased odds of hypertension has been confirmed by the SADHS survey.[26] Other smaller-scale studies found similar relationships between alcohol and blood pressure.[42, 48, 49]

3.8 Smoking

Acute effects of smoking result in a transient rise of the blood pressure, usually lasting less than 30 minutes, and some studies suggest a positive interaction with coffee drinking.[50, 51].

However, the evidence of increased risk of hypertension among smokers is scarce,[52] and most observational studies show that habitual smokers have lower blood pressures than non-smokers.[53, 54] This seeming contradiction has been explained mainly by the inverse relationship of smoking with body weight, and by the vasodilator effect of cotinine, the major metabolite of nicotine.[55, 56]

In South Africa, the THUSA study reported a direct association between smoking and both systolic and diastolic blood pressure in women, but no association in men.[43]

3.9 Stress

Psychological stress has also been related to raised blood pressure, and the positive results in clinical trials on the effects of relaxation techniques in the treatment of mild hypertension seems to support the existence of a causal link.[29].

Some studies have identified, as a partial mediator of this relationship, the increased heart rate at rest associated with stress,[57], which has been also observed in the study of Poulter *et al* on Kenyan migrants.[52] The evidence of this association is, nevertheless, still inconclusive.

4 SES and blood pressure in sub-Saharan Africa

4.1 Socioeconomic status

The concept of socioeconomic status refers to a finely graded hierarchy of social positions which can be used to describe a person's overall social position. It is usually considered as a multi-dimensional concept, indicated by a number of sub-components, among which those most frequently considered are employment status, type of occupation, educational attainment, income, and wealth. Despite that fact that the subject has been extensively studied, no standard measure or consensus on how to evaluate or quantify SES exists. Moreover, it is largely agreed that some of the indicators most widely used to quantify SES in high-income countries — like household and individual income — perform poorly in the developing world and particularly in contexts of widespread poverty.[7, 58]

In this review, following the definition of Grotto *et al*, the term *socioeconomic status* is used broadly to refer to the whole set of "*socially derived economic factors that influence the positions held by individuals or groups within the stratified structure of a society*".[8, p. 335]

4.2 Observed relationships

As in the general case of LMICs, the pattern of association between SES and blood pressure emerging from studies in sSA is more diversified and complex than in high-income countries. Table 1 summarises the findings of some of the studies which have reported data on this subject, extending to more recent research the results reported in Colhoun *et al.*[2]

Comparisons across studies are difficult, because of the heterogeneity of the samples, the variety of designs and adjustment techniques, and the use of different measurements for blood pressure/hypertension and SES. However, some general observations can be made.

The first observation is that the relationship between SES indicators and blood pressure is not necessarily the same for men and women, even in the same context. Relationships are often found to be stronger in women than in men, both in high- and low-income

Table 1: Selection of studies reporting data on the relationship between socioeconomic status, blood pressure and hypertension in sub-Saharan Africa

Study Country *Sample*	SES measure	Adjustments	Association with systolic blood pressure	Association with diastolic blood pressure	Association with hypertension
Scotch, 1963.[59] South Africa *505 urban Zulu*	Income	None	NR	NR	Inverse in women
Poulter, 1984.[40] Kenya *1 737 men*	Education	Age Body weight Electrolytes	Direct	NR	Direct
Lang, 1988.[60] Senegal *1 315 men*	Education Occupation	Age BMI Race	Inverse	Inverse (education)	Inverse
Bunker, 1992.[61] Nigeria *542 civil servants*	Occupation	Age BMI Alcohol	NR	NR	Direct in men
Steyn, 2001.[26] South Africa *13 803 adults* *(SADHS 1998 dataset)*	Assets Education	Age Gender Race	NR	NR	Inverse (education)
Norman, 2001.[62] South Africa *13 803 adults* *(SADHS 1998 dataset)*	Assets Education	Age Race	NR	NR	Direct in men Inverse in women
Schneider, 2009.[63] South Africa *13 803 adults* *(SADHS 1998 dataset)*	Assets	Age	NR	NR	Direct
Bovet, 2002.[64] Tanzania *9 294 adults*	Education Occupation Assets	Age Gender	Inverse	NR	NR
Adedoyin, 2005.[65] Nigeria *1 067 sedentary adults*	Assets Education Self-rating	None	Inverse	NR	NR
De Ramirez, 2010.[36] Malawi Rwanda Tanzania *1 485 rural adults*	Assets	Age Gender Country	NR	NR	Direct (TV ownership)
Ardington, 2009.[66] South Africa *13 843 adults* *(NIDS 2008 dataset)*	Assets	Age Education Race Urban/Rural	NR	NR	Inverse in women (education)

NR=not reported

countries.[2] For example, the analysis by Norman *et al* of the results of the SADHS in South Africa found a direct relationship between assets and hypertension in men, and an inverse relationship with education in women.[62]. These facts could partly explain the discrepancies between studies which analysed the data pooling male and female samples

(i.e. considering gender as a confounder, but not as an effect modifier), and those which considered the sub-samples separately.

The second observation relates to possible dissimilar relationships between SES and different blood pressure measurements. Few studies in sSA describe the association between socieoeconomic indicators and systolic/diastolic blood pressure separately, while the great majority report only data on systolic pressure, or on the prevalence of hypertension which *collapses* the effects of SES on SBP and DBP in a single indicator.

The study of Lang *et al*[60] among Senegalese male workers found that socioeconomic variables (namely education and occupational category) were more strongly associated with SBP than with DBP, with effect sizes — calculated with multivariate linear models adjusted for common biological confounders — more than three times higher in the former case. A result confirmed by other studies in LMICs, as, for example, in a sample of general population in Trinidad and Tobago.[9]

The THUSA study in the South African Northern Province, which analysed the relationship between blood pressure and level of urbanization,[43] also found different pattern of association with SBP and DBP. The results are consistent with the the Lang's study in showing a stronger relationship of the considered socioeconomic indicator with systolic than with diastolic blood pressure among men. Among women, interestingly, the study found also different relationships, but in the opposite direction, with effect sizes 2.4 times *higher* for DBP than for SBP.

The dearth of data does not allow one to draw any strong conclusion, but the results above suggest that the relationships of socioeconomic variables with SBP and with DBP are not necessarily the same, and what affects the former might not affect the latter, and vice versa. This observation is coherent with the results of more general studies which suggest that different blood pressure measurements have different bio-behavioural and psychological determinants.[67]

Causal mechanisms underlying this apparent different effect of socioeconomic variables on SBP and DBP are unclear. However, results of studies investigating the effect of stress on the cardiovascular system suggest that higher levels of stress — which are associated with living conditions, particularly with very low SES — affects the average levels of systolic

rather than diastolic blood pressure.[68] These findings offer, as suggested by Van Rooyen *et al* in the discussion of the THUSA study,[43, p. 784], a possible explanation for the observed pattern of association between socioeconomic variables and the different blood pressure indices.

4.3 SES and race

In the examination of the relationships between SES and blood pressure in sub-Saharan Africa the complex intervening factor of race/ethnicity deserves some specific considerations.

As summarised in section 3.3, growing evidence supports the use of the racial/ethnic categorization as a proxy for environmental and cultural patterns, rather than for population level genetic characteristics, and this is especially true in sub-Saharan Africa, where a colonial heritage of racial differentiation is widespread. Therefore, almost everywhere, race is strongly correlated with SES, and this fact poses significant questions on how to consider this variable in multivariate analyses, specifically whether it should be included in statistical models as a confounder or, alternatively, among the indicators of SES, analogous to education, income, and occupation. It is beyond the scope of this review to examine the implications of the racial categorization for epidemiological studies. Some of the major issues surrounding this topic are summarised in the commentary by Jones.[69]

South Africa's history is permeated with discrimination based on race and its consequences on the health of its citizens and on the distribution of both communicable and non-communicable disease are well known.[70] South Africa's population is characterised by large differences in health, extremely evident along racial lines, and this pattern is commonly attributed to the strong association between race and socioeconomic status, which is a product of South Africa's long history of inequality and unofficial and official discrimination on the basis of race.[71] Official statistics of income distribution offer evidence of this persistent relationship, showing how this distribution is still notably skewed in favour of whites.[72]

4.4 SES and bio-behavioural risk factors for hypertension

Body weight and obesity: Various studies have found a significant association between SES and body weight, BMI, obesity and measures of central obesity, like waist or waist-to-hip ratio.[64, 73, 74] In affluent countries, these associations are typically inverse,[75] whereas in sSA these studies show most commonly a direct relationship between measures of SES and weight/obesity.

In South Africa, an analysis of the 1998 South African Demographic and Health Survey found a significant direct association between education, BMI and waist circumference in men. Being white was also found associate with increased values of these variables. Among women the relationship was U-shaped: subjects with either no education or with tertiary education showed significantly higher values of BMI and waist circumference than those with primary or secondary education.[76] Multivariate analyses of the National Income Dynamics Study (NIDS) survey, done a decade later, and adjusted for age, sex and race, showed yet a different pattern of association between the socioeconomic variables and obesity in men and women. In both genders household wealth (measured by number of assets) was directly associated with BMI and obesity (although each *additional* asset had a larger effect on the odds of being obese among women than among men), but a statistically significant, direct, relationship with education was only found in men.[66]

Smoking: Sound evidence relates smoking to socioeconomic status among populations in sub-Saharan Africa. Population-based data from 16 Demographic Health Surveys in 14 countries have been recently reviewed by Pampel.[77] Among men aged 15–54 years, higher prevalence of cigarette smoking was significantly related to lower education and lower occupational status. Results for women (age 15-49 years) showed much lower smokers prevalence than men but similar socioeconomic patterns of use. Similar inverse relationships between SES and smoking has been found by Bovet *et al* in Tanzania.[64]

Overall, these findings are consistent with the research findings in high-income countries.[78]

South Africa does not differentiate itself from this general trend. Data from the SADHS in 1998 show that people in the lowest wealth quintile have the greatest overall prevalence of

smoking, albeit light smoking.[63] The study of Mfenyana *et al* in the Northern Province show, similarly, an inverse relationship between education and smoking, after adjustment for age and gender.[74] The same results were found in the 2003 wave of the SADHS, but caution should be used in the interpretation, because analyses in the official report are not adjusted for age, which can be a significant confounder in the relationship, being strongly associated both with education and smoking.[79]

Alcohol: In the general epidemiological literature — relating almost exclusively to high-income countries — the association between alcohol use and misuse and socioeconomic status is complex, and different patterns are shown in different studies, depending on gender, race, context, SES indicators and outcome metrics (alcohol use, misuse, or dependence).[78]

Little research in sub-Saharan Africa has explicitly focused on the relationship between alcohol consumption and socioeconomic markers in adults, beyond the ubiquitous finding of different level of consumption and pattern of use across racial/ethnic groups and across genders (with women showing lower consumptions than men). Results are far from established, buts some studies indicate that low socioeconomic status is associated with problem drinking, while consumption *per se* shows a varying pattern depending on the sub-population. Two large-scale population surveys support the hypothesis of an inverse association between problem drinking and SES. The first SADHS shows that lower economic status is associated with higher problem drinking among adult South Africans,[63, 80] and, similarly, the analyses of a representative sample of 3 265 Mozambicans aged 25–64 years indicated an inverse association between SES and binge drinking, albeit only statistically significant in women.[81] Both studies found no consistent association between amount of alcohol use in itself and socioeconomic variables (excluding race/ethnicity, when considered as a proxy for SES).

Physical activity: A systematic review of studies published in high-income countries showed consistent evidence of a higher prevalence of leisure-time physical activity in those at the top of the socioeconomic strata compared with those at the bottom, but failed to provide evidence of a consistent gradient across intermediate SES levels. Education produced the most stable relationships with physical activity, less susceptible to the con-

founding effects of ethnicity and environment.[82]

In LMICs, published research on the socioeconomic determinants of physical activity is quite sparse, more frequently based on total physical activity (i.e. including occupation, commuting and recreational activities) rather than leisure-time or sports activity alone. It is often acknowledged that an active lifestyle tends to be a necessity for those with very low SES, while adoption of more sedentary, westernised, lifestyles is a privilege affordable only among those with medium-high socioeconomic position.[82] Therefore, measures of physical activity based only on leisure time are less representative of the global level of physical activity and tend to be positively associated with health only in the upper socioeconomic strata of the population.

A recently published review identified 68 studies on correlates and determinants of physical activity in LMICs. In most of the studies, a direct relationship between SES and physical activity was found.[83] However, among the studies analyses, only one was carried out in Africa (the already cited study of Forrest *et al* on 799 Nigerian civil servants), and its results indicated a lower level of physical activity among senior staff (a marker of higher socioeconomic status) compared to junior staff, in most age classes.[34]

Heart rate: Finally, even less literature has focused on the relationships between socioeconomic variables and resting heart rate, which is another biological factor likely associated with blood pressure level. A significant exception is the previously cited THUSA migrant study,[43] which investigated the relationship of heart rate and level of urbanization. The study found that subjects living in informal shacks in peri-urban areas had the highest age-adjusted resting pulse rates, while the lowest levels belonged to farm-workers and to the urban upper class, even though the results were only statistically significant in women. The authors linked these observations to the findings that among urban informal dwellers (recently moved to the city from rural areas) the prevalence of systolic, but not diastolic, hypertension was particularly elevated. They suggested a "stress-mediated" explanation: because of the large load of unfamiliar stimuli that they need to process "*their cardiovascular system is in a hyperkinetic state where the cardiac output and heart rates are high with high systolic pressure and normal vascular resistance*".[43, p. 784]

5 Conclusions

A relatively large number of studies have provided data about the prevalence of hypertension in sSA and have shown its extreme variability across a broad class of indicators of SES. The studies reviewed above — and other — suggest a causal role of education, employment status, type of occupation, income, wealth and race as a proxy of SES in the determination of blood pressure levels and risk of hypertension. However, and in contrast to what happens in high-income countries — where an inverse relationship between SES and blood pressure is well-established, no matter how SES is measured — in LMICs and in sSA in particular, the patterns of association vary across countries, populations, races and gender, and the reasons of this heterogeneity are still largely unclear.

Many biological and behavioural factors are known to affect blood pressure. Among others, a large body of literature has identified significant — and, plausibly, causal — relationships between systolic and/or diastolic blood pressure and age, gender, eating habits, alcohol intake, smoking, physical activity, resting heart rate and, most of all, BMI and various measures of central obesity. Most of these factors have also shown some kind of association with socioeconomic factors, which makes them suitable candidates to the role of biological mediators of the observed associations between SES and blood pressure.

Epidemiological research aimed at the identification of these causal pathways has relevance from a public health perspective. Specifically it is a precondition to design and implement effective population-based preventive interventions, which are badly needed in sSA to blunt the growing epidemic of hypertension and reduce the need of high-cost health services for vascular disease which absorb an increasing amount of resources from already over-burdened health systems. However, this kind of research is extremely scant in LMICs, and, even though some studies have provided data about the association between some bio-behavioural risk factors and blood pressure from one side, and bio-behavioural risk factors and SES from the other side, in sSA no large-scale study has addressed explicitly and comprehensively the issue of the mediators of the association between SES and blood pressure/hypertension.

The field is, therefore, largely unexplored, and this analysis is aimed at reducing this knowledge gap.

6 References

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Part C: Article[†]

Contents

Figures

[†]The article meets the requirements set out in the Instructions for Authors of *Hypertension*, peer-reviewed journal of the American Heart Association. An extract of these instructions is appended in E. For readability purposes, figures and tables are inserted in the text rather than appended as required by the Journal, and spacing and justification match the other parts of the dissertation. Moreover, references are made to supplementary material in the appendices instead to the online supplement allowed by the Publisher.

Tables

1 Article abstract

Epidemiological research has long observed that the prevalence of hypertension varies across populations' socioeconomic strata. However, patterns of association and underlying causal mechanisms are poorly understood in sub-Saharan Africa, where little specific research has been done.

To reduce this knowledge gap, we investigated the extent to which socioeconomic status is linked to blood pressure in the first wave of the National Income Dynamics Study — a South African longitudinal study of more than 15 000 adults — and whether bio-behavioural risk factors mediate the association. A latent variables approach was used to reduce bias due to measurement error in physiological variables, which is a major strength of this study.

Multivariate analyses adjusted for age and antihypertensive treatment showed that education and income were independently associated with blood pressure levels. However, in contrast with the majority of the studies, the relationships were different across genders, with higher education and income associated with higher blood pressure in men and with lower blood pressure in women.

Analysis through structural equation modelling suggested that body mass index is an important mediator of a *harmful* effect of increasing socioeconomic status on blood pressure, explaining a sizable proportion of the overall association in men, and contributing to reduction of the overall protective effect found in women. The mediating role of the other bio-behavioural factors was, overall, modest.

Results reinforce previous evidence that the pattern of association between socioeconomic status and blood pressure in countries undergoing epidemiological transition do not replicate those found in Europe and the US.

Key Words: Systolic Blood Pressure, Diastolic Blood Pressure, Hypertension, Body Mass Index, Socioeconomic Status, Sub-Saharan Africa

2 Introduction

Hypertension is among the most common risk factors for coronary hearth disease and stroke worldwide, and consequences of raised blood pressure include cardiac failure, peripheral arterial disease, renal failure, retinopathy and visual impairment.[1] The World Health Organization estimated that nearly 1 billion people aged 25 years and over were hypertensive in 2008, with the highest age-adjusted prevalences recorded in Africa (46% vs. a world average of 40%), and a well documented increasing burden on the population and health systems especially in sub-Saharan Africa (sSA).[1–3]

Socioeconomic disparities in the prevalence of hypertension have long since observed in high-income countries. Sound epidemiological evidence associates higher socioeconomic status (SES) with lower prevalence of high blood pressure and cardiovascular disease, and the relationship is consistent across a variety of indicators of social position.[4, 5] By contrast, the pattern of association appears more diversified in sSA, and a mix of positive as well as negative gradients have been found in different studies, and in some studies also between women and men.[6–9]

Methodological differences, heterogeneity of samples and different degrees of economic development have been advocated as possible explanations of the conflicting results of studies in low- and middle-income countries (LMICs), as well as inconsistencies in SES measurements.[10, 11] However, the overall picture is far from complete and a better understanding of the reasons of this heterogeneity is needed in order to implement population-based preventive interventions. This requires, as pointed out by Colhoun *et al*,[5] going beyond simply describing the overall association between SES and hypertension, to identifying potentially modifiable mediating factors and causal pathways though which education, income or other socioeconomic factors affect blood pressure.

Two recent studies have addressed this subject, and analysed the extent to which a set of well-known lifestyle related factors mediate the observed effects of socioeconomic variables on blood pressure.[12, 13] Their findings suggests that variations in body shape, heart rate, and alcohol use account for a sizable proportion of the socioeconomic variation noted in average blood pressure levels and prevalence of hypertension. However, both studies were carried out in high-income countries, while equivalent studies in sSA are lacking.

Recently, the South African National Income Dynamics Study (NIDS) made available good quality anthropometric, sociodemographic and behavioural data from a large sample of the South African population — a middle-income country undergoing rapid epidemiological transition — offering an opportunity to reduce this knowledge gap and to improve the understanding of the relationships between SES and hypertension in sSA.

The aim of the present study was (1) to assess the independent association between different SES indicators and blood pressure in this national dataset, and (2) to examine the extent to which differences in body mass, resting heart rate, smoking and alcohol use explain these relationships in the adult population of South Africa.

3 Methods

3.1 Participants

The current study uses data from the first wave of the NIDS, a nationally representative panel survey of 28 255 individuals who were resident in 7 305 households in South Africa in 2008.[14]

The survey collected a broad range of information on participants, including education, income, household assets, health status, alcohol and tobacco use and physical exercise. Anthropometric measurements — namely height, weight, waist circumference, systolic blood pressure (SBP), diastolic blood pressure (DBP) and resting heart rate — were also taken.

The NIDS study was reviewed and approved by the Commerce Faculty Ethics Committee at the University of Cape Town.

This study considers only the adult sub-sample of the NIDS dataset, consisting of 15 574 subjects 15 years and over.

3.2 Measures

Sociodemographic variables: Various sociodemographic characteristics of participants were considered: age, gender, race, individual and parental education, employment status, income, household assets.

Age was considered as a continuous variable. Race was self-defined by participants according to the historical "population group" categorization used in South Africa (Black/African, Asian/Indian, Coloured, White).

Individual education was measured in years of completed schooling. Parental education recorded the highest education level reached by either parent.

Employment status was coded in three categories for descriptive purposes, but its values were collapsed in a binary variable *employed/not employed* in the multivariate analyses.

The total number of durable goods owned by the household, chosen from a closed list of 32 items, was also approximated with a continuous variable. Total individual monthly income was calculated as the summation of a series of individual questions on different sources, which is considered a more reliable method than the use of single questions.[15]

SBP, DBP and resting heart rate: Supine brachial blood pressure and heart rate were measured twice by trained field workers in the left arm after a 5 minute rest period, using an automated blood pressure monitor (Omron M7 upper arm BP monitor, multi-size cuff fitting 22-42 *cm* arm sizes, factory calibrated). Measurements were retained in the datasets if SBP was between 80 and 240 $mmHg$, DBP was $\geq$ 30 $mmHg$, and their difference was $\geq$ 15$mmHg$. Heart rate was also recorded, and values $\geq$ 30 *bpm* and $<$ 150 *bpm* were retained. The average of the values for each subject was used for all analyses, except for the structural equation models in which the individual readings were introduced (see below).

Data quality of measurement of blood pressure in field studies is an acknowledged limitation, and various procedures have been used to estimate validity and reliability of survey data after collection.[16] Digit preference score and proportion of identical duplicate readings are among the most used quality indicators.[17] The values of all these indices in the

NIDS survey are comparable with those of other high quality surveys, and do not offer evidence of gross inaccuracy. Details of this quality assessment and the actual values of these indicators are reported in Appendix C.

Antihypertensive medication use Current antihypertensive medication use was assessed with a direct question addressed to subjects who declared themselves as having been diagnosed with high blood pressure by a health care professional.

Bio-behavioural risk factors of hypertension Body mass index (BMI), waist circumference, smoking, alcohol use and physical exercise were considered, together with heart rate, as possible mediators of the association between socioeconomic variables and blood pressure.

Duplicate measures of weight, height and waist circumference were recorded in the NIDS dataset, with a third measure taken if the difference between the first two was greater than a pre-specified cut-off. Excluding measures with implausible values, the average of the available readings was used for the analyses. BMI, in kg/m^2, was calculated from these averaged values.

Subjects were asked during the interview about their past and current regular smoking status. A continuous variable *smoking* was created, containing the average daily number of cigarettes for current smokers, and 0 otherwise.

Subjects were classified in categories ordered according to the average number of drinks per drinking occasion, with non drinkers in the first class and those with 13 or more standard drink per occasion in the seventh. Physical exercise was measured by asking the respondents about the average number of days a week in which they exercised. The resulting variable was coded 0 (never) to 6 (more than 3 times a week). Both variables, though ordinal in nature, where included as continuous in the multivariate models.

3.3 Statistical analysis

Sample characteristics were described as median and interquartile range (IQR) for continuous variables and frequency for categorical measures. Statistical models were adjusted

for the multi-stage, stratified sampling scheme of the NIDS survey, using untrimmed post-stratification sampling weights (version 4.1, may 2012 release) as provided by the Southern Africa Labour and Development Research Unit (SALDRU).[18] The Taylor linearization method was used for variances estimation. In view of previous evidence that relationships differ by gender, separate analyses were conducted for women and men.

Statistical analyses were carried out using Stata® Statistical Software Version 12 for Windows.[19]

Objective 1: association between socioeconomic variables and blood pressure: A series of linear regression analyses were conducted to estimate the association of SES indicators with systolic and diastolic blood pressure, adjusting for age and use of anti-hypertensive medication. The variable income was log-transformed to improve statistical properties and for substantive reasons, considering its extremely skewed distribution (90% of the sample earned less than 3 300 $ZAR/month$, while the remaining 10% ranged from ZAR 3 300 to 1.5 million) and because of the reasonable assumption that the impact on the subject's lives of a given income increment decreases as income increases.[20]

Given the known non-linear relationship between age and blood pressure, which is confirmed in our sample, the former was introduced into the models as a linear spline with a single knot corresponding to 55 years.

For the analysis, predictors were first introduced one at a time in the regression models. Those which showed significant association ($p \leq 0.05$) with systolic and/or diastolic blood pressure were subsequently included in *full* models to determine their independent effects.

Objective 2: mediation analyses: A structural equation (SEM) model was fitted to assess the extent to which the bio-behavioural factors above explained the observed relationship between socioeconomic variables and blood pressure levels.

Possible causal paths were introduced based on *a priori* considerations of their theoretical and epidemiological relevance, and the overall compatibility of the proposed models with the observed data was estimated by the use of multiple indices of fit.[21]

To minimise the bias in the estimation of the paths coefficients due to random measurement error, DBP and heart rate were introduced in the model as latent variables, with the observed multiple readings as indicators.

Latent variables are variables that are not directly observed but rather inferred, through mathematical relationships, from other variables directly measured (indicators). They are used in SEM models either to represent abstract concepts (like behavioural or mental states) or — as in our case — aspects of physical reality which could in principle be measured but may not be for practical reasons, including measurement error. The use of latent variables allows for estimation and removal of the random measurement error associated with the directly observed variables.[22] In the case of multiple blood pressure measurements, it has been shown that this procedure, under relatively broad assumptions, produces better results than the approximation of the subjects' physiological parameters with the average of the multiple readings.[23]

Estimated model coefficients were then used to analyse direct and indirect causal pathways connecting SES indicators and blood pressure levels. Following the approach of Ditlevsen *et al*,[24] the share of the association between socioeconomic variables and blood pressure statistically explained by the most relevant mediating risk factors (mediation proportion) was then calculated as the ratio between the product of regression coefficients in the path involving the mediating variable and the sum of the coefficients expressing the total effect (see Appendix D).

4 Results

Unweighted sample characteristics are described in Table 1. The great majority of participants were black (78.5%) and Coloured (11.2%). Whites were largely under-represented in the sample, compared to the racial distribution of South African population, owing to their low response rate in the NIDS survey (36% response rate at household level, vs. an average 69% in the whole sample).[14] Generalizability of results to this population group is, therefore, unwarranted and no specific comments on white participants will be reported hereinafter. Based on the cut-off points from the Seventh Joint National Committee report (JNC-7), 28.4% of male participants would be classified as hypertensive, and

48.1% as pre-hypertensive (30.6% and 40.2% for women, respectively). Isolated systolic hypertension was recorded in 18.2% of cases, and isolated diastolic hypertension in 25.9%. Current use of antihypertensive medication was reported by 7.4% of men and 16.0% of women.

Taking into account the sampling scheme, the estimated average SBP in the South African adult population was 122.8 $mmHg$ in women (95%CI: 122.0 to 123.7) and 125.7 $mmHg$ in men (95%CI: 124.8 to 126.6). Average DBP was 80.62 $mmHg$ in women (95%CI: 80.0 to 81.3) and 78.89 $mmHg$ in men (95%CI: 78.2 to 79.6). Including all subjects on medication, regardless of their actual measurements, the prevalence of hypertension was 33.4% among women (95%CI: 31.5 to 35.4), and 28.0% among men (95%CI: 26.0 to 30.0). These values were remarkably higher (by 5.1% in men and 8.8% in women) than the values recorded during the first South African Demographic and Health Survey (SADHS), 10 years before the NIDS[8].

The relationships between age and blood pressure are depicted in Figure 1, and are consistent with the findings of the great majority of studies in literature. Both systolic and diastolic blood pressure rise during childhood and adulthood. Afterwards, systolic pressure maintains the trend until the eighth or ninth decade, while diastolic pressure tends to decline slightly after the age of 55/60 years.[25]

Socioeconomic predictors of blood pressure: After adjusting for age and use of antihypertensive medication, being Coloured was consistently associated with higher SBP and DBP in both men and women. Asian women had, in contrast, lower SBP than the reference category (Blacks).

Among women, education, income and number of household assets were negatively associated with SBP. The same relationship held for DBP, but it was statistically significant only for education (Tables 2 and 3).

Table 4 shows that, among men, *no* relationship was found between SES and SBP, while higher levels of DBP were associated with *higher* education, higher income, and being employed (Table 5).

Table 6 shows the *full* models, in which the variables with a statistically significant uni-

Table 1: Sample descriptive statistics

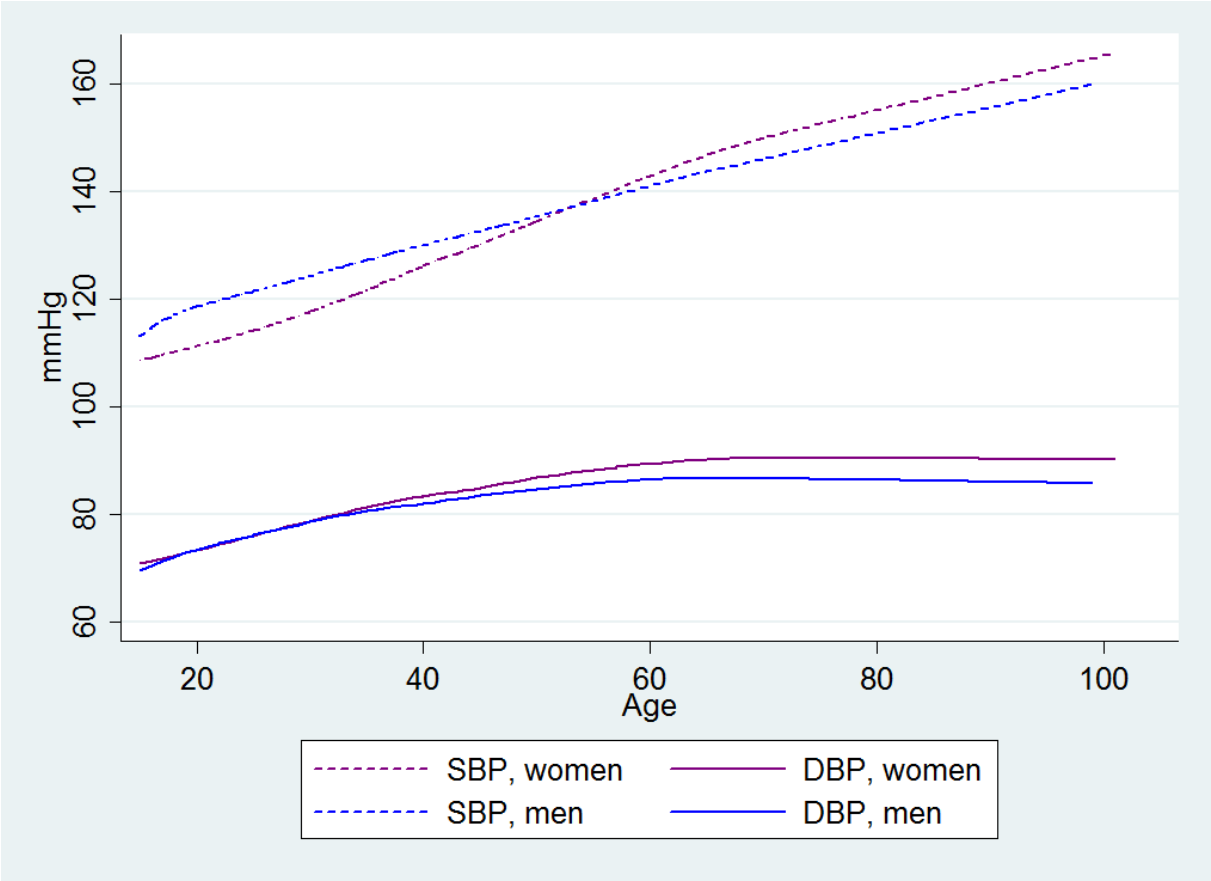
Variable	N	Median / percentage	IQR / frequency	Range
Age (*years*)	15 549	35	[22 ; 50]	[15 ; 105]
Men	15 574	40.2%	6 260	
Race	15 574			
Black		78.5%	12 221	
Coloured		14.2%	1 215	
Asian		1.4%	224	
White		5.9%	914	
Individual Income (ZAR)	15 276	600	[0 ; 1 200]	[0 ; 1 517 000]
Household assets (No)	15 568	6	[3 ; 9]	[0 ; 22]
Employment Status	15 424			
Not Economically Active		42.8%	6 606	
Unemployed		18.2%	2 812	
Employed		39.0%	6 006	
Education	15 545			
None		14.0%	2 178	
Primary		16.7%	2 603	
Secondary		60.17%	9 353	
Tertiary		9.1%	1 411	
Highest Parental Education	10 993			
None		48.5%	5 332	
Primary		15.8%	1 736	
Secondary		35.7%	3 920	
Tertiary		0.05%	5	
Average quantity of alcohol per drinking occasion	15 505			
Non drinker		75.8%	11 747	
1/2 standard drinks		7.2%	1 121	
3/4 standard drinks		6.7%	1 041	
5/6 standard drinks		4.8%	747	
7/8 standard drinks		2.3%	363	
9/12 standard drinks		1.7%	264	
13+		1.4%	222	
Ever smoked	15 505	25.6%	3 971	
Current smokers	15 513	21.2%	3 283	
Cigarettes/day (current smokers)	2 983	5	[4 ; 10]	[1 ; 60]
Physical exercise	15 471			
Never		70.1%	10 845	
$<$ once a week		5.8%	900	
Once a week		5.6%	863	
Twice a week		6.1%	944	
$\geq$ three times a week		12.4%	1 919	
SBP ($mmHg$)	13 852	121.5	[110 ; 137]	[80 ; 240]
DBP ($mmHg$)	13 836	79.5	[71 ; 89.5]	[31.5 ; 137]
HR (bpm)	14 025	75.5	[67 ; 84]	[32.5 ; 147]
BMI (kg/m^2)	13 858	24.4	[20.9 ; 29.7]	[7.1 ; 97.3]
Waist Circumference (cm)	13 858	83.3	[74.4 ; 95.5]	[45.1 ; 200]

Note: N=number of nonmissing cases, IQR=Interquartile Range. Values are unweighted.

variate association with SBP or DBP were introduced simultaneously.

Among women, each year of education was associated with 0.30 $mmHg$ drop in SBP and 0.10 $mmHg$ drop in DBP. A doubling of the monthly income was related to a decrease of

Figure 1: Systolic and diastolic blood pressure vs. age in the sample (smoothed curves)



SBP by 0.16 $mmHg$ ($0.23 \cdot \log 2 = 0.16$), but not statistically significant effect on DBP.

In men, education was still directly associated with DBP (an increase of 0.11 $mmHg$ per year of schooling), while the relationship with income was not statistically significant.

Coloured participants had higher values of blood pressure than Blacks, and this result was statistically significant for SBP and DBP in both sexes (+2.45 and 2.61 $mmHg$ in women and +5.07 and 2.67 in men). Differences in the average blood pressure between Asians and Blacks were small in magnitude and with wide CIs including the null value.

In this multivariate analysis, neither employment status nor household assets were associated with blood pressure.

Overall, it is worth noticing the consistent opposite relationship between SES and blood pressure in women and men. In fact, all considered SES indicators showed positive coefficients in their linear relationship with average blood pressure levels among men, whereas

Table 2: Systolic blood pressure vs. socioeconomic variables in **women**: linear regression coefficients and 95% confidence intervals

	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age $<$ 55 (*years*)	0.69‡ (0.63;0.75)	0.68‡ (0.63;0.74)	0.64‡ (0.58;0.70)	0.71‡ (0.64;0.78)	0.68‡ (0.62;0.75)
Age $\geq$ 55	0.58‡ (0.39;0.76)	0.55‡ (0.36;0.74)	0.49‡ (0.29;0.69)	0.55‡ (0.36;0.75)	0.55‡ (0.36;0.75)
Antihypertensive Medication	10.09‡ (7.46;12.72)	10.26‡ (7.63;12.89)	9.85‡ (7.26;12.44)	10.54‡ (8.04;13.05)	10.11‡ (7.44;12.79)
Race (ref: Black)					
Coloured	2.44* (0.04;4.84)				
Asian	-2.10 (-7.49;3.28)				
White	-4.31† (-7.28;-1.34)				
Household Assets (*number*)		-0.20* (-0.37;-0.03)			
Education (*years*)			-0.36‡ (-0.49;-0.23)		
(Log) Income				-0.34† (-0.54;-0.13)	
Employed					-0.94 (-2.51;0.64)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

the opposite was true among women. The only exception was employment status, which association with DBP in the univariate model showed a positive coefficient also in women as well as men, although not statistically significant in women.

Mediators: Two structural equation models were fitted (for men and women) including education, income and race as socioeconomic predictors; SBP and DBP as outcome variables; age and use of hypertensive medication as confounders; and BMI, smoking, alcohol use, physical exercise and resting heart rate as possible mediators. Even though the simultaneous introduction of BMI and waist circumference, significantly correlated ($\rho = 0.70$ and $\rho = 0.61$ in women and men), did not produce the estimation problems that were the case in other studies,[12] their role in mediating the association tended to be similar. Therefore, following the approach of Brummett *et al*,[13] the variables were introduced one at a time, and only the models including BMI are discussed below.

Mediation paths between predictors and outcomes were drawn through each possible mediator. Based on epidemiological and biological evidence, extra paths were included

Table 3: Diastolic blood pressure vs. socioeconomic variables in **women**: linear regression coefficients and 95% confidence intervals

	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age < 55 (*years*)	0.43‡ (0.39;0.46)	0.42‡ (0.39;0.46)	0.41‡ (0.37;0.45)	0.42‡ (0.38;0.47)	0.41‡ (0.37;0.45)
Age ≥ 55	0.07 (-0.17;0.02)	-0.08 (-0.18;0.01)	-0.11* (-0.20;-0.01)	-0.08 (-0.18;0.02)	-0.06 (-0.16;0.04)
Antihypertensive Medication	5.86‡ (4.21;7.51)	5.97‡ (4.34;7.61)	5.84‡ (4.20;7.48)	6.01‡ (4.35;7.67)	6.07‡ (4.45;7.68)
Race (ref: Black)					
Coloured	2.52† (0.66;4.38)				
Asian	-0.45 (-4.69;3.79)				
White	-1.64 (-3.45;0.18)				
Household Assets (*number*)		-0.04 (-0.16;0.08)			
Education (*years*)			-0.12† (-0.21;-0.04)		
(Log)Income				-0.01 (-0.16;0.14)	
Employed					0.79 (-0.29;1.87)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

connecting alcohol use, smoking and exercise to BMI, and smoking and exercise to heart rate.[26–30]

Model results relative to pathways connecting education and/or income and blood pressure for which the *total* association (see Appendix D) was statistically significant are displayed in figures 2 to 5. Estimates were produced from a single model that included all the variables and SBP/DBP simultaneously, but are shown separately for clarity. Thicker lines represent statistically significant associations ($p < 0.05$).

A note of caution is warranted regarding precision of estimates. The choice to use untrimmed sampling weights for statistical adjustment (see Appendix D) — as well as the assumption of normal distribution of variables in the Structural Equation Modelling (SEM) models — surely reduced the statistical power of our analyses, and may partly explain the lack of precision in our estimates compared to other studies with similar sample sizes. Therefore, the width of the confidence intervals reported below is very likely overestimated.

Table 4: Systolic blood pressure vs. socioeconomic variables in **men**: linear regression coefficients and 95% confidence intervals

	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age $<$ 55 (*years*)	0.52‡ (0.46;0.58)	0.52‡ (0.46;0.59)	0.53‡ (0.47;0.59)	0.51‡ (0.43;0.58)	0.51‡ (0.44;0.58)
Age $\geq$ 55	0.37‡ (0.16;0.58)	0.36‡ (0.15;0.56)	0.37‡ (0.16;0.58)	0.36‡ (0.17;0.56)	0.42‡ (0.21;0.63)
Antihypertensive Medication	5.51* (0.37;10.66)	5.66* (0.43;10.89)	5.73* (0.46;11.00)	5.71* (0.40;11.02)	5.75* (0.46;11.03)
Race (ref: Black)					
Coloured	5.07† (1.78;8.35)				
Asian	0.05 (-6.09;6.19)				
White	0.48 (-3.56;2.59)				
Household Assets (*assets*)		0.09 (-0.09;0.28)			
Education (*years*)			0.08 (-0.08;0.23)		
(Log) Income				0.20 (-0.00;0.40)	
Employed					1.33 (-0.34;3.01)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

Among women, education was directly associated with BMI and exercise, and inversely with smoking and resting heart rate. Heavier smoking was associated with increased heart rate. Higher income predicted higher BMI, greater alcohol intake and smoking (data not shown).

The major factor involved in the association between education and blood pressure in women was, by far, BMI, which, increasing with increased education, significantly contributed to reduce the total protective association. The proportion of the total effect explained by the mediating path through BMI (*mediation proportion*) was, respectively -10.98% (95%CI: -19.27 to -2.69) for SBP and -22.09% (-42.49 to -1.59) for DBP. The overall protective effect of education remained largely unexplained. The only mediating path which showed a statistically significant, albeit small in magnitude, contribution to explaining the total effect was, in fact, the one through exercise and BMI, with mediation proportion for 1.9% (95%CI: 0.36% to 3.49%) SBP and 3.87% (95%CI: 0.33% to 7.40%) for DBP.

Among men, higher education was associated with higher BMI and exercise frequency, and

Table 5: Diastolic blood pressure vs. socioeconomic variables in **men**: linear regression coefficients and 95% confidence intervals

	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age $<$ 55 (*years*)	0.41‡	0.41‡	0.42‡	0.38‡	0.39‡
(0.37;0.45)	(0.37;0.45)	(0.38;0.46)	(0.33;0.43)	(0.35;0.44)	
Age $\geq$ 55	-0.16*	-0.17†	-0.14*	-0.15*	-0.11
	(-0.29;-0.04)	(-0.29;-0.05)	(-0.26;-0.03)	(-0.27;-0.03)	(-0.23;0.02)
Antihypertensive Medication	2.50	2.57	2.65	2.69	2.72
	(-0.29;5.28)	(-0.24;5.37)	(-0.21;5.50)	(-0.20;5.57)	(-0.14;5.59)
Race (ref: Black)					
Coloured	3.05†				
	(1.14;4.96)				
Asian	0.13				
	(-3.11;3.36)				
White	0.38				
	(-1.75;2.51)				
Household Assets (*assets*)		0.11			
		(-0.02;0.25)			
Education (*years*)			0.13*		
			(0.03;0.24)		
(Log)Income				0.24†	
				(0.09;0.38)	
Employed					1.33*
					(0.18;2.49)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

lower smoking. Income was positively associated with BMI, alcohol intake and smoking. Higher BMI and heart rate predicted higher DBP. Smoking was inversely associated with BMI and positively with heart rate, while higher exercise frequency predicted lower heart rate.

The analysis showed statistically a significant path connecting education and income to DBP through BMI, in the same direction of the observed total association. In both cases — especially for education — the mediation proportion was large, albeit it did not reach the conventional significance level of 5%: the paths via BMI explained 34.32% (95%CI: -2.10% to 70.79%) of the increase in blood pressure associated with higher education, and 14.21% (-0.18% to 28.61%) of the increase associate with income. Education also affected DBP via the decreased heart rate associated with the lower level of smoking and higher exercise frequency which characterised the most educated subject. This effect was small in magnitude but statistically significant (coefficient: -0.01; 95%CI: -0.01 to -0.001), and tended to reduce the overall positive association. The corresponding mediation proportion was -5.43% (-12.11 to 1.25).

Table 6: Systolic and diastolic blood pressure vs. socioeconomic variables: fully adjusted linear regression coefficients and 95% confidence intervals

	Women		**Men**	
	SBP	DBP	SBP	DBP
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Age $<$ 55 (*years*)	0.68‡ (0.61;0.75)	0.41‡ (0.38;0.45)	0.52‡ (0.46;0.58)	0.39‡ (0.34;0.45)
Age $\geq$ 55	0.50‡ (0.30;0.70)	-0.10* (-0.19;-0.00)	0.37‡ (0.16;0.57)	-0.11 (-0.24;0.03)
Antihypertensive Medication	10.12‡ (7.61;12.63)	5.76‡ (4.11;7.42)	5.51* (0.37;10.66)	2.53 (-0.33;5.41)
Race (ref: Black)				
Coloured	2.45* (0.03;4.87)	2.61† (0.75;4.46)	5.07† (1.78;8.35)	2.67† (0.70;4.63)
Asian	-1.23 (-6.40;3.94)	-0.16 (-4.24;3.92)	-0.05 (-6.09;6.19)	-0.15 (-3.01;2.70)
White	-2.36 (-5.44;0.72)	-0.91 (-2.74;0.92)	-0.48 (-3.56;2.59)	-0.92 (-3.08;1.24)
Household Assets (*number*)	0.03 (-0.15;0.21)			
Education (*years*)	-0.30‡ (-0.43;-0.16)	-0.10* (-0.19;-0.02)		0.11* (0.01;0.21)
(Log) Income	-0.23* (-0.44;-0.01)			0.14 (-0.11;0.34)
Employed				0.37 (-1.49;2.23)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

Being coloured versus Black was significantly associated with higher smoking both in women (+2.26 cigarettes/day; 95%CI: 1.80 to 2.72) and in men (+2.41 cigarettes/day; 95%CI: 1.63 to 3.20). Coloured women had also higher alcohol consumption (coefficient: 0.52; 95%CI: 0.28 to 0.76) and exercised more frequently than Black women (coefficient: 0.35; 95%CI: 0.14 to 0.55). The overall mediation paths through these factors were, nevertheless, not statistically significant.

A full representation of the model used for in the analyses, details of statistical procedures, fit indices and further results are reported in Appendix D.

5 Discussion

Coherently with the findings of most studies in LMICs, in this representative sample of the South African adult population the patterns of association between SES indicators

Figure 2: Mediation analysis: systolic blood pressure vs. education in **women**

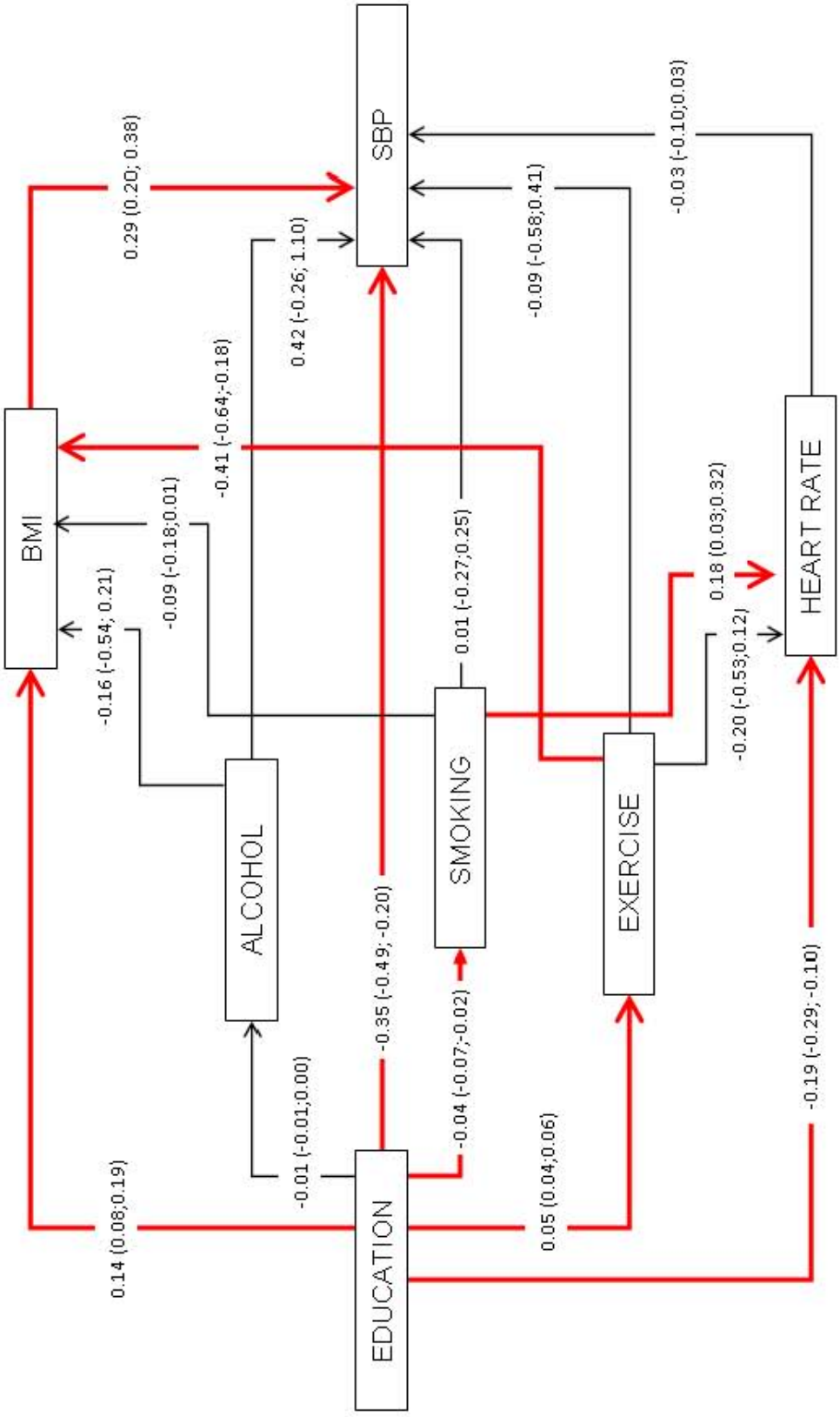


Figure 3: Mediation analysis: diastolic blood pressure vs. education in **women**

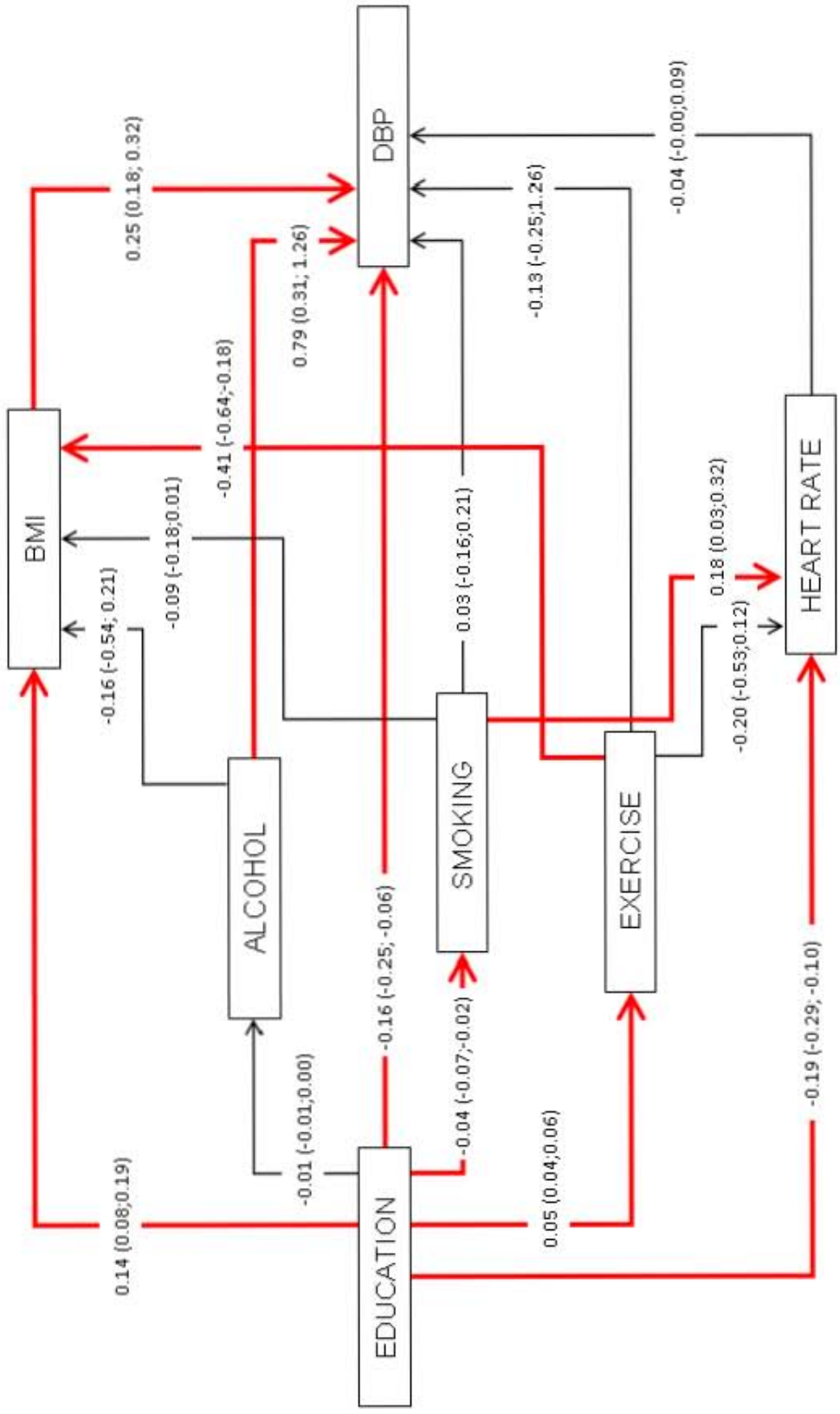


Figure 4: Mediation analysis: Diastolic blood pressure vs. education in **men**

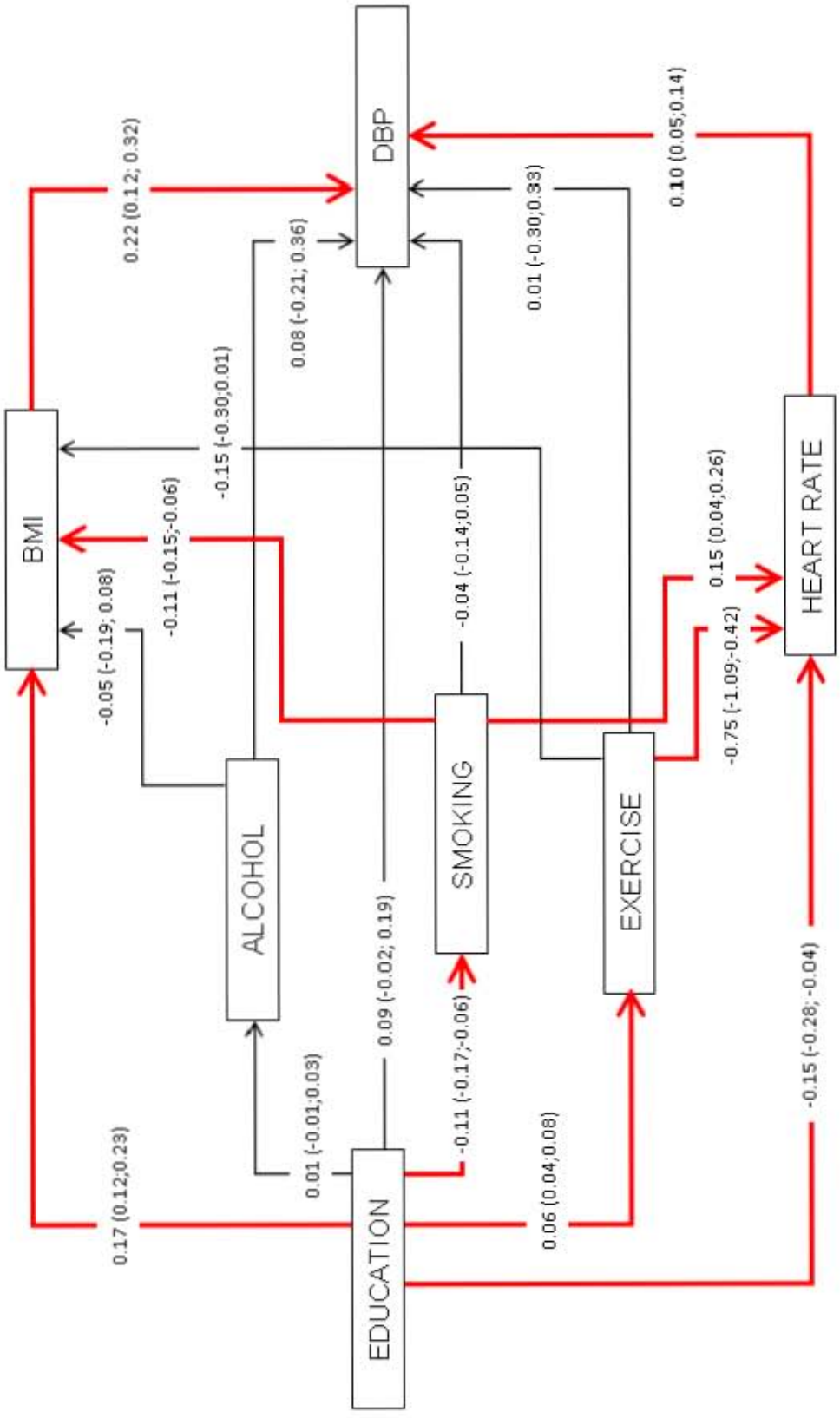
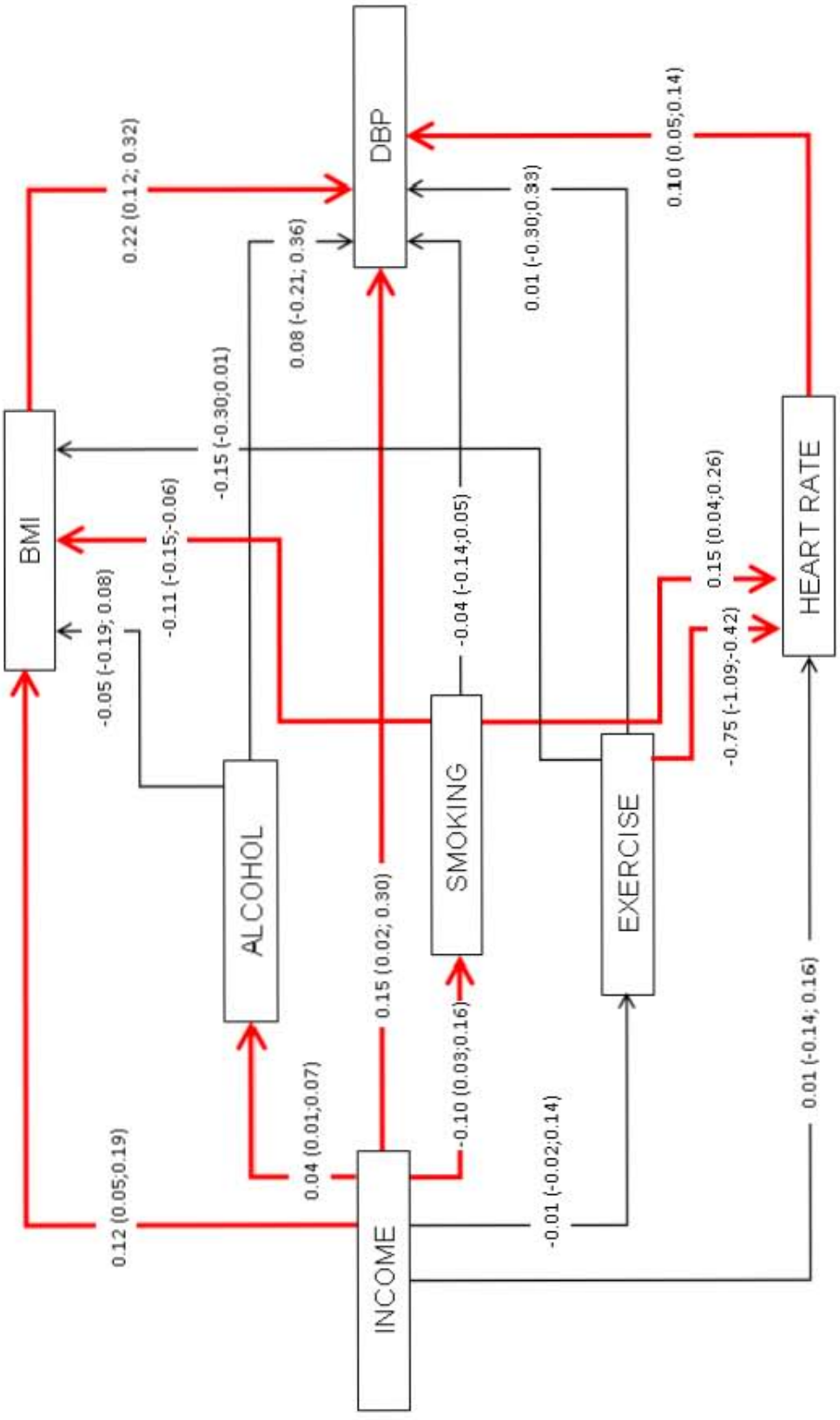


Figure 5: Mediation analysis: Diastolic blood pressure vs. income in **men**



and blood pressure were more complex than those in similar studies from high-income countries. By contrast with the consistent inverse relationships found in almost all studies in the US and in Europe, our study revealed opposite gradients between SES and blood pressure by gender. This partly confirms the analyses by Norman *et al* of the data from the first SADHS, also suggesting an opposite association between SES and blood pressure among men and women.[31] We also found that SES indicators were more strongly associated with SBP in women and with DBP in men.

The results of our mediation analysis agree with those of Chaix *et al*[12] and Brummett *et al*[13] in identifying BMI as a major factor involved in the causal pathways leading from SES to raised blood pressure, in finding a direct association between heart rate and blood pressure, and in confirming a protective effect of physical exercise and smoking on blood pressure.

However, our findings diverge in many aspects from both the French and the American studies. The most striking difference is that, in our middle-income population at an earlier stage of the epidemiological transition, BMI appears as a powerful mediator of a *harmful* effect of increasing SES on blood pressure, explaining a sizable proportion of the overall association in men, and contributing to reduction of the overall protective effect found in women. This seeming contradictory result may be partly explained by the average much lower level of income and education in our sample. It is plausible that, among people living around or below the poverty line, the increased knowledge of health risk and greater motivation to control weight associated with increasing SES — which have been argued as an explanation of the inverse relationship SES/BMI in high-income countries — played a less significant role then the weight increase associated with greater access to energy-dense processed food among those with relatively higher SES.

A separate analysis for the $n = 810$ subjects (5.3% of the total sample) with higher level of income ($> 8\,000\ ZAR/month$) offers some support for this hypothesis, showing that, in that subsample, the associations between income and BMI become inverse (coefficient: -0.71; 95%CI: -1.18 to -0.24, adjusting for age, race and gender)

A second difference is that the mediation role of all other factors appears to be much weaker in our sample than in the cited studies, though consistent with them in term of general pattern of association. Factors other than BMI contributed to mediate some of

the indirect relationships between education and/or income and SBP and/or DBP, but, overall their contribution to the total association was modest. Resting heart rate was a partial exception and, even though its contribution to the overall association between SES and blood pressure was small, it explained almost all the small but significant associations of smoking and exercise with DBP in men. Stress-mediated explanations have been used to link socioeconomic variables to heart rate, also in sSA (see, for example, the THUSA migrant study[32]). However, analysis (not shown in this article) of the correlation between heart rate and some other variables in the NIDS dataset plausibly correlated with chronic stress (e.g. sleep disturbances, perceived level of neighbourhood social cohesion and recent negative events) did not support the hypothesis.

Overall, the findings of this study suggest that the observed effect of SES on blood pressure is the result of contrasting effects mediated by different biologic and behavioural factors, and that the relative weight of these effects is different depending on gender. Given the modest proportion of the overall association explained by the considered mediators, it is plausible that other contextual determinants not analysed in this study such as food availability and the labour market contribute to these association as well. This finding may partially explain why the observed global effect appears to be so inconsistent in LMICs undergoing epidemiological and socioeconomic transition.

In our sample we found high proportions of isolated systolic and diastolic hypertension. Given the different responsiveness of SBP and DBP to variations in socioeconomic risk factors, also affected by gender, this results may also contribute to explain some incongruences between results of studies using systolic blood pressure as outcome variable, and studies analysing hypertension prevalence (defined in terms of both SBP and DBP).

Finally, our study confirmed the frequent finding that race, in the South African "population group" sense, is a strong predictor of SBP and DBP, a result not surprising in South Africa, in which large differences in health along racial lines are extremely evident. The uneven distributions of some risk factors (smoking, alcohol use and physical exercise) is coherent with the higher level of blood pressure found among Coloureds compared to Blacks, but, overall, the mediation analysis does not explain an appreciable proportion of these differences.

Strengths of the present study include the use of a large nationally sample and the Struc-

tural Equation Modelling analytical approach which allowed the testing simultaneously of mediation pathways involving multiple variables, thus identifying relationships which would have been undetectable in independent analyses. This approach also allowed the modelling of blood pressure and heart rate as latent variables and to reduce the influence of random measurement error on the coefficient estimates. Moreover, this study is the first, in our knowledge, to perform mediation analysis in a large sample modelling simultaneously both diastolic and systolic blood pressure.

The major limitations were the intrinsic lack of temporal information in our cross-sectional dataset — which limits the interpretation of the temporal sequence of the relationships and therefore their causal meaning — and the possibility that unmeasured important confounding variables (e.g. dietary patterns, likely associated both with SES and blood pressure) have introduce a substantial amount of bias in the study results.

Low reliability of self-report measures of physical exercise, alcohol and tobacco use, and incorrect techniques in anthropometric measurement are also well-known problems in population-based surveys. However, this kind of error tends usually to bias the observed associations towards the null,[33] and therefore more precise measurements are likely to strengthen the result of our analysis rather than invalidate them.

The choice of approximating some intrinsically ordinal mediating factors with continuous variables, and assuming a linear relationship with SES indicators and blood pressure across their whole range of values, is also arguable. Exploratory analyses have been done to assess the plausibility of these assumptions, but we cannot exclude the possibility that the smaller proportion of the SES/blood pressure association that these factors mediated in our sample than in other studies, is partly due to this overly stringent assumption. We also did not consider in our analysis interaction effects, and, in particular we did not take into account explicitly the plausible interaction effect between race and other SES indicators.

6 Perspectives

The findings of this study strengthen the case that SES is a risk factor for hypertension but, in contrast with studies in high-income populations, they suggest that in LMICs

in epidemiological transition, effects of SES on blood pressure may vary by gender and depend on whether SBP or DBP is considered. BMI appears to be an important mediator of a *harmful* effect of both education and income, while the contribution of other bio-behavioural factors is much less clear. From a public health viewpoint, these results imply that interventions that promote weight loss would reduce the negative impact of rising SES on blood pressure in men, and reinforce its protective effect in women.

7 Source of funding

None.

8 Conflict of interest

None.

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Appendices

Appendix A

NIDS ethical approval

University of Cape Town

ETHICS IN RESEARCH COMMITTEE

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12 December 2007

Dear Prof. Murray Leibbrandt and Dr. Ingrid Woolard

Project Title: National Income Dynamics Study (NIDS)

Having received your documentation associated with your project titled **"National Income Dynamics Study (NIDS),** the Acting Chair (Dr. Justine Burns) hereby gives your project final approval on behalf of the Commerce Faculty Ethics in Research Committee.

I wish you good success with your research.

Regards,

Andile P. Mhlahlo

For Dr. Justine Burns and Mr. Jacques Rousseau
Acting Chairs: Ethics in Research Committee

Appendix B

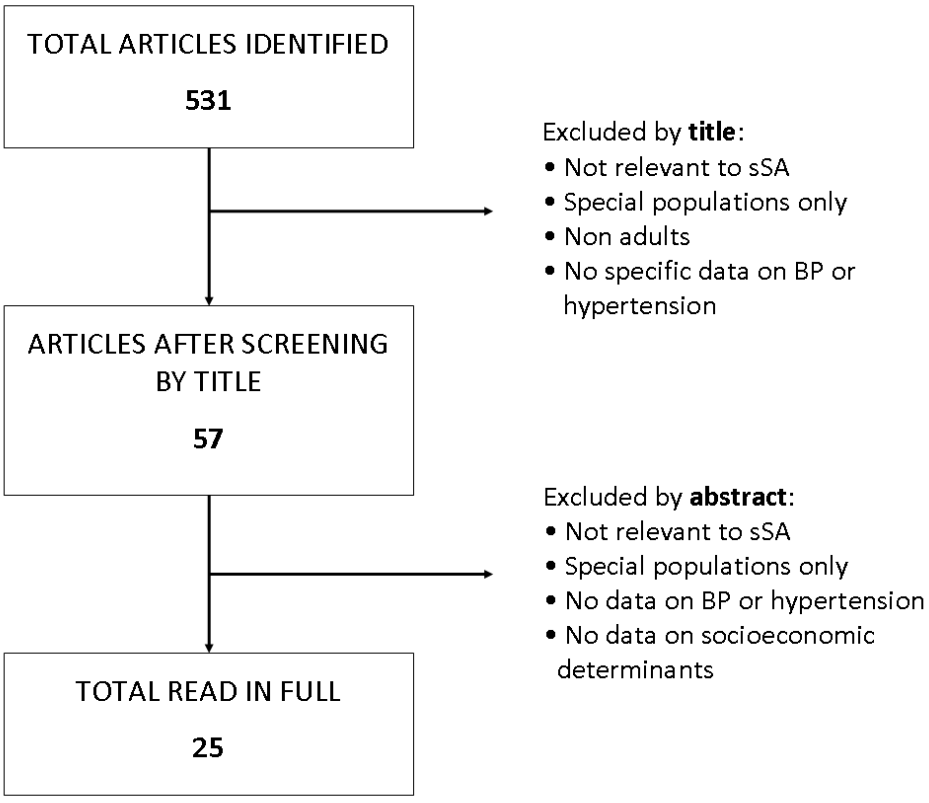
Literature review: search strategy

The initial search on the database was performed using the following search string:

> ("Africa South of the Sahara"[Mesh] OR "Developing Countries"[Mesh]) AND "Hypertension"[Mesh] AND ("2002/08/01"[PDat] : "2012/08/01"[PDat] AND "humans"[MeSH Terms] AND "adult"[MeSH Terms])

The search was carried out on the 30th of July, 2012. Figure B.1 summarises the results of the screening procedure.

Figure B.1: Screening of search results



Appendix C

Quality of blood pressure readings in NIDS

Digit Preference Score (DPS): The digit preference score (DPS) was calculated for each field-worker, when the number of measurements performed was large enough to ensure a reliable use of a χ^2 test of homogeneity ($N \geq 30$).

The DPS ranges form 0 to 100 and it is calculated as:

$$DPS = 100\sqrt{\frac{\chi^2}{N(k-1)}}$$

where

χ^2 =Pearson χ^2 test of the null hypothesis that all possible terminal digits were observed with equal frequency
N =number of observations per field interviewer
k = number of terminal digits (10 in this case)

Values over 20 are usually considered suggestive of data fabrication. The values in the NIDS survey are summarised in table C.1. A relatively low number of fieldworkers showed values greater than 20, and the total number of measurements coming for "dubious" fieldworkers account for less than 10% of the whole sample.

Analysing the dataset as a whole, including all valid measurements regardless of which fieldworker carried them out lead to the distribution of last digits shown in figure C.1.

The graph shows a statistically significant ($p < 0.001$) digit preference for even readings and, especially, for last digit 0 and 8. The overall DPSs range from 2.17 and 2.78.

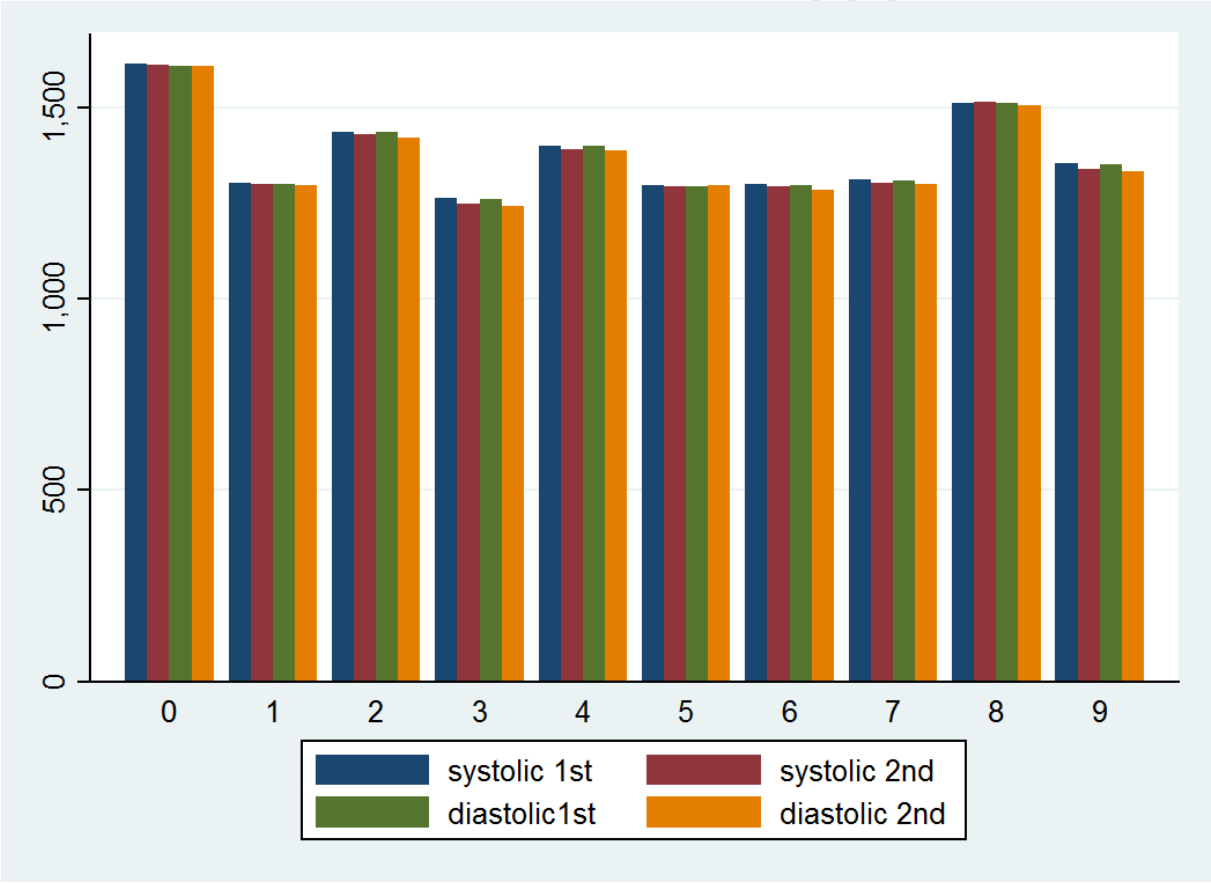
Similar patterns have been observed elsewhere,[1] and both the distribution of individual DPSs and the overall distribution of last digits are comparable with the results of other large scale surveys.[2, 3] Overall, they do not suggest gross inaccuracy or important problems of data fabrication.

Table C.1: Digit Preference Scores (DPS)

Measure	Number valid	median DPS	IQR	Range	DPS> 20
SBP first measurement	132	12.02	9.00;16.40	4.84;23.39	6
SBP second measurement	132	12.44	9.02;16.31	4.15;33.08	9
DBP first measurement	132	11.16	8.14;15.53	3.34;34.93	14
DBP second measurement	132	11.69	8.49;16.11	3.23;34.22	11

DPS > 20 = number of fieldworkers with DPS > 20
Eighty-eight fieldworkers who carried out less than 30 valid measurements were excluded from this analysis

Figure C.1: Number of readings vs. last digit



Proportion of identical readings (PIR): The proportion of identical readings (PIR) was 11.49% for systolic blood pressure and 13.76% for diastolic blood pressure. Values of PIR $\leq$ 33% for both pressure readings are considered an index of good data quality.[4, 5]

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Appendix D

Notes on statistical analyses

Structural equation models and fit indexes: Figure D.1 depicts graphically the overall structure of the model used to analyse the possible pathways explaining the association between race, education, income and SBP/DBP.

Ovals represent latent variables and boxes represent measured variables. Circles represent the latent error or disturbance terms. Error terms reflect random variation in measured variables, while disturbance terms represent variation in a latent variable not explained by other variables in the model. The variables are related by single-headed arrows that are hypothesized causal paths estimated by linear regression coefficients, and by double headed arrows that represent covariances not implying a causal relationship. An overview of principles of Structural Equation Modelling and a more precise definition of the terms above is reported in the article by Stein *et al* and in the comprehensive book by Kline. [1, 2]

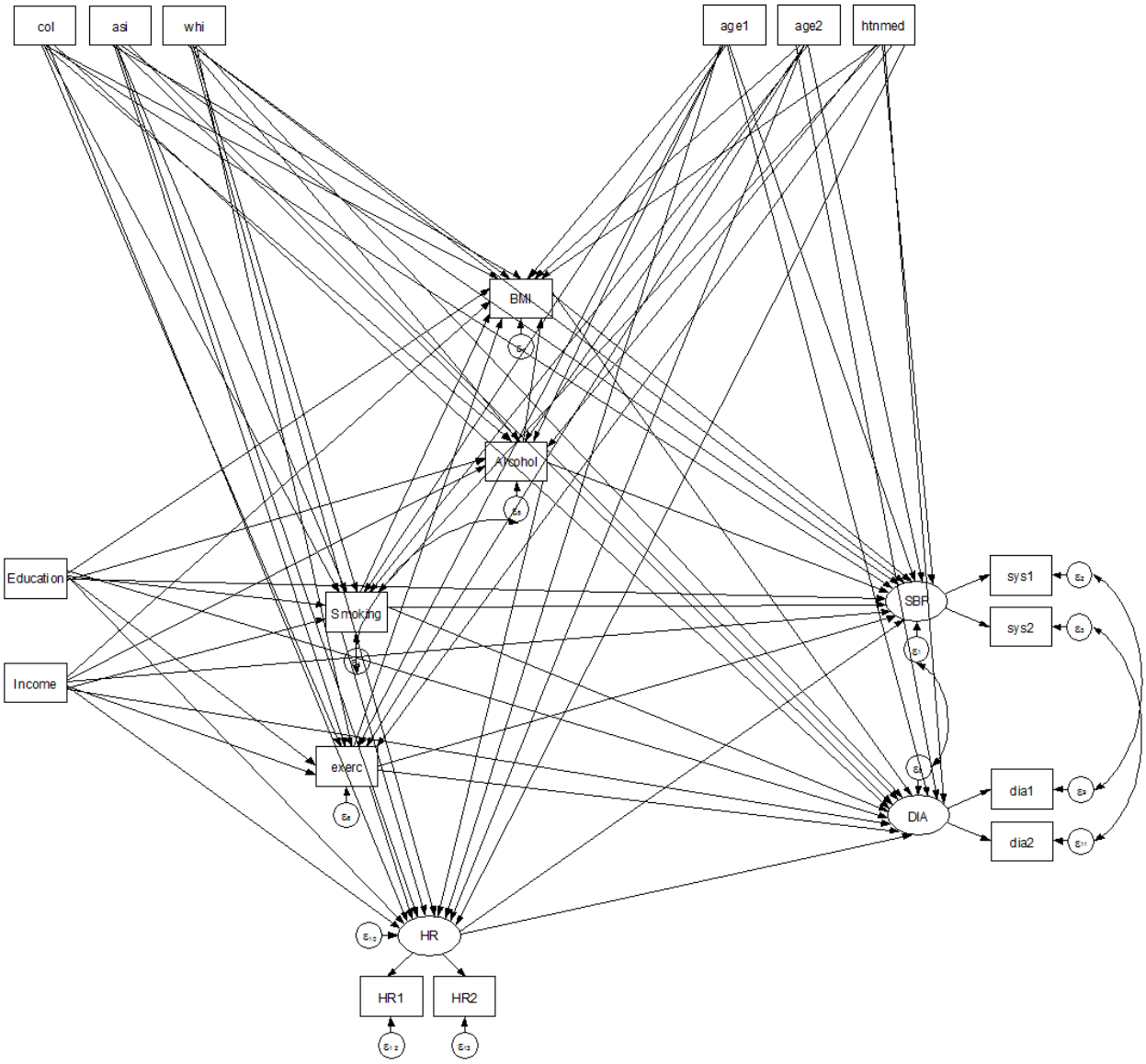
The presence of double headed paths means that other factors, external to the model, influence the association between the variables. Four of these paths were introduced in the model, and all were supported by substantive reasons.

- The path connecting the latent variables SBP and DBP indicates that part of the covariance between systolic and diastolic blood pressure in the same individual depends on factors which are not represented in the model, for example individual physiological characteristics.
- The double headed paths connecting single measurements of systolic and diastolic blood pressure take into account, for example, the variability in the techniques and/or in the environment (room temperature, hour of the day, etc.) during the measurement.
- The path connecting alcohol use and smoking accounts, for example, for environmental and psychological factors not included in the model which influence both alcohol and smoking habits.

We tested the effect of the removal of the above paths from the model. As expected, it worsened the global fit, but it did not affect substantially the values of the coefficients of the causal paths of interest.

The above model was fitted, separately for men and women, adjusting for survey design using the Taylor linearization method for variance estimation.[3] Because this kind of adjustment prevents the calculations of most of the indices commonly used to assess the

Figure D.1: Structural equation model for the relationship between SES and blood pressure



col, asi, whi= dummy variables for racial groups (ref=black); htnmed=antihypertensive medication; age1=age $<$ 55; age2=age$\geq$ 55; smoking=average number of cigarettes per day; alcohol=average drinks per drinking occasion class; exercise=weekly physical exercise class; BMI=body mass index; sys1/2, dia1/2, HR1/2=duplicate readings for systolic blood pressure, diastolic blood pressure, and heart rate; SBP, DBP, HR=latent systolic blood pressure, diastolic blood pressure, and heart rate; education=years of education; income=natural logarithm of individual monthly income

global fit of the models, these were preliminarily calculated without survey adjustment, using a maximum likelihood (ML) estimation procedure. The ML procedure assumes multivariate normality of the predicted variables, but it has been shown to be robust for relatively large violations of this assumption. The results did not change appreciably when the models, to confirm the applicability of ML estimation, were refitted with

the asymptotic distribution free (ADF) estimation method, which does not rely on this assumption.[4] Models were fitted using listwise deletion method to deal with missing data.

Table D.1 shows the results. The χ^2 test of badness-of-fit is statistically significant ($p < 0.001$), but this is a ubiquitous result with samples exceeding few thousands of observations. All other indices show a good fit, both in males and females.[5, 6]

Table D.1: Model fit indices

Model	$\chi^2(df)$	RMSEA (95%CI)	CFI	TLI	SRMR	CD
Women	351.7 (43)	0.031 (0.028;0.034)	0.994	0.984	0.005	0.619
Men	230.3 (43)	0.030 (0.026;0.034)	0.994	0.984	0.004	0.541

$\chi^2(df)$=Pearson's χ^2(degrees of freedom), RMSEA=Root mean square error of approximation,
CFI=Comparative fit index, TLI= Tucker-Lewis index, SRMR= Standardised root mean square residual

The models were subsequently re-calculated with proper adjustment for survey design, and their fit assessed analysing the values of the normalised residuals, showed in tables D.4 and D.5. All residuals were lower than the usual cut-off of 4, and the values of the standardised root mean square residual (SRMR=0.005 for women and men) and the coefficient of determination (CD=0.607 for women and 0.505 for men) show values similar to the unadjusted models.

In SEM, a good overall model fit — beside the statistical significance of the single estimates — is a precondition to interpret meaningfully path coefficients. Both the results of the unadjusted analyses of goodness of fit and the examination of the matrix of the residuals supported this assumption and did not offer evidence of gross misspecification of the model. Moreover, the modification indices calculated with the Stata® post-estimation command *estat mindices*[4] did not suggest that significant paths were missing in the model specification (data not shown).

Stata® code and full model results: The code for the model for Women was the following:

```
. svy linearized : sem (SBP -> sys1) (SBP -> sys2) (col -> SBP) (col -> smokq) (col -> alcq) (col -> exerc) (col ->
> bmi) (col -> DIA) (col -> HR) (asi -> SBP) (asi -> smokq) (asi -> alcq) (asi -> exerc) (asi -> bmi) (asi -> DIA) (
> asi -> HR) (whi -> SBP) (whi -> smokq) (whi -> alcq) (whi -> exerc) (whi -> bmi) (whi -> DIA) (whi -> HR) (age1 ->
>  SBP) (age1 -> smokq) (age1 -> alcq) (age1 -> exerc) (age1 -> bmi) (age1 -> DIA) (age1 -> HR) (age2 -> SBP) (age2
> -> smokq) (age2 -> alcq) (age2 -> exerc) (age2 -> bmi) (age2 -> DIA) (age2 -> HR) (htnmed -> SBP) (htnmed -> smokq
> ) (htnmed -> alcq) (htnmed -> exerc) (htnmed -> bmi) (htnmed -> DIA) (htnmed -> HR) (edu -> SBP) (edu -> smokq) (e
> du -> alcq) (edu -> exerc) (edu -> bmi) (edu -> DIA) (edu -> HR) (l_inc -> SBP) (l_inc -> smokq) (l_inc -> alcq) (
> l_inc -> exerc) (l_inc -> bmi) (l_inc -> DIA) (l_inc -> HR) (smokq -> SBP) (smokq -> bmi) (smokq -> DIA) (smokq ->
>  HR) (alcq -> SBP) (alcq -> bmi) (alcq -> DIA) (alcq -> HR) (exerc -> SBP) (exerc -> bmi) (exerc -> DIA) (exerc ->
>  HR) (bmi -> SBP) (bmi -> DIA) (DIA -> dia1) (DIA -> dia2) (HR -> SBP) (HR -> DIA) (HR -> HR1) (HR -> HR2) if ge
> nder==0, latent(SBP DIA HR ) cov( e.SBP*e.DIA e.sys1*e.dia1 e.sys2*e.dia2 e.smokq*e.alcq) nocapslatent
(running sem on estimation sample)
```

The full output is reported below:

```
Survey: Structural equation model
```

```
Number of strata   =        53                  Number of obs      =      7639
Number of PSUs     =       393                  Population size    =  12548940
                                                Design df          =       340

 ( 1)  [sys1]SBP = 1
 ( 2)  [dia1]DIA = 1
 ( 3)  [HR1]HR = 1
------------------------------------------------------------------------------
             |             Linearized
             |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
Structural   |
  smokq <-   |
         col |   2.262504   .2348566     9.63   0.000     1.800549    2.724459
         asi |   .7731518   .5311171     1.46   0.146    -.2715373    1.817841
         whi |   4.151475   .5930056     7.00   0.000     2.985053    5.317897
        age1 |  -.0002216    .007073    -0.03   0.975     -.014134    .0136909
        age2 |   -.041875   .0143085    -2.93   0.004    -.0700193   -.0137308
      htnmed |  -.2933488   .2061171    -1.42   0.156     -.698774    .1120764
         edu |  -.0423394   .0134023    -3.16   0.002    -.0687013   -.0159776
       l_inc |   .0153625    .020745     0.74   0.459    -.0254423    .0561673
       _cons |   .5850785   .3178569     1.84   0.067    -.0401351    1.210292
  -----------+----------------------------------------------------------------
  alcq <-    |
         col |   .5155545   .1219601     4.23   0.000     .2756633    .7554458
         asi |   .3469767   .3324264     1.04   0.297    -.3068947    1.000848
         whi |   .5912599   .1276798     4.63   0.000     .3401182    .8424016
        age1 |  -.0038384   .0019659    -1.95   0.052    -.0077052    .0000285
        age2 |  -.0071758   .0024703    -2.90   0.004    -.0120348   -.0023169
      htnmed |  -.0460674   .0536302    -0.86   0.391    -.1515562    .0594214
         edu |  -.0052606   .0043983    -1.20   0.233    -.0139119    .0033908
       l_inc |   .0172495   .0053714     3.21   0.001     .0066842    .0278149
       _cons |   .3183041    .088789     3.58   0.000     .1436591    .4929491
  -----------+----------------------------------------------------------------
  exerc <-   |
         col |   .3462082   .1038385     3.33   0.001     .1419613    .5504551
         asi |   1.044964   .3065344     3.41   0.001     .4420209    1.647906
         whi |   1.480087   .1553411     9.53   0.000     1.174536    1.785637
        age1 |  -.0048499   .0027465    -1.77   0.078    -.0102521    .0005524
        age2 |   .0022226   .0047169     0.47   0.638    -.0070553    .0115006
      htnmed |   .0641543   .0724226     0.89   0.376    -.0782985    .2066072
         edu |   .0500996   .0057275     8.75   0.000     .0388337    .0613655
       l_inc |  -.0043314   .0086218    -0.50   0.616    -.0212902    .0126274
       _cons |   1.169477   .1182058     9.89   0.000     .9369698    1.401983
  -----------+----------------------------------------------------------------
  bmi <-     |
       smokq |  -.0880057   .0476444    -1.85   0.066    -.1817206    .0057092
        alcq |  -.1649803   .1917865    -0.86   0.390    -.5422178    .2122573
       exerc |  -.4131564   .1148684    -3.60   0.000    -.6390987   -.1872141
         col |   .1431493   .5515813     0.26   0.795    -.9417922    1.228091
         asi |  -1.391374   .7888856    -1.76   0.079    -2.943084    .1603373
         whi |  -1.263144   .7175002    -1.76   0.079    -2.674443    .1481541
        age1 |   .1673444   .0114857    14.57   0.000     .1447525    .1899364
        age2 |  -.1492079   .0245401    -6.08   0.000    -.1974775   -.1009383
      htnmed |   3.749384   .4437348     8.45   0.000     2.876572    4.622195
         edu |   .1352136   .0298048     4.54   0.000     .0765885    .1938387
       l_inc |   .1145531   .0372373     3.08   0.002     .0413087    .1877975
       _cons |   20.73499   .6171224    33.60   0.000     19.52113    21.94885
  -----------+----------------------------------------------------------------
  SBP <-     |
       smokq |  -.0108988   .1315476    -0.08   0.934    -.2696485    .2478509
        alcq |   .4223188   .3468457     1.22   0.224    -.2599147    1.104552
       exerc |  -.0883931   .2521584    -0.35   0.726      -.58438    .4075938
         bmi |   .2882289   .0448593     6.43   0.000     .1999922    .3764657
          HR |   -.033914   .0325532    -1.04   0.298     -.097945     .030117
         col |    2.18646   1.323671     1.65   0.099    -.4171563    4.790076
         asi |  -.2095223   2.470028    -0.08   0.932    -5.067983    4.648938
         whi |  -1.205008   1.848287    -0.65   0.515    -4.840525    2.430509
        age1 |   .6127263   .0394172    15.54   0.000     .5351941    .6902585
        age2 |    .604895    .110665     5.47   0.000     .3872207    .8225694
      htnmed |   9.236705   1.261474     7.32   0.000     6.755428    11.71798
         edu |  -.3454301   .0747205    -4.62   0.000    -.4924028   -.1984574
```

```
      l_inc |  -.2667706    .117724    -2.27   0.024    -.4983298   -.0352114
  ----------+------------------------------------------------------------------
  DIA <-    |
      smokq |   .0255329   .0936007     0.27   0.785    -.1585764    .2096422
       alcq |   .7895657   .2396527     3.29   0.001      .318177    1.260954
      exerc |   .1345873    .196139     0.69   0.493    -.2512114    .5203861
        bmi |    .252945   .0343622     7.36   0.000     .1853557    .3205343
         HR |    .041742   .0225039     1.85   0.064    -.0025224    .0860065
        col |   1.847121   1.014824     1.82   0.070    -.1490029    3.843246
        asi |  -.0314746    2.07963    -0.02   0.988    -4.122035    4.059086
        whi |  -.7932733   1.185417    -0.67   0.504    -3.124947    1.538401
       age1 |   .3665986    .025544    14.35   0.000     .3163545    .4168427
       age2 |  -.0379941   .0501318    -0.76   0.449    -.1366017    .0606135
     htnmed |    4.95968   .8638998     5.74   0.000     3.260419    6.658942
        edu |   -.157973   .0497785    -3.17   0.002    -.2558856   -.0600604
      l_inc |  -.0103106   .0837635    -0.12   0.902    -.1750706    .1544494
  ----------+------------------------------------------------------------------
  HR <-     |
      smokq |   .1769424    .072658     2.44   0.015     .0340266    .3198582
       alcq |   .2773443   .2579136     1.08   0.283    -.2299628    .7846515
      exerc |  -.2037358   .1668118    -1.22   0.223    -.5318489    .1243773
        col |   .4897255   .8157546     0.60   0.549    -1.114836    2.094287
        asi |   2.936908   2.028327     1.45   0.149    -1.052742    6.926557
        whi |  -.3635529   1.461896    -0.25   0.804    -3.239053    2.511947
       age1 |  -.0920957   .0209446    -4.40   0.000     -.133293   -.0508984
       age2 |  -.1139778   .0512629    -2.22   0.027    -.2148101   -.0131455
     htnmed |   1.812806   .9073223     2.00   0.047     .0281344    3.597478
        edu |  -.1941804   .0503585    -3.86   0.000    -.2932338   -.0951269
      l_inc |  -.1157219   .0620801    -1.86   0.063    -.2378313    .0063874
-------------+------------------------------------------------------------------
Measurement  |
  sys1 <-    |
        SBP |          1  (constrained)
      _cons |   96.53959   1.695084    56.95   0.000     93.20541    99.87376
  ----------+------------------------------------------------------------------
  sys2 <-    |
        SBP |   .9792374   .0127574    76.76   0.000     .9541441    1.004331
      _cons |   94.97056   1.712757    55.45   0.000     91.60162    98.33949
  ----------+------------------------------------------------------------------
  dia1 <-    |
        DIA |          1  (constrained)
      _cons |   61.98225   1.239782    49.99   0.000     59.54364    64.42086
  ----------+------------------------------------------------------------------
  dia2 <-    |
        DIA |   .9775008   .0141535    69.06   0.000     .9496613     1.00534
      _cons |   61.06961   1.210514    50.45   0.000     58.68857    63.45065
  ----------+------------------------------------------------------------------
  HR1 <-     |
         HR |          1  (constrained)
      _cons |   84.11884   .9816483    85.69   0.000     82.18797    86.04971
  ----------+------------------------------------------------------------------
  HR2 <-     |
         HR |   1.072271   .0880594    12.18   0.000     .8990614    1.245481
      _cons |   84.02023    1.25407    67.00   0.000     81.55351    86.48694
-------------+------------------------------------------------------------------
Variance     |
      e.sys1 |   47.49823   6.678547                     36.02182    62.63099
      e.sys2 |   42.74563   5.853273                     32.65262    55.95841
     e.smokq |   8.146993   1.389976                     5.824427    11.39571
      e.alcq |   .7413125   .0790877                     .6009876    .9144018
     e.exerc |   1.358344   .0582642                     1.248442    1.477921
       e.bmi |   46.97036   1.883733                      43.4075    50.82566
      e.dia1 |   29.61326    2.77191                      24.6335    35.59971
      e.dia2 |   26.68333   3.046431                     21.31627    33.40171
      e.HR1  |   32.60837   11.06999                     16.72354    63.58137
      e.HR2  |   11.47126   11.66158                     1.553087    84.72783
       e.SBP |   320.4547   12.83455                     296.1784    346.7209
       e.DIA |   130.0062   4.554722                     121.3489    139.2811
        e.HR |   120.7459   11.74912                     99.71278    146.2157
-------------+------------------------------------------------------------------
Covariance   |
  e.sys1     |
      e.dia1 |   14.51192   3.013062     4.82   0.000     8.585326    20.43851
```

```
  -----------+------------------------------------------------------------------
  e.sys2     |
      e.dia2 |   9.831006   2.577379     3.81   0.000     4.761391    14.90062
  -----------+------------------------------------------------------------------
  e.smokq    |
      e.alcq |   .4510675   .0942278     4.79   0.000     .2657246    .6364105
  -----------+------------------------------------------------------------------
  e.SBP      |
       e.DIA |   163.4286   5.834276    28.01   0.000     151.9528    174.9044
------------------------------------------------------------------------------
```

For men, the code and the results were the following:

```
. svy linearized : sem (SBP -> sys1) (SBP -> sys2) (col -> SBP) (col -> smokq) (col -> alcq) (col -> exerc) (col ->
> bmi) (col -> DIA) (col -> HR) (asi -> SBP) (asi -> smokq) (asi -> alcq) (asi -> exerc) (asi -> bmi) (asi -> DIA) (
> asi -> HR) (whi -> SBP) (whi -> smokq) (whi -> alcq) (whi -> exerc) (whi -> bmi) (whi -> DIA) (whi -> HR) (age1 ->
>  SBP) (age1 -> smokq) (age1 -> alcq) (age1 -> exerc) (age1 -> bmi) (age1 -> DIA) (age1 -> HR) (age2 -> SBP) (age2
> -> smokq) (age2 -> alcq) (age2 -> exerc) (age2 -> bmi) (age2 -> DIA) (age2 -> HR) (htnmed -> SBP) (htnmed -> smokq
> ) (htnmed -> alcq) (htnmed -> exerc) (htnmed -> bmi) (htnmed -> DIA) (htnmed -> HR) (edu -> SBP) (edu -> smokq) (e
> du -> alcq) (edu -> exerc) (edu -> bmi) (edu -> DIA) (edu -> HR) (l_inc -> SBP) (l_inc -> smokq) (l_inc -> alcq) (
> l_inc -> exerc) (l_inc -> bmi) (l_inc -> DIA) (l_inc -> HR) (smokq -> SBP) (smokq -> bmi) (smokq -> DIA) (smokq ->
>  HR) (alcq -> SBP) (alcq -> bmi) (alcq -> DIA) (alcq -> HR) (exerc -> SBP) (exerc -> bmi) (exerc -> DIA) (exerc ->
>  HR) (bmi -> SBP) (bmi -> DIA) (DIA -> dia1) (DIA -> dia2) (HR -> SBP) (HR -> DIA) (HR -> HR1) (HR -> HR2) if ge
> nder==1, latent(SBP DIA HR ) cov( e.SBP*e.DIA e.sys1*e.dia1 e.sys2*e.dia2 e.smokq*e.alcq) nocapslatent
(running sem on estimation sample)


Survey: Structural equation model

Number of strata   =        53                  Number of obs      =      4938
Number of PSUs     =       394                  Population size    = 9464735.8
                                                Design df          =       341

 ( 1)  [sys1]SBP = 1
 ( 2)  [dia1]DIA = 1
 ( 3)  [HR1]HR = 1
------------------------------------------------------------------------------
             |             Linearized
             |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
Structural   |
  smokq <-   |
         col |   2.412532   .3996388     6.04   0.000     1.626465      3.1986
         asi |   2.721514    1.11638     2.44   0.015     .5256557    4.917371
         whi |   4.826758   .8448688     5.71   0.000     3.164947    6.488569
        age1 |   .0665684    .013184     5.05   0.000     .0406363    .0925005
        age2 |  -.2367742   .0272006    -8.70   0.000    -.2902764   -.1832721
      htnmed |  -1.526043    .536436    -2.84   0.005    -2.581183   -.4709028
         edu |   -.116673   .0294046    -3.97   0.000    -.1745103   -.0588357
       l_inc |   .0951546   .0344641     2.76   0.006     .0273656    .1629435
       _cons |   1.043277   .5493117     1.90   0.058    -.0371893    2.123743
  -----------+----------------------------------------------------------------
  alcq <-    |
         col |   .2498858   .1712382     1.46   0.145    -.0869302    .5867019
         asi |   .0286781   .2109346     0.14   0.892    -.3862186    .4435748
         whi |   .0781629   .1773839     0.44   0.660    -.2707415    .4270672
        age1 |   .0123266    .003553     3.47   0.001     .0053379    .0193153
        age2 |  -.0413949   .0072055    -5.74   0.000    -.0555677   -.0272222
      htnmed |  -.0482515   .1318527    -0.37   0.715    -.3075985    .2110955
         edu |   .0098619   .0088259     1.12   0.265    -.0074981     .027222
       l_inc |   .0396075   .0140443     2.82   0.005     .0119832    .0672318
       _cons |   .4259736   .1341914     3.17   0.002     .1620264    .6899208
  -----------+----------------------------------------------------------------
  exerc <-   |
         col |   .0552953   .1626844     0.34   0.734     -.264696    .3752865
         asi |   .2350382   .1982453     1.19   0.237    -.1548995    .6249759
         whi |   .5229583   .1773301     2.95   0.003     .1741598    .8717568
        age1 |  -.0369752   .0034839   -10.61   0.000    -.0438279   -.0301225
        age2 |   .0218486   .0079464     2.75   0.006     .0062183    .0374788
      htnmed |    .083314   .1709034     0.49   0.626    -.2528436    .4194716
         edu |   .0597216   .0089556     6.67   0.000     .0421064    .0773367
```

```
      l_inc |  -.0051511    .010048    -0.51   0.609     -.024915    .0146129
      _cons |   3.027714   .1621408    18.67   0.000     2.708792    3.346636
------------+----------------------------------------------------------------
bmi <-      |
      smokq |  -.1069124   .0226577    -4.72   0.000    -.1514789   -.0623459
       alcq |  -.0541792   .0691809    -0.78   0.434    -.1902543     .081896
      exerc |  -.1500308   .0796635    -1.88   0.061    -.3067246    .0066629
        col |     .59989   .5341768     1.12   0.262    -.4508065    1.650587
        asi |     1.0338   .9107974     1.14   0.257    -.7576885    2.825289
        whi |   1.602372   .5034128     3.18   0.002     .6121861    2.592557
       age1 |    .120697   .0103517    11.66   0.000     .1003358    .1410583
       age2 |  -.1066101   .0265079    -4.02   0.000    -.1587496   -.0544706
     htnmed |   2.872387   .5834157     4.92   0.000      1.72484    4.019933
        edu |   .1739224    .028436     6.12   0.000     .1179904    .2298544
      l_inc |   .1230435   .0362257     3.40   0.001     .0517896    .1942974
      _cons |    17.6684   .4875814    36.24   0.000     16.70936    18.62745
------------+----------------------------------------------------------------
SBP <-      |
      smokq |  -.0410537   .0772112    -0.53   0.595     -.192924    .1108166
       alcq |   .0583595   .2463288     0.24   0.813    -.4261557    .5428747
      exerc |   .1865976   .2409966     0.77   0.439    -.2874296    .6606248
        bmi |   .2537823   .0818643     3.10   0.002     .0927597     .414805
         HR |   .0193124   .0341818     0.56   0.572    -.0479214    .0865463
        col |   2.917952   1.430955     2.04   0.042     .1033431    5.732561
        asi |  -.6491476   3.000345    -0.22   0.829    -6.550661    5.252366
        whi |  -1.161493   1.618266    -0.72   0.473    -4.344533    2.021547
       age1 |    .475828   .0379787    12.53   0.000      .401126     .55053
       age2 |   .3855101   .1061119     3.63   0.000     .1767937    .5942265
     htnmed |   5.313747   2.724977     1.95   0.052    -.0461342    10.67363
        edu |   .0205227    .080043     0.26   0.798    -.1369176    .1779629
      l_inc |   .1166186   .1008519     1.16   0.248    -.0817516    .3149888
------------+----------------------------------------------------------------
DIA <-      |
      smokq |  -.0447608   .0502451    -0.89   0.374    -.1435901    .0540684
       alcq |   .0756158   .1455186     0.52   0.604    -.2106113    .3618429
      exerc |   .0166899   .1596926     0.10   0.917    -.2974168    .3307965
        bmi |   .2218302   .0540116     4.11   0.000     .1155923     .328068
         HR |   .0995344   .0229608     4.33   0.000     .0543718     .144697
        col |    2.16299   .9435649     2.29   0.022     .3070497    4.018931
        asi |   -.598978   1.506767    -0.40   0.691    -3.562705    2.364749
        whi |  -1.016363   1.149981    -0.88   0.377    -3.278313    1.245586
       age1 |   .3586901   .0257615    13.92   0.000     .3080187    .4093616
       age2 |  -.1061817   .0640531    -1.66   0.098    -.2321707    .0198073
     htnmed |   2.063648    1.48999     1.39   0.167    -.8670804    4.994375
        edu |   .0893226   .0533079     1.68   0.095     -.015531    .1941762
      l_inc |   .1506327   .0757369     1.99   0.048     .0016625     .299603
------------+----------------------------------------------------------------
HR <-       |
      smokq |   .1502762   .0563291     2.67   0.008     .0394799    .2610726
       alcq |   .3301433    .181753     1.82   0.070     -.027355    .6876415
      exerc |  -.7543938   .1721615    -4.38   0.000    -1.093026   -.4157616
        col |  -.6498616   1.049048    -0.62   0.536    -2.713282    1.413559
        asi |   3.146948   1.581163     1.99   0.047     .0368866     6.25701
        whi |   -.229228   1.486083    -0.15   0.878    -3.152272    2.693816
       age1 |   .0819159   .0263056     3.11   0.002     .0301742    .1336576
       age2 |  -.1041356   .0626498    -1.66   0.097    -.2273644    .0190931
     htnmed |   .8780162   .9496511     0.92   0.356    -.9898954    2.745928
        edu |  -.1481184   .0681347    -2.17   0.030    -.2821357   -.0141011
      l_inc |   .0104432   .0777519     0.13   0.893    -.1424905    .1633769
------------+----------------------------------------------------------------
Measurement |
  sys1 <-   |
        SBP |          1  (constrained)
      _cons |   102.6443   2.211582    46.41   0.000     98.29426    106.9944
------------+----------------------------------------------------------------
  sys2 <-   |
        SBP |   1.039784   .0212243    48.99   0.000      .998037    1.081531
      _cons |   99.56855   2.190381    45.46   0.000     95.26019    103.8769
------------+----------------------------------------------------------------
  dia1 <-   |
        DIA |          1  (constrained)
      _cons |   60.33807    1.67405    36.04   0.000     57.04531    63.63083
------------+----------------------------------------------------------------
```

dia2 <-						
DIA	1.011712	.0197141	51.32	0.000	.9729356	1.050489
_cons	58.83475	1.651506	35.62	0.000	55.58633	62.08317
HR1 <-						
HR	1	(constrained)				
_cons	72.00368	1.266264	56.86	0.000	69.513	74.49435
HR2 <-						
HR	.9400882	.0494101	19.03	0.000	.8429012	1.037275
_cons	71.79477	1.17568	61.07	0.000	69.48227	74.10726
Variance						
e.sys1	61.52562	7.011276			49.17112	76.98425
e.sys2	23.57493	6.29029			13.94835	39.84538
e.smokq	26.06707	2.050898			22.32971	30.42996
e.alcq	2.685705	.128393			2.444673	2.950502
e.exerc	2.409174	.0551778			2.30305	2.520187
e.bmi	28.25222	2.533521			23.68368	33.70203
e.dia1	30.79043	3.269378			24.98687	37.94195
e.dia2	21.21585	3.058355			15.97788	28.17097
e.HR1	12.74608	7.413859			4.0598	40.01735
e.HR2	27.70838	7.518338			16.24894	47.2495
e.SBP	260.55	14.44047			233.6398	290.5596
e.DIA	113.9527	4.937961			104.6424	124.0913
e.HR	143.3939	8.557971			127.5113	161.2548
Covariance						
e.sys1						
e.dia1	15.36695	3.286958	4.68	0.000	8.901687	21.83222
e.sys2						
e.dia2	3.748544	3.363652	1.11	0.266	-2.867576	10.36466
e.smokq						
e.alcq	2.583561	.2879138	8.97	0.000	2.017251	3.149872
e.SBP						
e.DIA	135.3437	6.706048	20.18	0.000	122.1532	148.5341

Total effects, indirect effects and mediation proportion: Total effects of education and income on blood pressure were estimated from the SEM models using Stata® post-estimation command *estat teffects*.[4] The results are shown in Table D.2 and, as a further confirmation of the good overall model fit, their values are very similar to those obtained from the regression models shown in Table 6 in the main article. The only coefficient whose value changed noticeably was the coefficient for the association between income and DBP in men (+29%, from 0.14 to 0.18), plausibly due to the absence in the SEM model of the variable representing employment status, which accounted for part of the effect of SES on blood pressure. As a result, the association between income and DBP was statistically significant in the SEM model but not in the multivariate linear regression model.

The fact that the coefficients for the total effects did not change after introducing the bio-behavioural variables, as done in the SEM model, also supports the hypothesis of their major role as mediators, rather than confounders, in the relationships between SES and blood pressure.

Indirect effects through the various mediators were calculated as the product of the unstandardised coefficients along the paths connecting predictors to outcomes, and their 95% confidence intervals approximated with the delta-method, using the Stata® com-

Table D.2: Total effects of education and income on SBP and DBP from SEM models

	Women		Men	
	SBP	DBP	SBP	DBP
	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
Education (*years*)	-0.31‡ (-0.45;-0.17)	-0.14† (-0.23;-0.04)	0.08 (-0.07;0.23)	0.11* (0.01;0.22)
(Log) Income	-0.22 (-0.46;0.01)	0.03 (-0.14;0.19)	0.14 (-0.06;0.35)	0.18* (0.02;0.33)

* p<0.05 ; † p<0.01 ; ‡ p<0.001

mand *nlcom*.

The proportion of the total effect mediated by the different factors (as well as their 95% confidence interval) was estimated using the approach by Ditlevsen *et al*, as the ratio between the product of regression coefficients in the path involving the mediating variable and the sum of the coefficient of the direct effect γ_1 plus the coefficients of all possible causal paths connecting the predictor to the outcome (i.e. the total effect).[7]

For example, in the model shown in figure D.2 (where γ_i represents the unstandardised coefficient of path i), the proportion of the total effect of **A** on **B** mediated by the variable **E** is calculated as:

$$MediationProportion = \frac{\gamma_2\gamma_3}{\gamma_1 + \gamma_2\gamma_3 + \gamma_4\gamma_6\gamma_5}$$

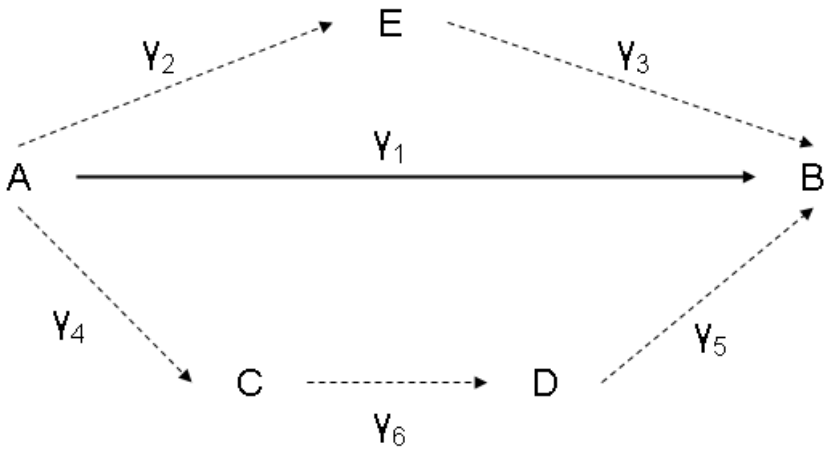
Table D.3 shows the proportion of the association between SES and blood pressure mediated by the considered risk factors. Only mediation proportions for which the total association was statistically significant are shown.

Table D.3: Mediation proportions from SEM models

	Women		Men	
	Education vs SBP	Education vs DBP	Education vs DBP	Income vs DBP
Variable	β (95% CI)	β (95% CI)	β (95% CI)	β (95% CI)
BMI	-10.98%† (-19.27;-2.69)	-22.09*% (-42.49;-1.59)	34.32% (-2.10;70.79)	14.21% (-0.18;28.61)
Alcohol	0.63% (-1.27;2.54)	2.91% (-2.84;8.65)	0.55% (-2.10;3.19)	1.42% (-5.22;8.1)
Smoking	-0.49% (-4.11;3.12)	0.10% (-6.12;6.33)	6.97% (-4.30;18.30)	-3.70% (-10.52;3.17)
Exercise	3.24% (-4.90;11.30)	0.80% (-14.94;13.34)	-4.77% (-2.33;13.70)	0.27% (-1.18;1.72)
Heart Rate	-2.31% (-6.89;2.26)	6.53% (-2.15;15.22)	-18.30% (-4.10;4.4)	1.61% (-6.76;9.98)

* p<0.05 ; † p<0.01
All variables are continuous: see article for definitions.

Figure D.2: Mediation Proportion: illustrative model



Sampling scheme and precision of the estimates: Extreme variation in the sampling weights (the inverse of the sampling probability) is known to produce excessively large sampling variances. A common technique to deal with the consequent loss of precision in the estimates is to *trim* the weights, i.e. to set a limit of their variation and to assign these limits to all weights outside the range. The expected result of weight trimming is a reduction in the sample variances (and, therefore, better precision), but more biased point estimates. The latter could be remarkable when the number of observations with very large weights is sizable.[8]

In the NIDS survey — owing to the adjustment for the largely unequal response rate among population groups, geographical regions and age classes and the calibration procedure — sampling weights show a very large variation, ranging from 0.57 to 29 545, and trimmed weights at the 95^{th} percentile are provided in the dataset.[9]

However, in our analyses we decided to avoid using trimmed weights in order to obtain unbiased estimates, accepting the corresponding loss in precision. As a result our estimates of the 95% confidence intervals should be considered as conservative, and *p-values* for the statistical tests probably overestimated.

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Table D.4: Normalised covariance residuals (women)

	sys1	sys2	smoking	alcohol	exercise	BMI	dia1	dia2	HR1	HR2	coloured	asian	white	age1	age2	htnmed	education	income
sys1	0.06																	
sys2	0.01	-0.04																
smoking	-0.10	0.19	0															
alcohol	-0.10	0.10	0	0														
exercise	-0.02	0.05	-3.58	-0.96	0													
BMI	-0.26	0.25	0.26	0.07	0.15	-0.02												
dia1	0.02	0.2	0.02	-0.28	0.13	-0.46	-0.07											
dia2	-0.20	-0.02	-0.05	0.26	-0.23	0.35	-0.02	0.04										
pul1	1.87	0.23	0.94	0.17	0.44	-1.17	2.58	0.50	0.01									
pul2	-0.49	-0.61	-0.20	-0.03	-0.40	-1.36	-2.16	0.72	0.01	0.01								
coloured	0.12	-0.11	0	0	0	0	0.14	-0.12	1.24	-0.41	0							
asian	-0.11	0.08	0	0	0	0	-0.42	0.40	-0.39	0.13	0	0						
white	-0.31	0.28	0	0	0	0	-0.32	0.28	-0.35	0.11	0	0	0					
age1	-0.08	0.07	0	0	0	0	-0.19	0.17	0.96	-0.32	0	0	0	0				
age2	0.18	-0.16	0	0	0	0	0.21	-0.18	0.57	-0.19	0	0	0	0	0			
htnmed	0.28	-0.27	0	0	0	0	0	0.04	0.45	-0.15	0	0	0	0	0	0		
education	-0.70	0.73	0	0	0	0	0.53	-0.62	0.034	-0.01	0	0	0	0	0	0	0	
income	-0.82	0.75	0	0	0	0	-0.72	0.60	0.33	-0.11	0	0	0	0	0	0	0	0

Table D.5: Normalised covariance residuals (men)

	sys1	sys2	smoking	alcohol	exercise	BMI	dia1	dia2	HR1	HR2	coloured	asian	white	age1	age2	htnmed	education	income
sys1	-0.02																	
sys2	-0.01	0.01																
smoking	1.15	-0.44	0															
alcohol	0.32	-0.13	0	0														
exercise	-0.35	0.19	-2.32	-0.87	0													
BMI	0.49	-0.16	0.10	0.038	0.25	-0.02												
dia1	0.02	-0.08	0.91	0.20	-0.09	0.57	0.04											
dia2	0.12	0.01	-0.41	-0.07	0.06	-0.32	0.02	-0.01										
pul1	-0.26	-0.38	0.28	-0.06	-0.22	-0.52	0.42	-0.97	0.03									
pul2	0.33	1.05	0.09	0.43	-0.10	1.72	-0.68	2.07	0.03	0.02								
coloured	0.47	-0.17	0	0	0	0	0.18	-0.05	-0.18	0.42	0							
asian	0.08	-0.03	0	0	0	0	0.03	-0.01	0.13	-0.31	0	0						
white	-0.93	0.35	0	0	0	0	-0.27	0.03	-0.28	0.66	0	0	0					
age1	-0.28	0.12	0	0	0	0	0.16	-0.18	-0.22	0.50	0	0	0	0				
age2	-0.37	0.15	0	0	0	0	0.16	-0.20	0.10	-0.24	0	0	0	0	0			
htnmed	-0.24	0.08	0	0	0	0	-0.24	0.13	-0.10	0.24	0	0	0	0	0	0		
education	-0.44	0.17	0	0	0	0	-0.08	-0.03	-0.44	1.02	0	0	0	0	0	0	0	
income	-0.04	0.03	0	0	0	0	0.33	-0.25	-0.38	0.88	0	0	0	0	0	0	0	0

Appendix E

Hypertension: instructions to authors

From: Hypertension Journal website
http://hyper.ahajournals.org/site/misc/ifora.xhtml, accessed 15/08/2012.

Irrelevant sections are omitted and indicated with [...]

Hypertension publishes scientific investigation of the highest quality in the broad field of blood pressure regulation and pathophysiology, clinical treatment, and prevention of hypertension. The editors encourage submission of original articles that deal with basic, clinical, and population studies of hypertension and related fields such as nephrology, endocrinology, neuroscience, vascular biology, physiology, pharmacology, cellular and molecular biology, and genetics.
Submitted manuscripts must not contain material previously published, except as an abstract, and must not be under consideration for publication elsewhere, in whole or in part. Manuscripts should conform to "Uniform Requirements for Manuscripts Submitted to Biomedical Journals" (*N Engl J Med*. 1991; 324:424-428). Manuscripts are examined by the editors and are usually sent to expert reviewers. Decisions will generally be communicated within 3 weeks after receipt of the manuscript. Acceptance is based on originality, scientific excellence, and topical balance of the journal.

Article Types

Original Scientific Communications: These are regular (original manuscripts) scientific contributions. Manuscripts should **not exceed 6000 words** including title page, abstract, acknowledgments, sources of funding, disclosures, references, novelty and significance, legends, tables, and figures. (Please note that a single bar graph is approximately 150 words, and table with 3 columns and 10 rows is approximately 100 words. For more detailed instructions on how to calculate words for figures, click **here**.) In exceptional circumstances, the editors may consider manuscripts longer than 6000 words when design complexity or research requires a greater length. For preparation, see "General Instructions."

[…..]

Manuscript Submissions

Online Submissions

Online Submissions: A formal online submission module to *Hypertension*is available. To submit your **original or revised** manuscript, please go tohttp://hype-submit.aha-journals.org and follow the detailed instructions located on our submission website. If you have any questions about the online submission process, please feel free to contact the Editorial Office athypertension@heart.org. If you do not receive confirmation of submission for a new manuscript within three days, please contact the Editorial Office. The following items should be uploaded at the time of submission:

1. A cover letter that includes a statement of submission: "All authors have read and approved the submission of the manuscript; the manuscript has not been published and is not being considered for publication elsewhere, in whole or in part, in any language, except as an abstract." The cover letter may include the names of six to eight potential reviewers, with address, email address, and fax number, who are experts in the area of research and who do not have a conflict of interest. It is especially helpful to suggest three to four members of the Editorial Board.

2. One copy of any potentially overlapping work that is in preparation, has been previously submitted or published, or is in-press, if applicable
3. One copy of any article currently in-press, which is cited in the References, if applicable
4. One copy of any abstracts published or submitted for publication, if applicable
5. All sources of support must be cited

If you are unable to submit the items above, please contact the *Hypertension*Editorial Office within 48 hours after completion of online manuscript submission for further instruction.

- **Authorship Responsibility and Copyright Transfer Agreement** All authors will be contacted AFTER submission is complete and instructed to complete the form on our submission site.
- All potential conflicts of interest related to the manuscript must be stated. **Conflict of Interest Disclosure Questionnaire** must be completed by each author on our submission site. All authors will be contacted AFTER submission is complete and instructed to complete the form on the submission site.

Instructions for Assembling Submissions

- Manuscripts must be typed, double-spaced using a 12-point font, including references, figure legends, and tables.
- Leave 1-inch margins on all sides. Do not use proportional spacing or justified margins.
- Number every page except the title page, including figures, tables, and references. Cite each figure and table in text in numerical order.
- Assemble manuscripts in this order:
    0. Title page
    1. Abstract
    2. Text, including Introduction, Methods, Results, Discussion, and Perspectives
    3. Acknowledgments
    4. Source(s) of Funding
    5. Conflict(s) of Interest/Disclosure(s)
    6. References
    7. Novelty and Significance: 1) What Is New, 2) What Is Relevant?, Summary
    8. Figure Legends
    9. Tables
    10. Figures
    11. Clinical Implications (Only by invitation)

- Cite each reference in text in numerical order and list in the References section. In-text reference numbers may be repeated but not omitted.
- Use SI units of measure in all manuscripts. For example, molar (M) should be changed to mol/L; mg/dL to mmol/L; and cm to mm. Units of measure previously reported as percentages (ie, hematocrit) are expressed as a decimal fraction. Measurements currently not converted

to SI units in biomedical applications are blood and oxygen pressures, enzyme activity, H+ concentration, temperature, and volume. The SI unit should be used in text, followed by the conventionally used measurement in parentheses.

- For style, consult the American Medical Association Manual of Style, 9th ed, Baltimore, MD, Williams & Wilkins, 1998. (NOTE: The use of et al. in the author listing of references is not allowed.)
- **Please note that if you use reference software tools (e.g. EndNote or Reference Manager), they do not always match our style, and you may need to manually correct your references.**
- Please provide sex-specific and/or racial/ethnic-specific data, when appropriate, in describing outcomes of epidemiologic analyses or clinical trials; or specifically state that no sex-based or racial/ethnic-based differences were present. See the Uniform Requirements for more details.
- Consult current issues of *Hypertension* for examples of format.

General Instructions for Revised Manuscripts

- In the top right-hand corner, indicate the manuscript number followed by R1 to denote a first revision.
- Responses to reviewers need to address all the topics addressed by a reviewer. Written responses to the reviewers' comments need to be specific and address each point separately. A global response, such as "We have addressed all of the concerns of the reviewers", will not be sufficient and will be sent back to the authors. Additionally, authors should give reasons for suggested changes that were not implemented, and identify any additional changes.
- Any changes made to the manuscript should be highlighted in yellow.
- Authorship Responsibility and Copyright Transfer Agreement online form must be individually completed by each author before a revised manuscript may be submitted.

- Conflict of Interest Disclosure Questionnaire online form must be individually completed by each author before a revised manuscript may be submitted.
- Revisions not received within three months will be administratively withdrawn. For further consideration the manuscript must be resubmitted de novo. In such cases, every effort will be made to retain the original reviewers.
- Respond to each referee's comments, indicating precisely the changes made in response to the critiques. Also, give reasons for suggested changes that were not implemented, and identify additional changes made.
- Ensure that the section "Novelty and Significance: 1) What Is New, 2) What Is Relevant?, Summary" is included.

General Instructions for Preparing a Manuscript

Title Page (Page 1, but do not number)

- Full title of manuscript, in capital letters, limited to 120 characters total.
- Authors' full names and affiliations
- A short title (total characters must not exceed 50, including spaces) to be typeset at the top of the journal page
- Word count of manuscript, including references, figures, legends, word count of abstract, and total number of figures
- The full name, title, and complete address for corresponding author, including street and post office box as well as telephone and fax numbers, and email address

Abstract

- Maximum abstract length is 250 words
- Do not use acronyms or abbreviations
- Do not use subheadings
- Do not cite references
- The abstract should include the rationale for the study, a brief description of methods and presentation of significant results, and a succinct interpretation of the data.
- Provide five to seven key words for your manuscript, using Index Medicus as a guide

Text

Abbreviations

Abbreviations should be defined at the first mention in the text.

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The methods section should provide sufficient detail for the experiments to be reproduced.

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  - To allow others to replicate and build on work published in ***Hypertension***, authors should make materials, data, and associated protocols available to readers or list the primary source of materials. Authors must disclose upon submission of the manuscript any restrictions on the availability of materials or information.
  - Authors should make Unique Materials (e.g., cloned DNAs; antibodies; bacterial or animal cells; viruses; and computer programs) promptly available on request by qualified researchers for their own use. It is reasonable for authors to charge a modest amount to cover the cost of preparing and shipping the requested material and some materials may require a Materials Transfer Agreement between institutions.

[.....]

- **Studies in Humans:** Indicate that the study was approved by an institutional review committee and that the subjects gave informed consent. All studies that involve the use of humans must adhere to the principles of the Declaration of Helsinki and Title 45, U.S. Code of Federal Regulations, Part 46, Protection of Human Subjects, Revised November 13, 2001, effective December 13, 2001. Describe the characteristics of human subjects or patients and indicate that the procedures followed were in accordance with institutional guidelines.
- **Blood Pressure Methods for Human Studies:** Blood pressure measurement methods should be described in detail in the text or by reference. Information should include number of readings, instrument type(s), cuff size(s), arm position, posture, and observer training.

[….]

- **Statistics:** A subsection on statistics should be included in the Methods section and the measures of variance, such as standard deviation or standard error, should be indicated.
- Methods should be limited to essential new information. To save space for the authors and the journal, if methods have been previously published, the author may refer to that paper and submit copies of that paper as reference material.
- The following information should be included as an **Online Data Supplement**:
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    - For human subjects or patients, describe their characteristics.
    - When describing surgical procedures on animals, identify the pre-anesthetic and anesthetic agents used and state the amount or concentration and the route and frequency of administration for each. The use of paralytic agents, such as curare or succinylcholine, is not an acceptable substitute for anesthetics. For other invasive procedures on animals, report the analgesic or tranquilizing drugs used. If none was used, provide justification for such exclusion. Generic names of drugs must be given.
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Discussion

This section should not be used to restate the results but rather to illuminate and place into perspective the results. Excessive discussion and reiteration of points that are obvious from the results are discouraged.

Perspectives

Authors should include a brief (fewer than 250 words) "Perspectives" section at the end of the Discussion Section. The "Perspectives" section should be clearly labeled with a separate heading. The purpose of "Perspectives" is to indicate the broad implications of the study, and to permit reasonable speculation on the overall importance and future directions of the work. Such perspectives should not replace the conclusions drawn from the study and should be limited to one paragraph. This section should, however, replace the "In summary..." paragraph that is often placed at the end of the discussion.

Acknowledgments

The Acknowledgments section lists substantive contributions of individuals.

Sources of Funding

Authors **must** list all sources of support for research in this section.

Conflict(s) of Interest/Disclosure(s) Statement

Authors **must** disclose any and all relationships that could be perceived as real or apparent conflict(s) of interest as a **FOOTNOTE** after the Sources of Funding section. Conflict-of-interest/disclosure will be published as a footnote to the accepted article. This pertains to relationships with pharmaceutical companies, biomedical device manufacturers, or other corporations whose products or services are related to the subject matter of the article. Such relationships include, but are not limited to, employment by an industrial concern, ownership of stock, membership on a standing advisory council or committee, being on the board of directors, or being publicly associated with the company or its products. Other areas of real or perceived conflict of interest related to the subject of the article could include receiving honoraria or consulting fees or receiving grants or funds from such corporations or individuals representing such corporations.

If no author has anything to disclose, please list "None".

References

- References must conform to the journal's style -- consult the American Medical Association Manual of Style, 9th ed, Baltimore, MD, Williams & Wilkins, 1998.(NOTE: References with 15 authors or fewer must list all authors.If there are more than 15 authors, list the first 3 authors followed by et al.)
  Please note that if you use reference software tools (e.g. EndNote or Reference Manager), they do not always match *Hypertension's* style, and you may need to manually correct your references.
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- Abstracts may be cited only if they are the sole source and must be identified in the reference as "Abstract."
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Novelty and Significance: 1) What Is New, 2) What Is Relevant?, Summary

When an author is preparing to submit a manuscript, he/she needs to ensure that there is a section following the references entitled "Novelty and Significance: 1) What Is New, 2) What Is Relevant?" written in a style that is understood by a general audience. This section, which should be about 100 words, comprises 3 subsections under the following headings:

1. What Is New?- with a few bullet points highlighting the novelty;
2. What Is Relevant?" - with a few bullet points indicating how the study relates to hypertension; and
3. Summary - of the conclusions of the study.

Tables

- Each table must begin on a separate page, double-spaced. The table number must be in Arabic numerals followed by a period and a brief informative title.
- Use same size type as in text.
- Supply a brief heading for each column.
- Indicate footnotes in tables by symbols in this order: *, †, ‡, §, ||, ¶, #, **.
- Do not use vertical lines in tables. Use horizontal lines above and below the column headings and at the bottom of the table only. Use extra space to delineate sections within the table.
- Do not duplicate data in figures and tables.
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- Figures may be black and white line drawings, graphs, color illustrations, or halftones (gel blots/stains).
- Authors are responsible for the cost of printing color illustrations.
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- Figure parts should be clearly labeled. Letters, symbols, arrows, etc. must be uniform in size and style within each figure, and when possible between figures. We prefer that you use at least 12 pt Arial Bold font.
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- Line art should not contain very thin lines, which are hard to reproduce.
- Supply a scale bar with photomicrographs.
- Provide figure legends on a separate page, double-spaced.
- If there are abbreviations or symbols in the figures, they must be defined in the figure or the figure legend.
- Limit white space between all panels and between panels and panel labels.
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The use of digital media for image acquisition and processing introduces the potential for inadvertent distortion of data. To prevent such distortion, the following guiding principles should be used:

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- The use of touch-up tools, such as cloning and healing tools in Photoshop, or any feature that deliberately obscures manipulations, is unacceptable.
    -
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1. Open graph in software that created the graph (i.e. programs such as SigmaPlot, Excel, Powerpoint, etc.)
2. Go to Print Menu
3. Change printer to Adobe
4. Name the file Fig1, Fig2, etc.

This will create a pdf of your figure.

NOTE: Do **not** create a pdf from graphs grouped in Adobe Photoshop or some type of tif or jpg file.

If you do not have Adobe Writer, the editorial office will accept Powerpoint, Excel, and Adobe Illustrator files, but please do not paste tif or jpg images of graphs in Powerpoint.

(Please note that a single bar graph is approximately 150 words. For more detailed instructions on how to calculate words for figures, click **here**.)

Clinical Implications (Only by invitation)

If a manuscript is provisionally accepted for publication, authors may be asked by the handling editor to provide a section entitled "Clinical Implications". This section is a 200 - 250 word summary highlighting key information in the article, which is meant to draw readers to the full article. It will appear at the beginning of the published issue. One single-paneled figure may be included.

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The editors encourage submission of color images for consideration as potential cover figures. These may be uploaded along with a figure legend as a supplemental file when a revised manuscript is submitted. Please make sure to clearly label this as a cover figure.

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-

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This optional section provides an opportunity for authors to present supporting materials to the manuscript. The manuscript appears both in the print version and online, whereas Online Supplements are independent from the manuscript and appear only online. Online Supplements undergo peer review and therefore must be submitted simultaneously with original submissions.

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- Number supplementary figures and tables as S1, S2, etc.
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