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Cohort profile: Research on Obesity and Diabetes among African Migrants in Europe and Africa Prospective (RODAM-Pros) cohort study

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Abstract

Purpose: The Research on Obesity and Diabetes among African Migrants (RODAM) prospective (RODAM-Pros) cohort study was established to identify key changes in environmental exposures and epigenetic modifications driving the high burden of cardiovascular disease (CVD) risk among Sub-Saharan African migrants.

Participants: All the participants in the RODAM cross-sectional study that completed the baseline assessment (n=5114) were eligible for the follow-up of which 2165 participants (n=638 from rural-Ghana, n=608 from urban-Ghana and n=919 Ghanaian migrants in Amsterdam, the Netherlands) were included in the RODAM-Pros cohort study. Additionally, we included a subsample of European-Dutch (n=2098) to enable a comparison to be made between Ghanaian migrants living in the Netherlands and the European-Dutch host population.

Findings to date: Follow-up data have been collected on demographics, socioeconomic status, medical history, psychosocial environment, lifestyle factors, nutrition, anthropometrics, blood pressure, fasting blood, urine, and stool samples. Biochemical analyses included glucose metabolism, lipid profile, electrolytes and renal function, liver metabolism, and inflammation. In a sub-sample, we assessed DNA methylation patterns using Infinium® 850K DNA Methylation BeadChip. Baseline results indicated that migrants have higher prevalence of CVD risk factors than non-migrants. Epigenome-wide association studies suggest important differences in DNA methylation between migrants and non-migrants. The follow-up study will shed further light on key specific environmental exposures and epigenetic modifications contributing to the high burden of CVD risk among Sub Saharan African migrants.

Future plans: Follow-up is planned at five-year intervals, baseline completed in 2015 and first follow-up completed in 2021.

Strengths and limitations

- The main strength of the RODAM-Pros cohort study is the longitudinal cohort design, including representative samples of Ghanaian migrants and their non-migrant compatriots of predominantly Akan ethnicity living in their country of origin, alongside a sample of the host European population, which is unique.

- The RODAM-Pros cohort study uses well standardised approaches across the study sites in rural Ghana, urban Ghana and Amsterdam, the Netherlands, and has collected a variety of data on demographics, socioeconomic status, psychosocial environment, lifestyle, nutrition, biological factors and epigenetics.

- This cohort may be limited by a relatively low response rates, especially in urban Ghana, due to the COVID-19 pandemic, but the response rates achieved will gain insight into the drivers of the high burden of CVD and its risk factors among these populations.

Introduction

Cardiovascular disease (CVD) is the main cause of death in the European Union (EU) accounting for 1.9 million deaths yearly in the EU, equivalent to 40% of all deaths each year in this region.[1] CVD is also a major health problem confronting migrant and ethnic minorities in Europe, and the rate of CVD incidence and mortality are higher among these populations than in the European host populations.[2-4] This inevitably contributes importantly to the widening health inequalities between migrant and ethnic minorities and the European host populations. Sub-Saharan Africa (SSA) migrants, especially West-Africans, have been particularly affected by stroke, being 1.5-2.5 times more common in these groups than in the European host populations.[2-5] SSA patients with hypertension are also at greater risk of developing cardiovascular complications, such as renal disease, than other populations. [2,6]

Hypertension, the single most important modifiable risk factor for CVD, is consistently highly prevalent among SSA origin populations and appears to be a major contributor to their elevated stroke risk.[7-9] Hypertension prevalence in SSA migrants e.g. West-African migrants is 1.5 to 3.5 times higher than in the European host population.[10] The HELIUS study in Amsterdam, the Netherlands, has shown that the prevalence of hypertension was 62% and 52% in Ghanaian migrant men and women compared with 34% and 19% in their European Dutch counterparts.[10] Similarly, the prevalence of type 2 diabetes is higher in SSA migrants than in the European host population.[11] A meta-analysis of papers published between 1994 and 2014 in Europe showed that the pooled odds ratio of type 2 diabetes was about two-and-a-half-fold higher in SSA migrants than in the European host population.[12] Moreover, overweight and obesity, too, have been shown to be higher among SSA migrants compared to individuals of European descent, especially in women.[12] These huge disparities in prevalence of CVDs risk factors, and related complications between SSA migrants and the European host population has led to the burning question: which factors are driving the increased burden of CVD and its risk factors among SSA migrants?

At present, the underlying reasons for the increased risk of CVD risk factors among SSA migrants are incompletely understood. Lack of understanding of the drivers of increased CVD risk in SSA migrants prohibits the development of strategies that can mitigate existing differences in CVD outcomes. This is happening at a time when preventive measures have led to reduction in CVDs and their risk factors in the European general populations for the last few decades.[1] More evidence on the underlying factors is clearly needed in order to develop adequate policy, clinical and public health responses to minimise the high burden of CVD risk factors and related complications among these populations.[13]

Notwithstanding, several factors have been proposed as the underlying factors for the high burden of CVD risk factors among SSA migrants, including migration-related lifestyle changes, psychosocial stress and low socioeconomic status, genetic susceptibility and gene-environment interactions, however, the key specific modifiable risk factors within these broad categories still remain to be determined.[14] Additionally, at the moment, very few genetic variants have been identified to directly influence CVD risk, but, analyses of several common polymorphisms associated with underlying mechanisms e.g. salt sensitivity and heat stress indicate that these polygenic traits might influence the tendency to develop CVD risk factors such as hypertension and diabetes.[15] Additionally, epigenetic alterations might also influence the risk of CVD among migrant populations.[16] Furthermore, the disparities in CVD risk may be affected by differences in the gut microbiome.[17] However, the current limited available knowledge is mainly based on cross-sectional analyses. Answering the critical question of what are causing the high burden of CVDs and their risk factors in SSA migrants requires a longitudinal design. The RODAM prospective (RODAM-Pros) cohort study was, therefore, set up to identify key changes in environmental exposures (e.g., socioeconomic status, lifestyle factors, psychosocial factors), biological factors and epigenetic modifications in the development of CVD risk factors among SSA migrants and their non-migrant peers living in SSA. Through the RODAM-Pros cohort study, we aim to provide better understanding on the factors driving the high rates of CVD risk factors among SSA migrants, and provide a knowledge base to improve diagnosis and treatment of CVD risk factors in this population.

Cohort description

This cohort profile describes the RODAM-Pros cohort study based on the RODAM study. The RODAM study was conducted between 2012 and 2015 and was based on a well-defined homogenous SSA population (i.e. Ghanaian migrants of mostly Akan ancestral heritage) living in three European cities (Amsterdam, the Netherlands; Berlin, Germany; and London, United Kingdom) and their compatriots that are living in rural and urban Akan region of Ghana.[18] The follow-up of the RODAM-Pros cohort conducted between 2019-2021, is restricted to the Netherlands, rural and urban Ghana because the recruitment strategies in these sites allowed the study participants to be followed over time. In addition, we also included participants of Ghanaian ethnicity and European-Dutch in the Healthy Life in an Urban Setting (HELIUS) study, who were not initially included in the RODAM study, to maximise the sample size and to allow comparison of migrants with the European host population. The HELIUS study is a multi-ethnic prospective cohort study on health and health care utilization among ethnic groups in Europe. The RODAM and the HELIUS studies used exactly the same sampling, recruitment and data collection methods at baseline and follow-up. The rationale and study design of the RODAM study [18] and HELIUS study [19] has been published before.

Baseline recruitment strategy in Ghana and the Netherlands (2012 – 2015)

At baseline, 15 villages in the Ashanti region and two cities (Kumasi and Obuasi) in Ghana served as the rural and urban recruitment sites using the list of enumeration areas (EAs) in the Ashanti region from the 2010 census as the initial sampling frame.[18] We used a multistage sampling procedure to arrive at the sampling of 30 EAs consisting of 15 rural EAs and 15 urban (Kumasi and Obuasi) EAs. These were selected from over 2000 urban EAs and 1000 rural EAs following the stratification and weighting of the EAs. The health and community authorities in all the selected EAs were informed by letters about the study. The RODAM team organised mini clinics in the various communities for a period of 1-2 weeks for data collection.

In the Netherlands, Ghanaian participants were randomly drawn from the Amsterdam Municipal register, which contains data on country of birth of each citizen and his/her parents. The Ghanaian participants identified from the register aged ≥25-70 years were sent an invitation letter combined with study information and an opt-out response card. An appointment for physical examination was made for those that agreed to participate in the study. In addition, participants completed questionnaires through face-to-face interviews by research assistants or independently by filling out the paper version or online version of the questionnaire depending on the preference of the participants. The participants were asked to consent for about five-yearly follow up and for their data to be linked to the national registry data on health outcomes and health care at the individual level to study changes in diseases experiences over time.

Patient and public involvement

The RODAM study engaged the Ghanaian community in both Europe and Ghana by working with religious communities and endorsement from local community leaders for the recruitment of the study participants and the dissemination of the study results. We also provided information about the study via local Ghanaian community organisations and local media via Ghanaian radio and television stations.

Follow-up recruitment strategy (2019 – 2021)

In Ghana, all participants contact details including house address, mobile numbers and next of kin contact details were compiled at baseline. In the follow up, the study participants were contacted by phone in urban Ghana (n=1452) and by home visits in rural Ghana (n=1111). If there were no means of contact available for a participant (e.g. because of changed phone numbers), then we relied on households head's contact details or the community members in each specific EA to reach the

participant. If a potential participant had moved to another village or a city, effort was made to reach them through the participant's contact details.

In Amsterdam, the Netherlands, all Ghanaian participants who participated in the baseline RODAM study assessment and agreed to be approached for future studies (n=1504) were invited for follow-up examination. As the RODAM and the HELIUS studies used exactly the same methods at baseline and follow up, we included Ghanaian participants in the HELIUS study (n=1047) to enlarge the RODAM-Pros cohort sample in Amsterdam. Furthermore, we included a sub-population of HELIUS study participants of European-Dutch origin (n=2098) to enable comparison to be made between the Ghanaian migrants in the Netherlands with the host European Dutch population. Effort was made to increase the response rate by means of repeated phone calls by the research team if individuals did not respond to the initial invitation. Furthermore, community sensitisations were carried out through radio, TV and community organisations such as churches and African mosques to create awareness about the importance of participating in the follow-up. In Ghana, the research team visited several houses in both rural and urban Ghana to motivate participants to take part in the study.

Follow-up data collection

Table 1 summarises the data collected from participants at baseline and follow up assessment. In both the Netherlands and in Ghana, all the participants that agreed to participate were invited for physical examination and to complete a questionnaire at the local research clinic or health centre. The study and procedures involved were explained to each participant by trained research assistants and informed consent was signed for participation, storage of biological materials in Biobank and to be approached for future (sub-) studies. Participants were asked to fast 8-12 hour before their physical measurement.

Table 1 Summary of physical and biological examination variables measured at baseline and follow-up

Measures	Variables	Instrument used where applicable	Baseline	Follow-up
Anthropometrics	Weight Height Waist circumference Hip circumference Body fat (Bio Impedance Analysis)	SECA 877 SECA 217 Measuring tape Measuring tape BODYSTAT 1500 MDD analyser for BIA	x x x x x	x x x x
Blood Pressure, office	Systolic BP, Diastolic BP, pulse, measured 3 times	Microlife BP A6 BT	x	x
24-h ABPM *In subsample only*	24-h ABPM	Spacelabs 90207/		x
Ankle-Brachial Index	PAD	Ankle-Brachial Index, measured in a supine position after at least 10 min rest	x	
Biological samples				
On the spot glucose *In Ghana only*		Nova Xpress meter + StatStrip GLU - test strip	x	x
Glucose metabolism	Glucose HbA1C		x	x
Lipid metabolism	Total cholesterol HDL LDL Triglycerides		x x x x	x x x x
Inflammation	hsCRP		x	x
Uric acid metabolism	Uric acid		x	
Oxidative stress	Ferritin		x	
Electrolytes and renal function	Creatinine Albumin Sodium Potassium Calcium		x x x x x	x
Liver metabolism	ALAT ASAT y-GT		x x x	x x x
Renin-angiotensin-aldosterone system *Subsample only*	Renin Aldosterone		x x	
Adipokines *Subsample only*	Adiponectin Leptin Non-esterified fatty acid		x x x	
Urine analysis				
Morning void	Albumin Creatinine Sodium Potassium		x x x x	x x x x
24-h urine collection *In subsample only*	24h Albumin 24h Creatinine 24h Sodium 24h Potassium 24 h Urea			x x x x x
Stool sample	Microbiome			x
(Epi-)Genetics				
Epigenetics *In subsample only*	DNA methylation RNA expression analysis	Infinium® Methylation EPIC BeadChip of Illumina (850K) -	x	x x

Physical measurements

Physical measurements were carried out using validated devices according to standardised operational procedures (SOP). Physical measurements included anthropometric indices (weight, height, waist circumference and hip circumference), and blood pressure (Table 1). Height was

measured using a portable stadiometer SECA 217; weight was measured with SECA 877 wearing light clothing and no shoes. Abdominal and hip circumference were measured with a measuring tape, at the point midway between the iliac crest and the costal margin, and over the trochanter major of the femur, respectively. All anthropometric measurements were taken twice. Blood pressure was measured three times with a validated semiautomated device (The Microlife WatchBP home) in a sitting position after at least 5 min rest, with appropriate cuffs around the left upper arm. In a subsample (n=55) of participants with newly detected, untreated hypertension during their study visit, 24h ambulatory blood pressure measurement (ABPM) was performed with a validated device (Spacelabs 90207/90217).

Questionnaire

After the physical examination, the participants completed a structured health questionnaire containing questions on demographics, socioeconomic status, migration-related factors, psychosocial vulnerability (perceived discrimination, social support, mastery, recent negative life events and current depression), health status and behaviour (self-reported general health and presence and history of diseases, family history of diseases, dietary behaviour, physical activity, alcohol and smoking, and adherence to medications) by using appropriate validated instruments where necessary (Table 2) by trained and ethnically matched interviewers. The questionnaires were conducted face to face by trained interviewers of Ghanaian background in the preferred language of the participant either in English, Dutch or a Ghanaian language and lasted for about 75 minutes. The European-Dutch participants completed an online digital shortened Dutch version of the structured health questionnaire.

Table 2 Summary of variables collected at baseline and follow-up by a questionnaire

Themes	Variables	Instrument used where applicable	Baseline	Follow-up
Questionnaire				
Demographics	Age, study, marital status, ethnicity, household composition, religion	NA	x	x
Socioeconomic status	1. Education 2. Employment status 3. Wealth 4. Parental socioeconomic status	1. NA 2. NA 3. Household Index; Wealth index 4. NA	x x x x	x x
Migration-related factors	1. Migration history 2. Generation, length of stay in Europe 3. Religion 4. Cultural distance and integration 5. Early factors	1. NA 2. NA 3. NA 4. Berry's Model of Acculturation 5. Parental SES, anthropometric indicators	x x x x x	 x
Health Status	1. General health 2. Questions for women only 3. Specific illnesses and disorders a. Blood pressure, hypertension b. Cholesterol, dyslipidaemia c. Blood sugar, diabetes mellitus, diabetes-related complications d. Awareness of chronic kidney disease e. Chest pain, angina, myocardial infarction f. Leg pain, intermittent claudication, artery stenosis g. Stroke h. Oral health 4. Family history, changes in the past five years	1. One item of SF-12 2. NA 3. Specific illnesses/disorders a. NA b. NA c. Diabetic Neuropathy Score d. NHANES e. Rose angina questionnaire f. WHO/Rose questionnaire g. NA h. Two questions GLOBE 2014 4. NA	x x x x x x x x x x x	x x x x x x x x x x x
Psychosocial factors	1. Dealing with everyday problems 2. Recent experiences 3. Psychological stress 4. Perceived discrimination 5. Recent well-being	1. Mastery 2. List of threatening experiences 3. Two items from INTERHEART 4. Everyday Discrimination Scale 5. Patient Health Questionnaire-9	x x x x x	x x x x x
Health behaviour	1. Smoking 2. Alcohol intake 3. Physical activity 4. Dietary behaviour 5. Dietary salt 6. Use of medication	1. NA 2. NA 3. WHO GPAQ V.2 4. Ghana-specific FPQ 5. WHO STEPS 6. Self-reported adherence	X x x x x	x x x x x x

NA, not available

Biological material

Blood samples: Fasting venous blood samples were collected by trained research assistants in the Netherlands and Ghana. Blood samples were manually processed and aliquoted immediately after collection by a trained technician according to SOPs, and then temporarily stored at 4-7°C at the local research location. The SOPs in both the Netherlands and Ghana were strictly followed to ensure that the samples were collected, handled, processed, transported and stored in the same way in both countries. The samples, including EDTA whole blood, PAX-gene blood, and heparin plasma, were then transported to the local laboratories in Kwame Nkrumah University of Science and Technology,

Kumasi, and Amsterdam University Medical Centres (UMC), Amsterdam, where samples were checked, registered and stored at -80°C.

Morning urine sample: All the study participants were asked to bring early morning, midstream, urine samples in a clean jar. In addition, 24-hour urine samples were collected in a subsample of the study population (n=408).

Stool Sample: The study participants were asked to bring fresh stool samples in a stool tube as has been provided by the research team. These samples were transported to the respective local laboratory and stored at -80°C.

Transfer of biological material for biochemical analyses and genotyping: All the samples in Ghana were shipped to Amsterdam, the Netherlands, in CXR500 dry shippers including an activated temperature logger with intervals of 30 minutes, filled with liquid nitrogen, to keep the samples frozen at -80°C. The staff involved with the shipment of the samples were trained in the preparation and filling of dryshippers and on legal and regulatory aspects of shipment of samples such as Material Transfer Agreement (MTA) in order to minimise factors that might affect the integrity of the samples such as temperature, packaging, import/export requirements, seasons, and transit time/ship days. We maintained a shipment log to record the receipt and dissemination of shipments; and each shipment entry was given a unique shipment number.

All the blood, urine and stool samples were transported to Amsterdam UMC Biobank and parts of the samples were processed for biochemical analyses at the Central Biochemical Laboratory of the Amsterdam UMC. All biochemical analyses were performed in the same laboratory in Amsterdam, to prevent bias of interlaboratory differences. Biochemical analysis of blood included glucose metabolism (fasting glucose, HbA1c), lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides), renal function (creatinine), liver metabolism (alanine transaminase, aspartate aminotransferase, γ-glutamyl transpeptidase), and inflammation (high-sensitivity C reactive protein). Urine samples were analysed for renal function and

electrolytes (albumin, creatinine, sodium, potassium, urea). Stool samples will be analysed to evaluate the role of microbiome and its impact on CVD risk factors among migrants.

Each participant received a summary of his/her main results accompanied by an explanation and recommendation to contact their GP if the results were abnormal.

Deceased participants

For RODAM participants who died in the period between baseline and follow-up data collection, efforts were made to retrieve information on causes of death. In the Netherlands, at baseline, participants gave informed consent to link up their information to the national statistics registration (Centraal Bureau voor de Statistiek, CBS) data on cause and date of death – based on medical certification of death, using the International Classification of Disease (ICD) version 10 classification. In Ghana, no reliable vital national registration system on cause of death exists. Therefore, information on causes of death of the deceased participants were collected using a validated verbal autopsy instrument. During verbal autopsy interviews with families, information about the events leading to death were collected, using the shortened Verbal Autopsy Instrument developed by the Population Health Metrics Research Consortium (PHMRC), based on the World Health Organization standards.[20] This Verbal Autopsy Instrument was then analysed using the SmartVA software (https://www.healthdata.org/verbal-autopsy/tools), resulting in most likely cause of death, classified based on the ICD-10.[21]

Epigenetics

We included around 1300 participants in the epigenetic studies. A core interest was to identify key epigenetic modifications driving the high burden of hypertension among African migrants. In a nested

case-control study, including 793 participants (n=174 rural Ghana, n=161 urban Ghana, n=145 Amsterdam Ghanaians and n=313 Dutch) an epigenome-wide association study (EWAS) will be conducted to assess differentially methylated positions and regions associated with incident hypertension at follow-up. An additional 507 participants (n=169 rural Ghana, n=169 urban Ghana, and n=169 Amsterdam Ghanaians) were randomly selected to study DNA methylation loci associated with (other) CVD risk factors. DNA was isolated from whole blood at the Core Facility Genomics of the Amsterdam UMC. DNA samples were sent to Erasmus University, Rotterdam for DNA methylation profiling using Infinium® Methylation EPIC BeadChip of Illumina (850K). Raw methylation data have been sent to Amsterdam UMC for quality control and data analysis. Data analyses will begin once quality control is completed. mRNA will be isolated from whole blood (PAXgene stored). mRNA expression analysis will be performed in a subset of randomly selected cases and controls using RNA sequencing (RNA-seq) depending on the results of the epigenetic analyses.

Findings to date

The follow-up data collection of the RODAM-Pros cohort study in rural and urban Ghana, and the Netherlands completed in October 2021. The mean time to follow-up was 6.4 years, with a range of 3.6 to 9.9 years. The response rates were 63.3% in rural Ghana, 43.9% in urban Ghana, 68.4% among Ghanaian migrants and 92.6% among European Dutch. Of the respondents, 90.8% of rural Ghanaian, 95.3% of urban Ghanaian, 52.7% of Amsterdam Ghanaian and 67.2% of European Dutch participants completed the physical examination (Figure 1). The response rate was affected by the COVID-19 pandemic, which started in the middle of the data collection. Following the outbreak, data collection was interrupted several times in both Ghana and the Netherlands because of the COVID-19 shutdowns. In urban Ghana, especially in Obuasi, several participants relocated to their hometowns due to COVID-19 shutdown and many were not traceable despite efforts to reach them. We carried out non-response analyses to assess the characteristics of the individuals who participated and those

who did not participate in the follow up. Among rural and urban Ghanaians, there were no differences in sex and educational levels between respondents and non-respondents, but respondents were less frequently living in urban Ghana than in rural Ghana (Table 3). Respondents were more frequently employed than non-respondents. Among Ghanaian migrants in the Netherlands, there was no differences in sex and educational level between respondents and non-respondents; but the respondents were older, and more frequently employed than their non-respondent peers (Table 3). Among the European-Dutch, the respondents were frequently males, older, had higher educational level, and were more frequently employed than non-respondents.

Table 3 Characteristics of Non-respondents and Respondents in follow-up data collection, for Ghana, Amsterdam Ghanaians and Dutch

		Non-respondents		Respondents		
		n	% (95% CI)	n	% (95% CI)	
Ghana						P-value
Sex	Male	441	33.9 (31.3, 36.5)	411	32.5 (30, 35.1)	ns
	Female	861	66.1 (63.5, 68.7)	853	67.5 (64.9, 70)	
Site	Rural Ghana	462	35.5 (32.9, 38.1)	649	51.3 (48.6, 54.1)	<0.05
	Urban Ghana	840	64.5 (61.9, 67.1)	615	48.7 (45.9, 51.4)	
Age at baseline, mean (SD)			47 (14)		47 (12)	
Educational level	None or elementary	629	51 (48.2, 53.8)	598	49.5 (46.6, 52.3)	ns
	Lower secondary	410	33.3 (30.7, 35.9)	455	37.6 (34.9, 40.4)	
	Higher secondary	134	10.9 (9.2, 12.7)	113	9.3 (7.8, 11.1)	
	Tertiary	60	4.9 (3.8, 6.2)	43	3.6 (2.6, 4.7)	
Employment status	Employed	1038	84.2 (81.1, 86.1)	1066	88.1 (86.2, 89.8)	<0.05
	Not in the labour force	46	3.7 (2.8, 4.9)	38	3.1 (2.3, 4.2)	
	Unemployed	54	4.4 (3.3, 5.6)	37	3.1 (2.2, 4.1)	
	Unable to work	95	7.7 (6.3, 9.3)	69	5.7 (4.5, 7.1)	
Amsterdam-Ghanaians						
Sex	Male	703	38.8 (36.5, 41)	361	39.2 (36.1, 42.4)	ns
	Female	1111	61.2 (59, 63.5)	559	60.8 (57.6, 63.9)	
Age at baseline, mean (SD)			43 (12)		46 (10)	<0.05
Educational level	None or elementary	441	27.6 (25.5, 29.9)	242	28.6 (25.7, 31.8)	ns
	Lower secondary	638	40 (37.6, 42.4)	338	40 (36.7, 43.3)	
	Higher secondary	422	26.5 (24.3, 28.7)	207	24.5 (21.7, 27.5)	
	Tertiary	94	5.9 (4.8, 7.1)	58	6.9 (5.3, 8.7)	
Employment status	Employed	912	57.6 (55.1, 60)	524	62.2 (58.9, 65.5)	<0.05
	Not in the labour force	145	9.2 (7.8, 10.6)	43	5.1 (3.8, 6.8)	
	Unemployed	379	23.9 (21.9, 26.1)	209	24.8 (22, 27.8)	
	Unable to work	148	9.3 (8, 10.9)	66	7.8 (6.2, 9.8)	
Dutch						
Sex	Male	792	42.9 (40.7, 45.2)	1354	47.9 (46.1, 49.8)	<0.05
	Female	1054	57.1 (54.8, 59.3)	1471	52.1 (50.2, 53.9)	
Age at baseline, mean (SD)			44 (15)		47 (13)	<0.05

Educational level	None or elementary	88	4.9 (3.9, 5.9)	65	2.3 (1.8, 2.9)	<0.05
	Lower secondary	323	17.8 (16.1, 19.6)	337	12 (10.9, 13.3)	
	Higher secondary	415	22.9 (21, 24.9)	603	21.5(20, 23.1)	
	Tertiary	985	54.4 (52.1, 56.7)	1799	64.2 (62.4, 65.9)	
Employment status	Employed	1240	68.3 (66.2, 70.4)	2172	77.2 (75.6, 78.7)	<0.05
	Not in the labour force	363	20 (18.2, 21.9)	451	16 (14.7, 17.4)	
	Unemployed	127	7.0 (5.9, 8.2)	129	4.6 (3.9, 5.4)	
	Unable to work	85	4.7 (3.8, 5.7)	61	2.2 (1.7, 2.8)	

SD, standard deviation; ns, non-significant

The RODAM baseline data have shed light on the high burden of CVD risk factors such as obesity, type 2 diabetes, hypertension, and dyslipidaemia among Ghanaian migrants and their non-migrant Ghanaian compatriots living in rural and urban Ghana.[22] For example, the prevalence ratio of obesity was five times higher in urban Ghanaian men and 11- to 15-fold higher among Ghanaian migrant men living in the various European countries compared with their rural Ghanaian men counterparts.[22] The baseline data of the RODAM-Pros cohort also show that despite the high burden of CVD risk factors among Ghanaian migrants, they have lower rates of microvascular and macrovascular complications as compared with non-migrant Ghanaians.[23-24] The RODAM study has identified various cross-sectional factors associated with CVD risk factors.[25-27] In addition, the study has resulted in the first EWAS for type 2 diabetes in SSA, in which we identified several CpG sites that were differentially methylated between type 2 diabetes cases and controls at an epigenome-wide level.[28] In our study of epigenome-wide DNA methylation differences between migrant and non-migrant Ghanaians, we identified 13 differentially methylated positions and three differentially methylated regions between migrants and non-migrants, with DNA methylation differences ranging from 0.1 to 4.5%.[29] The complete list of publications based on the baseline RODAM study data is available online in the RODAM study website (http://www.rod-am.eu/publications/).

The RODAM-Pros longitudinal cohort will shed further light on the key specific causal factors including lifestyle, psychosocial stressors, socioeconomic circumstances, physiological changes and epigenetic modifications among many factors that are driving the high burden of CVD and its risk factors in SSA migrants and their compatriots living in rural and urban SSA.

Strengths and limitations

The main strength of the RODAM-Pros cohort is the uniqueness of a longitudinal cohort of Ghanaian migrants and their non-migrant compatriots of predominantly Akan ethnicity living in their country of origin, alongside a cohort of the host European population. Another strength of the RODAM-Pros cohort is the use of well-standardised methods across the study sites in rural Ghana, urban Ghana and Amsterdam, the Netherlands. A further strength of the RODAM-Pros cohort is the large sample size and detailed characterisation of the study participants including data on demographics, socioeconomic status, psychosocial environment, lifestyle, nutrition, biochemical characterisation and epigenetics.

There are also limitations to the RODAM-Pros cohort. First, although the data collection was highly standardised across all sites, the recruitment strategies were adapted to suit the local circumstances due to differences in registration systems. In the Netherlands, the Ghanaian migrants and the European-Dutch participants were drawn from the Amsterdam Municipal population register, whereas Ghanaian participants living in Ghana were drawn from the list of EAs. It is possible that individuals who are not included in the register such as non-documented migrants differ in terms of demographics and socioeconomic status, which might somewhat affect the representativeness of Ghanaian migrants in Amsterdam, the Netherlands. Another limitation is the relatively low response due to impact of COVID-19 pandemic. The COVID-19 pandemic lockdowns deterred some participants to participate in the follow up because of fear of infection especially in urban Ghana where the entire data collection occurred within the pandemic period. In a non-response analysis, there were no differences in sex and educational levels between respondents and non-respondents; but non-respondents were more frequently living in urban Ghana than in rural Ghana, which might somewhat bias the results. Another limitation is the use of self-reported data through questionnaires such as WHO/Rose questionnaire, WHO GPAQ V.2 and Ghana-specific Food Propensity Questionnaire, which

may be subject to response bias. Despite these potential limitations, this unique RODAM-Pros longitudinal cohort study offers an important opportunity to gain insight into the drivers of the high burden of CVDs and their risk factors among SSA migrants.

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Data availability statement

We welcome potential collaboration with other researchers especially on epigenetics studies. Researchers can visit the RODAM-Pros cohort website (http://www.rod-am.eu/follow-up/about/) for more information about the study. Data are available on reasonable request. Requests for access to data can be made to the RODAM-Pros cohort coordinator Dr Erik Beune (e.j.beune@amsterdamumc.nl) or Principal Investigator Professor Charles Agyemang (c.o.agyemang@amsterdamumc.nl). Reuse of the data must be done in collaboration with the RODAM cohort team.

Contributors CA, EB, EL, PH, BJB & EOD established the cohort and provided intellectual inputs to the manuscript. CA, EL & EB conceived the present manuscript and prepared the final version for the submission. CA & EL drafted the manuscript. EL conducted the data analysis. All authors critically revised the manuscript. All authors reviewed and approved the final version of the manuscript.

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Competing interests None declared.

Patient and public involvement Community leaders were involved in the design, and dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval Ethical approval of the study protocols were obtained from the respective ethics committees in Ghana (School of Medical Sciences/Komfo Anokye Teaching Hospital Committee on Human Research, Publication & Ethical Review Board), and the Netherlands (Institutional Review Board of the AMC, University of Amsterdam). Interviewees provide informed consent prior to the start of the interview.

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References

1. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: Epidemiological update. Eur Heart J. 2014;35:2950–9.
2. Gill P, et al. Health Care Needs Assessment: Black and Minority Ethnic Groups. In: Raftery J (ed) Health Care Needs Assessment Third Series. Abingdon: Radcliffe Medical Press Ltd;
3. Agyemang C, Van Oeffelen AAM, Norredam M, Kappelle LJ, Klijn CJM, Bots ML, et al. Ethnic disparities in ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage incidence in the Netherlands. Stroke. 2014;45(11):3236–42.
4. Harding S, Rosato M, Teyhan A. Trends for coronary heart disease and stroke mortality among migrants in England and Wales, 1979-2003: slow declines notable for some groups. Heart. 2008;94(4):463–70.
5. Kunst A, Stronks K, Agyemang C. Non-communicable diseases. In: Rechel B, Mladovsky P, Devillé W, Rijks B, Petrova-Benedict R, McKee M, editors. Migration and health in the European Union. Birkshire: Open University Press; 2011. p. 101–20.
6. Agyemang C, Snijder MB, Adjei DN, Van Den Born BJH, Modesti PA, Peters RJG, et al. Ethnic disparities in CKD in the Netherlands: The healthy life in an Urban Setting (HELIUS) Study. Am J Kidney Dis. 2016;67(3):391–9.
7. Hajjar I, Kotchen TA. Trends in Prevalence, Awareness, Treatment, and Control of Hypertension in the United States, 1988-2000. J Am Med Assoc. 2003;290(2):199–206.
8. Agyemang C, Bhopal R. Is the blood pressure of people from African origin adults in the UK

higher or lower than that in European origin white people? A review of cross-sectional data. J Hum Hypertens. 2003;17(8):523–34.

9. Agyemang C, Bindraban N, Mairuhu G, Montfrans G Van, Koopmans R, Stronks K. Prevalence, awareness, treatment, and control of hypertension among Black Surinamese, South Asian Surinamese and White Dutch in Amsterdam, The Netherlands: the SUNSET study. J Hypertens. 2005;23(11):1971–7.
10. Agyemang C, Kieft S, Snijder MB, Beune EJ, Van Den Born BJ, Brewster LM, et al. Hypertension control in a large multi-ethnic cohort in Amsterdam, The Netherlands: The HELIUS study. Int J Cardiol. 2015;183:180–9.
11. Agyemang C, van der Linden EL, Bennet L. Type 2 diabetes burden among migrants in Europe: unravelling the causal pathways. Diabetologia. 2021 Dec;64(12):2665-2675.
12. Meeks KA, Freitas-Da-Silva D, Adeyemo A et al (2016) Disparities in type 2 diabetes prevalence among ethnic minority groups resident in Europe: a systematic review and meta-analysis. Intern Emerg Med 11(3):327–340.
13. World Health Organisation. Health of migrants: the way forward: report of a global consultation, Madrid, Spain, 3-5 March 2010. Madrid, Spain. 2010.
14. Agyemang C, van den Born BJ. Cardiovascular health and disease in migrant populations: a call to action. Nat Rev Cardiol. 2022 Jan;19(1):1-2.
15. Meeks KAC, Bentley AR, Adeyemo AA, Rotimi CN. Evolutionary forces in diabetes and hypertension pathogenesis in Africans. Hum Mol Genet. 2021 Apr 26;30(R1):R110-R118.
16. Chilunga FP, Henneman P, Elliott HR, Cronjé HT, Walia GK, Meeks KAC, Requena-Mendez A, Venema A, Bahendeka S, Danquah I, Adeyemo A, Klipstein-Grobusch K, Pieters M, Mannens MMAM, Agyemang C. Epigenetic age acceleration in the emerging burden of cardiometabolic diseases among migrant and non-migrant African populations: the population based cross-sectional RODAM study. Lancet Healthy Longev. 2021 May 17;2(6):E327-E339.
17. Verhaar, B. J. H. et al. Associations between gut microbiota, faecal short-chain fatty acids, and blood pressure across ethnic groups: the HELIUS study. Eur. Heart J. 41, 4259–4267 (2020).
18. Agyemang C, Beune E, Meeks K, Owusu-Dabo E, Agyei-Baffour P, Aikins Ad, Dodoo F, Smeeth L, Addo J, Mockenhaupt FP, Amoah SK, Schulze MB, Danquah I, Spranger J, Nicolaou M, Klipstein-Grobusch K, Burr T, Henneman P, Mannens MM, van Straalen JP, Bahendeka S, Zwinderman AH, Kunst AE, Stronks K. Rationale and cross-sectional study design of the Research on Obesity and type 2 Diabetes among African Migrants: the RODAM study. BMJ Open. 2014 Mar 21;4(3):e004877.
19. Stronks K, Snijder MB, Peters RJ, Prins M, Schene AH, Zwinderman AH. Unravelling the impact of

ethnicity on health in Europe: the HELIUS study. BMC Public Health. 2013;13(1):402.

20. Lozano R, Sazawal S, Fawzi W, Ali SM, Sanvictores D, Lopez AD, et al. A shortened verbal autopsy instrument for use in routine mortality surveillance systems. BMC Med. BMC Medicine; 2015;13(1):1–10.
21. Murray CJ, Lopez AD, Black R, Ahuja R, Ali SM, Baqui A, Dandona L, Dantzer E, Das V, Dhingra U, Dutta A, Fawzi W, Flaxman AD, Gómez S, Hernández B, Joshi R, Kalter H, Kumar A, Kumar V, Lozano R, Lucero M, Mehta S, Neal B, Ohno SL, Prasad R, Praveen D, Premji Z, Ramírez-Villalobos D, Remolador H, Riley I, Romero M, Said M, Sanvictores D, Sazawal S, Tallo V. Population Health Metrics Research Consortium gold standard verbal autopsy validation study: design, implementation, and development of analysis datasets. Popul Health Metr. 2011 Aug 4;9:27.
22. Agyemang C, Meeks K, Beune E, Owusu-Dabo E, Mockenhaupt FP, Addo J, de Graft Aikins A, Bahendeka S, Danquah I, Schulze MB, Spranger J, Burr T, Agyei-Baffour P, Amoah SK, Galbete C, Henneman P, Klipstein-Grobusch K, Nicolaou M, Adeyemo A, van Straalen J, Smeeth L, Stronks K. Obesity and type 2 diabetes in sub-Saharan Africans - Is the burden in today's Africa similar to African migrants in Europe? The RODAM study. BMC Med. 2016 Oct 21;14(1):166.
23. Hayfron-Benjamin CF, van den Born BJ, Maitland-van der Zee AH, Amoah AGB, van der Linden EL, Stronks K, Klipstein-Grobusch K, Bahendeka S, Danquah I, Beune E, Smeeth L, Agyemang C. Higher prevalence of peripheral arterial disease in Ghana compared to Ghanaian migrants in Europe: The RODAM study. Int J Cardiol. 2020 Apr 15;305:127-134.
24. Hayfron-Benjamin C, van den Born BJ, Maitland-van der Zee AH, Amoah AGB, Meeks KAC, Klipstein-Grobusch K, Bahendeka S, Spranger J, Danquah I, Mockenhaupt F, Beune E, Smeeth L, Agyemang C. Microvascular and macrovascular complications in type 2 diabetes Ghanaian residents in Ghana and Europe: The RODAM study. J Diabetes Complications. 2019 Aug;33(8):572-578.
25. van der Linden EL, Meeks KAC, Klipstein-Grobusch K, Bahendeka S, Beune EJAJ, van den Born BH, Agyemang C. Hypertension determinants among Ghanaians differ according to location of residence: RODAM study. J Hypertens. 2022 May 1;40(5):1010-1018.
26. Osei TB, van Dijk AM, Dingerink S, Chilunga FP, Beune E, Meeks KAC, Bahendeka S, Schulze MB, Agyemang C, Nicolaou M, Holleboom AG, Danquah I. Reduced Rank Regression-Derived Dietary Patterns Related to the Fatty Liver Index and Associations with Type 2 Diabetes Mellitus among Ghanaian Populations under Transition: The RODAM Study. Nutrients. 2021 Oct 20;13(11):3679.
27. Darko SN, Meeks KAC, Owiredu WKBA, Laing EF, Boateng D, Beune E, Addo J, de-Graft Aikins A, Bahendeka S, Mockenhaupt F, Spranger J, Agyei-Baffour P, Klipstein-Grobusch K, Smeeth L, Agyemang C, Owusu-Dabo E. Anthropometric indices and their cut-off points in relation to type

2 diabetes among Ghanaian migrants and non-migrants: The RODAM study. Diabetes Res Clin Pract. 2021;173:108687.

28. Meeks KAC, Henneman P, Venema A, Addo J, Bahendeka S, Burr T, Danquah I, Galbete C, Mannens MMAM, Mockenhaupt FP, Owusu-Dabo E, Rotimi CN, Schulze MB, Smeeth L, Spranger J, Zafarmand MH, Adeyemo A, Agyemang C. Epigenome-wide association study in whole blood on type 2 diabetes among sub-Saharan African individuals: findings from the RODAM study. Int J Epidemiol. 2019 Feb 1;48(1):58-70.
29. Chilunga FP, Henneman P, Venema A, Meeks KA, Gonzalez JR, Ruiz-Arenas C, Requena-Méndez A, Beune E, Spranger J, Smeeth L, Bahendeka S, Owusu-Dabo E, Klipstein-Grobusch K, Adeyemo A, Mannens MM, Agyemang C. DNA methylation as the link between migration and the major noncommunicable diseases: the RODAM study. Epigenomics. 2021 May;13(9):653-666.

Figure legends

Figure 1 – Response and participation rates

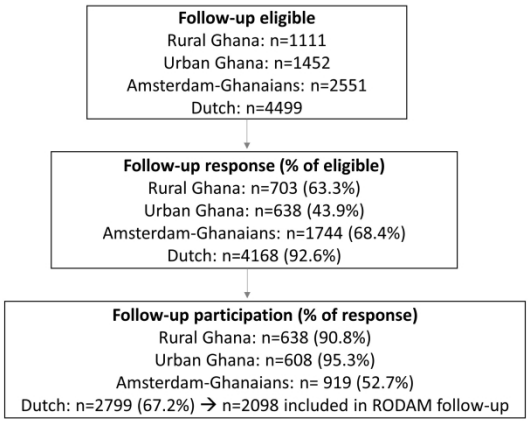

Figure 1 – Response and participation rates

338x190mm (300 x 300 DPI)

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Cohort profile: Research on Obesity and Diabetes among African Migrants in Europe and Africa Prospective (RODAM-Pros) cohort study

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Cohort profile: Research on Obesity and Diabetes among African Migrants in Europe and Africa Prospective (RODAM-Pros) cohort study

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Abstract

Purpose: The Research on Obesity and Diabetes among African Migrants (RODAM) prospective (RODAM-Pros) cohort study was established to identify key changes in environmental exposures and epigenetic modifications driving the high burden of cardiovascular disease (CVD) risk among Sub-Saharan African migrants.

Participants: All the participants in the RODAM cross-sectional study that completed the baseline assessment (n=5114) were eligible for the follow-up of which 2165 participants (n=638 from rural-Ghana, n=608 from urban-Ghana and n=919 Ghanaian migrants in Amsterdam, the Netherlands) were included in the RODAM-Pros cohort study. Additionally, we included a subsample of European-Dutch (n=2098) to enable a comparison to be made between Ghanaian migrants living in the Netherlands and the European-Dutch host population.

Findings to date: Follow-up data have been collected on demographics, socioeconomic status, medical history, psychosocial environment, lifestyle factors, nutrition, anthropometrics, blood pressure, fasting blood, urine, and stool samples. Biochemical analyses included glucose metabolism, lipid profile, electrolytes and renal function, liver metabolism, and inflammation. In a sub-sample, we assessed DNA methylation patterns using Infinium® 850K DNA Methylation BeadChip. Baseline results indicated that migrants have higher prevalence of CVD risk factors than non-migrants. Epigenome-wide association studies suggest important differences in DNA methylation between migrants and non-migrants. The follow-up study will shed further light on key specific environmental exposures and epigenetic modifications contributing to the high burden of CVD risk among Sub Saharan African migrants.

Future plans: Follow-up is planned at five-year intervals, baseline completed in 2015 and first follow-up completed in 2021.

Strengths and limitations

- The main strength of the RODAM-Pros cohort study is the longitudinal cohort design, including representative samples of Ghanaian migrants and their non-migrant compatriots of predominantly Akan ethnicity living in their country of origin, alongside a sample of the host European population, which is unique.

- The RODAM-Pros cohort study uses well standardised approaches across the study sites in rural Ghana, urban Ghana and Amsterdam, the Netherlands, and has collected a variety of data on demographics, socioeconomic status, psychosocial environment, lifestyle, nutrition, biological factors and epigenetics.

- This cohort may be limited by a relatively low response rates, especially in urban Ghana, due to the COVID-19 pandemic, but the response rates achieved will give insight into the drivers of the high burden of CVD and its risk factors among these populations.

Introduction

Cardiovascular disease (CVD) is the main cause of death in the European Union (EU) accounting for 1.9 million deaths yearly in the EU, equivalent to 40% of all deaths each year in this region.[1] CVD is also a major health problem confronting migrant and ethnic minorities in Europe, and the rate of CVD incidence and mortality are higher among these populations than in the European host populations.[2-4] This inevitably contributes importantly to the widening health inequalities between migrant and ethnic minorities and the European host populations. Sub-Saharan Africa (SSA) migrants, especially West-Africans, have been particularly affected by stroke, being 1.5-2.5 times more common in these groups than in the European host populations.[2-5] SSA patients with hypertension are also at greater risk of developing cardiovascular complications, such as renal disease, than other populations. [2,6]

Hypertension, the single most important modifiable risk factor for CVD, is consistently highly prevalent among SSA origin populations and appears to be a major contributor to their elevated stroke risk.[7-9] Hypertension prevalence in SSA migrants e.g. West-African migrants is 1.5 to 3.5 times higher than in the European host population.[10] The HELIUS study in Amsterdam, the Netherlands, has shown that the prevalence of hypertension was 62% and 52% in Ghanaian migrant men and women compared with 34% and 19% in their European Dutch counterparts.[10] Similarly, the prevalence of type 2 diabetes is higher in SSA migrants than in the European host population.[11] A meta-analysis of papers published between 1994 and 2014 in Europe showed that the pooled odds ratio of type 2 diabetes was about two-and-a-half-fold higher in SSA migrants than in the European host population.[12] Moreover, overweight and obesity, too, have been shown to be higher among SSA migrants compared to individuals of European descent, especially in women.[12] These huge disparities in prevalence of CVDs risk factors, and related complications between SSA migrants and the European host population has led to the burning question: which factors are driving the increased burden of CVD and its risk factors among SSA migrants?

At present, the underlying reasons for the increased risk of CVD risk factors among SSA migrants are incompletely understood. Lack of understanding of the drivers of increased CVD risk in SSA migrants prohibits the development of strategies that can mitigate existing differences in CVD outcomes. This is happening at a time when preventive measures have led to reduction in CVDs and their risk factors in the European general populations for the last few decades.[1] More evidence on the underlying factors is clearly needed in order to develop adequate policy, clinical and public health responses to minimise the high burden of CVD risk factors and related complications among these populations.[13]

Notwithstanding, several factors have been proposed as the underlying factors for the high burden of CVD risk factors among SSA migrants, including migration-related lifestyle changes, psychosocial stress and low socioeconomic status, genetic susceptibility and gene-environment interactions, however, the key specific modifiable risk factors within these broad categories still remain to be determined.[14] Additionally, at the moment, very few genetic variants have been identified to directly influence CVD risk, but, analyses of several common polymorphisms associated with underlying mechanisms e.g. salt sensitivity and heat stress indicate that these polygenic traits might influence the tendency to develop CVD risk factors such as hypertension and diabetes.[15] Additionally, epigenetic alterations might also influence the risk of CVD among migrant populations.[16] Furthermore, the disparities in CVD risk may be affected by differences in the gut microbiome.[17] However, the current limited available knowledge is mainly based on cross-sectional analyses. Answering the critical question of what are causing the high burden of CVDs and their risk factors in SSA migrants requires a longitudinal design. The RODAM prospective (RODAM-Pros) cohort study was, therefore, set up to identify key changes in environmental exposures (e.g., socioeconomic status, lifestyle factors, psychosocial factors), biological factors and epigenetic modifications in the development of CVD risk factors among SSA migrants and their non-migrant peers living in SSA. Through the RODAM-Pros cohort study, we aim to provide better understanding on the factors driving the high rates of CVD risk factors among SSA migrants, and provide a knowledge base to improve diagnosis and treatment of CVD risk factors in this population.

Cohort description

This cohort profile describes the RODAM-Pros cohort study based on the RODAM study. The RODAM study was conducted between 2012 and 2015 and was based on a well-defined homogenous SSA population (i.e. Ghanaian migrants of mostly Akan ancestral heritage) living in three European cities (Amsterdam, the Netherlands; Berlin, Germany; and London, United Kingdom) and their compatriots that are living in rural and urban Akan region of Ghana.[18] The follow-up of the RODAM-Pros cohort conducted between 2019-2021, is restricted to the Netherlands, rural and urban Ghana because the recruitment strategies in these sites allowed the study participants to be followed over time. In addition, we also included participants of Ghanaian ethnicity and European-Dutch in the Healthy Life in an Urban Setting (HELIUS) study, who were not initially included in the RODAM study, to maximise the sample size and to allow comparison of migrants with the European host population. The HELIUS study is a multi-ethnic prospective cohort study on health and health care utilization among ethnic groups in Europe. The RODAM and the HELIUS studies used exactly the same sampling, recruitment and data collection methods at baseline and follow-up. The rationale and study design of the RODAM study [18] and HELIUS study [19] has been published before.

Baseline recruitment strategy in Ghana and the Netherlands (2012 – 2015)

At baseline, 15 villages in the Ashanti region and two cities (Kumasi and Obuasi) in Ghana served as the rural and urban recruitment sites using the list of enumeration areas (EAs) in the Ashanti region from the 2010 census as the initial sampling frame.[18] We used a multistage sampling procedure to arrive at the sampling of 30 EAs consisting of 15 rural EAs and 15 urban (Kumasi and Obuasi) EAs. These were selected from over 2000 urban EAs and 1000 rural EAs following the stratification and weighting of the EAs. The health and community authorities in all the selected EAs were informed by letters about the study. The RODAM team organised mini clinics in the various communities for a period of 1-2 weeks for data collection.

In the Netherlands, Ghanaian participants were randomly drawn from the Amsterdam Municipal register, which contains data on country of birth of each citizen and their parents. The Ghanaian participants identified from the register aged ≥25-70 years were sent an invitation letter combined with study information and an opt-out response card. An appointment for physical examination was made for those that agreed to participate in the study. In addition, participants completed questionnaires through face-to-face interviews by research assistants or independently by filling out the paper version or online version of the questionnaire depending on the preference of the participants. The participants were asked to consent for future follow up, planned to be conducted every five years, and for their data to be linked to the national registry data on health outcomes and health care at the individual level to study changes in diseases experiences over time.

Patient and public involvement

The RODAM study engaged the Ghanaian community in both Europe and Ghana by working with religious communities and endorsement from local community leaders for the recruitment of the study participants and the dissemination of the study results. We also provided information about the study via local Ghanaian community organisations and local media via Ghanaian radio and television stations.

Follow-up recruitment strategy (2019 – 2021)

In Ghana, all participants contact details including house address, mobile numbers and next of kin contact details were compiled at baseline. In the follow up, the study participants were contacted by phone in urban Ghana (n=1452) and by home visits in rural Ghana (n=1111). If there were no means of contact available for a participant (e.g. because of changed phone numbers), then we relied on households head's contact details or the community members in each specific EA to reach the

participant. If a potential participant had moved to another village or a city, effort was made to reach them through the participant's contact details.

In Amsterdam, the Netherlands, all Ghanaian participants who participated in the baseline RODAM study assessment and agreed to be approached for future studies (n=1504) were invited for follow-up examination. As the RODAM and the HELIUS studies used exactly the same methods at baseline and follow up, we included Ghanaian participants in the HELIUS study (n=1047) to enlarge the RODAM-Pros cohort sample in Amsterdam. Furthermore, we included a sub-population of HELIUS study participants of European-Dutch origin (n=2098) to enable comparison to be made between the Ghanaian migrants in the Netherlands with the host European Dutch population. Effort was made to increase the response rate by means of repeated phone calls by the research team if individuals did not respond to the initial invitation. Furthermore, community sensitisations were carried out through radio, TV and community organisations such as churches and African mosques to create awareness about the importance of participating in the follow-up. In Ghana, the research team visited several houses in both rural and urban Ghana to motivate participants to take part in the study.

Follow-up data collection

Table 1 summarises the data collected from participants at baseline and follow up assessment. In both the Netherlands and in Ghana, all the participants that agreed to participate were invited for physical examination and to complete a questionnaire at the local research clinic or health centre. The study and procedures involved were explained to each participant by trained research assistants and informed consent was signed for participation, storage of biological materials in Biobank and to be approached for future (sub-) studies. Participants were asked to fast 8-12 hour before their physical measurement.

Table 1 Summary of physical and biological examination variables measured at baseline and follow-up

Measures	Variables	Instrument used where applicable	Baseline	Follow-up
Anthropometrics	Weight Height Waist circumference Hip circumference Body fat (Bio Impedance Analysis)	SECA 877 SECA 217 Measuring tape Measuring tape BODYSTAT 1500 MDD analyser for BIA	x x x x x	x x x x
Blood Pressure, office	Systolic BP, Diastolic BP, pulse, measured 3 times	Microlife BP A6 BT	x	x
24-h ABPM *In subsample only*	24-h ABPM	Spacelabs 90207/		x
Ankle-Brachial Index	PAD	Ankle-Brachial Index, measured in a supine position after at least 10 min rest	x	
Biological samples				
On the spot glucose *In Ghana only*		Nova Xpress meter + StatStrip GLU - test strip	x	x
Glucose metabolism	Glucose HbA1C		x	x
Lipid metabolism	Total cholesterol HDL LDL Triglycerides		x x x x	x x x x
Inflammation	hsCRP		x	x
Uric acid metabolism	Uric acid		x	
Oxidative stress	Ferritin		x	
Electrolytes and renal function	Creatinine Albumin Sodium Potassium Calcium		x x x x x	x
Liver metabolism	ALAT ASAT y-GT		x x x	x x x
Renin-angiotensin-aldosterone system *Subsample only*	Renin Aldosterone		x x	
Adipokines *Subsample only*	Adiponectin Leptin Non-esterified fatty acid		x x x	
Urine analysis				
Morning void	Albumin Creatinine Sodium Potassium		x x x x	x x x x
24-h urine collection *In subsample only*	24h Albumin 24h Creatinine 24h Sodium 24h Potassium 24 h Urea			x x x x x
Stool sample	Microbiome			x
(Epi-)Genetics				
Epigenetics *In subsample only*	DNA methylation RNA expression analysis	Infinium® Methylation EPIC BeadChip of Illumina (850K) -	x	x x

Physical measurements

Physical measurements were carried out using validated devices according to standardised operational procedures (SOP). Physical measurements included anthropometric indices (weight, height, waist circumference and hip circumference), and blood pressure (Table 1). Height was

measured using a portable stadiometer SECA 217; weight was measured with SECA 877 wearing light clothing and no shoes. Abdominal and hip circumference were measured with a measuring tape, at the point midway between the iliac crest and the costal margin, and over the trochanter major of the femur, respectively. All anthropometric measurements were taken twice. Blood pressure was measured three times with a validated semiautomated device (The Microlife WatchBP home) in a sitting position after at least 5 min rest, with appropriate cuffs around the left upper arm. In a subsample (n=55) of participants with newly detected, untreated hypertension during their study visit, 24h ambulatory blood pressure measurement (ABPM) was performed with a validated device (Spacelabs 90207/90217).

Questionnaire

After the physical examination, the participants completed a structured health questionnaire containing questions on demographics, socioeconomic status, migration-related factors, psychosocial vulnerability (perceived discrimination, social support, mastery, recent negative life events and current depression), health status and behaviour (self-reported general health and presence and history of diseases, family history of diseases, dietary behaviour, physical activity, alcohol and smoking, and adherence to medications) by using appropriate validated instruments where necessary (Table 2) by trained and ethnically matched interviewers. The questionnaires were conducted face to face by trained interviewers of Ghanaian background in the preferred language of the participant either in English, Dutch or a Ghanaian language and lasted for about 75 minutes. The European-Dutch participants completed an online digital shortened Dutch version of the structured health questionnaire.

Table 2 Summary of variables collected at baseline and follow-up by a questionnaire

Themes	Variables	Instrument used where applicable	Baseline	Follow-up
Questionnaire				
Demographics	Age, study, marital status, ethnicity, household composition, religion	NA	x	x
Socioeconomic status	1. Education 2. Employment status 3. Wealth 4. Parental socioeconomic status	1. NA 2. NA 3. Household Index; Wealth index 4. NA	x x x x	x x
Migration-related factors	1. Migration history 2. Generation, length of stay in Europe 3. Religion 4. Cultural distance and integration 5. Early factors	1. NA 2. NA 3. NA 4. Berry's Model of Acculturation 5. Parental SES, anthropometric indicators	x x x x x	 x
Health Status	1. General health 2. Questions for women only 3. Specific illnesses and disorders a. Blood pressure, hypertension b. Cholesterol, dyslipidaemia c. Blood sugar, diabetes mellitus, diabetes-related complications d. Awareness of chronic kidney disease e. Chest pain, angina, myocardial infarction f. Leg pain, intermittent claudication, artery stenosis g. Stroke h. Oral health 4. Family history, changes in the past five years	1. One item of SF-12 2. NA 3. Specific illnesses/disorders a. NA b. NA c. Diabetic Neuropathy Score d. NHANES e. Rose angina questionnaire f. WHO/Rose questionnaire g. NA h. Two questions GLOBE 2014 4. NA	x x x x x x x x x x x	x x x x x x x x x x x
Psychosocial factors	1. Dealing with everyday problems 2. Recent experiences 3. Psychological stress 4. Perceived discrimination 5. Recent well-being	1. Mastery 2. List of threatening experiences 3. Two items from INTERHEART 4. Everyday Discrimination Scale 5. Patient Health Questionnaire-9	x x x x x	x x x x x
Health behaviour	1. Smoking 2. Alcohol intake 3. Physical activity 4. Dietary behaviour 5. Dietary salt 6. Use of medication	1. NA 2. NA 3. WHO GPAQ V.2 4. Ghana-specific FPQ 5. WHO STEPS 6. Self-reported adherence	X x x x x	x x x x x x

NA, not available

Biological material

Blood samples: Fasting venous blood samples were collected by trained research assistants in the Netherlands and Ghana. Blood samples were manually processed and aliquoted immediately after collection by a trained technician according to SOPs, and then temporarily stored at 4-7°C at the local research location. The SOPs in both the Netherlands and Ghana were strictly followed to ensure that the samples were collected, handled, processed, transported and stored in the same way in both countries. The samples, including EDTA whole blood, PAX-gene blood, and heparin plasma, were then transported to the local laboratories in Kwame Nkrumah University of Science and Technology,

Kumasi, and Amsterdam University Medical Centres (UMC), Amsterdam, where samples were checked, registered and stored at -80°C.

Morning urine sample: All the study participants were asked to bring early morning, midstream, urine samples in a clean jar. In addition, 24-hour urine samples were collected in a subsample of the study population (n=408).

Stool Sample: The study participants were asked to bring fresh stool samples in a stool tube as has been provided by the research team. These samples were transported to the respective local laboratory and stored at -80°C.

Transfer of biological material for biochemical analyses and genotyping: All the samples in Ghana were shipped to Amsterdam, the Netherlands, in CXR500 dry shippers including an activated temperature logger with intervals of 30 minutes, filled with liquid nitrogen, to keep the samples frozen at -80°C. The staff involved with the shipment of the samples were trained in the preparation and filling of dryshippers and on legal and regulatory aspects of shipment of samples such as Material Transfer Agreement (MTA) in order to minimise factors that might affect the integrity of the samples such as temperature, packaging, import/export requirements, seasons, and transit time/ship days. We maintained a shipment log to record the receipt and dissemination of shipments; and each shipment entry was given a unique shipment number.

All the blood, urine and stool samples were transported to Amsterdam UMC Biobank and parts of the samples were processed for biochemical analyses at the Central Biochemical Laboratory of the Amsterdam UMC. All biochemical analyses were performed in the same laboratory in Amsterdam, to prevent bias of interlaboratory differences. Biochemical analysis of blood included glucose metabolism (fasting glucose, HbA1c), lipid profile (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol and triglycerides), renal function (creatinine), liver metabolism (alanine transaminase, aspartate aminotransferase, γ-glutamyl transpeptidase), and inflammation (high-sensitivity C reactive protein). Urine samples were analysed for renal function and

electrolytes (albumin, creatinine, sodium, potassium, urea). Stool samples will be analysed to evaluate the role of microbiome and its impact on CVD risk factors among migrants.

Each participant received a summary of their main results accompanied by an explanation and recommendation to contact their GP if the results were abnormal.

Deceased participants

For RODAM participants who died in the period between baseline and follow-up data collection, efforts were made to retrieve information on causes of death. In the Netherlands, at baseline, participants gave informed consent to link up their information to the national statistics registration (Centraal Bureau voor de Statistiek, CBS) data on cause and date of death – based on medical certification of death, using the International Classification of Disease (ICD) version 10 classification. In Ghana, no reliable vital national registration system on cause of death exists. Therefore, information on causes of death of the deceased participants were collected using a validated verbal autopsy instrument. During verbal autopsy interviews with families, information about the events leading to death were collected, using the shortened Verbal Autopsy Instrument developed by the Population Health Metrics Research Consortium (PHMRC), based on the World Health Organization standards.[20] This Verbal Autopsy Instrument was then analysed using the SmartVA software (https://www.healthdata.org/verbal-autopsy/tools), resulting in most likely cause of death, classified based on the ICD-10.[21]

Epigenetics

We included around 1300 participants in the epigenetic studies. A core interest was to identify key epigenetic modifications driving the high burden of hypertension among African migrants. In a nested

case-control study, including 793 participants (n=174 rural Ghana, n=161 urban Ghana, n=145 Amsterdam Ghanaians and n=313 Dutch) an epigenome-wide association study (EWAS) will be conducted to assess differentially methylated positions and regions associated with incident hypertension at follow-up. These participants were selected based on their hypertension status at baseline (normotensive) and at follow-up (either normotensive control or hypertensive case). An additional 507 participants (n=169 rural Ghana, n=169 urban Ghana, and n=169 Amsterdam Ghanaians) were randomly selected to study DNA methylation loci associated with (other) CVD risk factors. DNA was isolated from whole blood at the Core Facility Genomics of the Amsterdam UMC. DNA samples were sent to Erasmus University, Rotterdam for DNA methylation profiling using Infinium® Methylation EPIC BeadChip of Illumina (850K). Raw methylation data have been sent to Amsterdam UMC for quality control and data analysis. Data analyses will begin once quality control is completed. mRNA will be isolated from whole blood (PAXgene stored). mRNA expression analysis will be performed in a subset of randomly selected cases and controls using RNA sequencing (RNA-seq) depending on the results of the epigenetic analyses.

Findings to date

The follow-up data collection of the RODAM-Pros cohort study in rural and urban Ghana, and the Netherlands completed in October 2021. The mean time to follow-up was 6.4 years, with a range of 3.6 to 9.9 years. The response rates were 63.3% in rural Ghana, 43.9% in urban Ghana, 68.4% among Ghanaian migrants and 92.6% among European Dutch. Of the respondents, 90.8% of rural Ghanaian, 95.3% of urban Ghanaian, 52.7% of Amsterdam Ghanaian and 67.2% of European Dutch participants completed the physical examination (Figure 1). The response rate was affected by the COVID-19 pandemic, which started in the middle of the data collection. Following the outbreak, data collection was interrupted several times in both Ghana and the Netherlands because of the COVID-19 shutdowns. In urban Ghana, especially in Obuasi, several participants relocated to their hometowns

due to COVID-19 shutdown and many were not traceable despite efforts to reach them. We carried out non-response analyses to assess the characteristics of the individuals who participated and those who did not participate in the follow up. Among rural and urban Ghanaians, there were no differences in sex and educational levels between respondents and non-respondents, but respondents were less frequently living in urban Ghana than in rural Ghana (Table 3). Respondents were more frequently employed than non-respondents. Among Ghanaian migrants in the Netherlands, there was no differences in sex, region of origin, and educational level between respondents and non-respondents; but the respondents were older, had been residing in Amsterdam for longer, and were more frequently employed than their non-respondent peers (Table 3). Among the European-Dutch, the respondents were frequently males, older, had higher educational level, and were more frequently employed than non-respondents.

Table 3 Baseline characteristics of Non-respondents and Respondents in follow-up data collection, for Ghana, Amsterdam Ghanaians and Dutch

		Non-respondents		Respondents		
		n	% (95% CI)	n	% (95% CI)	
Ghana						P-value
Sex	Male	441	33.9 (31.3, 36.5)	411	32.5 (30, 35.1)	ns
	Female	861	66.1 (63.5, 68.7)	853	67.5 (64.9, 70)	
Site	Rural Ghana	462	35.5 (32.9, 38.1)	649	51.3 (48.6, 54.1)	<0.05
	Urban Ghana	840	64.5 (61.9, 67.1)	615	48.7 (45.9, 51.4)	
Age, mean (SD)			47 (14)		47 (12)	
Educational level	None or elementary	629	51 (48.2, 53.8)	598	49.5 (46.6, 52.3)	ns
	Lower secondary	410	33.3 (30.7, 35.9)	455	37.6 (34.9, 40.4)	
	Higher secondary	134	10.9 (9.2, 12.7)	113	9.3 (7.8, 11.1)	
	Tertiary	60	4.9 (3.8, 6.2)	43	3.6 (2.6, 4.7)	
Employment status	Employed	1038	84.2 (81.1, 86.1)	1066	88.1 (86.2, 89.8)	<0.05
	Not in the labour force	46	3.7 (2.8, 4.9)	38	3.1 (2.3, 4.2)	
	Unemployed	54	4.4 (3.3, 5.6)	37	3.1 (2.2, 4.1)	
	Unable to work	95	7.7 (6.3, 9.3)	69	5.7 (4.5, 7.1)	
Amsterdam-Ghanaians						
Sex	Male	703	38.8 (36.5, 41)	361	39.2 (36.1, 42.4)	ns
	Female	1111	61.2 (59, 63.5)	559	60.8 (57.6, 63.9)	
Age, mean (SD)			43 (12)		46 (10)	<0.05
Length of stay in Europe, years, mean (SD)			18 (8)		19 (8)	<0.05
Region of origin	Rural Ghana	27	4.0 (2.7-5.6)	12	3.2 (1.8-5.4)	ns
	Urban Ghana	652	96.0 (94.4-97.3)	362	96.8 (94.6-98.2)	
Educational level	None or elementary	441	27.6 (25.5, 29.9)	242	28.6 (25.7, 31.8)	ns
	Lower secondary	638	40 (37.6, 42.4)	338	40 (36.7, 43.3)	
	Higher secondary	422	26.5 (24.3, 28.7)	207	24.5 (21.7, 27.5)	
	Tertiary	94	5.9 (4.8, 7.1)	58	6.9 (5.3, 8.7)	
Employment status	Employed	912	57.6 (55.1, 60)	524	62.2 (58.9, 65.5)	<0.05
	Not in the labour force	145	9.2 (7.8, 10.6)	43	5.1 (3.8, 6.8)	

	Unemployed	379	23.9 (21.9, 26.1)	209	24.8 (22, 27.8)	
	Unable to work	148	9.3 (8, 10.9)	66	7.8 (6.2, 9.8)	
Dutch						
Sex	Male	792	42.9 (40.7, 45.2)	1354	47.9 (46.1, 49.8)	<0.05
	Female	1054	57.1 (54.8, 59.3)	1471	52.1 (50.2, 53.9)	
Age, mean (SD)			44 (15)		47 (13)	<0.05
Educational level	None or elementary	88	4.9 (3.9, 5.9)	65	2.3 (1.8, 2.9)	<0.05
	Lower secondary	323	17.8 (16.1, 19.6)	337	12 (10.9, 13.3)	
	Higher secondary	415	22.9 (21, 24.9)	603	21.5(20, 23.1)	
	Tertiary	985	54.4 (52.1, 56.7)	1799	64.2 (62.4, 65.9)	
Employment status	Employed	1240	68.3 (66.2, 70.4)	2172	77.2 (75.6, 78.7)	<0.05
	Not in the labour force	363	20 (18.2, 21.9)	451	16 (14.7, 17.4)	
	Unemployed	127	7.0 (5.9, 8.2)	129	4.6 (3.9, 5.4)	
	Unable to work	85	4.7 (3.8, 5.7)	61	2.2 (1.7, 2.8)	

SD, standard deviation; ns, non-significant; Characteristics of non-respondents and respondents were compared using Student's t-test for normally distributed continuous variables (Age), Mann-Whitney U test for non-normally distributed continuous variables (length of stay in Europe), and Chi-square test for categorical variables.

The RODAM baseline data have shed light on the high burden of CVD risk factors such as obesity, type 2 diabetes, hypertension, and dyslipidaemia among Ghanaian migrants and their non-migrant Ghanaian compatriots living in rural and urban Ghana.[22] For example, the prevalence ratio of obesity was five times higher in urban Ghanaian men and 11- to 15-fold higher among Ghanaian migrant men living in the various European countries compared with their rural Ghanaian men counterparts.[22] The baseline data of the RODAM-Pros cohort also show that despite the high burden of CVD risk factors among Ghanaian migrants, they have lower rates of microvascular and macrovascular complications as compared with non-migrant Ghanaians.[23-24] The RODAM study has identified various cross-sectional factors associated with CVD risk factors.[25-27] In addition, the study has resulted in the first EWAS for type 2 diabetes in SSA, in which we identified several CpG sites that were differentially methylated between type 2 diabetes cases and controls at an epigenome-wide level.[28] In our study of epigenome-wide DNA methylation differences between migrant and non-migrant Ghanaians, we identified 13 differentially methylated positions and three differentially methylated regions between migrants and non-migrants, with DNA methylation differences ranging from 0.1 to 4.5%.[29] The complete list of publications based on the baseline RODAM study data is available online in the RODAM study website (http://www.rod-am.eu/publications/).

The RODAM-Pros longitudinal cohort will shed further light on the key specific causal factors including lifestyle, psychosocial stressors, socioeconomic circumstances, physiological changes and epigenetic

modifications among many factors that are driving the high burden of CVD and its risk factors in SSA migrants and their compatriots living in rural and urban SSA.

Strengths and limitations

The main strength of the RODAM-Pros cohort is the uniqueness of a longitudinal cohort of Ghanaian migrants and their non-migrant compatriots of predominantly Akan ethnicity living in their country of origin, alongside a cohort of the host European population. Another strength of the RODAM-Pros cohort is the use of well-standardised methods across the study sites in rural Ghana, urban Ghana and Amsterdam, the Netherlands. A further strength of the RODAM-Pros cohort is the large sample size and detailed characterisation of the study participants including data on demographics, socioeconomic status, psychosocial environment, lifestyle, nutrition, biochemical characterisation and epigenetics.

There are also limitations to the RODAM-Pros cohort. First, although the data collection was highly standardised across all sites, the recruitment strategies were adapted to suit the local circumstances due to differences in registration systems. In the Netherlands, the Ghanaian migrants and the European-Dutch participants were drawn from the Amsterdam Municipal population register, whereas Ghanaian participants living in Ghana were drawn from the list of EAs. It is possible that individuals who are not included in the register such as non-documented migrants differ in terms of demographics and socioeconomic status, which might somewhat affect the representativeness of Ghanaian migrants in Amsterdam, the Netherlands. Another limitation is the relatively low response due to impact of COVID-19 pandemic. The COVID-19 pandemic lockdowns deterred some participants to participate in the follow up because of fear of infection especially in urban Ghana where the entire data collection occurred within the pandemic period. In a non-response analysis, there were no differences in sex and educational levels between respondents and non-respondents; but non-respondents were more frequently living in urban Ghana than in rural Ghana, which might somewhat

bias the results. Another limitation is the use of self-reported data through questionnaires such as WHO/Rose questionnaire, WHO GPAQ V.2 and Ghana-specific Food Propensity Questionnaire, which may be subject to response bias. Additionally, bias could have been introduced as questionnaires were completed during an interview rather than by self-completion. To limit this bias, interviewers were trained to conduct the interview in a structured and objective manner. Despite these potential limitations, this unique RODAM-Pros longitudinal cohort study offers an important opportunity to gain insight into the drivers of the high burden of CVDs and their risk factors among SSA migrants.

Collaboration

We welcome potential collaboration with other researchers especially on epigenetics studies. Researchers can visit the RODAM-Pros cohort website (http://www.rod-am.eu/follow-up/about/) for more information about the study. Data are available on reasonable request. Requests for access to data can be made to the RODAM-Pros cohort coordinator Dr Erik Beune (e.j.beune@amsterdamumc.nl) or Principal Investigator Professor Charles Agyemang (c.o.agyemang@amsterdamumc.nl). Reuse of the data must be done in collaboration with the RODAM cohort team.

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Data availability statement

Data are available on reasonable request. These requests can be made to de RODAM-Pros cohort coordinator Dr Erik Beune (e.j.beune@amsterdamumc.nl) or Principal Investigator Professor Charles Agyemang (c.o.agyemang@amsterdamumc.nl).

Contributors CA, EB, EL, PH, BJB & EOD established the cohort and provided intellectual inputs to the manuscript. CA, EL & EB conceived the present manuscript, CA & EL drafted the manuscript, and EL conducted the data analysis. DAB, SND, STA, KM, BJB, PH & EOD critically revised the manuscript. CA, EL & EB prepared the final version for the submission. All authors reviewed and approved the final version of the manuscript.

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References

1. Nichols M, Townsend N, Scarborough P, Rayner M. Cardiovascular disease in Europe 2014: Epidemiological update. Eur Heart J. 2014;35:2950–9.
2. Gill P, et al. Health Care Needs Assessment: Black and Minority Ethnic Groups. In: Raftery J (ed)

Health Care Needs Assessment Third Series. Abingdon: Radcliffe Medical Press Ltd;

3. Agyemang C, Van Oeffelen AAM, Norredam M, Kappelle LJ, Klijn CJM, Bots ML, et al. Ethnic disparities in ischemic stroke, intracerebral hemorrhage, and subarachnoid hemorrhage incidence in the Netherlands. Stroke. 2014;45(11):3236–42.
4. Harding S, Rosato M, Teyhan A. Trends for coronary heart disease and stroke mortality among migrants in England and Wales, 1979-2003: slow declines notable for some groups. Heart. 2008;94(4):463–70.
5. Kunst A, Stronks K, Agyemang C. Non-communicable diseases. In: Rechel B, Mladovsky P, Devillé W, Rijks B, Petrova-Benedict R, McKee M, editors. Migration and health in the European Union. Birkshire: Open University Press; 2011. p. 101–20.
6. Agyemang C, Snijder MB, Adjei DN, Van Den Born BJH, Modesti PA, Peters RJG, et al. Ethnic disparities in CKD in the Netherlands: The healthy life in an Urban Setting (HELIUS) Study. Am J Kidney Dis. 2016;67(3):391–9.
7. Hajjar I, Kotchen TA. Trends in Prevalence, Awareness, Treatment, and Control of Hypertension in the United States, 1988-2000. J Am Med Assoc. 2003;290(2):199–206.
8. Agyemang C, Bhopal R. Is the blood pressure of people from African origin adults in the UK higher or lower than that in European origin white people? A review of cross-sectional data. J Hum Hypertens. 2003;17(8):523–34.
9. Agyemang C, Bindraban N, Mairuhu G, Montfrans G Van, Koopmans R, Stronks K. Prevalence, awareness, treatment, and control of hypertension among Black Surinamese, South Asian Surinamese and White Dutch in Amsterdam, The Netherlands: the SUNSET study. J Hypertens. 2005;23(11):1971–7.
10. Agyemang C, Kieft S, Snijder MB, Beune EJ, Van Den Born BJ, Brewster LM, et al. Hypertension control in a large multi-ethnic cohort in Amsterdam, The Netherlands: The HELIUS study. Int J Cardiol. 2015;183:180–9.
11. Agyemang C, van der Linden EL, Bennet L. Type 2 diabetes burden among migrants in Europe: unravelling the causal pathways. Diabetologia. 2021 Dec;64(12):2665-2675.
12. Meeks KA, Freitas-Da-Silva D, Adeyemo A et al (2016) Disparities in type 2 diabetes prevalence among ethnic minority groups resident in Europe: a systematic review and meta-analysis. Intern Emerg Med 11(3):327–340.
13. World Health Organisation. Health of migrants: the way forward: report of a global consultation, Madrid, Spain, 3-5 March 2010. Madrid, Spain. 2010.
14. Agyemang C, van den Born BJ. Cardiovascular health and disease in migrant populations: a call to action. Nat Rev Cardiol. 2022 Jan;19(1):1-2.

15. Meeks KAC, Bentley AR, Adeyemo AA, Rotimi CN. Evolutionary forces in diabetes and hypertension pathogenesis in Africans. Hum Mol Genet. 2021 Apr 26;30(R1):R110-R118.
16. Chilunga FP, Henneman P, Elliott HR, Cronjé HT, Walia GK, Meeks KAC, Requena-Mendez A, Venema A, Bahendeka S, Danquah I, Adeyemo A, Klipstein-Grobusch K, Pieters M, Mannens MMAM, Agyemang C. Epigenetic age acceleration in the emerging burden of cardiometabolic diseases among migrant and non-migrant African populations: the population based cross-sectional RODAM study. Lancet Healthy Longev. 2021 May 17;2(6):E327-E339.
17. Verhaar, B. J. H. et al. Associations between gut microbiota, faecal short-chain fatty acids, and blood pressure across ethnic groups: the HELIUS study. Eur. Heart J. 41, 4259–4267 (2020).
18. Agyemang C, Beune E, Meeks K, Owusu-Dabo E, Agyei-Baffour P, Aikins Ad, Dodoo F, Smeeth L, Addo J, Mockenhaupt FP, Amoah SK, Schulze MB, Danquah I, Spranger J, Nicolaou M, Klipstein-Grobusch K, Burr T, Henneman P, Mannens MM, van Straalen JP, Bahendeka S, Zwinderman AH, Kunst AE, Stronks K. Rationale and cross-sectional study design of the Research on Obesity and type 2 Diabetes among African Migrants: the RODAM study. BMJ Open. 2014 Mar 21;4(3):e004877.
19. Stronks K, Snijder MB, Peters RJ, Prins M, Schene AH, Zwinderman AH. Unravelling the impact of ethnicity on health in Europe: the HELIUS study. BMC Public Health. 2013;13(1):402.
20. Lozano R, Sazawal S, Fawzi W, Ali SM, Sanvictores D, Lopez AD, et al. A shortened verbal autopsy instrument for use in routine mortality surveillance systems. BMC Med. BMC Medicine; 2015;13(1):1–10.
21. Murray CJ, Lopez AD, Black R, Ahuja R, Ali SM, Baqui A, Dandona L, Dantzer E, Das V, Dhingra U, Dutta A, Fawzi W, Flaxman AD, Gómez S, Hernández B, Joshi R, Kalter H, Kumar A, Kumar V, Lozano R, Lucero M, Mehta S, Neal B, Ohno SL, Prasad R, Praveen D, Premji Z, Ramírez-Villalobos D, Remolador H, Riley I, Romero M, Said M, Sanvictores D, Sazawal S, Tallo V. Population Health Metrics Research Consortium gold standard verbal autopsy validation study: design, implementation, and development of analysis datasets. Popul Health Metr. 2011 Aug 4;9:27.
22. Agyemang C, Meeks K, Beune E, Owusu-Dabo E, Mockenhaupt FP, Addo J, de Graft Aikins A, Bahendeka S, Danquah I, Schulze MB, Spranger J, Burr T, Agyei-Baffour P, Amoah SK, Galbete C, Henneman P, Klipstein-Grobusch K, Nicolaou M, Adeyemo A, van Straalen J, Smeeth L, Stronks K. Obesity and type 2 diabetes in sub-Saharan Africans - Is the burden in today's Africa similar to African migrants in Europe? The RODAM study. BMC Med. 2016 Oct 21;14(1):166.
23. Hayfron-Benjamin CF, van den Born BJ, Maitland-van der Zee AH, Amoah AGB, van der Linden EL, Stronks K, Klipstein-Grobusch K, Bahendeka S, Danquah I, Beune E, Smeeth L, Agyemang C. Higher prevalence of peripheral arterial disease in Ghana compared to Ghanaian migrants in

Europe: The RODAM study. Int J Cardiol. 2020 Apr 15;305:127-134.

24. Hayfron-Benjamin C, van den Born BJ, Maitland-van der Zee AH, Amoah AGB, Meeks KAC, Klipstein-Grobusch K, Bahendeka S, Spranger J, Danquah I, Mockenhaupt F, Beune E, Smeeth L, Agyemang C. Microvascular and macrovascular complications in type 2 diabetes Ghanaian residents in Ghana and Europe: The RODAM study. J Diabetes Complications. 2019 Aug;33(8):572-578.
25. van der Linden EL, Meeks KAC, Klipstein-Grobusch K, Bahendeka S, Beune EJAJ, van den Born BH, Agyemang C. Hypertension determinants among Ghanaians differ according to location of residence: RODAM study. J Hypertens. 2022 May 1;40(5):1010-1018.
26. Osei TB, van Dijk AM, Dingerink S, Chilunga FP, Beune E, Meeks KAC, Bahendeka S, Schulze MB, Agyemang C, Nicolaou M, Holleboom AG, Danquah I. Reduced Rank Regression-Derived Dietary Patterns Related to the Fatty Liver Index and Associations with Type 2 Diabetes Mellitus among Ghanaian Populations under Transition: The RODAM Study. Nutrients. 2021 Oct 20;13(11):3679.
27. Darko SN, Meeks KAC, Owiredu WKBA, Laing EF, Boateng D, Beune E, Addo J, de-Graft Aikins A, Bahendeka S, Mockenhaupt F, Spranger J, Agyei-Baffour P, Klipstein-Grobusch K, Smeeth L, Agyemang C, Owusu-Dabo E. Anthropometric indices and their cut-off points in relation to type 2 diabetes among Ghanaian migrants and non-migrants: The RODAM study. Diabetes Res Clin Pract. 2021;173:108687.
28. Meeks KAC, Henneman P, Venema A, Addo J, Bahendeka S, Burr T, Danquah I, Galbete C, Mannens MMAM, Mockenhaupt FP, Owusu-Dabo E, Rotimi CN, Schulze MB, Smeeth L, Spranger J, Zafarmand MH, Adeyemo A, Agyemang C. Epigenome-wide association study in whole blood on type 2 diabetes among sub-Saharan African individuals: findings from the RODAM study. Int J Epidemiol. 2019 Feb 1;48(1):58-70.
29. Chilunga FP, Henneman P, Venema A, Meeks KA, Gonzalez JR, Ruiz-Arenas C, Requena-Méndez A, Beune E, Spranger J, Smeeth L, Bahendeka S, Owusu-Dabo E, Klipstein-Grobusch K, Adeyemo A, Mannens MM, Agyemang C. DNA methylation as the link between migration and the major noncommunicable diseases: the RODAM study. Epigenomics. 2021 May;13(9):653-666.

Figure legends

Figure 1 – Response and participation rates

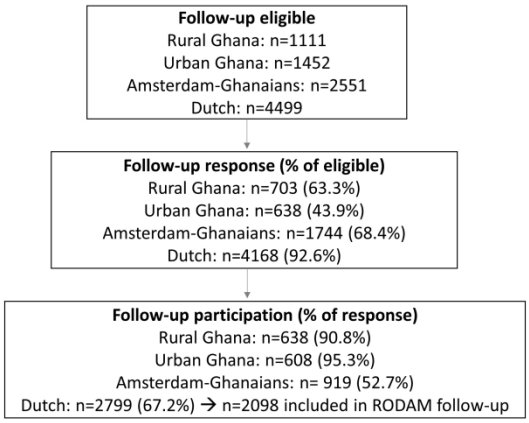

Figure 1 – Response and participation rates

338x190mm (300 x 300 DPI)