

PRESENTER: ANNE SUMNER (Posters not to be judged)

1.

Vitamin D status does not influence Bone Density in Africans

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Without regard to race, the Institute of Medicine states that to protect bone health vitamin D, measured as 25(OH)D, should be >20 ng/mL while levels of 12-19 ng/mL are inadequate and levels of <12 ng/mL are deficient. However, even when 25(OH)D levels are low, bone mineral density (BMD) is not compromised in African-Americans. The relationship of 25(OH)D levels to BMD in Africans is unknown. Therefore 78 African immigrants to the United States (77% male, median age 35y, age range 22-63y (95% CI: 36, 40)) had 25(OH)D levels and dual-energy X-ray absorptiometry (DXA) scans. Distribution of 25(OH)D levels by quartile was determined (Fig. 1). The distribution of whole body BMD across quartiles of 25(OH)D was assessed (Fig. 2). Median 25(OH)D levels was 21 ng/mL (95% CI: 20, 23) with 47% having 25(OH)D <20 ng/mL and 8% having 25(OH)D <12 ng/mL. BMD did not change across quartiles of 25(OH)D (Fig. 2). Spearman correlation between BMD and 25(OH)D was $r = 0.1$, $P = 0.5$. As there was no relationship between vitamin D levels and BMD, low 25(OH)D levels are not a predictor of low bone density in Africans.

Fig 1. Distribution of 25(OH)D by Quartile Quartiles

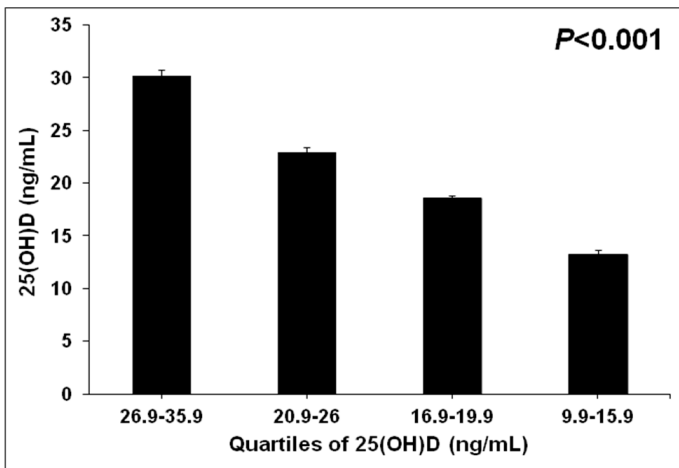
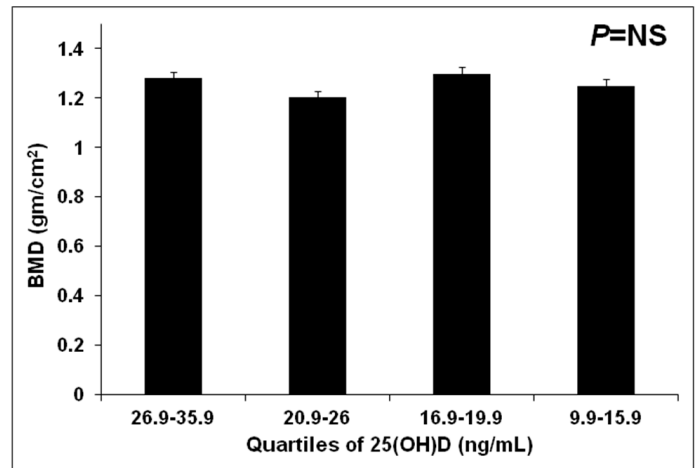


Fig 2. BMD across 25(OH)D



Low Vitamin D does not correlate with Cardiometabolic Risk in African Immigrants

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Controversy exists as to whether low vitamin D levels contribute to the development of cardiometabolic disease. As African descent populations have a high prevalence of low vitamin D levels and cardiometabolic disease, clarification is important. However, current cross-sectional studies linking low vitamin D concentrations to cardiometabolic disease not only provide conflicting results, data specifically on people of African descent is very limited. Therefore, we evaluated the association between between vitamin D levels, measured as 25(OH)D, and cardiometabolic risk factors in 78 African immigrants (77% male, age 35±y (mean±SD) age range 22-63y). Participants had oral glucose tolerance tests, insulin sensitivity index (S_I) determined with the minimal model and abdominal computerized tomographic scans to measure visceral adipose tissue (VAT). Cardiometabolic risk factors were related to 25(OH)D levels by Pearson correlations and one-way ANOVA across quartiles of 25(OH)D. Mean 25(OH)D levels were 22±7, range 10-36 ng/mL. BMI was 27.9±4.4 and 74% of Africans were either overweight or obese. Nine percent had newly identified diabetes and 33% had pre-diabetes. Mean arterial BP was 88±10 mmHg and 44% of Africans had either pre-hypertension or hypertension. Cardiometabolic variables did not change across quartiles of 25(OH)D (Table). In addition, there were no significant correlations between 25(OH)D and the cardiometabolic variables listed in the Table (all $r < 0.2$, all $P > 0.1$). As cardiometabolic risk factors do not become more severe as 25(OH)D levels decline, vitamin D may not modulate cardiometabolic risk in people of African descent.

Table: Distribution of Metabolic Variables Across Quartiles of 25(OH)D Levels

Variable (mean±SD)	Quartile 1 27-36 ng/mL	Quartile 2 21-26 ng/mL	Quartile 3 17-20 ng/mL	Quartile 4 10-16 ng/mL	P-value
BMI (kg/m ²)	29 ± 5	28 ± 4	28 ± 4	26 ± 4	0.43
Waist Circumference (cm)	93 ± 11	93 ± 12	92 ± 13	90 ± 13	0.93
VAT (cm ³)	125 ± 73	119 ± 97	109 ± 82	98 ± 71	0.77
Mean Arterial BP (mmHg)	89 ± 11	91 ± 13	85 ± 10	85 ± 5	0.20
Fasting Glucose (mg/dL)	99 ± 31	90 ± 9	88 ± 7	90 ± 10	0.22
2h Glucose (mg/dL)	155 ± 71	136 ± 28	124 ± 32	146 ± 41	0.20
SI (mU/L) ⁻¹ .min ⁻¹	2.8 ± 1.5	3.3 ± 1.9	2.9 ± 2.0	3.2 ± 1.7	0.87

3.

Worse Cardiometabolic Health in African Immigrants than African-Americans: Reconsideration of the Healthy Immigrant Effect

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In decades past, African immigrants were considered to have better cardiometabolic health than African Americans. Whether this health advantage continues to exist in the 21st century is unknown. To explore differences in markers of cardiometabolic health, oral glucose tolerance tests, blood pressure (BP), visceral adipose tissue (VAT) volume and the waist circumference (WC) which predicts insulin resistance were compared in 210 men (134 African immigrants, 76 African Americans, mean age 36±9y (mean±SD), range 20-64y) who self-identified as healthy. Insulin resistance was defined by the lowest quartile of the insulin sensitivity index ($S_I \leq 2.28 \text{mU/L}^{-1} \cdot \text{min}^{-1}$). Receiver operating characteristic curves and the Youden Index were used to identify the WC which optimally predicts insulin resistance. BMI was lower in African immigrants than African Americans (27.4 ± 3.9 vs. $29.3 \pm 5.5 \text{kg/m}^2$, $P < 0.01$). Adjusting for BMI, WC did not differ between groups (93 ± 5 vs. $94 \pm 5 \text{cm}$, $P = 0.55$); but African immigrants had more visceral adipose tissue (VAT) ($P < 0.001$) higher BP ($P \leq 0.01$), higher fasting glucose ($P \leq 0.001$) and 2h glucose ($P < 0.001$) as well as a higher prevalence of previously undiagnosed diabetes (7% (9 of 134) vs. 0% (0 of 76), $P < 0.01$) and pre-diabetes (35% (47 of 134) vs. 22% (17 of 76), $P < 0.01$). Degree of insulin resistance did not differ in African immigrants and African Americans (4.17 ± 2.88 vs. $4.24 \pm 2.61 (\text{mU/L})^{-1} \cdot \text{min}^{-1}$, $P = 0.88$). Yet, the WC which optimally predicted insulin resistance was lower in African immigrants than African Americans, specifically 92 cm and 102 cm, respectively. As African immigrants had higher VAT, BP and glucose levels than African Americans, the healthy immigrant effect may no longer be a valid concept. As insulin resistance occurred at a lower WC in African immigrants than African Americans, lower BMI in African immigrants does not appear to provide protection from cardiometabolic risk.

4.

APOL1 risk variants: Spectrum of Disease Associations, Prevalence, and Genetic Architecture

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APOL1 kidney disease is a unique case in the field of the genetics of common disease. Two variants (termed G1 and G2) with high population frequency have been repeatedly associated with non-diabetic chronic kidney diseases, with very strong effect size (odds-ratios 3-29) in admixed populations of west African descent. *APOL1* encodes Apolipoprotein L1, which exhibits trypanolytic potential against *T.b.rhodensiense* but not against *T.b.gambiense*, the causes of human African sleeping sickness. Combining published and new data, we show G1 and G2 alleles frequencies for 34 sub-Saharan populations, representing 4408 chromosomes, with frequencies from 0% to ~45% for G1 and to ~20% for G2, with the lowest frequencies in East Africa and the highest frequencies observed in West Africa. Although the prevailing hypothesis is that the G1 allele, and to a lesser degree G2, have been under recent selection in West Africa by *T.b. rhodensiense*, the highest prevalence of these alleles are found in *T.b.gambiense* endemic regions. Of the 34 African populations with *APOL1* data, G1 variants were detected in 23, only 7 of which were from *T.b. rhodensiense* endemic regions. Similarly, G2 was found in 79% of populations, most of which were in *T.b.gambiense* endemic regions. It remains unclear why G2 has not been as strongly selected as G1, given that G2 is a more potent killer of *T.b. rhodensiense* and arose earlier than G1. This suggests that there may be aspects of the evolutionary story that remain to be learned and raises the possibility that some other pathogen is responsible for the selective sweep in West Africa. We provide an overview of the spectrum of renal and cardiovascular phenotypes, the strength of the associations in African Americans and West Africans, and provide new data from South Africa showing the exceptionally strong association of *APOL1* variants with HIV-associated nephropathy. The impact of *APOL1* variants on renal and cardiovascular disease in populations subject to different infectious and environmental exposures has not been investigated in sub-Saharan Africa, where the majority of surveyed ethnic groups carry G1 and/or G2 alleles at frequency >5%.

5.

Description of F cells in Sickle Cell Anemia in Tanzania

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Background

High levels of HbF are associated with decrease in disease severity in SCA. Measured HbF is contained in F cells. There is limited information on F-cells in SCA in Tanzania.

Objectives

To determine F cell levels in SCA by exploring the association between HbF and F cells and determining the amount of HbF/ F cell.

Method

SCA patients aged ≥ 5 years who were not on hydroxyurea were recruited. HbF levels were measured by HPLC and F cells by Flow cytometry using anti- HbF antibody.

Results

130 individuals were recruited (105 HbSS and 25 HbAA). Median HbF for SCA was 8.9% (6.9- 11.6) and AA was 0.4% (0.2 - 1.1). Median F-cell for SCA and non-SCA was 38.25% (30.19 - 47.82) and 4.58% (2.92 - 6.94) respectively. 3.8% of HbSS had RBC containing ≥ 10 pg. R^2 for the association between HbF and F cell was 0.87.

Conclusion

HbF and F-cell were high in SCA patients compared to AA in Tanzania. A positive correlation between HbF and F cells is found. A critical level of intracellular HbF ≥ 10 pg is thought to inhibit HbS polymer formation. This study does not provide a spread of the amount of HbF/ F cell.

6.

MITRAL VALVE REPLACEMENT FOR RHEUMATIC HEART DISEASE IN SOUTHERN AFRICA

Jithan Koshy; Paul Human; Peter Zilla

Background: Threshold countries like South Africa provide cardiac surgery to a largely indigent population with rheumatic heart disease. Although repairs are a preferred treatment modality many rheumatic mitral valves can only be replaced. In view of significantly improved primary health care and broad access of the indigent population to communication technology we revisited the efficacy of mitral valve replacement (MVR) at the interface of the developing and developed world.

Methods: A cohort of 280 patients (mean age 40.7 ± 13.7 y/range 12-80y/median 41y; 76.4% female) with rheumatic heart disease (21% MR; 11% MS; 68% mixed) undergoing mitral valve replacement (MVR) (88.2% mechanical versus 11.8% tissue valves) was analyzed.

Results: Follow-up for the entire cohort was 94% complete (median follow-up period 3.5 years). Actuarial 5-year freedom from valve related reoperation/death was $81.5 \pm 2.9\%$ / $96.7 \pm 1.3\%$ in the mechanical and $81.8 \pm 6.7\%$ / $100 \pm 0\%$ in the tissue valve group ($p=0.562/0.970$). There was no significant difference in freedom from death or reoperation irrespective of whether INR tests were performed or not. In the mechanical group, partition modeling demonstrated a significant difference with respect to freedom from death ($95.3 \pm 3.2\%$ versus $82.9 \pm 4.1\%$ %; $p=0.013$) but not with respect to freedom from reoperation ($98.2 \pm 1.8\%$ versus $96.2 \pm 3.8\%$; $p=0.329$) between patients divided by an INR cut point of 34% of tests falling within the therapeutic range. Compared to the tissue valve group, the mechanical group with poor INR control was statistically equivalent with respect to survival and reoperation rate.

Conclusion: Overall circumstances for patients with rheumatic heart disease needing mitral valve replacement in a developing country have become conducive for the use of mechanical prostheses. Yet, the remaining inferior outcome in patients with suboptimal INR control highlights the need for alternative anticoagulation agents that require less stringent dosing.

LONG TERM OUTCOME AND VALIDITY OF THE EUROSCORE-II IN NATIVE-VALVE SURGERY FOR ACTIVE ENDOCARDITIS IN A SOUTH AFRICAN COHORT

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ABSTRACT

OBJECTIVES

To evaluate the major risk factors for adverse short and long term outcomes in patients with active native valve infective endocarditis needing cardiac surgery and to validate the EuroSCORE II in our cohort of patients.

METHODS

We retrospectively studied all patients (n=149) who had cardiac surgery for infective endocarditis between June 2000 and May 2011 at our tertiary referral center. Ninety-six patients met the inclusion criteria for the study and those included in the analysis were 29 aortic valve replacements (AVR), 27 mitral valve replacements (MVR), 28 aortic/mitral (double) valve replacements (DVR), and 12 mitral valve repair (MV Repair).

RESULTS

Mechanical valves were implanted in 68 patients (70.8%), bioprosthetic valves in 16 (16.7%), mitral annuloplasty rings in 12 (12.5%). Cox proportional hazard model showed that the most important risk factors for early 30 day mortality were critical preoperative state, emergency surgery, EuroSCORE II > 12%, low cardiac output state (LCOS), HIV positive status, preoperative embolic episodes, vegetation size > 1cm and postoperative ventilation > 24 hours. The EuroSCORE II underestimated early mortality for the entire cohort but the discriminatory ability and precision were evaluated as the area under the receiver operating characteristic (AUROC) curve of 0.796 and a C-statistic of 12.4 (p-value = 0.13) with the Hosmer-Lemeshow test, respectively. When this was evaluated within the subgroups the AUROC curve was poorer for MVR (0.696), 0.837 for DVR and better for AVR group (0.92). The highest sensitivity (76%) and specificity (88%) was at a EuroSCORE II category “>12%” in predicting 30-day mortality for the entire cohort; and a positive predictive value of 44%. Kaplan Meier analysis of patients with a EuroSCORE II ≤12% versus >12% showed that the former had significantly higher early to midterm mortality and similar late mortality (84.6 ± 7.1% vs.

97.1 ± 1.9% p = 0.0001 at 30 days; 57.7 ± 9.7% vs. 85 ± 4.8% p = 0.0001 at 5 years; and 49.5 ± 11.3 vs. 39.6 ± 28.3 p = 0.69 at 10 years).

CONCLUSIONS

We concluded that the EuroSCORE II generally underestimated mortality in our cohort of patients; however, the discriminatory ability and precision were evaluated to be good. We also concluded that the EuroSCORE II > 12%, not only predicts early mortality also medium term mortality until 5 years in our cohort.

8.

Familial Aggregation of Dilated Cardiomyopathy in Patients with Postpartum Cardiomyopathy

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Introduction

Peripartum cardiomyopathy (PPCM) is a form of unexplained pregnancy-associated heart failure that is associated with considerable morbidity and mortality. Most patients present with acute postpartal heart failure that otherwise resembles the clinical presentation of dilated cardiomyopathy (DCM). Insufficient data exists to formally evaluate any genetic contribution; most being case reports of PPCM cases whose mothers or sisters had the same diagnosis. Two recent Western studies and one local study favour theories that some cases of PPCM may be part of the spectrum of familial DCM (FDCM). Mutations in the Lamin A/C gene (LMNA) have been shown to be associated with some of the more severe forms of DCM, although the two studies in Western populations has not yet documented these mutations to be present in PPCM. We hereby report a study of familial aggregation of PPCM, which incorporated genetic screening for mutations in the LMNA gene, to see if they also played a role in PPCM.

Methods

Of prevalent and incident PPCM patients seen at two tertiary hospitals across South Africa, 51 were approached for consent to screen their first degree relatives.

Consenting relatives underwent screening for DCM that included interview, clinical examination, ECG, 2D-transthoracic echocardiography, and, only in relatives thought to bear signs of DCM, the necessary additional investigations to exclude other causes of heart failure. For the sake of comparison, a subset of 9 patients manifesting hypertensive heart failure of pregnancy (HHFP; ie. pregnancy-associated heart failure with current or prior history of hypertension) also underwent family screening.

Patients who consented for genetic testing also had blood samples taken and DNA extracted and analysed for anomalies using local standard laboratory technique.

Results

A total of 18 index patients with PPCM had at least one first-degree relative who was screened for DCM. Of these, 4 index cases (22%) had confirmed familial disease (i.e., DCM on echocardiography), whilst an additional 3 (17%) had possible familial disease, (i.e., early echocardiographic signs of DCM). Of these, autosomal dominant patterns of inheritance were observed in 4 families, while 3 families displayed autosomal recessive inheritance. None of the HHFP cases had confirmed familial DCM, but one (11%) had possible familial disease; and displayed autosomal dominance. Of the 51 PPCM patients approached, 38 underwent successful screening for LMNA mutations. Although a number of known single nucleotide polymorphisms (SNP)s were identified, no novel mutation was yet identified in this cohort.

Conclusion

Our findings support the notion that over a third of PPCM cases bear familial DCM, thus confirming the notion that PPCM is part of the spectrum of familial DCM. Our study also suggests that while HHFP are at far lower risk of familial disease, larger studies will still be needed to better quantify this risk. Detailed family history and routine family screening may be as much merited in PPCM as it is in DCM. Although PPCM may differ from DCM in that LMNA mutations do not appear to occur commonly in PPCM, larger studies in PPCM would be needed before this can be stated with confidence.

POSTER PRESENTER: MATT HALL

9.

Authors: **Matt Hall**, Ann Dufton, Roy Katso, Sally Gatsi, Mike Strange & Pauline Williams

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Abstract:

In March 2014 GlaxoSmithKline announced new strategic investments in Africa to increase access to medicines, build capacity and deliver sustainable growth. Part of these investments includes £25 million to create the world's first R&D Open Lab to increase understanding of non-communicable diseases (NCDs) in Africa. The vision is to create a new global R&D effort with GSK working in partnership with major funders, academic groups and governments to share expertise and resources to conduct high quality research. The R&D Open Lab for NCDs in Africa will see GSK scientists collaborate with research and scientific centres across Africa from its hub at GSK's Stevenage R&D facility in the UK. An independent governing board of leading scientists and clinicians will oversee the implementation of NCD research projects within a dynamic and networked open innovation environment. The Open Lab aims to improve understanding of NCD variations seen in the Africa setting. It is hoped that these insights will inform prevention and treatment strategies and will enable researchers across academia and industry to discover and develop new medicines to address the specific needs of African patients. The Open Lab will directly support the training and education of African scientific researchers. The vision is to collaborate with, and build upon existing African training programmes, creating a new generation of African NCD experts while instilling a deep vein of 'African thinking' within GSK's own R&D organisation. The poster will outline the concept and vision for the Open Lab.

10.

Abstract

Title: Stroke Genomics in people of African Ancestry- Charting new paths

Authors: RO Akinyemi, B Ovbiagele, A Akpalu, C Jenkins, K Sagoe, L Owolabi, F Sarfo, R Obiako, M Gebreziabher, S Melikam, O Arulogun, D Lackland, *MO Owolabi

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Stroke has attracted global attention as 1 in 6 people will develop stroke in their lifetime. There is also a burgeoning epidemic of stroke in Africa but the full contributions of genomic factors are unknown. Despite intense research and recent progress, the genomic architecture of stroke is yet to be fully unraveled. Studies exploring the genetic underpinnings of the peculiarities of stroke in populations of African ancestry in the US are still in their infancy while there are hardly any data on negroid populations living in Africa. Evidence from twin studies, family history studies, animal models and heritability studies of vascular risk factors and intermediate phenotypes suggest a modest and likely significant contribution of genomic factors to the neurobiology and phenomenology of stroke. The SIREN Project proposes to explore genomic factors in stroke in native Africans in comparison with African Americans (80 per cent of whom migrated from West Africa) and white Americans in the REGARDS Study (comparison among three tracks).

The wide genomic variation of African populations offers a unique opportunity to identify genomic variants with causal relationship to stroke across different ethnic groups. An ethnically diverse sample increases the scope and generalizability of findings, because pan-ethnic replicability of association between a candidate SNP and trait outcome provides support for a causal relationship. Thus, ethnically diverse patterns of linkage disequilibrium may help resolve causal from non-causal relationships. Overall, unraveling the genomic underpinnings of stroke using such approaches as 'pathway-based hypothesis - driven genomic analysis' would improve our understanding of the molecular pathways of stroke and this may unmask new and better prevention and treatment options for stroke in people of African ancestry and other global populations. We present a critical appraisal of the literature on the genomics of stroke with special reference to populations of African origin.

The SIREN Project is supported by NIH 1U54HG007479-01.

11.

ABSTRACT

TITLE: RATIONALE AND DESIGN OF THE STUDY OF GENETICCS OF ATRIAL FIBRILLATION IN AN AFRICAN POPULATION

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Background: Atrial fibrillation (AF) is the most common sustained arrhythmia in high-income countries. While underlying conditions such as hypertensive and rheumatic heart disease cause the vast majority of cases of AF in developing countries, AF can also present as an isolated finding without other concomitant cardiovascular diseases. Genetic mutations in several potassium channel genes (i.e., *KCNQ1*, *KCNJ2*, *KCNE2* and *KCNA5*) have been associated with AF. Whether mutations in the genes known to cause lone AF in Caucasians are also causing AF among Kenyan patients is unknown. Identification of the frequency of mutations in these genes in patients with AF in Kenya may shed light into the causal pathways of AF in this population.

Objectives: To characterize (phenotypically and genotypically) patients with AF in Western Kenya.

Methods: This is a case control study, approximately 70 patients with non-valvular AF, 70 patients with valvular AF and 140 non-AF controls will be enrolled between October 1, 2013 - June, 2014. Each patient will undergo standardized interview and physical examination. An electrocardiogram, echocardiogram and blood sample for biochemical and genetic analysis will also be obtained. Mutations analysis in potassium channel genes will be performed using automated sequencing.

Results: Of the 411 patients screened, 269 patients (65%) were enrolled by April 2014. This represents 96% enrollment. Patients mean age was 49.4 ± 19.7 years. Thirty-one percent of patients were male and sixty-nine percent were females. Data cleaning and genetic analyses are underway.

Conclusion:

Results from the this study will describe the clinical characteristics and morbidity of AF patients in Western Kenya which will put AF patients unique needs in proper context. In addition, the results from mutation analysis will contribute towards enhancing prediction of development of disease and outcomes in African individuals, improve preventive medicine and potentially contribute towards the development of novel therapies.

POSTER PRESENTER: UCHECHUKWU SAMPSON

12.

H3Africa Cardiovascular Workshop

The Burden of High Body Mass Index from 1990 to 2010: A Comparison of Sub-Saharan Africa and Developed Regions

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Disclaimer:

The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung, and Blood Institute, National Institutes of Health, Department of Health and Human Services or any other government entity.

Abstract

Introduction: Recent population studies report increasing burden of cardiovascular disease (CVD) and related risk factors in sub-Saharan Africa (SSA). The nutrition transition and related changes in high body mass index (BMI) are considered important drivers of these adverse CVD trends. Therefore we evaluated trends in deaths and disability-adjusted life years (DALYs) associated with high BMI in SSA compared to developed world regions.

Methods: We estimated deaths and disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) attributable to the independent effects of high BMI in 1990 and 2010. We estimated exposure distributions for each year, region, sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesizing published and unpublished data. We used these estimates, together with estimates of cause-specific deaths and DALYs from the Global Burden of Disease Study 2010, to calculate the burden attributable to high BMI exposure compared with the theoretical-minimum-risk exposure. We incorporated uncertainty in disease burden, relative risks, and exposures into our estimates of attributable burden.

Results: In developed regions the age-standardized deaths per 100,000 population associated with high BMI decreased from 77.42 (CI: 65.37 to 89.31) in 1990 to 68.23 (CI: 59.09 to 77.06) in 2010, however in SSA the rates increased from 21.01 (CI: 14.73 to 28.28) to 37.85 (CI: 29.80 to 46.70) during the study period. Similarly, in developed regions the age-standardized DALYs associated with high-BMI decreased from 1978.99 (CI: 1660.99 to 2299.62) in 1990 to 1914.45 (CI: 1649.36 to 2190.76) in 2010. On the contrary the rates in SSA increased from 623.03 (431.17 to 842.82) in 1990 to 1141.23 (CI: 889.99 to 1412.23) in 2010. Throughout the study period, there was a consistent increase in deaths (Figure 1) and DALYs (Figure 2) associated with high BMI in SSA.

Conclusions: The SSA region has experienced persistent increase in the burden of high BMI over the past two decades. The increasing burden of high-BMI in SSA is concerning and calls for appropriately measured response to mitigate the observed trend.

Figure 1.

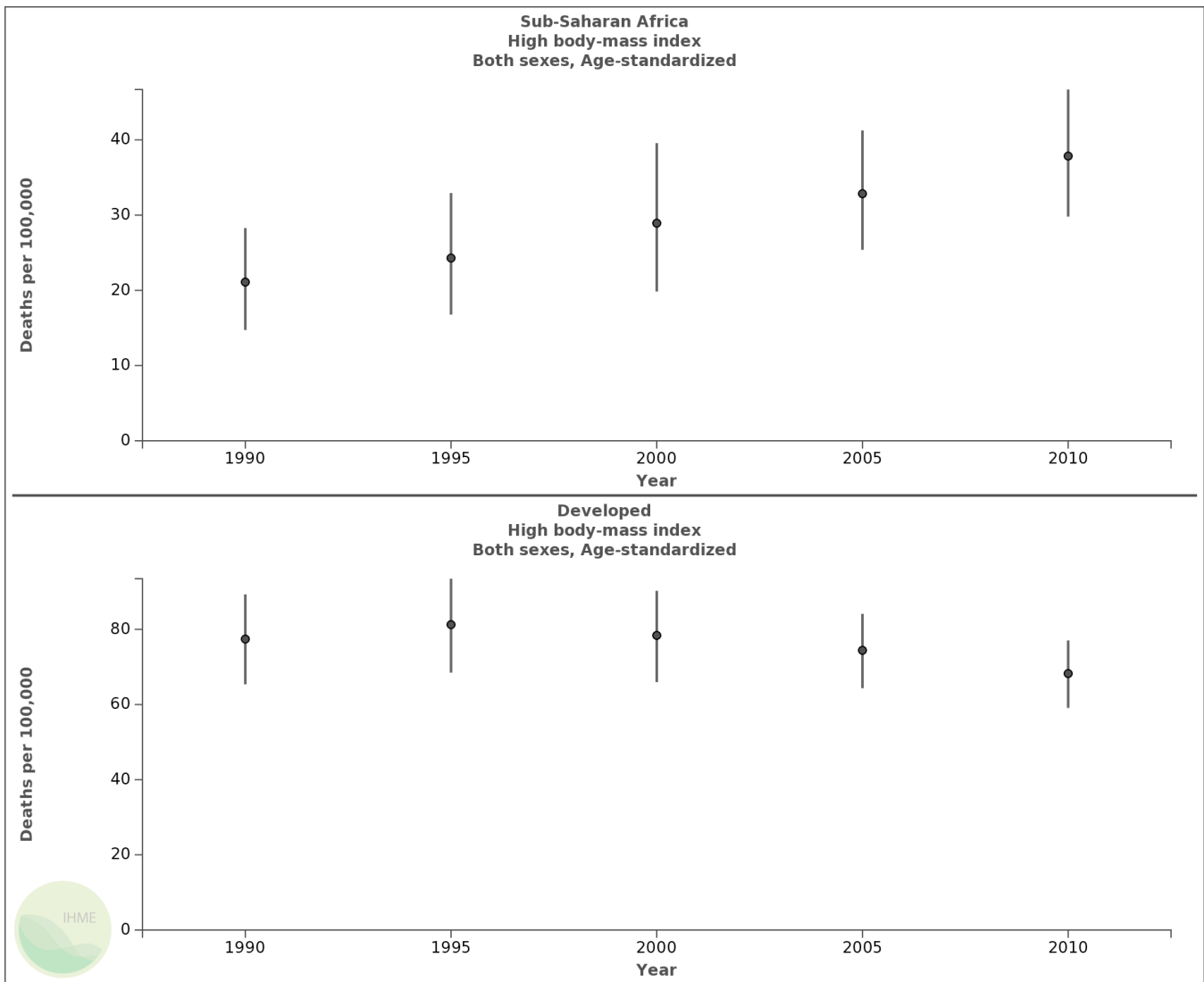
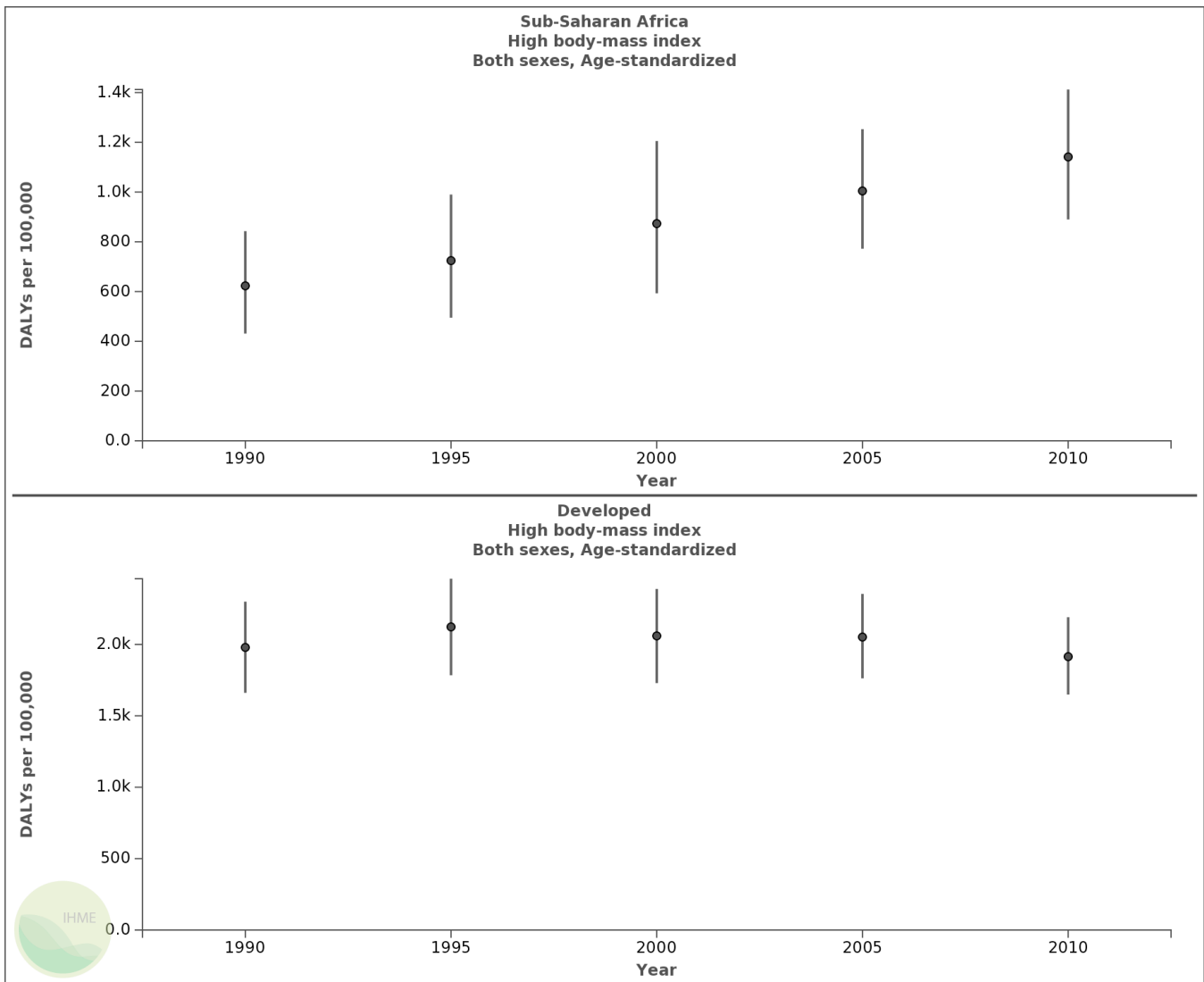


Figure 2



H3Africa Cardiovascular Workshop

The Burden of Diabetes in Sub-Saharan Africa and Developed World Regions: 1990 to 2010

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Abstract

Introduction: The increasing burden of cardiovascular disease (CVD) in sub-Saharan Africa (SSA) is now a subject of many reports. Since diabetes is a risk equivalent for CVD, we evaluated the trends in deaths and disability-adjusted life years (DALYs) associated with high fasting plasma glucose (diabetes) in Sub-Saharan Africa (SSA) compared to developed world regions.

Methods: We estimated deaths and disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) attributable to the independent effects of high fasting plasma glucose in 1990 and 2010. We estimated exposure distributions for each year, region, sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesizing published and unpublished data. We used these estimates, together with estimates of cause-specific deaths and DALYs from the Global Burden of Disease Study 2010, to calculate the burden attributable to high fasting plasma glucose exposure compared with the theoretical-minimum-risk exposure. We incorporated uncertainty in disease burden, relative risks, and exposures into our estimates of attributable burden.

Results: In developed regions the age-standardized DALYs per 100,000 population associated with diabetes decreased from 1171.52 (CI: 979.18 to 1380.87) in 1990 to 988.20 (CI: 814.72 to 1185.65) in 2010, however in SSA the rates increased modestly from 1435.59 (CI: 1244.21 to 1649.75) to 1524.73 (CI: 1297.73 to 1747.99) during the study period. Similarly, in developed regions the age-standardized deaths associated with diabetes decreased from 46.33 (CI: 38.13 to 55.50) in 1990 to 35.70 (CI: 28.29 to 43.99) in 2010, while the rates in SSA increased marginally from 57.77 (49.70 to 66.70) in 1990 to 61.06 (CI: 51.83 to 69.79) in 2010. During the study period, there was a decreasing trend in deaths (Figure 1) and DALYs (Figure 2) in developed regions but not in SSA.

Conclusions: The disease burden attributable to diabetes is now greater in SSA than the developed world regions. The reduction of this burden will require treatment as well as prevention strategies that elucidate and address the underlying causes of diabetes.

Figure 1.

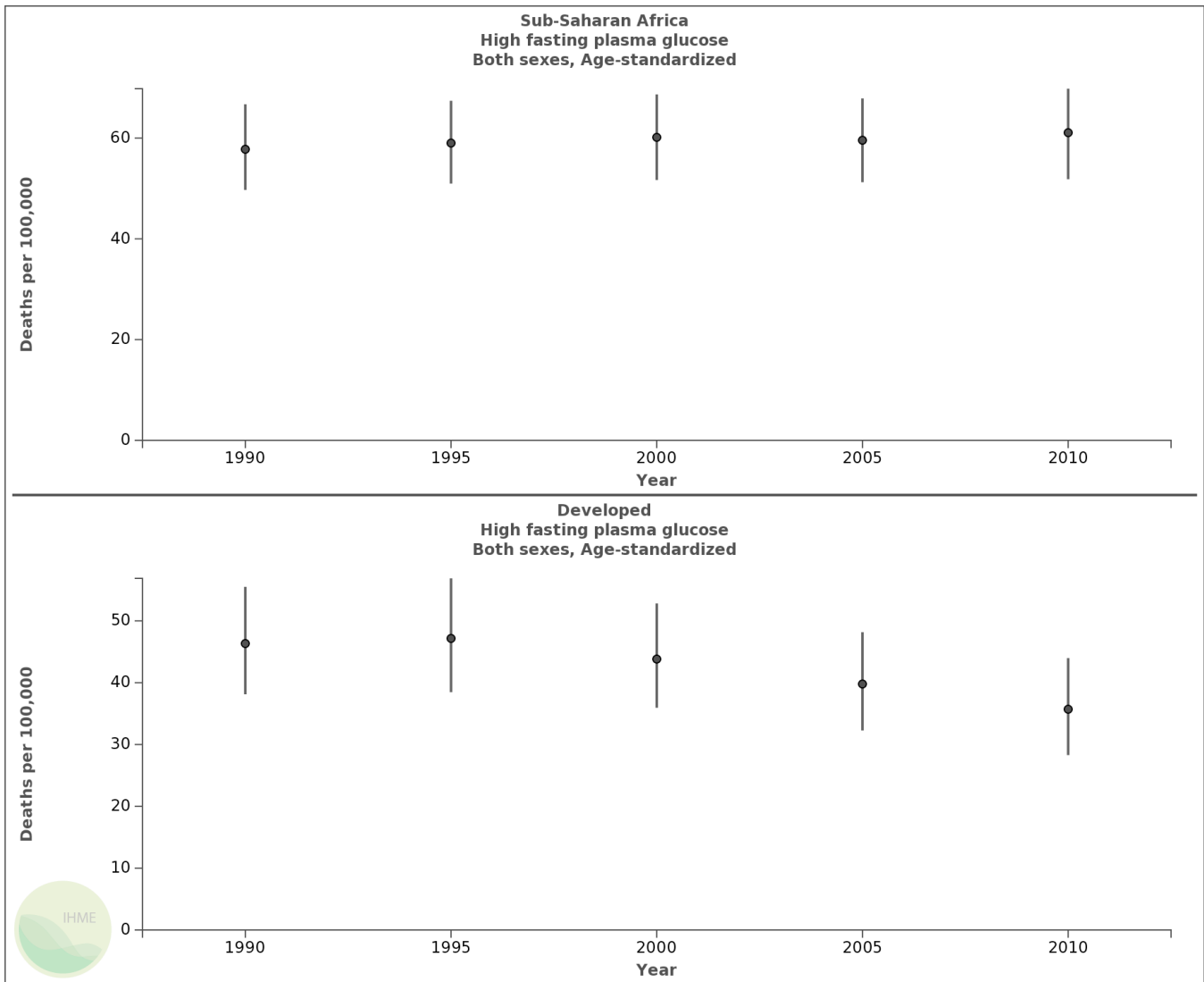
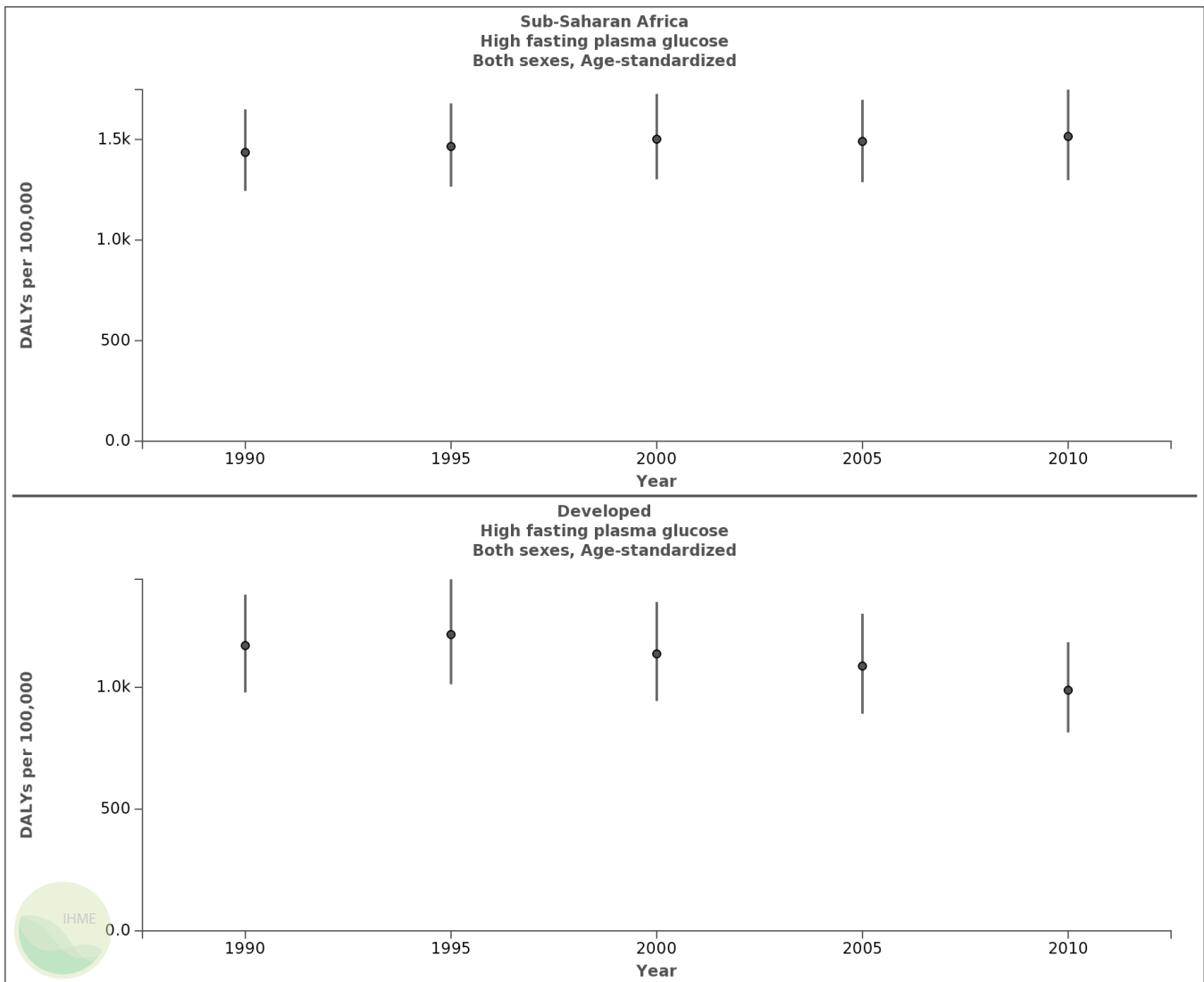


Figure 2.



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The Burden of High Blood Pressure in Sub-Saharan Africa: A 21st Century Dilemma

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Abstract

Introduction: Hypertension (HTN) is a well-established risk factor for all-cause and cardiovascular mortality, thus an assessment of its burden would shape disease control priorities and strategies. Therefore we estimated the deaths and disability-adjusted life years (DALYs) associated with HTN, in sub-Saharan Africa (SSA) compared to developed regions of the world.

Methods: We estimated deaths and disability-adjusted life years (DALYs; sum of years lived with disability [YLD] and years of life lost [YLL]) attributable to the independent effects of high blood pressure in 1990 and 2010. We estimated exposure distributions for each year, region, sex, and age group, and relative risks per unit of exposure by systematically reviewing and synthesizing published and unpublished data. We used these estimates, together with estimates of cause-specific deaths and DALYs from the Global Burden of Disease Study 2010, to calculate the burden attributable to high blood pressure exposure compared with the theoretical-minimum-risk exposure. We incorporated uncertainty in disease burden, relative risks, and exposures into our estimates of attributable burden.

Results: HTN was the 4th leading risk factor for DALYs per 100, 000 in 1990 but became the number one risk factor in 2010 (Figure 1). In the developed world the age-standardized deaths per 100, 000 associated with HTN dropped appreciably from 196.44 (CI: 183.02 to 209.90) in 1990 to 122.6 (CI: 111.23 to 132.90) in 2010, however in SSA the 1990 estimate was 151.75 (CI: 135.07 to 169.07) versus 144.46 (CI: 129.86 to 163.94) in 2010, reflecting a very modest decrease. Of note, among women there was a greater disparity in the 2010 death rates in SSA compared to the developed world: 145.86 (126.11 to 169.26) vs. 102.20 (90.73 to 112.47). In 2010 the HTN-associated DALYs in SSA was 2946.58 (CI: 2654.41 to 3303.11) far exceeding the estimated 2224.90 (2007.05 to 2435.34) for the developed world regions. In developed world there was an apparent decline in the DALYs associated with HTN between 1990 and 2010, but a similar decline was not witnessed in SSA (Figure 2).

Conclusions: The burden of HTN is now a dilemma in SSA. However, the estimation of HTN-associated disease burden in SSA is based upon paucity of data available for the region. The public health significance of HTN should provide impetus for concerted efforts to augment disease surveillance data for the region in order to improve the analysis of disease burden and response strategies.

Figure 1.

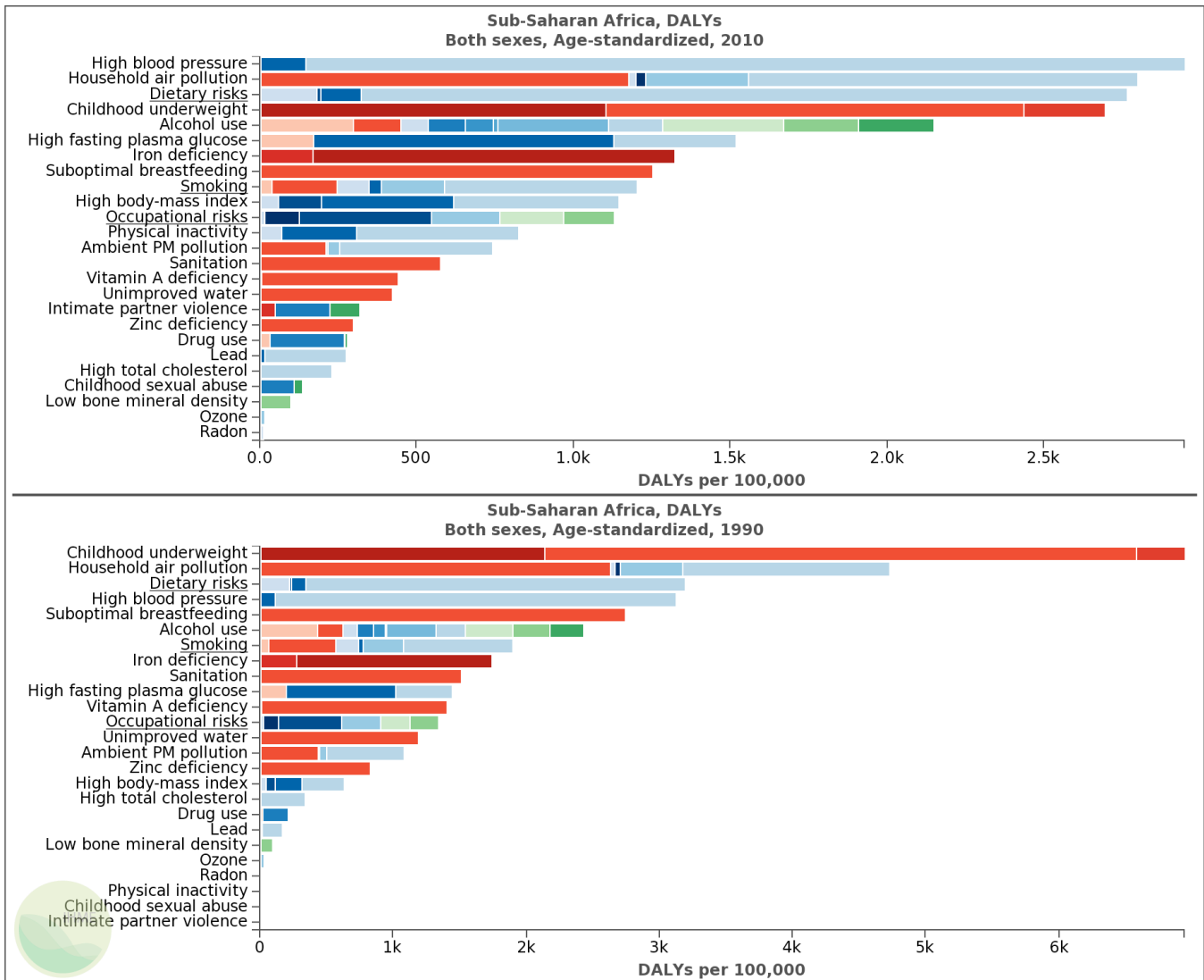
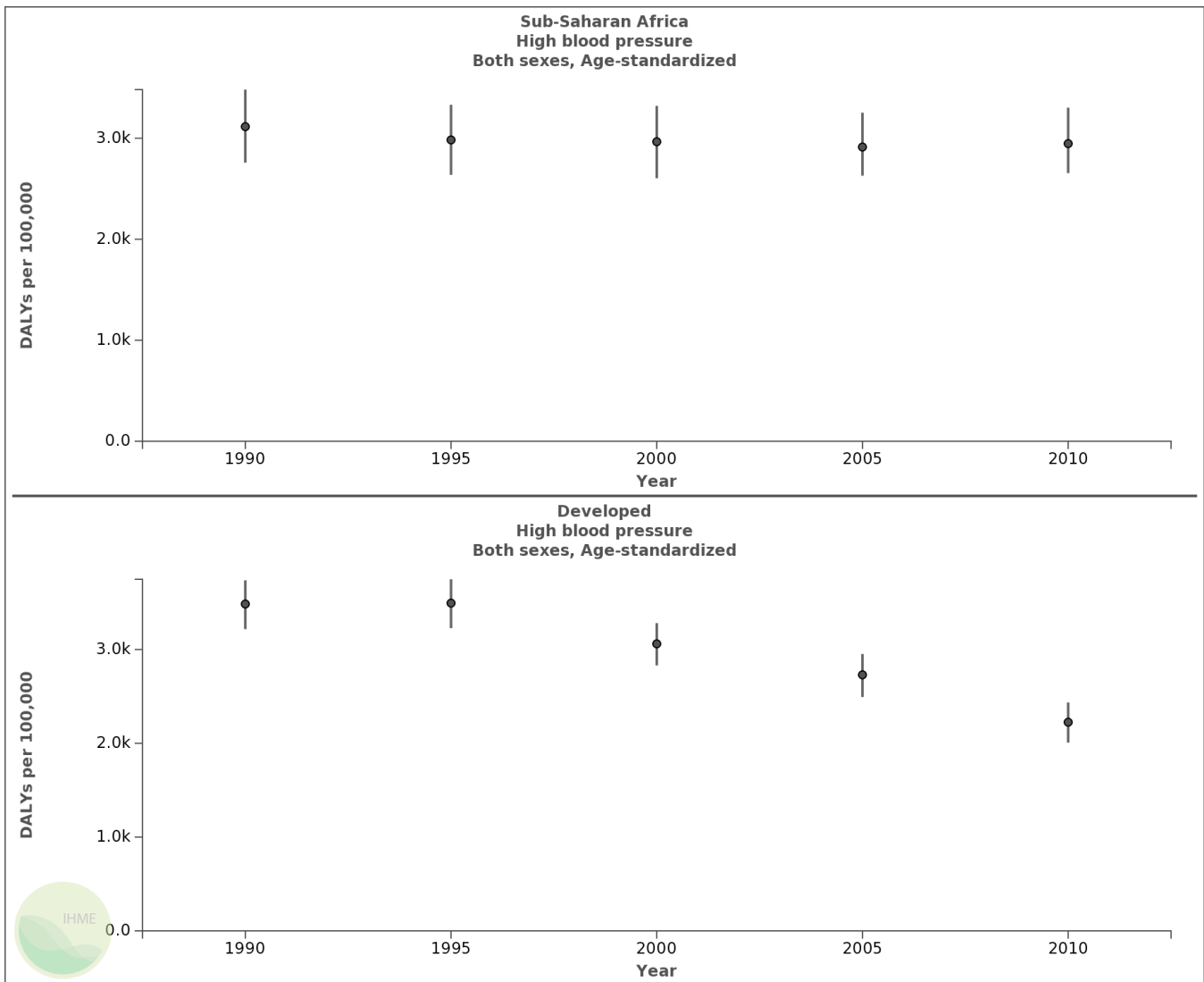


Figure 2.



15.

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The Burden of Sickle Cell Disease: A Comparison of Global and Sub-Saharan African Estimates of Disability Adjusted Life Years.

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Abstract

Introduction: A comprehensive and systematic assessment of the burden of sickle cell disorders (SCD) is needed to inform disease control priorities. Therefore we estimated the disability-adjusted life years (DALYs) associated with SCD globally and in sub-Saharan Africa (SSA) as a summary measure of premature mortality and years lived with disability.

Methods: We used the global burden of disease (GBD) causes of death database, and the cause of death ensemble modeling (CODEm) approach to assess levels of DALYs associated with SCD. Assessment of DALYs employed estimates of SCD prevalence from systematic reviews of epidemiologic data using a Bayesian meta-regression method (DisMod-MR).

Results: In 2010 the global age-standardized DALYs per 100,000 population associated with SCD was 80.09 (CI: 60.00 to 102.40) compared to 281.16 (CI: 196.70 to 368.44) in SSA, which was in excess of the estimated 77.86 (CI: 58.01 to 98.96) for other developing regions (Figure 1). The under-5 child age-specific DALYs per 100,000 population associated with SCD in SSA was 1024.03 (CI: 645.82 to 1452.36) compared to 338.71 (CI: 236.46 to 462.44) globally. There was incremental disparity in the estimates of post neonatal (PN), late neonatal (LN), and early neonatal (EN) DALYs for SSA vs. global: PN, 1513.69 (CI: 949.64 to 2142.41) vs. 467.30 (CI: 317.42 to 630.61); LN, 1894.54 (CI: 1113.56 to 2847.5) vs. 473.73 (CI: 291.50 to 697.36); EN, 2560.59 (CI: 1854.70 to 3563.85) vs. 637.34 (CI: 470.79 to 874.78) (Figure 2). Among 5 to 14 year olds the age-specific DALYs in 2010 for SSA was 326.64 (CI: 221.42 to 434.16) vs. 120.71 (CI: 85.90 to 164.07) globally.

Conclusions: Despite the well-characterised pathology and genetic underpinnings of SCD, its associated disease burden in SSA remains disproportionately high compared to the rest of the world. Our findings suggest that concerted efforts are needed to accelerate the identification and implementation of the best strategies for optimal reduction of this burden.

Figure 1.

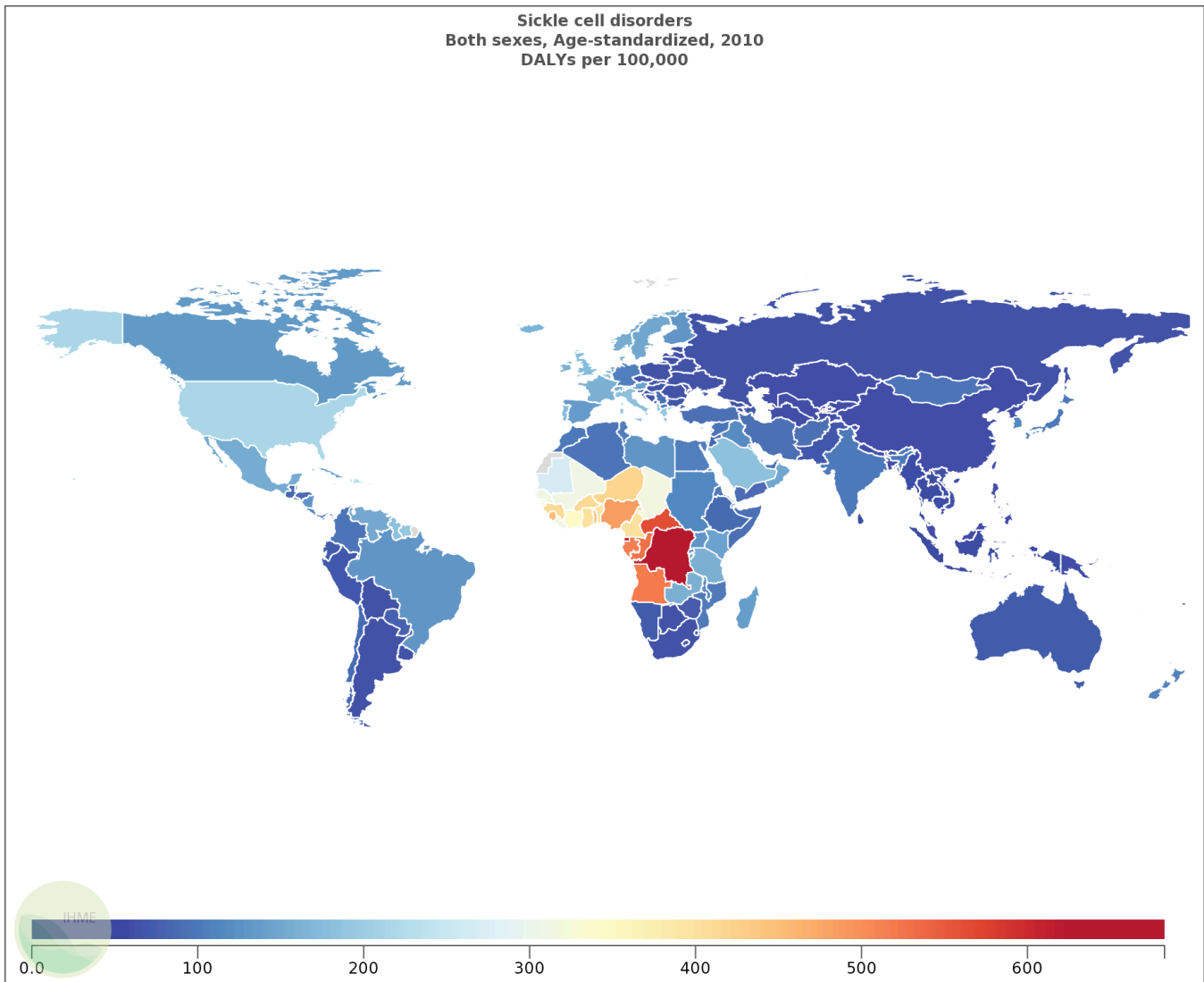
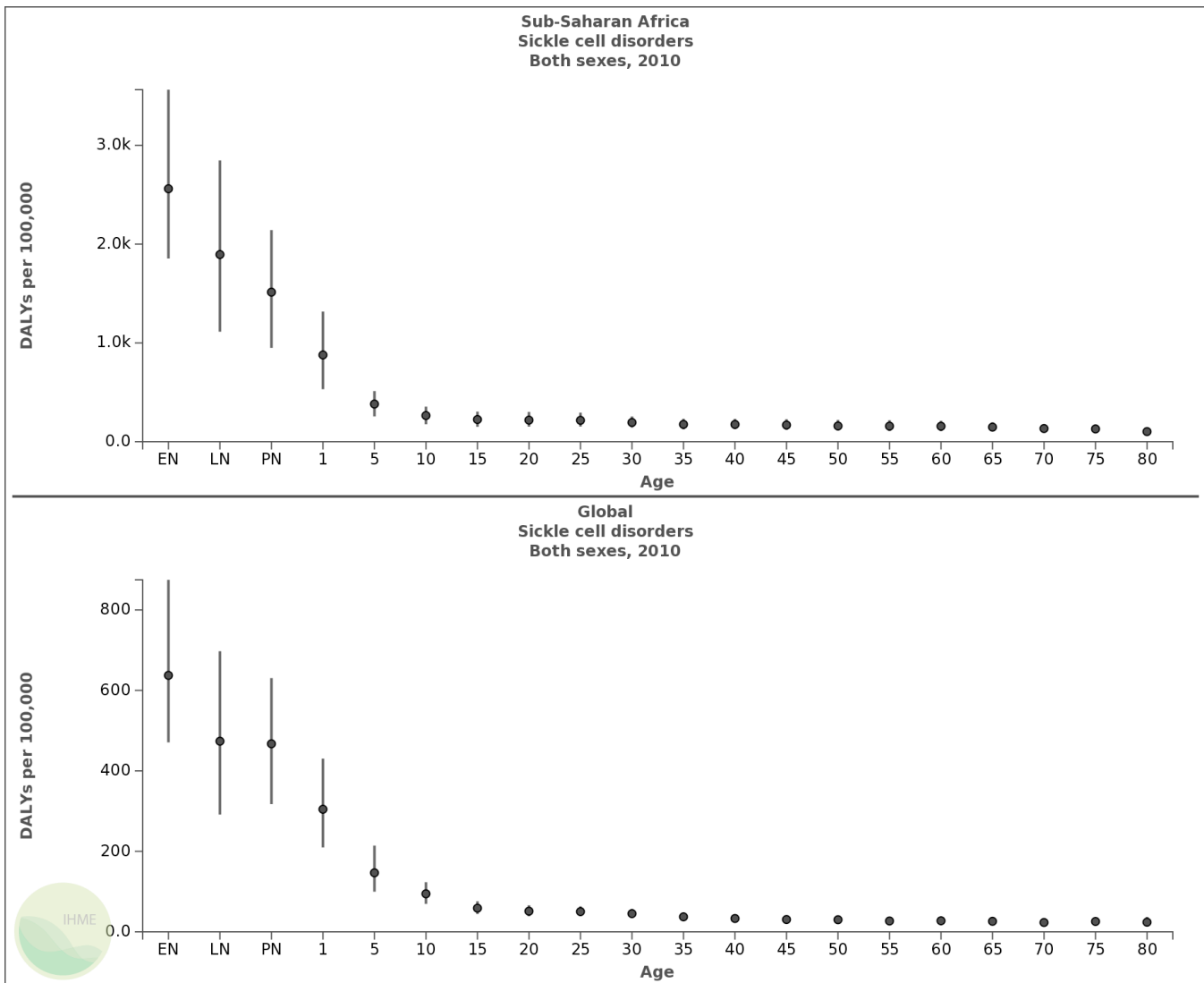


Figure 2.



EN, Early neonatal period

LN, Late neonatal period

PN, Post neonatal period

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The Burden of Stroke in Sub-Saharan Africa Compared With Developed World Regions: 1990 to 2010.

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Abstract

Introduction: In the light of prevailing knowledge about the rising burden of cardiovascular risk factors in Sub-Saharan Africa (SSA), a comprehensive and systematic assessment of the burden of stroke is needed to inform strategies for disease control. Accordingly, we evaluated trends in deaths and disability-adjusted life years (DALYs) associated with stroke (ischemic, haemorrhagic, and other non-ischemic) in SSA compared to developed world regions.

Methods: We used the global burden of disease (GBD) causes of death database, and the cause of death ensemble modeling (CODEm) approach to assess levels of deaths and DALYs associated with stroke from 1990 to 2010. Assessment of DALYs employed prevalence estimates of stroke from systematic reviews of epidemiologic data using a Bayesian meta-regression method (DisMod-MR).

Results: In 2010 the age-standardized DALYs per 100, 000 population associated with stroke was 982.31 (CI: 920.90 to 1068.91) in developed regions compared to a higher rate of 1779.97 (CI: 1492.32 to 2001.28) in SSA. Similarly, the rates in 1990 were 1537.72 (CI: 1406.99 to 1624.48) and 2162.32 (CI: 1718.97 to 2417.57) for developed and SSA regions, respectively. In the developed world the age-standardized deaths per 100, 000 associated with stroke dropped appreciably from 96.44 (CI: 88.31 to 102.17) in 1990 to 60.54 (CI: 57.21 to 67.00) in 2010, however in SSA the 1990 estimate was 110.11 (CI: 88.47 to 122.09) versus 94.16 (CI: 78.77 to 106.21) in 2010, reflecting a modest decrease. During the study period we observed a more appreciable decline in the deaths (Figure 1) and DALYs (Figure 2) associated with stroke in developed world regions.

Conclusions: During the twenty-year study period, the burden of stroke in SSA was high and did not decline appreciably compared with developed regions. This observed pattern requires careful assessment to determine the contributory factors and the best strategies for optimal reduction of disease burden.

Figure 1.

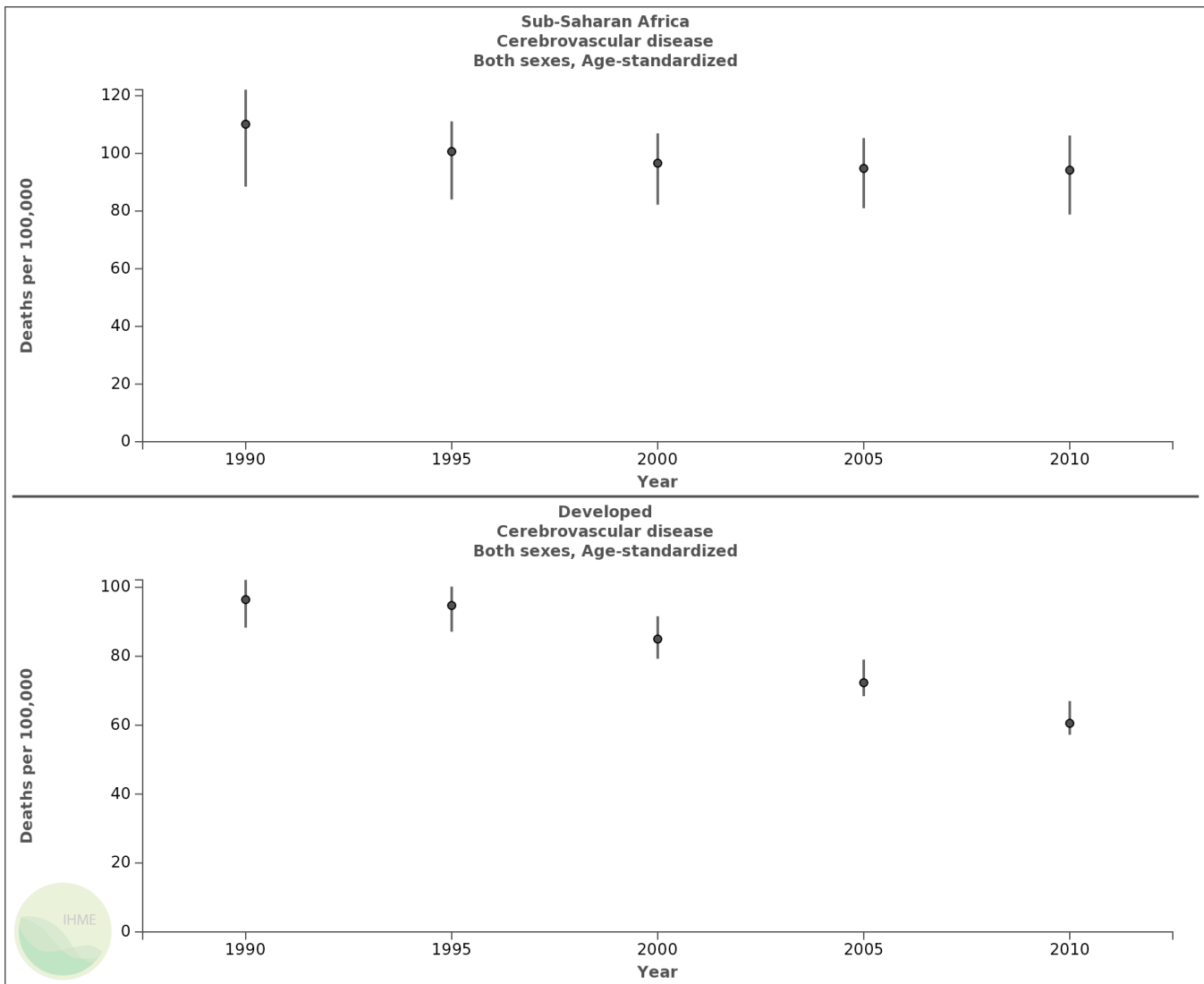
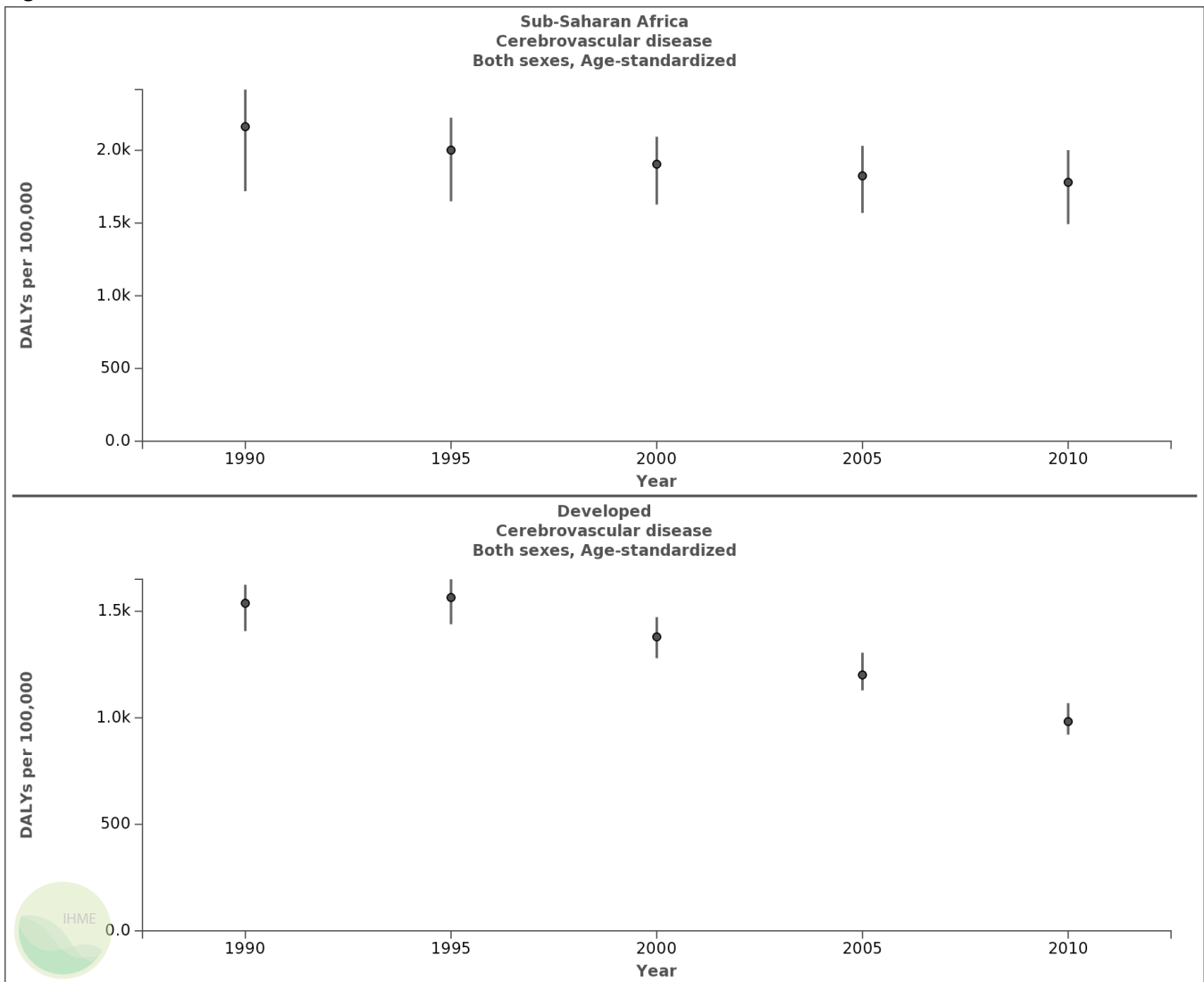


Figure 2.



17.

Possible genetic origins of the increased C-reactive protein levels in the black South African population

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Introduction: In Africa, it is estimated that cardiovascular disease (CVD) will affect approximately 1.3 million people per annum over the following 20 years. C-reactive protein (CRP) is a predictor of CVD risk and certain *CRP* gene polymorphisms can result in altered CRP concentrations. The distribution of *CRP* gene polymorphisms is ethnic-specific and extrapolating information from other populations to the black South African population, reported to harbour considerable genetic variation, should be avoided. This highlights the fact that genetic research among black South Africans is necessary.

Objectives: The main aim of this dissertation was to determine the association between various polymorphisms (reported and novel [single nucleotide polymorphisms (SNPs)]) within the *CRP* gene with CRP concentrations [measured as high sensitivity (hs)-CRP concentrations] in a black South African population undergoing an epidemiological transition. Interactions between specific *CRP* polymorphisms and certain environmental factors on hs-CRP concentrations were also investigated.

Methods: This cross-sectional study (n=1,588) was nested within the Prospective Urban and Rural Epidemiological (PURE) study. Genotyping was performed using Illumina VeraCode technology on the BeadXpress[®] platform. Hs-CRP concentrations were measured by the use of a sequential multiple analyser computer (SMAC) through a particle-enhanced immunoturbidometric assay.

Results: All the SNPs adhered to the assumptions of Hardy-Weinberg equilibrium, although the distribution of several SNPs differed from that reported in other population groups. Three SNPs (rs3093058, rs3093062 and rs3093068) were associated with a significant ($p \leq 0.05$) increase in CRP concentrations. Five SNPs (rs1205, rs1341665, rs2794520, rs7553007 and rs2027471) were associated with a significant ($p \leq 0.05$) decrease in CRP concentrations. This difference in effect was most probably due to changes in gene function brought about by the localisation of these SNPs in the *CRP* gene. Men and urban individuals were more likely to present with significant associations between the SNPs investigated and CRP concentrations. The difference in the prevalence of the alleles associated with higher CRP concentrations in this population compared to non-African populations could possibly explain the increased CRP concentrations that are observed in the black South African population. Gene-gender (rs1205, rs1341665 and rs2027474) as well as gene-environmental (rs3093068) interactions were also observed.

Conclusions: CRP concentrations are in themselves a complex trait and there are many factors at play that influence their expression. Numerous factors (both genetic and environmental) are involved and no single factor acting alone is likely to have enough of an influence to be used as a clinical diagnostic test of CRP concentrations. These results provide valuable information on the regulation of CRP in a black South African population as well as contribute to the literature of CRP on a global level.

Key words: cardiovascular disease; C-reactive protein; *CRP* polymorphisms; BeadXpress[®]; South African black population

18.

Title: Risk Factors for Chronic Kidney Disease in Relatives of patient with Chronic Kidney Disease.

Authors: Raji YR, Mabayoje MO, Bello BT.

First degree relatives (FDR) of patient with CKD have higher CKD risk. Studies have suggested clustering of risk factors for CKD among relatives of patient with CKD, none of these studies was in the Sub-Saharan African (SSA) population. The aim was to assess clustering of CKD risk factors among FDR of patient with CKD. We carried out a cross sectional survey of 230 FDR and 230 healthy controls at the Lagos University Teaching Hospital, Nigeria. Questionnaire was administered on all subjects, information regarding family member with CKD and demographic characteristics, chronic diseases, lifestyle and medications obtained. Anthropometric measurement and blood pressure were taken, urine and blood samples were collected for microalbuminuria, fasting plasma glucose, lipids, creatinine and uric acid. The study showed that hypertension 24.3%, diabetes mellitus (DM) 8.7%, overweight 31.7%, obesity 17.4%, dyslipidaemia 74.3%, hyperuricemia 5.7% and herbal use 50.9% were more prevalent in FDR. DM (OR, 3.6) and hyperuricemia (OR, 3.4) had the highest odds ratio while obesity (OR, 1.8) and dyslipidaemia (OR, 1.9) had the lowest odds ratio. CKD risk factors are more prevalent in the FDR of patient with CKD in the SSA population. This finding supports the need for screening FDR of patient with CKD for CKD risk factors, most of which are modifiable. Incorporating screening of relatives for CKD risk factors into the preventive health scheme will be a cost effective approach