



Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Neighborhood greenness and burden of non-communicable diseases in Sub-Saharan Africa: A multi-country cross-sectional study

Hari S. Iyer^{a,b,*}, Peter James^c, Linda Valeri^d, Francis Bajunirwe^e, Joan Nankya-Mutyoba^f, Marina Njelekela^{g,h,i}, Faraja Chiwanga^h, Vikash Sewram^j, IkeOluwapo Ajayi^k, Clement Adebamowo^{l,m}, Shona Dalal^b, Todd G. Reid^{n,o}, Timothy R. Rebbeck^{a,b}, Hans-Olov Adami^{b,p,q}, Michelle D. Holmes^{b,r}

^a Department of Medical Oncology, Dana-Farber Cancer Institute, Boston, USA

^b Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, USA

^c Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, USA

^d Department of Biostatistics, Columbia University Mailman School of Public Health, New York, USA

^e Department of Community Health, Mbarara University of Science and Technology, Mbarara, Uganda

^f Department of Epidemiology & Biostatistics, School of Public Health, Makerere University College of Health Sciences, Kampala, Uganda

^g Department of Physiology, Muhimbili University of Health and Allied Sciences, Dar Es Salaam, Tanzania

^h Department of Internal Medicine, Muhimbili National Hospital, Dar Es Salaam, Tanzania

ⁱ Deloitte Consulting Limited, Dar Es Salaam, Tanzania

^j African Cancer Institute, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

^k Department of Epidemiology and Medical Statistics, Faculty of Public Health, College of Medicine, University of Ibadan, Ibadan, Nigeria

^l Institute of Human Virology, Abuja, Nigeria

^m Greenebaum Comprehensive Cancer Center and Institute of Human Virology, University of Maryland School of Medicine, Baltimore, USA

ⁿ Media Lab and Connection Science, Massachusetts Institute of Technology, Boston, USA

^o Department of Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health, Boston, USA

^p Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden

^q Clinical Effectiveness Research Group, Institute of Health and Society, University of Oslo, Oslo, Norway

^r Channing Division of Network Medicine, Brigham & Women's Hospital, Harvard Medical School, Boston, USA

ARTICLE INFO

Keywords:

Non-communicable diseases
Greenness
Vegetation
Sub-saharan Africa
Obesity
Environmental epidemiology

ABSTRACT

Population growth, demographic transitions and urbanization in sub-Saharan Africa (SSA) will increase non-communicable disease (NCD) burden. We studied the association between neighborhood greenness and NCDs in a multi-country cross-sectional study. Among 1178 participants, in adjusted models, a 0.11 unit NDVI increase was associated with lower BMI (β : -1.01 , 95% CI: -1.35 , -0.67), and lower odds of overweight/obesity (aOR: 0.73 , 95% CI: 0.62 , 0.85), diabetes (aOR: 0.77 , 95% CI: 0.62 , 0.96), and having ≥ 3 allostatic load components compared to none (aOR: 0.66 , 95% CI: 0.52 , 0.85). Except for diabetes, these remained statistically significant after Bonferroni correction. We observed no association between NDVI and hypertension or cholesterol. Our findings are consistent with health benefits of neighborhood greenness reported in other countries, suggesting greening strategies could be considered as part of broader public health interventions for NCDs.

1. Introduction

Sub-Saharan Africa's (SSA) population is projected to increase from 1.05 billion in 2018 to 2.2 billion in 2050, resulting in an older, more urban population (UN Economic and Social Affairs 2018; Population Reference Bureau, 2018). Non-communicable disease (NCD) burden is

expected to rise alongside these demographic changes (Dalal et al., 2011; NCD Risk Factor Collaboration – Africa Working Group 2017; Jemal et al., 2012; Mensah et al., 2015). The Global Burden of Disease Study estimated a 67% increase in disability-adjusted life-years attributable to NCDs in SSA from 1990 to 2017, with burden of cancer (79.5%) and diabetes (83.1%) exhibiting the largest relative increases

* Corresponding author. Division of Population Sciences Dana-Farber Cancer Institute 450 Brookline Avenue, Boston, MA, 02215, USA.

E-mail address: Hari.Iyer@dfci.harvard.edu (H.S. Iyer).

<https://doi.org/10.1016/j.envres.2020.110397>

Received 29 March 2020; Received in revised form 15 October 2020; Accepted 23 October 2020

Available online 31 October 2020

0013-9351/© 2020 Elsevier Inc. All rights reserved.

over this period (Gouda et al., 2019). National health ministries in SSA are developing strategies to control NCDs by expanding medical services and promoting lifestyle changes (Farmer et al., 2013; Stefan et al., 2013; Binagwaho et al., 2014; Kwan et al., 2016; WHO 2018; Tapela et al., 2019). Increased investments in health care delivery are necessary to limit the spread of NCDs in SSA countries (Alwan et al., 2011). However, experience from other parts of the world suggests that in order to be effective, public health strategies for NCD control must consider socioeconomic and contextual factors, such as income, education, catastrophic health expenditures, availability of spaces for active transport, healthy diets, and incentives for promoting healthy lifestyles (Nugent et al., 2018). Analytic models that incorporate relationships between risk factors and underlying social and environmental context are therefore needed to accurately inform NCD prevention policy (Krieger 2011; Frumkin and Haines 2019).

Neighborhood greenness, or the natural green vegetation in a given area, is increasingly understood as an important health promoting contextual environmental factor. African scientists have called for more parks and street trees in cities, citing benefits including reductions of adverse health impacts of temperature and air pollution, as well as space for active transport (such as bicycling) and exercise (Cilliers et al., 2013; Ezeh 2016; Abernethy et al., 2016; Toit et al., 2018). Cohort studies in western countries have reported multiple health benefits of green spaces, including promotion of physical activity, lower risk of obesity and diabetes, improved mental health, enhanced social capital, and reduced all-cause and cardiovascular mortality (James et al. 2015, 2016; Crouse et al., 2017; Vienneau et al., 2017; Fong et al., 2018; Twohig-Bennett and Jones 2018; Bratman et al., 2019; Orioli et al., 2019; Rojas-Rueda et al., 2019; Iyer et al., 2020). Researchers have estimated the effects of nature visits on physiologic stress response, reporting reduced inflammation, enhanced glucose and cardiometabolic profile, and reduced sympathetic nervous system activation (Li et al., 2008; Park et al., 2010). Cross-sectional studies in the United States reported associations between neighborhood greenness and allostatic load, an index made up of biomarkers capturing physiologic response to cumulative biologic stress (McEwen 1998), and sympathetic stress response (Egorov et al., 2017; Yeager et al., 2018). While studies in SSA have assessed the association between neighborhood greenness and mental health (Tomita et al., 2017), little evidence exists regarding associations between neighborhood greenness and other NCDs.

We conducted a cross-sectional study using data from a multi-country sample of urban and rural community members in SSA to evaluate the association between neighborhood greenness and cardiometabolic NCDs. We hypothesized that neighborhood greenness would be associated with lower NCD prevalence, lower prevalence of lifestyle risk factors, and lower cardiometabolic allostatic load.

2. Materials and methods

2.1. Study setting and population

We used participant data from the Africa/Harvard Partnership for Cohort Research and Training (PaCT), launched in 2011 as a collaboration between the Harvard T. H. Chan School of Public Health (USA), Makerere University (Uganda), Mbarara University (Uganda), Muhimbili University (Tanzania), University of Ibadan (Nigeria), and Stellenbosch University (South Africa). For this study, we included participants from sites with available location data (Uganda, South Africa, Tanzania). In Uganda, participants were recruited from villages in peri-urban (Kampala) and rural (Mbarara) settings. In Tanzania and South Africa, occupational samples of teachers were recruited from cities (Dar Es Salaam, Tanzania and Cape Town, South Africa). Standardized, culturally-adapted questionnaires were administered to capture information on demographics, socioeconomic status, diet and lifestyle factors, medical history, and care seeking behaviors. Anthropometric data and blood measurements were taken by trained study staff. Participants

provided names of the village where they lived (Uganda sites) or school where they worked (Tanzania, South Africa sites). Full details regarding study procedures are described elsewhere (Dalal et al., 2015).

One of the investigators (HSI) collected geocodes for locations by entering names of villages and schools into Google Maps and extracting coordinates at the center of the village or school. Site investigators (FB, JNM, MN, VS) verified the accuracy of these coordinates and resolved discrepancies (10/81, 12%). Of 1215 participants, 3% ($n = 37$) were excluded due to missing geocodes resulting in a final sample of 1178.

2.2. Exposure

We estimated exposure to neighborhood greenness at participant locations using the Normalized Difference Vegetation Index (NDVI), a satellite-derived measure of natural green vegetation (Kriegler et al., 1969). NDVI is calculated by taking the difference of near infrared light (reflected by leaves) and visible red light (absorbed), and dividing by the sum of these measures. Values range from -1 to $+1$, with values below 0 reflecting bodies of water. NDVI was obtained from the Moderate Resolution Imaging Spectroradiometer (MODIS) with resolution of 250 m. We extracted the NDVI value for the area that included the participant's school (Tanzania, South Africa) or village (Uganda) geocodes, and collected four (January, April, July, September) images each year from 2010 to 2011, to account for seasonal changes in NDVI at these locations. Google Earth Engine was used to extract images and select the least cloudy image in each month (Mutanga & Kumar 2019). In order to capture recent exposure and account for seasonal differences in NDVI, we averaged over the eight seasonal measures at each location. We were able to assign geocodes to schools with greater precision than for villages. We therefore conducted sensitivity analyses using zonal statistics to assign mean NDVI to village locations using polygon boundaries rather than points. Use of this metric did not change our conclusions, and so we used a point-based approach to assign NDVI for consistency across villages and schools.

2.3. Outcomes

We studied the association between neighborhood greenness and the prevalence of multiple NCD endpoints including specific diseases (diabetes, hypertension), overweight/obesity ($\text{BMI} > 25 \text{ kg/m}^2$), and cardiometabolic profile (allostatic load, total cholesterol). Whenever possible, we relied on measurements taken by trained study staff. However, because access to NCD services varied across sites and prior disease status could affect measurements taken during the study, we also included information about prior history of diagnosis and treatment to define outcomes.

Diabetes was reported on questionnaires by participants and, when available, estimated based on blood glucose measures taken during the study. Participants were classified as diabetic if they reported history of diabetes (62/139, 45%), or if they reported a fasting glucose level $\geq 7 \text{ mmol/l}$ (77/139, 55%) (Chiwanga et al., 2016). Hypertension was reported on questionnaires, and, when available, confirmed by blood pressure measurements. We used World Health Organization (WHO) classifications for hypertension as follows: Hypertensive (SBP: 140 mm Hg and/or DBP: 90 mm Hg based on blood pressure measurement (297/448, 66%), self-reported being on regular anti-hypertensive therapy (94/448, 21%), or self-reported history of hypertension (57/448, 13%)) (Guwatudde et al., 2015). We modeled obesity using the body mass index (BMI) as a continuous scale, and using WHO classification (under-weight: $\text{BMI} < 18.5 \text{ kg/m}^2$; normal weight: BMI in $18.5\text{--}24.9 \text{ kg/m}^2$; overweight: BMI in $25\text{--}29.9 \text{ kg/m}^2$; obese: 30 kg/m^2 and over). We also dichotomized BMI categories into overweight/obese vs normal/under-weight. Total cholesterol was ascertained by trained nurses who visited schools to collect blood samples at pre-specified times, while in villages, trained staff conducted blood draws in the community (Dalal et al., 2015). Cholesterol was modeled as a

continuous variable, and dichotomized, defining high cholesterol as any value above 6.22 mmol/L based on clinical guidelines used in 2011 (Craig et al., 2000).

We developed a minimal allostatic load score to assess the association between NDVI and chronic stress in this population focusing on metabolic measures available in our data. We adapted the full allostatic load measure developed by Seeman et al. which incorporated ten components reflecting multiple homeostatic regulatory systems (Seeman et al., 1997). Our score was comprised of a subset of four variables: systolic blood pressure, diastolic blood pressure, blood glucose (on the natural logarithm scale), and body mass index (as a proxy for waist-to-hip ratio). We used this abridged score because it was consistent with cardiovascular contributions to allostatic load used elsewhere, and because other individual components were missing for entire sites (McEwen 1998; Seeman et al., 1997). To calculate the allostatic load score, we first created quartiles for each of the components, and then assigned a score of 1 if the component was in the highest quartile and 0 otherwise (Seeman et al., 1997). Allostatic load was then calculated using the sum of component scores, ranging from 0 to 4, with four being the least healthy. Individuals with three or more components were grouped together due to few participants with four allostatic load components ($n = 17$), yielding a four-level categorical variable (0, 1, 2 or ≥ 3 components).

2.4. Ethics

Written informed consent from each participant was provided through a signed form along with mailed completed questionnaire (South Africa, Tanzania) or during enrollment interviews with study staff (Uganda). This study was approved by the Harvard T. H. Chan School of Public Health Institutional Review Board; the Health Research Ethics Committee of the Faculty of Medicine and Health Sciences, Stellenbosch University; Makerere University School of Public Health Higher Degrees Research and Ethics Committee; National Institute for Medical Research, Tanzania; Mbarara University of Science and Technology Research Ethics Committee; and the Uganda National Council of Science and Technology.

2.5. Statistical analysis

Since 369 participants (31%) were missing values for at least one outcome or covariate, we used multiple imputation with chained equations to fit models for missingness, assuming data were missing at random (Rubin 1987). To multiply impute missing continuous covariates (age, BMI, systolic blood pressure, diastolic blood pressure, blood glucose level) we used linear regression, and for missing categorical and binary covariates (private health care seeking, piped vs other water source, overweight/obesity, allostatic load category) we used the discriminant function. We used the following covariates as predictors of missingness: age, sex, marital status, educational attainment, cooking fuel type, NDVI, smoking status, and site. These variables were chosen based on examination of missingness patterns in the data and strength of correlations between these predictors and variables with missing values. For models estimating the association between NDVI and cholesterol, we excluded the peri-urban Uganda site because no cholesterol measurements were taken. Using these models, we imputed values for covariates with missing data to generate 10 datasets.

Next, we fit multiple linear regression models for continuous outcomes (BMI, cholesterol) and logistic regression models for binary outcomes (obese/overweight, diabetes, hypertension, high cholesterol). Models for categorical allostatic load were fit using multiple multinomial logistic regression. NDVI was modeled as a continuous exposure, and effect estimates correspond to a 0.11 unit increase in NDVI (0.58 standard deviation) to facilitate comparisons with previous studies. We tested for linearity between NDVI and each outcome using quadratic terms. Models were sequentially adjusted for (1) age at interview

(continuous), sex; (2) educational attainment (primary school or lower vs other), cooking fuel source (electric or gas vs other), marital status (married/cohabiting vs other), smoking status (current smoker or not), site (Uganda/rural, Uganda/peri-urban, Tanzania/urban, South Africa/urban), care sought in private sector (binary). Covariates were selected based on previous studies by PaCT investigators (Guwatudde et al., 2015; Chiwanga et al., 2016; Ajayi et al., 2016; Laurence et al., 2016) and literature on common causes of NDVI and NCDs (James et al., 2015; Fong et al., 2018; Twohig-Bennett and Jones 2018). Since these models were fit in imputed datasets, standard errors were estimated using Rubin's Rules (Rubin 1987). We provided results from a complete case analysis as a sensitivity analysis. As an additional sensitivity analysis, we restricted the analysis to urban sites only (excluding the rural Uganda site).

In addition, we explored the role of BMI as a mediator of the association between NDVI and NCD outcomes. Following methods described by Valeri and VanderWeele (Valeri and VanderWeele 2013), we fit regression models adjusting for the full set of covariates above, and tested for interaction between NDVI and BMI at the $\alpha = 0.05$ level. If interactions were present, we presented estimates for the NDVI-outcome association at three levels of BMI (20, 25, 30). For binary outcomes, we replaced the logistic model with a log-linear model with Poisson distribution to model prevalence ratios. Log-linear models were used because risk ratio estimates from these models can be directly compared in models with and without the mediator, a property not shared by odds ratios obtained using logistic regression (Valeri and VanderWeele 2013).

Since we studied the association between NDVI and multiple outcomes, we used VanderWeele's Outcome-wide Epidemiology approach (VanderWeele 2017). This approach facilitates comparisons between multiple exposure-outcome associations simultaneously. We report E-values as a sensitivity analysis to quantify the minimum unmeasured confounding bias required to explain away our findings (VanderWeele and Ding 2017). The E-value for a point estimate corresponds to the minimum bias, conditional on covariates, necessary to attenuate the point estimate to the null value of 1. Confidence interval E-value quantifies the bias required to shift the confidence interval to include 1. To limit type 1 error, we applied a Bonferroni correction to all significance tests for association between NDVI and NCD outcomes in fully adjusted outcome models performed (7 tests in total population, 5 tests in urban sites only, for a total of 12 tests). This correction resulted in an alpha type 1 error cutoff of 0.0042. All analyses were done using SAS version 9.4. Detailed formulae for each of the regression models are provided in the supplementary appendix (Supplementary Appendix A).

3. Results

After exclusions, 1178 participants were included in the study, with 275 (23%) from Peri-urban Uganda, 200 (17%) from rural Uganda, 477 (40%) from South Africa, and 226 (19%) from Tanzania. The NDVI distribution varied by site, with Tanzania and South Africa exhibiting lower levels of NDVI than the Uganda sites (Table 1). Higher levels of NDVI were associated with lower median age (NDVI Q5: 36, NDVI Q1: 46.7), lower proportion reporting female gender (NDVI Q5: 51%, NDVI Q1: 81%), and lower educational attainment (NDVI Q5: 82% with primary school or lower, NDVI Q1: 3%). We observed high reported prevalence of overweight (31%) and obesity (33%) in the total study population. Prevalence of diabetes was 12%, and prevalence of hypertension was 38%. In analysis excluding the peri-urban Uganda site, the prevalence of high cholesterol was 14%.

Results of our outcome-wide regression analysis using multiple imputation are presented in Table 2. In fully adjusted models, a 0.11 unit increase in NDVI was associated with a 1.01 unit decrease in BMI ($\beta: -1.01$, 95% CI: $-1.35, -0.67$). Similarly, in fully adjusted models, we observed 27% lower odds of overweight/obesity associated with a 0.11 unit increase in NDVI (aOR: 0.73, 95% CI: 0.62, 0.85) in the total study population. Both were statistically significant after applying the

Table 1
Descriptive characteristics of study participants from four sites in three Sub-Saharan African countries.

	Normalized Difference Vegetation Index (NDVI)					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
No.	233	229	245	240	231	1178
Age ^a	46.7 [40.7, 52.3]	44.2 [37.1, 51.4]	43.4 [34.29, 51.14]	33.2 [26, 47.42]	36.1 [27.2, 42.94]	41.9 [32.6, 50.32]
Female	189 (81.1)	178 (77.7)	160 (65.3)	125 (52.1)	117 (50.7)	769 (65.3)
BMI ^a	30.1 [26.8, 34.8]	29.9 [25.7, 33.2]	27.6 [23.7, 32.3]	24.1 [21.7, 28.6]	24.2 [21.8, 27.3]	27.1 [23.3, 31.4]
Ever Smoke	27 (11.6)	20 (8.7)	26 (10.6)	28 (11.7)	28 (12.1)	129 (11)
Systolic Blood Pressure (mm/Hg) ^a	133.8 [124, 145.5]	130 [120, 145]	124.3 [116, 137]	123.5 [114, 133.5]	118.8 [109.5, 125]	125 [115.5, 138.5]
Diastolic Blood Pressure (mm/Hg) ^a	79.3 [73, 87.5]	80 [74.5, 90]	80 [70, 87]	75.5 [68.5, 82.5]	77.3 [70.5, 82.5]	79 [70.5, 85.5]
Blood glucose ^a	5.2 [4.6, 5.8]	4.8 [4.4, 5.5]	5.2 [4.5, 5.8]	5.1 [4.5, 5.7]	5.7 [5.1, 6.4]	5.2 [4.6, 5.8]
NDVI (two-year seasonal average) ^a	0.23 [0.23, 0.24]	0.31 [0.29, 0.33]	0.40 [0.37, 0.41]	0.61 [0.54, 0.67]	0.73 [0.72, 0.75]	0.40 [0.29, 0.67]
Site						
Kampala, Uganda (peri-urban)	.	.	89 (36.3)	169 (70.4)	17 (7.4)	275 (23.3)
Mbarara, Uganda (rural)	200 (86.6)	200 (17)
Cape Town, South Africa (urban)	195 (83.7)	119 (52)	93 (38)	70 (29.2)	.	477 (40.5)
Dar Es Salaam, Tanzania (urban)	38 (16.3)	110 (48)	63 (25.7)	1 (0.4)	14 (6.1)	226 (19.2)
Primary School Education or Lower	6 (2.6)	14 (6.1)	38 (15.5)	63 (26.3)	190 (82.3)	311 (26.4)
Currently Married/Cohabiting	160 (68.7)	159 (69.4)	163 (66.5)	162 (67.5)	190 (82.3)	834 (70.8)
Fuel (not electricity, natural gas, biogas)	39 (16.7)	111 (48.5)	149 (60.8)	165 (68.8)	231 (100)	695 (59)
Piped drinking water	193 (82.8)	136 (59.4)	122 (49.8)	136 (56.7)	5 (2.2)	592 (50.3)
Seek health care at private facility						
Yes	181 (77.7)	195 (85.2)	143 (58.4)	117 (48.8)	77 (33.3)	713 (60.5)
No	52 (22.3)	34 (14.9)	98 (40)	122 (50.8)	153 (66.2)	459 (39.0)
(Missing)	.	.	4 (1.6)	1 (0.4)	1 (0.4)	6 (0.5)
Have you ever been told by a doctor or other health worker that you have DM?						
Yes	24 (10.3)	23 (10.0)	21 (8.6)	6 (2.5)	2 (0.9)	76 (6.5)
No	162 (69.5)	171 (74.7)	198 (80.8)	225 (93.8)	228 (98.7)	984 (83.5)
(Missing)	47 (20.2)	35 (15.3)	26 (10.6)	9 (3.8)	1 (0.4)	118 (10)
Family member with diabetes						
Yes	105 (45.1)	87 (38.0)	85 (34.7)	63 (26.3)	28 (12.1)	368 (31.2)
No	111 (47.6)	131 (57.2)	152 (62.0)	174 (72.5)	202 (87.5)	770 (65.4)
(Missing)	17 (7.3)	11 (4.8)	8 (3.3)	3 (1.3)	1 (0.4)	40 (3.4)
Have you ever been told by a doctor or other health worker that you have HPT?						
Yes	75 (32.2)	78 (34.1)	57 (23.3)	23 (9.6)	14 (6.1)	247 (21.0)
No	145 (62.2)	140 (61.1)	174 (71.0)	209 (87.1)	177 (93.9)	885 (75.1)
(Missing)	13 (5.6)	11 (4.8)	14 (5.7)	8 (3.3)	.	46 (3.9)
Family member with hypertension						
Yes	137 (58.8)	118 (51.5)	122 (49.8)	118 (49.2)	66 (28.6)	561 (47.6)
No	84 (36.1)	99 (43.2)	116 (47.4)	120 (50.0)	164 (71.0)	583 (49.5)
(Missing)	12 (5.2)	12 (5.2)	7 (2.9)	2 (0.8)	1 (0.4)	34 (2.9)

^a Median [Interquartile Range].

Bonferroni correction. In fully adjusted models, a 0.11 unit increase in NDVI was associated with a 23% lower odds of prevalence of diabetes in the total study population (aOR: 0.77, 95% CI: 0.62, 0.96), but this association was not statistically significant after correcting for multiple testing. We did not observe statistically significant associations between NDVI and prevalence of hypertension, or between NDVI and cholesterol (continuous or dichotomous outcome) after adjustment for covariates. In fully adjusted multinomial regression models for allostatic load a 0.11 unit increase NDVI was associated with 34% lower odds of having 3 or more allostatic load components (worst) compared to none (best) (aOR: 0.66, 95% CI: 0.52, 0.85), and 33% lower odds of having 2 allostatic load components compared to none (aOR: 0.67, 95% CI: 0.52, 0.85). This association was statistically significant after correction for multiple testing. The magnitude and direction of reported associations were similar when restricting to urban populations only.

Table 3 presents results from our exploratory mediation analysis. Further adjustment for BMI attenuated the association between NDVI and diabetes prevalence towards the null (aPR: 0.87, 95% CI: 0.71, 1.06). In models for hypertension, we found a significant interaction between NDVI and BMI ($P_{het} = 0.019$), so we estimated prevalence ratios at different levels of BMI. Results suggest that a joint hypothetical intervention to increase NDVI while fixing BMI of all participants to 20 would be associated with a 13% reduced prevalence of hypertension (aPR: 0.87, 95% CI: 0.77, 0.98). However, fixing BMI to levels above 20 would attenuate the association between NDVI and hypertension prevalence.

In complete case analyses, associations between NDVI and NCD outcomes remained largely unchanged (Table B1). There were however a few differences: a 0.11 unit increase in NDVI was associated with 20% lower odds of hypertension (aOR: 0.80, 95% CI: 0.68, 0.93), remaining statistically significant after multiple testing in urban sites only. Associations between NDVI and allostatic load in complete case analysis were of similar magnitude but not statistically significant following Bonferroni correction for multiple testing.

E-values for point estimates and 95% confidence intervals are reported in Table B2. Estimates for BMI, overweight/obesity, and allostatic load would require moderate amounts of unmeasured confounding bias to attenuate point estimates to the null or shift confidence intervals to contain 1 (point estimates range: 1.59–1.76, confidence intervals range: 1.39–1.44). An omitted variable would have to be associated with a 59%–76% increased relative risk or prevalence comparing exposed to unexposed, conditional on covariates, to attenuate point estimates to the null. E-values for estimates and confidence intervals did not change following restriction to urban sites.

4. Discussion

In this multi-country sample of urban and rural study participants in SSA, we observed statistically significant inverse associations between NDVI and a number of NCDs and risk factors. Participants in locations with higher NDVI had lower BMI and lower allostatic load based on cardiovascular components. Though we observed an inverse association

Table 2

Cross-sectional associations between Normalized Difference Vegetation Index (0.11 unit increase) and components of allostatic load using multiple imputation^a among participants from four sites in three Sub-Saharan African countries.

Outcome	Total Population (N = 1178)			Urban Population (N = 978)		
	β (95% CI)	OR (95% CI)	p	β (95% CI)	OR (95% CI)	p
BMI (continuous)						
Unadjusted	-1.65 (-1.84, -1.45)		<.0001	-1.87 (-2.17, -1.58)		<.0001
Age + Sex	-1.38 (-1.58, -1.17)		<.0001	-1.52 (-1.84, -1.21)		<.0001
Full Adjustment ^b	-1.01 (-1.35, -0.67)		<.0001 ^d	-0.97 (-1.37, -0.57)		<.0001 ^d
Overweight/Obese						
Unadjusted		0.57 (0.53, 0.62)	<.0001		0.52 (0.46, 0.58)	<.0001
Age + Sex		0.64 (0.58, 0.70)	<.0001		0.60 (0.53, 0.68)	<.0001
Full Adjustment ^b		0.73 (0.62, 0.85)	<.0001 ^d		0.73 (0.63, 0.85)	<.0001 ^d
Diabetes						
Unadjusted		0.87 (0.79, 0.97)	0.0153		0.74 (0.63, 0.87)	0.0003
Age + Sex		0.93 (0.83, 1.05)	0.2381		0.76 (0.64, 0.91)	0.0032
Full Adjustment ^b		0.77 (0.62, 0.96)	0.0193		0.77 (0.62, 0.95)	0.0167
Hypertension						
Unadjusted		0.68 (0.63, 0.74)	<.0001		0.75 (0.68, 0.82)	<.0001
Age + Sex		0.76 (0.70, 0.82)	<.0001		0.84 (0.75, 0.94)	0.0017
Full Adjustment ^b		0.92 (0.80, 1.05)	0.1996		0.91 (0.79, 1.04)	0.1531
Cholesterol (continuous)^c						
Unadjusted	-0.24 (-0.30, -0.18)		<.0001			
Age + Sex	-0.17 (-0.23, -0.11)		<.0001			
Full Adjustment ^b	0.04 (-0.07, 0.14)		0.4875			
Cholesterol (binary)^c						
Unadjusted		0.99 (0.90, 1.11)	0.9252			
Age + Sex		1.07 (0.95, 1.20)	0.2626			
Full Adjustment ^b		1.15 (0.93, 1.42)	0.2093			
Allostatic Load						
Unadjusted						
0 (Low)						
1		0.86 (0.79, 0.94)	0.0016		0.80 (0.71, 0.91)	0.0005
2		0.66 (0.58, 0.75)	<.0001		0.60 (0.50, 0.70)	<.0001
≥3 (High)		0.61 (0.52, 0.70)	<.0001		0.58 (0.48, 0.69)	<.0001
Age + Sex						
0 (Low)		Ref				
1		0.94 (0.86, 1.04)	0.1376		0.90 (0.78, 1.03)	0.1376
2		0.74 (0.65, 0.84)	<.0001		0.66 (0.55, 0.79)	<.0001
≥3 (High)		0.69 (0.59, 0.81)	<.0001		0.66 (0.54, 0.8)	<.0001
Full Adjustment ^b						
0 (Low)		Ref				
1		0.87 (0.74, 1.02)	0.1702		0.88 (0.74, 1.05)	0.1702
2		0.67 (0.52, 0.85)	0.0004 ^d		0.65 (0.51, 0.82)	0.0004 ^d
≥3 (High)		0.66 (0.52, 0.85)	0.0014 ^d		0.67 (0.52, 0.85)	0.0014 ^d

^a Imputation models were fit using multiple chained equations to impute missing data for body mass index and the following covariates: age, sex, educational attainment, fuel source, marital status, NDVI, smoking status, site.

^b Multiple regression models were fit for categorical (multinomial logistic), binary (logistic) or continuous (linear) outcome variables, using the following covariates: age, sex, educational attainment, fuel source, marital status, smoking status, site, seeking health care in private sector.

^c Since cholesterol was missing for one site (peri-urban Uganda), these models were fit only on remaining sites (Tanzania, South Africa, and Rural Uganda) with a sample size of 903.

^d $p < 0.05$ after Bonferroni correction applied to final fully adjusted outcome models (the p-value cutoff for Bonferroni correction = $0.05/12$ outcomes = 0.0042).

Table 3

Cross-sectional associations between Normalized Difference Vegetation Index (0.11 unit increase) and non-communicable disease prevalence using log-linear models using multiple imputation^a to evaluate mediation by body mass index among participants from four sites in three Sub-Saharan African countries.

Outcome	Total Population (N = 1178)			Urban Population (N = 978)		
	β (95% CI)	aPR (95% CI)	<i>p</i>	β (95% CI)	aPR (95% CI)	<i>p</i>
Diabetes						
Full Adjustment		0.80 (0.65, 0.98)	0.030		0.80 (0.65, 0.97)	0.026
Full + BMI ^b		0.87 (0.71, 1.06)	0.17		0.86 (0.71, 1.06)	0.16
Hypertension						
Full Adjustment		0.95 (0.86, 1.05)	0.32		0.95 (0.86, 1.04)	0.27
Full + BMI ^b		0.98 (0.89, 1.09)	0.75		0.98 (0.88, 1.08)	0.64
BMI: 20 ^c		0.87 (0.77, 0.98)	0.025		0.87 (0.77, 0.99)	0.029
BMI: 25 ^c		0.93 (0.85, 1.01)	0.10		0.93 (0.85, 1.01)	0.088
BMI: 30 ^c		0.99 (0.92, 1.07)	0.83		0.99 (0.92, 1.06)	0.71
Cholesterol (continuous)						
Full Adjustment	0.04 (−0.07, 0.14)		0.49			
Full + BMI ^b	0.02 (−0.08, 0.13)		0.66			
Cholesterol (binary)						
Full Adjustment		1.11 (0.92, 1.34)	0.28			
Full + BMI ^b		1.09 (0.90, 1.32)	0.37			

Abbreviations Normalized Difference Vegetation Index (NDVI), Body Mass Index (BMI), PR (prevalence ratio).

^a Imputation models were fit using multiple chained equations to impute missing data for BMI and the following covariates: age, sex, educational attainment, fuel source, marital status, NDVI, smoking status, site.

^b Multiple log-linear regression models were fit for the outcome, using the following covariates: age, sex, educational attainment, fuel source, marital status, smoking status, site, seeking health care in private sector, BMI.

^c Multiple log-linear regression models were fit for prevalence of hypertension, using the following covariates: age, sex, educational attainment, fuel source, marital status, smoking status, site, seeking health care in private sector, interaction between BMI and NDVI ($P_{het} = 0.019$ for Total Population, $P_{het} = 0.042$ for Urban Population).

between NDVI and prevalence of diabetes, this finding was not statistically significant after accounting for multiple testing. The strength of associations between NDVI and NCDs were attenuated following adjustment for BMI, suggesting that BMI could play an explanatory role, though this cannot be confirmed in our cross-sectional study. Restricting analyses to urban sites alone did not change our inference.

Our results are largely in agreement from studies of neighborhood greenness, BMI and diabetes conducted in other parts of the world. Following results from a large cross-sectional study in Australia (Astell-Burt et al., 2014), several authors have reported an association between NDVI and lower odds of diabetes. A recent meta-analysis summarizing evidence across multiple studies investigating health effects of exposure to green spaces estimated higher greenness exposure was associated with 28% lower odds of type II diabetes (aOR: 0.72, 95% CI: 0.61, 0.85) (Twohigg-Benett and Jones 2018). In addition, others have previously reported inverse associations between NDVI and BMI (James et al., 2015; Villeneuve et al., 2018). Studies in Europe and China have reported inverse associations between NDVI and glucose levels in children and adults, consistent with our findings (Tamosiunas et al., 2014; Thiering et al., 2016; Yang et al., 2019a,b).

We did not observe statistically significant associations between NDVI and hypertension or cholesterol. While studies from high income countries consistently report increased levels of neighborhood greenness are associated with lower cardiovascular disease (Wang et al., 2019), evidence of the relationship between neighborhood greenness, blood pressure and hypertension is mixed (Brown et al., 2016; Twohigg-Benett and Jones 2018). Studies in Korea and China reported lower levels of lipidemia associated with increasing neighborhood greenness (Kim et al., 2016; Yang et al., 2019a,b), while a study among 10–15 year old children in Lithuania using NDVI as greenness exposure found no association (Markevych et al., 2016). Another cross-sectional study in China reported associations between neighborhood greenness and lower hypertension prevalence, but did not control for income (Jia et al., 2018). While we did not observe an association between NDVI and total cholesterol, others have reported inverse associations between NDVI and high-density lipoprotein cholesterol (Egorov et al., 2017) and high overall levels of cholesterol (Plans et al., 2019). Future studies employing prospective designs, that take advantage of recent developments in wireless technologies and mobile phone based

applications to measure the environment and behaviors, could clarify the relationship between NDVI, hypertension, and cholesterol in SSA.

Our exploratory mediation analysis suggests that BMI, a modifiable lifestyle risk factor, could explain the inverse associations between neighborhood greenness and cardiometabolic risk factors in this African population. An important omitted variable in this analysis is physical activity, which we were unable to evaluate due to site-level differences in physical activity assessment. Rural populations in SSA experience much higher levels of physical activity compared to urban populations due to differences in occupation (agricultural work vs office work) and modes of travel (biking or walking vs motorized transport) (Guwatudde et al., 2016; Mashili et al., 2018). In our study, physical activity would be expected to be associated with both NDVI and cardiometabolic risk and therefore could have led to confounding in our primary analysis and mediation analysis. The fact that associations between NDVI and NCDs in our study did not change when restricting to urban populations suggests that differences in unmeasured physical activity between sites cannot completely explain our findings. It is possible that the association between neighborhood greenness and physical activity is weaker in an African population, and varies based on geography. Cross-sectional studies in Europe and New Zealand evaluating the role of physical activity as a mediator of the effect of neighborhood greenness on cardiovascular disease and mortality generally have found little explanatory power (Richardson et al., 2013; Lachowycz and Jones 2014). A Chinese study reported strong inverse associations between neighborhood greenness and physical activity, but did not control for income, an important confounder (Jia et al., 2018). Longitudinal designs incorporating precise physical activity measurements could improve assessment of this modifiable pathway through which neighborhood greenness could influence cardiometabolic health in African and other settings.

Additional limitations of our study include its cross-sectional design which hampers causal inference. Our study further relied on discrete, spatially diffuse locations, assuming that these locations (villages and schools) would be sufficient to capture relevant exposure to neighborhood greenness. If such exposure occurs outside these locations, we could introduce non-differential exposure measurement error. For diabetes and hypertension, self-reports could have led to outcome misclassification. Higher NCD detection in urban compared to rural areas is possible, and since urban areas had lower NDVI, failure to

account for this relationship could have resulted in residual bias. Control for factors associated with urbanicity, NDVI and NCDs, and our sensitivity analysis restricting to urban sites should mitigate this bias. While NDVI is an objective measure of neighborhood greenness, it does not capture specific types of vegetation that could drive the associations, which would be needed to develop interventions. Study participants represent a unique mix of urban vs rural, as well as occupational-vs population-based samples, which limits the overall generalizability of these findings because population characteristics may vary in other African settings. Future studies should explore more detailed residential histories and assess movement patterns at the individual-rather than area-level.

5. Conclusions

We found that higher levels of neighborhood greenness are associated with lower BMI, overweight/obesity, and lower cardiometabolic allostatic load in a multi-country study of participants from South Africa, Tanzania and Uganda, supporting evidence from other countries. There was no association between neighborhood greenness and hypertension or cholesterol. Excluding rural participants did not change study findings. Studies with prospective follow-up and more detailed measurement of contextual environmental exposure are needed to strengthen evidence for these associations. Given growing interest in green infrastructure and urban planning for public health in SSA, confirmation could help inform evidence-based urban public health interventions to control NCD burden in SSA.

Credit statement

Hari S. Iyer: Conceptualization, Data Curation, Software, Formal Analysis, Writing – Original draft preparation, Writing – Reviewing and Editing. **Peter James:** Conceptualization, Methodology, Software, Writing – Review and Editing. **Linda Valeri:** Conceptualization, Methodology, Formal analysis, Writing – Review & Editing. **Francis Bajunirwe:** Resources, Project administration, Data Curation, Writing – Review & Editing. **Joan Nankya-Mutyoba:** Resources, Project administration, Data Curation, Writing – Review & Editing. **Marina Njelekela:** Resources, Project administration, Data Curation, Writing – Review & Editing. **Faraja Chiwanga:** Project administration, Data Curation, Writing – Review & Editing. **Vikash Sewram:** Resources, Project administration, Data Curation, Writing – Review & Editing. **IkeOluwapo Ajayi:** Resources, Project administration, Data Curation, Writing – Review & Editing. **Clement Adebamowo:** Writing – Review & Editing. **Shona Dalal:** Writing – Review & Editing. **Todd G. Reid:** Writing – Review & Editing. **Timothy R. Rebbeck:** Conceptualization, Resources, Methodology, Supervision. **Hans-Olov Adami:** Funding Acquisition, Writing – Review & Editing. **Michelle D. Holmes:** Funding Acquisition, Methodology, Supervision.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Holmes declares receipt of aspirin for trial NCT 02927249 from Bayer AG, consulting for Arla Foods, United States Social Security Administration, VISIONS Inc., and service on Cambridge Savings Bank's advisory board. The remaining authors declare they have no actual or potential competing financial interests.

Acknowledgements

We are grateful to the participants in Uganda, Tanzania and South Africa who contributed data to the Africa/Harvard Partnership for Cohort Research and Training study. We thank Jeffrey C. Blossom at the Harvard Center for Geographic Analysis for providing technical support

with Geographic Information Systems for this analysis. This work was funded through grants from the Dean's office and Department of Nutrition of the Harvard T. H. Chan School of Public Health, and Karolinska Institutet Distinguished Professor Award (grant no. Dnr: 2368/10–221). Hari Iyer was supported in part by the National Institutes of Health research training grant (NIH, T32 CA 009001) and the Harvey Fineberg Fellowship in Cancer Prevention. Dr. Peter James was supported in part by NCI (R00 CA201542). Dr. Timothy Rebbeck was supported in part by NCI (U01 CA184734). Dr. Clement Adebamowo received funding from the Office Of The Director, National Institutes of Health (OD) (U54HG006947) and the National Human Genome Research Institute (NHGRI); and funds through the Maryland Department of Health's Cigarette Restitution Fund Program.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envres.2020.110397>.

Funding

This work was funded through grants from the Dean's office and Department of Nutrition of the Harvard T. H. Chan School of Public Health, and Karolinska Institutet Distinguished Professor Award (grant no. Dnr: 2368/10–221). Hari Iyer was supported in part by the National Institutes of Health research training grant (NIH, T32 CA 009001) and the Harvey Fineberg Fellowship in Cancer Prevention. Dr. Peter James was supported in part by NCI (R00 CA201542). Dr. Timothy Rebbeck was supported in part by NCI (U01 CA184734). Dr. Clement Adebamowo received funding from the Office Of The Director, National Institutes Of Health (OD) (U54HG006947) and the National Human Genome Research Institute (NHGRI); and funds through the Maryland Department of Health's Cigarette Restitution Fund Program. Dr. Holmes declares receipt of aspirin for trial NCT 02927249 from Bayer AG, consulting for Arla Foods, United States Social Security Administration, VISIONS Inc., and service on Cambridge Savings Bank's advisory board. The remaining authors declare they have no actual or potential competing financial interests.

References

- Abernethy, K., Maisels, F., White, L.T.J., 2016. Environmental issues in central Africa. *Annu. Rev. Environ. Resour.* 41, 1–33.
- Ajayi, I.O., Adebamowo, C., Adami, H.O., et al., 2016. Urban-rural and geographic differences in overweight and obesity in four sub-Saharan African adult population: a multi-country cross-sectional study. *BMC Publ. Health* 16 (1), 1126.
- Alwan, A., Evans, D., Edejer, T.T., et al., 2011. Scaling up Action against Noncommunicable Diseases: How Much Will it Cost? World Health Organization, Geneva.
- Astell-Burt, T., Feng, X., Kolt, G.S., 2014. Is neighborhood green space associated with a lower risk of type 2 diabetes? Evidence from 267,072 Australians. *Diabetes Care* 37, 197–201.
- Binagwaho, A., Muhimpundu, M.A., Bukhman, G., 2014. 80 under 40 by 2020: an equity agenda for NCDs and injuries. *Lancet* 383 (9911), 3–4.
- Bratman, G.N., Anderson, C.B., Berman, M.G., Cochran, B., de Vries, S., Flanders, J., et al., 2019. Nature and mental health: an ecosystem service perspective. *Sci. Adv.* 5 (7), eaax0903.
- Brown, S.C., Lombard, J., Wang, K., et al., 2016. Neighborhood greenness and chronic health conditions in medicare beneficiaries. *Am. J. Prev. Med.* 51 (1), 78–89.
- Chiwanga, F.S., Njelekela, M.A., Diamond, M.B., et al., 2016. Urban and rural prevalence of diabetes and pre-diabetes and risk factors associated with diabetes in Tanzania and Uganda. *Glob. Health Action* 9, 31440.
- Cilliers, S., Cilliers, J., Lubbe, R., Siebert, S., 2013. Ecosystem services of urban green spaces in African countries-perspectives and challenges. *Urban Ecosyst.* 16, 681–702.
- Craig, S.R., Amin, R.V., Russell, D.W., et al., 2000. Blood cholesterol screening influence of fasting state on cholesterol results and management decisions. *J. Gen. Intern. Med.* 15 (6), 395–399.
- Crouse, D.L., Pinault, L., Balram, A., Hystad, P., Peters, P.A., Chen, H., van Donkelaar, A., Martin, R.V., Ménard, R., Robichaud, A., Villeneuve, P.J., 2017. Urban greenness and mortality in Canada's largest cities: a national cohort study. *Lancet Planet Health* 1 (7), e289–e297.

- Dalal, S., Beunza, J.J., Volmink, J., Adebamowo, C., Bajunirwe, F., Njelekela, M., et al., 2011. Non-communicable diseases in sub-Saharan Africa: what we know now. *Int. J. Epidemiol.* 40 (4), 885–901.
- Dalal, S., Holmes, M.D., Laurence, C., et al., 2015. Feasibility of a large cohort study in sub-Saharan Africa assessed through a four-country study. *Glob. Health Action* 8, 27422.
- Egorov, A.L., Griffin, S.M., Converse, R.R., et al., 2017. Vegetated land cover near residence is associated with reduced allostatic load and improved biomarkers of neuroendocrine, metabolic and immune functions. *Environ. Res.* 158, 508–521.
- Ezeh, A., 2016. Addressing planetary health challenges in Africa. *Publ. Health Rev.* 37, 27.
- Farmer, P., Basilio, M., Kerry, V., et al., 2013. Global health priorities for the early twenty-first century. In: Farmer, P.E., Kim, J.Y., Basilio, M., Kleinman, A. (Eds.), *Reimagining Global Health*. University of California Press, Berkeley and Los Angeles, California, pp. 320–329.
- Fong, K.C., Hart, J.E., James, P., 2018. A review of epidemiologic studies on greenness and health: updated literature through 2017. *Curr. Environ. Health Rep.* 5 (1), 77–87.
- Frumkin, H., Haines, A., 2019. Global environmental change and noncommunicable disease risks. *Annu. Rev. Publ. Health* 40, 261–282.
- Gouda, H.N., Charlson, F., Sorsdahl, K., Ahmadzade, S., Ferrari, A.J., Kerslake, H., et al., 2019. Burden of non-communicable diseases in sub-Saharan Africa, 1990–2017: results from the global burden of disease study 2017. *Lancet Glob. Health* 7 (10), e1375–e1387.
- Guwatudde, D., Kirunda, B.E., Wesonga, R., et al., 2016. Physical activity levels among adults in Uganda: findings from a countrywide cross-sectional survey. *J. Phys. Activ. Health* 13 (9), 938–945.
- Guwatudde, D., Nankya-Mutyoba, J., Kalyesubula, R., et al., 2015. The burden of hypertension in sub-Saharan Africa: a four-country cross sectional study. *BMC Publ. Health* 15, 1211.
- Iyer, H.S., Valeri, L., James, P., Chen, J.T., Hart, J.E., Laden, F., et al., 2020. The Contribution of Neighborhood Greenness to Mortality Among Men with Prostate Cancer: A Registry-Based Cohort Study of Black and White Men. *Environmental Epidemiology*. Press.
- James, P., Banay, R.F., Hart, J.E., et al., 2015. A review of the health benefits of greenness. *Curr. Epidemiol. Rep.* 2 (2), 131–142.
- James, P., Hart, J.E., Banay, R.F., Laden, F., 2016. Exposure to greenness and mortality in a nationwide prospective cohort study of women. *Environ. Health Perspect.* 124 (9), 1344–1352.
- Jemal, A., Bray, F., Forman, D., O'Brien, M., Ferlay, J., Center, M., et al., 2012. Cancer burden in Africa and opportunities for prevention. *Cancer* 118 (18), 4372–4384.
- Jia, X., Yu, Y., Xia, W., et al., 2018. Cardiovascular diseases in middle aged and older adults in China: the joint effects and mediation of different types of physical exercise and neighborhood greenness and walkability. *Environ. Res.* 167, 175–183.
- Kim, H.J., Min, J.Y., Kim, H.J., Min, K.B., 2016. Parks and green areas are associated with decreased risk for hyperlipidemia. *Int. J. Environ. Res. Publ. Health* 13 (12), E1205.
- Krieger, N. (Ed.), 2011. *Epidemiology and the People's Health: Theory and Context*. Oxford University Press, New York, pp. 202–235 (Chapter 7): *Ecosocial Theory of Disease Distribution: Embodying Societal and Ecologic Context*.
- Kriegler, F.J., Malila, W.A., Nalepka, R.F., et al., 1969. Preprocessing transformations and their effects on multispectral recognition. In: *Proceedings of the Sixth International Symposium on Remote Sensing of Environment*. Institute of Science and Technology of the University of Michigan; 1969, Ann Arbor, MI, pp. 97–131.
- Kwan, G.F., Bongani, M.M., Mocumbi, A.O., et al., 2016. Endemic cardiovascular diseases of the poorest billion. *Circulation* 133 (24), 2561–2575.
- Lachowycz, K., Jones, A.P., 2014. Does walking explain associations between access to greenspace and lower mortality? *Soc. Sci. Med.* 107, 9–17.
- Laurence, E.C., Volmink, J., Esterhuizen, T.M., et al., 2016. Risk of cardiovascular disease among teachers in Cape Town: findings of the South African PaCT pilot study. *S. Afr. Med. J.* 106 (10), 996–1001.
- Li, Q., Morimoto, K., Kobayashi, M., et al., 2008. Visiting a forest, but not a city, increases human natural killer activity and expression of anti-cancer proteins. *Int. J. Immunopathol. Pharmacol.* 21 (1), 117–127.
- Markevych, I., Standl, M., Sugiri, D., et al., 2016. Residential greenness and blood lipids in children: a longitudinal analysis in GINIplus and LISAPLUS. *Environ. Res.* 151, 168–173.
- Mashili, F.L., Kagaruki, G.B., Mbatia, J., et al., 2018. Physical activity and associated socioeconomic determinants in rural and urban Tanzania: results from the 2012 WHO-steps survey. *Int. J. Popul. Res.* 4965193.
- McEwen, B.S., 1998. Stress, adaptation and disease. Allostasis and allostatic load. *Ann. N. Y. Acad. Sci.* 840, 33–44.
- Mensah, G.A., Sampson, U.K., Roth, G.A., Forouzanfar, M.H., Naghavi, M., Murray, C.L., et al., 2015. Mortality from cardiovascular diseases in sub-Saharan Africa, 1990–2013: a systematic analysis of data from the Global Burden of Disease Study 2013. *Cardiovasc. J. Afr.* 26 (2 H3Africa Suppl. 1), S6–S10.
- Mutanga, O., Kumar, L., 2019. Google earth engine applications. *Rem. Sens.* 11, 591.
- NCD Risk Factor Collaboration (NCD-RisC) – Africa Working Group, 2017. Trends in obesity and diabetes across Africa from 1980 to 2014: an analysis of pooled population-based studies. *Int. J. Epidemiol.* 46 (5), 1421–1432.
- Nugent, R., Bertram, M.Y., Jan, S., et al., 2018. Investing in non-communicable disease prevention and management to advance the Sustainable Development Goals. *Lancet* 391 (10134), 2029–2035.
- Orioli, R., Antonucci, C., Scortichini, M., Cerza, F., Marando, F., Ancona, C., et al., 2019. Exposure to residential greenness as a predictor of cause-specific mortality and stroke incidence in the rome longitudinal study. *Environ. Health Perspect.* 127 (2), 27002.
- Park, B.J., Tsunetsugu, Y., Kasetani, T., et al., 2010. The physiologic effects of Shinrin-yoku (taking in the forest atmosphere or forest bathing): evidence from field experiments in 24 forests across Japan. *Environ. Health Prev. Med.* 15 (1), 18–26.
- Plans, E., Gullón, P., Cebrecos, A., Fontán, M., Diez, J., Nieuwenhuijsen, M., et al., 2019. Density of green spaces and cardiovascular risk factors in the city of madrid: the heart healthy woods study. *Int. J. Environ. Res. Publ. Health* 16 (24), E4918.
- Population Reference Bureau, 2018. *World Population Data Sheet* (accessed June 26, 2019). <https://www.prb.org/wp-content/uploads/2018/08/2018-WPDS.pdf>.
- Richardson, E.A., Pearce, J., Mitchell, R., Kingham, S., 2013. Role of physical activity in the relationship between urban green space and health. *Publ. Health* 127 (4), 318–324.
- Rojas-Rueda, D., Nieuwenhuijsen, M.J., Gascon, M., Perez-Leon, D., Mudu, P., 2019. Green spaces and mortality: a systematic review and meta-analysis of cohort studies. *Lancet Planet Health* 3 (11), e469–e477.
- Rubin, D.B., 1987. *Multiple Imputation for Nonresponse in Surveys*. Wiley.
- Seeman, T.E., Singer, B.H., Rowe, J.W., et al., 1997. Price of adaptation—allostatic load and its health consequences. *MacArthur studies of successful aging. Arch. Intern. Med.* 157 (19), 2259–2268.
- Stefan, D.C., Elzawawy, A.M., Khaled, H.M., Ntaganda, F., Asimwe, A., Addai, B.W., et al., 2013. Developing cancer control plans in Africa: examples from five countries. *Lancet Oncol.* 14 (4), e189–e195.
- Tamosiunas, A., Grazuleviciene, R., Luksiene, D., et al., 2014. Accessibility and use of urban green spaces, and cardiovascular health: findings from a Kaunas cohort study. *Environ. Health* 13 (1), 20.
- Tapela, N.M., Tshisimogo, G., Shatera, B.P., et al., 2019. Integrating noncommunicable disease services into primary care, Botswana. *Bull. World Health Organ.* 97 (2), 142–153.
- Thiering, E., Markevych, I., Bruske, I., et al., 2016. Associations of residential long-term air pollution exposures and satellite-derived greenness with insulin resistance in German adolescents. *Environ. Health Perspect.* 124 (8), 1291–1298.
- Toit, M.J., Cilliers, S.S., Dallimer, M., et al., 2018. Urban green infrastructure and ecosystem services in sub-Saharan Africa. *Landsc. Urban Plann.* 180, 249–261.
- Tomita, A., Vandormael, A.M., Cuadros, D., et al., 2017. Green environment and incident depression in South Africa: a geospatial analysis and mental health implications in a resource-limited setting. *Lancet Planet Health* 1 (4), e152–e162.
- Towhig-Bennett, C., Jones, A., 2018. The health benefits of the great outdoors: a systematic review and meta-analysis of greenspace exposure and health outcomes. *Environ. Res.* 166, 628–637.
- UN Economic & Social Affairs. *World urbanization prospects: the 2018 revision*. Available at: (accessed June 26, 2019). <https://esa.un.org/unpd/wup/Publications/Files/WUP2018-KeyFacts.pdf>.
- Valeri, L., VanderWeele, T.J., 2013. Mediation analysis allowing for exposure-mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychol. Methods* 18 (2), 137–150.
- VanderWeele, T., Ding, P., 2017. Sensitivity analysis in observational research: introducing the E-value. *Ann. Intern. Med.* 167 (4), 268–274.
- VanderWeele, T.J., 2017. Outcome-wide Epidemiology. *Epidemiology* 28 (3), 399–402.
- Vienneau, D., de Hoogh, K., Faeh, D., Kaufmann, M., Wunderli, J.M., Röösli, M., SNC Study Group, 2017. More than clean air and tranquility: residential green is independently associated with decreasing mortality. *Environ. Int.* 108, 176–184.
- Villeneuve, P., Jerrett, M., Su, J.G., et al., 2018. Association of residential greenness with obesity and physical activity in a US cohort of women. *Environ. Res.* 160, 372–384.
- Wang, K., Lombard, J., Rundek, T., Dong, C., Gutierrez, C.M., Byrne, M.M., et al., 2019. Relationship of neighborhood greenness to heart disease in 249,405 US medicare beneficiaries. *J. Am. Heart Assoc.* 8 (6), e010258.
- WHO, 2018. *Time to Deliver: Report of the WHO Independent High-Level Commission on Noncommunicable Diseases*. World Health Organization, Geneva. Licence: CC BY-NC-SA 3.0 IGO.
- Yang, B., Markevych, I., Heinrich, J., et al., 2019a. Associations of greenness with diabetes mellitus and glucose-homeostasis markers: the 33 Communities Chinese Health Study. *Int. J. Hyg Environ. Health* 222, 283–290.
- Yang, B.Y., Markevych, I., Heinrich, J., Bloom, M.S., Qian, Z., Geiger, S.D., et al., 2019b. Residential greenness and blood lipids in urban-dwelling adults: the 33 Communities Chinese Health Study. *Environ. Pollut.* 250, 14–22.
- Yeager, R., Riggs, D.W., DeJarnett, N., et al., 2018. Association between residential greenness and cardiovascular disease risk. *J. Am. Heart Assoc.* 7 (24), e009117.