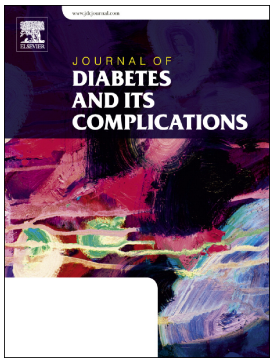

Microvascular and macrovascular complications in type 2 diabetes Ghanaian residents in Ghana and Europe: The RODAM study

Charles Hayfron-Benjamin, Bert-Jan van den Born, Anke H. Maitland - van der Zee, Albert G.B. Amoah, Karlijn A.C. Meeks, Kerstin Klipstein-Grobusch, Silver Bahendeka, Joachim Spranger, Ina Danquah, Frank Mockenhaupt, Erik Beune, Liam Smeeth, Charles Agyemang

PII: S1056-8727(19)30181-3
DOI: https://doi.org/10.1016/j.jdiacomp.2019.04.016
Reference: JDC 7369

To appear in: *Journal of Diabetes and Its Complications*

Received date: 27 February 2019
Revised date: 5 April 2019
Accepted date: 30 April 2019

Please cite this article as: C. Hayfron-Benjamin, B.-J. van den Born, A.H. Maitland - van der Zee, et al., Microvascular and macrovascular complications in type 2 diabetes Ghanaian residents in Ghana and Europe: The RODAM study, Journal of Diabetes and Its Complications, https://doi.org/10.1016/j.jdiacomp.2019.04.016

Title: Microvascular and macrovascular complications in type 2 diabetes Ghanaian residents in Ghana and Europe: The RODAM Study

Charles Hayfron-Benjamin MBChB,[1-3,15] Bert-Jan van den Born Ph.D.,[1,2] Anke H. Maitland - van der Zee Ph.D.,[3] Albert G. B. Amoah Ph.D.,[4] Karlijn A. C. Meeks Ph.D.,[1,5] Kerstin Klipstein-Grobusch Ph.D.,[6,7] Silver Bahendeka Ph.D.,[8] Joachim Spranger MD.,[9,10] Ina Danquah Ph.D.,[11,12] Frank Mockenhaupt MD.,[13] Erik Beune Ph.D.,[1] Liam Smeeth Ph.D.,[14] Charles Agyemang Ph.D. [1]

1. Department of Public Health, Amsterdam UMC, University of Amsterdam, Amsterdam Public Health research institute, Amsterdam, The Netherlands.
2. Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, The Netherlands.
3. Department of Respiratory Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands.
4. Department of Medicine & Therapeutics, University of Ghana Medical School, Accra, Ghana ; National Diabetes Management & Research Centre, Korle-Bu Teaching Hospital, Accra, Ghana.
5. Center for Research on Genomics and Global Health, National Human Genome Research Institute, Bethesda, MD, USA.
6. Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, The Netherlands.
7. Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.
8. MKPGMS-Uganda Martyrs University, Kampala, Uganda.
9. Department of Endocrinology and Metabolism, Charité Universitätsmedizin Berlin, Berlin, Germany.
10. Center for Cardiovascular Research (CCR), Charite-Universitaetsmedizin Berlin, Berlin, Germany.
11. Institute for Social Medicine, Epidemiology and Health Economics, Charité Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universitaet zu Berlin, and Berlin Institute of Health, Berlin, Germany.
12. Department of Molecular Epidemiology, German Institute of Human Nutrition Potsdam-Rehbrücke, Nuthetal, Germany.
13. Institute of Tropical Medicine and International Health, Charité Universitätsmedizin Berlin, Berlin, Germany.
14. Department of Non-communicable Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom.
15. Department of Physiology, University of Ghana Medical School, Accra, Ghana ; Department of Anaesthesia, Korle-Bu Teaching Hospital, Accra, Ghana.

CORRESPONDING AUTHOR

Charles Hayfron-Benjamin

Departments of Public Health, Respiratory Medicine and Vascular Medicine, Amsterdam UMC, University of Amsterdam, The Netherlands

E-mail: charlesfhb1@gmail.com; c.hayfronbenjamin@amc.nl

P O Box DC 605, Dansoman, Accra, Ghana.

Telephone: +233 20 042 7790

STRUCTURED ABSTRACT

AIMS: To compare microvascular and macrovascular complication rates among Ghanaians with type 2 diabetes (T2D) living in Ghana and in three European cities (Amsterdam, London and Berlin).

METHODS: Data from the multicenter Research on Obesity and Diabetes among African Migrants (RODAM) study were analyzed. 650 Ghanaian participants with T2D (206 non-migrant and 444 migrants) were included. Logistic regression analyses were used to determine the association between migrant status and microvascular (nephropathy and retinopathy) and macrovascular (coronary artery disease (CAD), peripheral artery disease (PAD) and stroke) complications with adjustment for age, gender, socioeconomic status, alcohol, smoking, physical activity, hypertension, BMI, total-cholesterol, and HbA1c.

RESULTS: Microvascular and macrovascular complications rates were higher in non-migrant Ghanaians than in migrant Ghanaians (nephropathy 32.0% vs. 19.8%; PAD 11.2% vs. 3.4%; CAD 18.4% vs. 8.3%; and stroke 14.5% vs. 5.6%), except for self-reported retinopathy (11.0% vs. 21.6%). Except nephropathy and stroke, the differences persisted after adjustment for the above-mentioned covariates: PAD (OR 7.48; 95%CI, 2.16-25.90); CAD (2.32; 1.09-4.93); and retinopathy (0.23; 0.07-0.75).

CONCLUSIONS: Except retinopathy, the rates of microvascular and macrovascular complications was higher in non-migrant than in migrant Ghanaians with T2D. Conventional cardiovascular risk factors did not explain the differences except for nephropathy and stroke.

KEYWORDS: Diabetes complications, microvascular, macrovascular, Ghana, RODAM study, ethnic minority groups.

1. INTRODUCTION

Worldwide, the prevalence of diabetes is increasing, but substantial variations exist between regions (1). According to the International Diabetes Federation in 2017, about 16 million people in sub-Saharan Africa had diabetes, with the burden projected to increase to 41 million people by 2045, the highest projected increase anywhere in the world (2).

Diabetes increases the risk of macrovascular disease, including coronary heart disease (CAD), peripheral vascular disease (PAD), and stroke (3,4). Diabetes also causes specific microvascular complications such as retinopathy, nephropathy and neuropathy, and remains a leading cause of blindness, end stage kidney disease, and lower limb amputation (3,5–8). The microvascular and macrovascular complications of diabetes contribute to reduced quality of life, increased risk of hospitalization, disability and mortality, that pose a burden on the economies of all countries, especially the low and middle income ones (9,10).

In high-income countries, migrant populations including those from sub-Saharan Africa are disproportionately affected by diabetes, and tend to develop the disease at a younger age than the host populations (11). For example, the prevalence of type 2 diabetes was two to three times higher in populations of sub-Saharan Africa origin than in European host populations (11). Further, migrants resident in high-income countries have higher prevalence of diabetes than their counterparts in rural sub-Saharan Africa (12). These disparities may suggest a role of environmental factors in the development of diabetes among these populations (12).

In a previous Research on Obesity & Diabetes among African Migrants (RODAM) study, we observed higher diabetes prevalence in migrant-Ghanaians in three European cities compared to non-migrant Ghanaians (12). The prevalence of diabetes-related microvascular and macrovascular complications in the two populations, however, is not known. Therefore, we assessed the prevalence of microvascular (nephropathy and retinopathy) and macrovascular

(CAD, PAD and stroke) complications in the RODAM cohorts with type 2 diabetes in Europe and in Ghana. Furthermore, we assessed whether the rates of diabetic microvascular and macrovascular complications vary between Ghanaian migrants in Europe and their non-migrant compatriots living in Ghana.

2. METHODS

2.1 Study Design

The rationale, conceptual framework, design and methodology of the RODAM study have been described in detail elsewhere (13). For the current analysis only participants with type 2 diabetes were included in the analyses. This included data from 206 participants in Ghana and 444 Ghanaian migrants resident in Amsterdam, Berlin and London (figure 1). Type 2 diabetes was defined according to the World Health Organization diagnostic criteria (self-reported diabetes, documented use of glucose-lowering medication(s), fasting plasma glucose $\geq$ 7.0 mmol/L) or HbA1c $\geq$ 6.5% or $\geq$48 mmol/mol (14). Participants who met the diagnostic criteria for diabetes but who had no prior diabetes and who were not on glucose-lowering medication(s) were considered to have undiagnosed diabetes.

2.2 Participants' Baseline Measurements

A structured questionnaire (13) was used to record the demographic, socioeconomic, health-related behaviors, and microvascular and macrovascular complications (retinopathy, CAD, and strokes) of the study participants. The assessment of educational status was adapted to local circumstances at the different study sites and comprised four categories: never been to school or elementary school; lower vocational schooling or lower secondary schooling; intermediate vocational schooling or intermediate/higher secondary schooling; and higher vocational schooling or university. Smoking was assessed as a positive reply to the question 'Do you smoke at all?' Alcohol intake in grams per day was estimated using standard portion seizes combined with frequencies of intake based on a standardised Food Propensity Questionnaire. Physical activity was derived for each participant using International physical

activity questionnaire (15). Respondents were classified into three categories of total physical activity, namely low, moderate and high level. Eyesight was graded by the response to the question 'At the present time, would you say your eyesight using both eyes (with glasses or contact lenses, if you wear them) is excellent, good, fair, poor, or very poor or are you completely blind?'

Physical examinations were performed with validated devices according to standardized operational procedures across all study sites. Weight was measured in light clothing and without shoes with SECA 877 scales to the nearest 0.1 kg. Height was measured without shoes with a portable stadiometer (SECA 217) to the nearest 0.1 cm. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). Waist circumference (WC) was measured in centimeters at the midpoint between the lower margin of the least palpable rib and the top of the iliac crest. Hip circumference (HC) was measured in centimeters around the widest portion of the buttocks, at the level of the greater trochanters, with the tape parallel to the floor. Waist-to-hip ratio (WHR) was determined as the ratio of WC to HC. All the anthropometrics were measured twice by the same assessor and the average of the two measurements was used for analyses. Body fat was determined using arm-leg bio-impedance measurements using a Bodystat 1500 analyzer (Bodystat Ltd, Isle of Man, UK). The body fat percentage was calculated using the African-specific formula by Kyle et al. (16)

Blood pressure (BP) was measured three times using a validated semi-automated device (Microlife Watch BP home, Widnau, Switzerland), with appropriate sized cuffs after at least 5 minutes rest while seated. The mean of the last two BP measurements was used for the analyses. Hypertension was defined as systolic BP $\geq$140 mmHg and/or diastolic BP $\geq$90 mmHg, and/or being on antihypertensive medication treatment. Ankle brachial index (ABI), the ratio of the resting systolic blood pressure at the ankle to the resting systolic

brachial pressure at the arm, was obtained from two blood pressure measurements on the left side (leg and arm) and two on the right side (leg and arm) using the Microlife Watch BP Office ABI with appropriate sized cuffs, after at least 10 minutes of supine rest. The cuffs for measuring the ankle and brachial pressures were placed just above the ankle and at the upper arm, respectively.

2.3 Biochemical Analyses

Fasting venous blood samples were processed and aliquoted into Sarstedt tubes after collection according to standard operation procedures, and then temporarily stored at the local research location at −20 °C. Two aliquoted blood samples and one first early morning urine sample were transported to the local research centres, where they were checked, registered and stored at −80 °C before being shipped to the laboratory at Charité–University Medicine Berlin (Berlin, Germany) for determination of biochemical variables. Shipping of the samples from European sites was carried out using Styrofoam boxes filled with dry ice and from Ghana in dry shippers filled with liquid nitrogen. Extensive quality checks were done during the biochemical analysis, including blinded serial measurements.

Fasting glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides levels were determined using the ABX Pentra 400 chemistry analyzer (HORIBA ABX, Montpellier, France). Fasting plasma glucose concentration was measured using an enzymatic method (hexokinase). Concentration of total cholesterol was assessed by using colorimetric test kits.. HbA1c was measured by high-performance liquid chromatography (TOSOH G8 HPLC analyzer). Serum creatinine concentration was determined by a kinetic colorimetric spectrophotometric isotope dilution mass spectrometry calibration method (Roche Diagnostics). Estimated glomerular filtration rate (eGFR) was calculated using the 2009

CKD-EPI (CKD Epidemiology Collaboration) creatinine equation and the severity of kidney disease categorized according to the 2012 KDIGO guidelines (17).

Urinary albumin concentration (in mg/L) was measured by an immunochemical turbidimetric method (Roche Diagnostics). Urinary creatinine concentration (in μmol/L) was measured by a kinetic spectrophotometric method (Roche Diagnostics). Urinary albumin–creatinine ratio (ACR; expressed in mg/g) was calculated by taking the ratio between urinary albumin and urinary creatinine and stratified according to the 2012 KDIGO classifications: A1, <3 mg/mmol (normal to mildly increased); A2, 3 to 30 mg/mmol (moderately increased); and A3, > 30 mg/mmol (severely increased).

2.4 Determination of Microvascular and Macrovascular Complications

Nephropathy was defined as albuminuria or microalbuminuria based on the report from Joint Committee on Diabetic Nephropathy (18). PAD was defined as ankle brachial index <0.9 (19). Retinopathy was assessed by a positive reply to the question 'Have you ever been told by a doctor or health care worker that you have eye disease or eye damage as a result of your diabetes (diabetic retinopathy)?' (13). Coronary artery disease (CAD) was assessed using the WHO Rose angina questionnaire (20). Possible myocardial infarction was defined as a positive reply to the question 'have you ever had a severe pain across the front of your chest lasting for half an hour or more?' Angina was defined as a positive reply to the questions 'Have you ever had any pain or discomfort in your chest?' and 'Do you get this pain or discomfort when you walk uphill or hurry?' Stroke was assessed by a positive reply to the question 'Have you ever had a stroke?' (13).

2.5 Statistical Analysis

Data were analyzed using the IBM SPSS version 22 for Windows. Data with normal distribution was presented as mean ± standard deviation whereas those not normally distributed presented as median (interquartile range). Categorical data were presented as frequencies (percentages). Differences in demographic, clinical and micro- and macrovascular function between migrants and non-migrants with type 2 diabetes were assessed by chi-square test or two-sample independent sample t-test for categorical or continuous covariates, respectively.

Multivariable logistic regression was used to build a model of factors associated with the microvascular and macrovascular complications including nephropathy, retinopathy, CAD, PAD, and stroke (dependent variables); and the sites of residence in Ghana and Europe (independent variable) with adjustments for potential covariates. Four models were used to examine the data: model 1 was unadjusted for any covariate; model 2 was adjusted for age and gender; model 3 was additionally adjusted for socioeconomic status (level of education); and model 4 was additionally adjusted for the conventional cardiovascular risk factors including, smoking; physical activity, hypertension, BMI, hypercholesterolemia, HbA1c and amount of alcohol consumed. The data as presented as odds ratios (OR) with their corresponding 95% confidence intervals (CI). The analyses were performed for Ghanaian and European sites using Europe as reference. In a sensitivity analysis, we further compared the proportions of microvascular and macrovascular complications between migrant and non-migrant Ghanaians stratified by previously known and unknown diabetes. A statistical test of significance was set at p-value < 0.05.

3. RESULTS

3.1 General Characteristics

The baseline characteristics for the migrants and non-migrants with type 2 diabetes are described in table 1. Although there was no difference in age, migrants were more frequently male than non-migrants. Migrants generally had a higher level of education, had a higher proportion of current smokers, and consumed more alcohol than their non-migrant counterparts. While there was no difference in the percent body fat between the two groups, the BMI and WHR were higher in the migrant group than in non-migrants. There was no difference in the duration of diabetes between migrants and non-migrants. The systolic blood pressure and diastolic blood pressure were also higher in the migrant group than in non-migrants. However, the non-migrant group had a higher proportion of undiagnosed diabetes, lower proportion of participants taking glucose lowering medications, poorer glycemic control and worse eyesight compared to migrants. Additionally, non-migrants had higher concentrations of blood triglyceride and LDL-cholesterol and lower HDL-cholesterol concentration than migrants.

3.2 Differences in microvascular and macrovascular complications between migrants and non-migrants

Table 2 shows the differences in the prevalence of microvascular and macrovascular complications between the migrant and non-migrant Ghanaians with type 2 diabetes. Overall, the proportion of nephropathy was higher in non-migrants than in migrants (32.0% vs. 19.8%). Additionally, non-migrants were more likely to have moderate to severe forms of albuminuria (categories A2 and A3; ACR >3 mg/mmol). There was no difference in the

eGFR categories between the two groups. Non-migrants also had higher prevalence of PAD (11.2% vs. 3.4%), CAD (18.4% vs. 8.3%) and s stroke (14.5% vs. 5.6%) than migrants. However, migrants had higher prevalence of self-reported diabetic retinopathy previously diagnosed by a doctor or health worker than non-migrants (21.6% vs. 11.0%).

The odds ratios (ORs) of the microvascular and macrovascular complications for Ghanaians with type 2 diabetes living in rural and urban Ghana compared with Ghanaians living in the three European cities are shown in table 3. After adjusting for age and gender, living in Ghana was still associated with higher odds for developing nephropathy (OR 2.01, 95% CI, 1.35-3.01), PAD (OR 3.14, 95% CI, 1.58-6.24), CAD (OR 2.31, 95% CI, 1.40-3.83) and stroke (OR 2.74, 95% CI, 1.52-4.93). Similar results were obtained after additionally adjusting for socioeconomic status. However, after further adjustments for the conventional cardiovascular risk factors, the proportion of the nephropathy and self-reported strokes was no longer statistically significant, but the differences persisted for the macrovascular complications PAD (OR 7.48, 95% CI, 2.16-25.90) and CAD (OR 2.32, 95% CI, 1.09-4.93). Adjustment for age, gender and socioeconomic status explained the differences in retinopathy diagnosed by a doctor.

The prevalence rates of microvascular and macrovascular complications were generally similar between newly diagnosed diabetes and established diabetes participants (Supplementary Table 1). When the analysis was further stratified by participants with previously known diabetes and undiagnosed diabetes (Supplemental Table 2), the proportions of nephropathy (35.8% vs. 17.1%, $p<0.001$), PAD (10.6% vs. 4.3%, $p=0.028$) and CAD (20.8% vs. 8.4%, $p=0.001$) were higher, but self-reported diabetic retinopathy (11.0% vs. 22.2%, $p=0.022$) was lower in non-migrants than in migrants among previously known diabetes participants. For participants with undiagnosed diabetes, the proportions of

nephropathy, CAD and PAD were similarly higher in non-migrants than in migrants although the differences were not significant except for PAD (12.0% vs. 1.9%, p=0.002).

4. DISCUSSION

4.1 Key findings

Our study shows that the prevalence of both microvascular (nephropathy) and macrovascular (coronary artery disease, peripheral artery disease and self-reported stroke) complications are higher in non-migrant than in migrant-Ghanaians with type 2 diabetes. Correction for conventional cardiovascular risk factors attenuated differences in the complication rates. However, after correction for conventional cardiovascular risk factors, the difference in PAD and CAD remained statistically significant.

4.2 Discussion of key findings

There is limited published data on community level of diabetes-related microvascular and macrovascular complications among sub-Saharan Africans with type 2 diabetes. Most studies are either diabetes clinic-based or hospital-based surveys (21–26). Moreover, on account of differences in study methodology and diagnostic criteria used in defining the diabetes-related microvascular and macrovascular complications, reports show wide variations (21–27). With the exception of CAD, our findings for non-migrant Ghanaians with type 2 diabetes compare well with these studies. The differences in the proportion of CAD could be due to the diagnostic criteria for CAD used in previous studies (26). In the study on coronary heart disease in the diabetic African, Touze *et al*. assessed CAD via stress test and/or coronary arteriography (26). In this study, we evaluated CAD using the WHO Rose angina questionnaire. The WHO Rose angina questionnaire has been shown to overestimate CAD prevalence, with higher sensitivity among people from lower socio-economic status (28,29).

This could explain the relatively higher prevalence of CAD observed in non-migrant Ghanaians with type 2 diabetes, compared with the findings from Touze et al.

Published studies comparing the burden of microvascular complications in sub-Saharan Africans with type 2 diabetes and their migrant counterparts are limited. Choukem *et al*. previously compared microvascular complications between Cameroonians with type 2 diabetes living in Cameroon and those who migrated to France (30). After adjusting for the conventional cardiovascular risk factors, Cameroonians with type 2 diabetes living in Cameroon were found to have a 5.6 higher odds of nephropathy than their counterparts living in France (30). Although less marked compared with the findings by Choukem *et al*., this present study shows that non-migrant Ghanaians had higher prevalence of nephropathy than migrants. Our non-migrant participants with type 2 diabetes had better glycemic control than the non-migrant Cameroonians studied by Choukem et al. This could explain why we had less marked differences in the prevalence of nephropathy between migrant and non-migrant Ghanaians with type 2 diabetes.

Contrary to the other microvascular and macrovascular complications, retinopathy diagnosed by a doctor or health worker was higher in migrants than in non-migrants. This may reflect the better access to healthcare by migrants and hence increased likelihood of diagnosis of the complication. Therefore, retinopathy assessed this way may reflect diagnosis of the complication by a doctor or healthcare worker instead of true prevalence of the disease. In this study, when participants were asked to grade their eyesight as excellent, good, fair, poor, or very poor or completely blind, in contrast to the retinopathy previously diagnosed by a doctor or healthcare worker, non-migrant Ghanaians were more likely to report poor vision to total blind compared with their migrant peers. This highlights the need for more objective measures such as fundus photography in making diagnoses of retinopathy.

With the exception of factors related to glycemic control and blood lipids, living in Europe was associated with a worse cardiovascular risk profile in Ghanaians with type 2 diabetes. This is consistent with findings from previous studies that have compared cardiovascular disease risk factors among residents with or without type 2 diabetes living in rural and urbanized cities in their respective countries or overseas (31,32). Using data from the RODAM study, we have previously reported that European residence was associated with higher odds for elevated 10-year risk of cardiovascular disease among Ghanaian men with or without diabetes (33). It is thus interesting to observe that despite their overall poorer cardiovascular risk profiles, migrants had lower complication rates than their non-migrant counterparts. Therefore, poor glycemic control (evidenced by the higher HbA1c in non-migrant Ghanaians), instead of the other conventional cardiovascular risk factors, could be the key driving force for the development of these diabetic microvascular complications. This supports the existing pathophysiological explanation for microvascular injury that highlights chronic hyperglycemia as the central mechanism (34). Further, it underscores the importance of glycemic control in preventing diabetes-related complications and the need for implementation of strategies to improve glycemic control among people with diabetes in Ghana.

Although the higher prevalence of microvascular and macrovascular complications in non-migrant Ghanaians is likely to reflect poorer diabetes care, it remains unclear whether the observed differences is due to differences in the access to quality care or related to the microvascular and macrovascular complications rates at the time of diagnosis. While this study did not directly address the impact of healthcare on the development of microvascular and macrovascular complications, it is conceivable that access to healthcare and timely initiation of medical treatment could explain some of the differences. The attenuation of differences in microvascular and macrovascular complications after correction for

conventional cardiovascular risk factors is supportive of this assumption. Indeed a previous report from Ghana had indicated limited health infrastructure and access for diabetes care (35). In people with diabetes, both lack of health care coverage and low utility of available health care service are known to be associated with poor glycemic control (36).

In this study, we observed a higher proportion of undiagnosed diabetes in non-migrants compared to migrants. However, the microvascular and macrovascular complication rates in the undiagnosed and previously diagnosed diabetes groups were similar. Given the above facts, the higher proportion of undiagnosed diabetes in the non-migrant group may not explain all the observed differences in the complication rates between migrant and non-migrant Ghanaians with type 2 diabetes. Thus, just improving targeted screening for type 2 diabetes without appropriate treatment and management of complications may not necessarily decrease the rates of diabetes-related microvascular and macrovascular complications. Therefore care of diabetes after diagnosis as well as controlling the modifiable risk factors for vascular complications may play important roles in reducing the rates and severity of diabetes-related microvascular and macrovascular complications. This is evidenced by the lower rates of complications in migrants who reside in Europe where diabetes is likely to be diagnosed earlier and complication screening and care instituted. Previous studies have shown that the asymptomatic phase of type 2 diabetes (lasting at least 4 to 7 years) is known to be associated with increased risk of developing microvascular complications (37). Additionally, early diagnosis and treatment of hyperglycemia is known to prevent disease progression and delay the development of diabetes related complications (38).

Although the strength of association between migrant status and diabetes complications differ in the subgroups with unknown diabetes and previously known diabetes, the pattern of associations are similar. This may imply that aside hyperglycemia, other risk factors may be

important in driving development of diabetic microvascular and macrovascular complications. In this study, we observed higher LDL-cholesterol concentrations and lower HDL-cholesterol concentrations in non-migrants compared to migrant Ghanaians. Diabetic dyslipidemia is known to cause or exacerbate diabetic microvascular and macrovascular complications via multiple mechanisms including alterations in the coagulation-fibrinolytic system, changes in membrane permeability, damage to endothelial cells and increased atherosclerosis (39)

Diabetic microvascular and macrovascular complications have similar etiologic characteristics, with chronic hyperglycemia driving several metabolic and structural derangements including the formation of advanced glycation end products, activation of inflammatory pathways, and increased oxidative stress (34). Further, diabetics with microvascular complications are prone to accelerated atherosclerosis and subsequent macrovascular injury (34). It would, therefore, have been expected that the risk factors driving microvascular injury and atherosclerosis would explain the differences in the prevalence of macrovascular complications in our cohort. However, adjusting for these risk factors could not explain the differences in PAD and CAD suggesting that other unmeasured factors may play a role. It is worth noting that the time dependent effects of blood pressure, poor glycemic control and persistent dyslipidemia on microvascular and macrovascular complications were not assessed in this study due to the cross-sectional design nature of our study. More work is needed to identify other potential factors driving the differences in macrovascular complications among migrant and non-migrant Ghanaians. This could possibly inform complication prevention strategies and treatment efforts.

4.3 Strengths and limitations

Key strengths of our study are that we used a relatively homogenous multi-centered study population of Ghanaians and well-standardized study protocols across the various study sites. Additionally, we eliminated the limitation of intra-laboratory variability by using the same standard operating procedures in the same laboratory for running all samples across all sites. Our study is limited in a number of ways. First, we used both objective and subjective measures for microvascular and macrovascular complications, but both pointed to the same direction. We assessed CAD via the Rose Angina Questionnaire. Although the Rose Angina Questionnaire has moderate sensitivity, it has a high specificity to detect CAD and is valuable for screening individuals at risk of CAD in large-scale epidemiological surveys (28). CAD and stroke were self-reported, which could have led to reporting bias. While the question used to assess diabetic retinopathy is a very sensitive measure for proliferative retinopathy and has a high specificity for measuring the prevalence of diabetic retinopathy, it is less sensitive for non-proliferative retinopathy (40). Additionally, neuropathy, another microvascular complication, was not assessed. Finally, the duration of diabetes was not included as a covariate in the multivariable analysis because a large number of study participants did not provide this information.

4.4 Conclusion

Our study shows that Ghanaian migrants with T2D had lower prevalence of microvascular and macrovascular complications than their non-migrant counterparts. Unlike the CAD and PAD, the differences in the nephropathy and stroke were explained by poorer glycemic control in non-migrant Ghanaians. Therefore, the higher prevalence of microvascular complications in non-migrants is likely to reflect poorer diabetic care. Thus, interventions aimed at improving glycemic control among non-migrant Ghanaians may help to reduce the

prevalence of some diabetic microvascular and macrovascular complications in Ghana. More work is needed to identify potential factors driving the high prevalence of microvascular and macrovascular complications among non-migrant Ghanaians to assist the prevention and treatment efforts.

Acknowledgments

We are grateful to the research assistants, interviewers, and other staff of the 5 research locations who have taken part in gathering the data and, most of all, the Ghanaian volunteers participating in the RODAM study (Research on Obesity and Diabetes Among African Migrants). We gratefully acknowledge the advisory board members for their valuable support in shaping the RODAM study methods, Jan van Straalen from the Amsterdam University Medical Centre with standardization of the laboratory procedures, and the Amsterdam University Medical Centre Biobank for their support in biobank management and high-quality storage of collected samples.

Funding

This work was supported by the European Commission under the Framework Programme (Grant Number: 278901). K.M. is supported by the Intramural Research Program of the National Institutes of Health in the Center for Research on Genomics and Global Health (CRGGH). The CRGGH is supported by the National Human Genome Research Institute, the National Institute of Diabetes and Digestive and Kidney Diseases, the Center for Information Technology, and the Office of the Director at the National Institutes of Health (1ZIAHG200362). The study sponsor was not involved in the design of the study; the

collection, analysis and interpretation of data; writing the report; nor the decision to submit the report for publication.

Authorship Contributions

All authors have contributed substantially to this article and approved the submission. C.H-B, B.B., A.H.M, A.G.B.A and C.A. conceived the idea. C.H-B., E.B., and C.A. were responsible for data acquisition; C.H-B., and C.A. were responsible for statistical analysis. C.H-B, B.B., A.H.M, A.G.B.A., K.A.C.M, K.K.-G., S.B., J.S., I.D., F.M., E.B., L.S., and C.A. were responsible for data analysis/interpretation. Each author contributed important intellectual content during article drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. C.H-B. takes responsibility for the fact that this study has been reported honestly, accurately and transparently, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained

Disclosures of Interests

None declared

References

1. Ogurtsova K, da Rocha Fernandes JD, Huang Y, Linnenkamp U, Guariguata L, Cho NH, et al. IDF Diabetes Atlas: Global estimates for the prevalence of diabetes for 2015 and 2040. Diabetes Res Clin Pract. 2017 Jun 1;128:40–50.

2. IDF diabetes atlas - Home [Internet]. [cited 2017 Oct 28]. Available from: http://www.diabetesatlas.org/

3. Association AD. Standards of Medical Care in Diabetes—2014. Diabetes Care. 2014 Jan 1;37(Supplement 1):S14–80.

4. Deshpande AD, Harris-Hayes M, Schootman M. Epidemiology of Diabetes and Diabetes-Related Complications. Phys Ther. 2008 Nov;88(11):1254–64.

5. Fong DS, Aiello L, Gardner TW, King GL, Blankenship G, Cavallerano JD, et al. Diabetic Retinopathy. Diabetes Care. 2003 Jan 1;26(suppl 1):s99–102.

6. Chance WW, Rhee C, Yilmaz C, Dane DM, Pruneda ML, Raskin P, et al. Diminished Alveolar Microvascular Reserves in Type 2 Diabetes Reflect Systemic Microangiopathy. Diabetes Care. 2008 Aug;31(8):1596–601.

7. Association AD. Diabetic Nephropathy. Diabetes Care. 2003 Jan 1;26(suppl 1):s94–8.

8. Pop-Busui R, Boulton AJM, Feldman EL, Bril V, Freeman R, Malik RA, et al. Diabetic Neuropathy: A Position Statement by the American Diabetes Association. Diabetes Care. 2017 Jan 1;40(1):136–54.

9. Guariguata L, Whiting DR, Hambleton I, Beagley J, Linnenkamp U, Shaw JE. Global estimates of diabetes prevalence for 2013 and projections for 2035. Diabetes Res Clin Pract. 2014 Feb 1;103(2):137–49.

10. Liu NF, Brown AS, Younge MF, Guzman SJ, Close KL, Wood R. Stigma in People With Type 1 or Type 2 Diabetes. Clin Diabetes. 2017 Jan 1;35(1):27–34.

11. Meeks KAC, Freitas-Da-Silva D, Adeyemo A, Beune EJAJ, Modesti PA, Stronks K, et al. Disparities in type 2 diabetes prevalence among ethnic minority groups resident in Europe: a systematic review and meta-analysis. Intern Emerg Med. 2016 Apr;11(3):327–40.

12. Agyemang C, Meeks K, Beune E, Owusu-Dabo E, Mockenhaupt FP, Addo J, et al. 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 [Internet]. 2016 Oct 21;14. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5075171/

13. Agyemang C, Beune E, Meeks K, Owusu-Dabo E, Agyei-Baffour P, Aikins A de-Graft, et al. Rationale and cross-sectional study design of the Research on Obesity and type 2 Diabetes among African Migrants: the RODAM study. BMJ Open [Internet]. 2014 Mar 21 [cited 2019 Feb 3];4(3). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3963103/

14. WHO | Definition and diagnosis of diabetes mellitus and intermediate hyperglycaemia [Internet]. WHO. [cited 2018 Mar 27]. Available from: http://www.who.int/diabetes/publications/diagnosis_diabetes2006/en/

15. Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003 Aug;35(8):1381–95.

16. Kyle UG, Genton L, Karsegard L, Slosman DO, Pichard C. Single prediction equation for bioelectrical impedance analysis in adults aged 20--94 years. Nutr Burbank Los Angel Cty Calif. 2001 Mar;17(3):248–53.

17. Lamb EJ, Levey AS, Stevens PE. The Kidney Disease Improving Global Outcomes (KDIGO) guideline update for chronic kidney disease: evolution not revolution. Clin Chem. 2013 Mar;59(3):462–5.

18. Haneda M, Utsunomiya K, Koya D, Babazono T, Moriya T, Makino H, et al. A new Classification of Diabetic Nephropathy 2014: a report from Joint Committee on Diabetic Nephropathy. J Diabetes Investig. 2015 Mar;6(2):242–6.

19. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, et al. Measurement and Interpretation of the Ankle-Brachial Index: A Scientific Statement From the American Heart Association. Circulation. 2012 Dec 11;126(24):2890–909.

20. Rose Chest Pain Questionnaire. Occas Pap R Coll Gen Pract. 2002 Feb;(82):43.

21. Burgess PI, MacCormick IJC, Harding SP, Bastawrous A, Beare N a. V, Garner P. Epidemiology of diabetic retinopathy and maculopathy in Africa: a systematic review. Diabet Med J Br Diabet Assoc. 2013 Apr;30(4):399–412.

22. Noubiap JJN, Naidoo J, Kengne AP. Diabetic nephropathy in Africa: A systematic review. World J Diabetes. 2015 Jun 10;6(5):759–73.

23. Yeboah K, Puplampu P, Boima V, Antwi DA, Gyan B, Amoah AGB. Peripheral sensory neuropathy in type 2 diabetes patients: A case control study in Accra, Ghana. J Clin Transl Endocrinol. 2016 Sep 1;5:26–31.

24. Okello S, Millard A, Owori R, Asiimwe SB, Siedner MJ, Rwebembera J, et al. Prevalence of lower extremity Peripheral artery disease among adult diabetes patients in Southwestern Uganda. BMC Cardiovasc Disord. 2014 Jun 10;14(1):75.

25. Kalk WJ, Joffe BI. Differences in coronary heart disease prevalence and risk factors in African and White patients with type 2 diabetes. Diabetes Res Clin Pract. 2007 Jul;77(1):107–12.

26. Touze JE, Ekra A, Darracq R, Mardelle T, Adoh A, Ake E, et al. Coronary heart disease in the diabetic African: frequency clinical and angiographic features. Diabete Metab. 1987 Oct;13(5):529–33.

27. Danquah I, Bedu-Addo G, Terpe K-J, Micah F, Amoako YA, Awuku YA, et al. Diabetes mellitus type 2 in urban Ghana: characteristics and associated factors. BMC Public Health. 2012 Mar 20;12(1):210.

28. Rahman MA, Spurrier N, Mahmood MA, Rahman M, Choudhury SR, Leeder S. Rose Angina Questionnaire: validation with cardiologists' diagnoses to detect coronary heart disease in Bangladesh. Indian Heart J. 2013 Feb;65(1):30–9.

29. Biloglav Z, Ivanković D, Campbell H, Rudan I. Performance of WHO Angina Questionnaire in measuring burden of coronary heart disease in human isolate populations. Coll Antropol. 2004 Jun;28(1):205–13.

30. Choukem SP, Fabreguettes C, Akwo E, Porcher R, Nguewa JL, Bouche C, et al. Influence of migration on characteristics of type 2 diabetes in sub-Saharan Africans. Diabetes Metab. 2014 Feb;40(1):56–60.

31. Kodaman N, Aldrich MC, Sobota R, Asselbergs FW, Poku KA, Brown NJ, et al. Cardiovascular Disease Risk Factors in Ghana during the Rural-to-Urban Transition: A Cross-Sectional Study. PloS One. 2016;11(10):e0162753.

32. Miranda JJ, Gilman RH, Smeeth L. Differences in cardiovascular risk factors in rural, urban and rural-to-urban migrants in Peru. Heart Br Card Soc. 2011 May;97(10):787–96.

33. Boateng D, Agyemang C, Beune E, Meeks K, Smeeth L, Schulze M, et al. Migration and Cardiovascular Disease Risk Among Ghanaian Populations in Europe: The RODAM Study (Research on Obesity and Diabetes Among African Migrants). Circ Cardiovasc Qual Outcomes. 2017 Nov;10(11).

34. Orasanu G, Plutzky J. The pathologic continuum of diabetic vascular disease. J Am Coll Cardiol. 2009 Feb 3;53(5 Suppl):S35-42.

35. Amoah AG, Owusu SK, Saunders JT, Fang WL, Asare HA, Pastors JG, et al. Facilities and resources for diabetes care at regional health facilities in southern Ghana. Diabetes Res Clin Pract. 1998 Nov;42(2):123–30.

36. Zhang X, Bullard KM, Gregg EW, Beckles GL, Williams DE, Barker LE, et al. Access to Health Care and Control of ABCs of Diabetes. Diabetes Care. 2012 Jul;35(7):1566–71.

37. Spijkerman AMW, Dekker JM, Nijpels G, Adriaanse MC, Kostense PJ, Ruwaard D, et al. Microvascular Complications at Time of Diagnosis of Type 2 Diabetes Are Similar Among Diabetic Patients Detected by Targeted Screening and Patients Newly Diagnosed in General Practice: The Hoorn Screening Study. Diabetes Care. 2003 Sep 1;26(9):2604–8.

38. Engelgau MM, Narayan KM, Herman WH. Screening for type 2 diabetes. Diabetes Care. 2000 Oct;23(10):1563–80.

39. Misra A, Kumar S, Kishore Vikram N, Kumar A. The role of lipids in the development of diabetic microvascular complications: implications for therapy. Am J Cardiovasc Drugs Drugs Devices Interv. 2003;3(5):325–38.

40. Klein R, Klein BEK, Moss SE, Dements DL. The validity of a survey question to study diabetic retinopathy. Am J Epidemiol. 1986 Jul 1;124(1):104–10.

Table 1: Baseline characteristics of subjects

	Migrants*	**Non-migrants†**	***p* value**
	Migrants	Non-migrants	*p* value
Participants	*n*=444	*n*=206	
Female gender	222 (50.0%)	142 (68.9%)	<0.001
Age (y)	52.22 (±8.83)	52.86 (±9.99)	0.408
Education			<0.001
None or elementary	103 (24.8%)	96 (48.2%)	
Lower secondary	159 (38.2%)	70 (35.2%)	
Higher secondary	97 (23.3%)	25 (12.6%)	
Tertiary education	57 (13.7%)	8 (4.0%)	
Physical activity			0.217
Low level	118 (34.8%)	82 (41.2%)	
Moderate level	74 (21.8%)	44 (22.1%)	
High level	147 (43.4%)	73 (36.7%)	
Eyesight			0.011
Excellent	37 (10.6%)	8 (4.0%)	
Good	159 (45.4%)	78 (39.0%)	
Fair	125 (35.7%)	88 (44.0%)	
Poor	28 (8.0%)	23 (11.5%)	
Very poor	1 (0.3%)	2 (1.0%)	
Completely blind	0 (0.0%)	1 (0.5%)	
Body Fat Percentage (%)	33.49 (±8.88)	32.41 (±8.24)	0.164
BMI, kg/m^2	30.42 (±5.36)	26.92 (±5.94)	<0.001
Waist-to-hip ratio	0.95 (±0.07)	0.94 (±0.06)	0.016
Current smokers (%)	18 (4.3%)	0 (0.0%)	0.009
Consume alcohol, %	210 (73.4%)	110 (53.9%)	<0.001
Alcohol consumed, g/day	1.65 (7.48)	0.06 (0.61)	<0.001
Systolic BP, mmHg	140.43 (±17.38)	133.58 (±21.81)	<0.001

Diastolic BP, mmHg	85.97 (±10.56)	82.47 (±11.69)	<0.001
Diagnosis of Hypertension	364 (82.0%)	128 (62.1%)	<0.001
Duration of Diabetes (y)	5.00 (8.00)	3.00 (7.00)	0.053
Undiagnosed diabetes	158 (35.6%)	100 (48.5%)	0.002
Glucose-lowering medications	197 (44.4%)	50 (24.3%)	<0.001
Blood glucose, mmol/L	7.34 (±3.64)	9.99 (±4.75)	<0.001
HbA1c, mmol/mol	55.11 (±17.73)	67.76 (±28.86)	<0.001
Total cholesterol, mmol/l	4.99 (±1.31)	5.52 (±1.24)	<0.001
Triglycerides, mmol/l	1.08 (±0.59)	1.56 (±0.84)	<0.001
LDL-cholesterol, mmol/l	3.16 (±1.16)	3.62 (±1.10)	<0.001
HDL-cholesterol, mmol/l	1.34 (±0.33)	1.19 (±0.35)	<0.001

Values for categorical variables are given as number (percentage); for continuous variables, as mean (±standard deviation) or median (interquartile range). Definition of abbreviations: BMI = Body mass index; BP = Blood pressure; bpm=beats per minute; HbA1c = Glycosylated Hemoglobin; HDL = High-density lipoprotein; LDL = Low-density lipoprotein.

*Ghanaian residents living in Europe; † Ghanaian residents living in Ghana

Table 2: Microvascular and Macrovascular Complications among migrants and non-migrants

	Migrants*	**Non-migrants†**	***p* value**
Participants	*n*=444	*n*=206	
CKD-EPI eGFR, mL/min/1.73 m^2	90.8 (±19.0)	90.2 (±20.7)	0.708
CKD-EPI eGFR categories			0.219
G1 and G2	393 (94.7%)	189 (92.2%)	
G3 – G5	22 (5.3%)	16 (7.8%)	
Albuminuria category			<0.001
A1, normal: <3 mg/mmol	382 (88.6%)	150 (73.9%)	
A2, moderate: 3-30 mg/mmol	41 (9.5%)	46 (22.7%)	
A3, severe: >30 mg/mmol	8 (1.9%)	7 (3.4%)	
Nephropathy	88 (19.8%)	66 (32.0%)	0.001
Retinopathy	38 (21.6%)	11 (11.0%)	0.033
ABI	1.20 (±0.11)	1.11 (±0.11)	<0.001
PAD	15 (3.4%)	23 (11.2%)	<0.001
CAD	37 (8.3%)	38 (18.4%)	<0.001
Stroke	23 (5.6%)	29 (14.5%)	<0.001

Values for categorical variables are given as number (percentage); for continuous variables, as mean (±standard deviation) or median (interquartile range).

Definition of abbreviations: ABI, Ankle Brachial Index; ACR, Albumin-creatinine ratio; CKD-EPI, Chronic Kidney Disease - Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; PAD, Peripheral Artery Disease

*Ghanaian residents living in Europe; † Ghanaian residents living in Ghana

Table 3: Multivariable logistic regression models for nephropathy, retinopathy, PAD, CAD and strokes among Ghanaians living in Ghana and Ghanaians living in Europe (reference = Europe) (*n* = 603)

	Model 1				Model 2				Model 3				Model 4			
	OR	95% C.I		*P*	OR	95% C.I		*p*	OR	95% C.I		*P*	OR	95% C.I		*P*
		Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper	
Nephropathy	1.85	1.26	2.73	0.002	2.01	1.35	3.01	0.001	2.03	1.34	3.07	0.001	1.41	0.80	2.50	0.232
Retinopathy	0.44	0.21	0.92	0.028	0.40	0.19	0.85	0.017	0.47	0.22	1.02	0.055	0.23	0.07	0.75	0.014
PAD	3.42	1.74	6.71	<0.001	3.14	1.58	6.24	0.001	2.72	1.34	5.53	0.006	7.48	2.16	25.90	0.010
CAD	2.29	1.40	3.74	<0.001	2.31	1.40	3.83	0.001	2.22	1.32	3.74	0.003	2.32	1.09	4.93	0.029
Stroke	2.85	1.60	5.07	<0.001	2.74	1.52	4.93	0.001	2.66	1.45	4.91	0.002	1.45	0.42	5.00	0.553

Definition of abbreviations: CAD = Coronary artery disease; CI = Confidence interval; OR = odds ratio; PAD = Peripheral arterial disease.

Model 1 – unadjusted for covariates

Model 2 – adjusted for age and gender

Model 3 – adjusted for age, gender, and socioeconomic status

Model 4 – adjusted for age, gender, socioeconomic status, alcohol consumption, smoking; physical activity, hypertension, BMI, total cholesterol, and HbA1c

Online-only supplemental table 1: Microvascular and Macrovascular Indices among newly-diagnosed diabetes patients and previously known diabetes

	Undiagnosed Diabetes	Previously known diabetes	*p* value
	N = 258	N = 392	
CKD-EPI eGFR, mL/min/1.73 m^2	92.01 (±19.23)	89.72 (±19.74)	0.154
CKD-EPI eGFR categories			0.332
G1 and G2	236 (91.5%)	346 (88.3%)	
G3 – G5	11 (4.3%)	27 (6.9%)	
Albuminuria category			0.925
A1, normal: <3 mg/mmol	209 (81.0%)	323 (82.4%)	
A2, moderate: 3-30 mg/mmol	36 (14.0%)	51 (13.0%)	
A3, severe: >30 mg/mmol	7 (2.7%)	8 (2.0%)	
Nephropathy	67 (26.0%)	87 (22.2%)	0.300
ABI	1.16(±0.11)	1.18 (±0.12)	0.016
PAD	15 (5.8%)	23 (5.9%)	0.532
CAD	29 (11.2%)	46 (11.7%)	0.901
Stroke	25 (10.7%)	27 (7.1%)	0.137

Values for categorical variables are given as number (percentage); for continuous variables, as mean (±standard deviation) or median (interquartile range).

Definition of abbreviations: ABI, Ankle Brachial Index; ACR, Albumin-creatinine ratio; CKD-EPI, Chronic Kidney Disease - Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; PAD = peripheral artery disease

Online-only supplemental table 2: Microvascular and Macrovascular complications among migrants and non-migrants with previously diagnosed diabetes and undiagnosed diabetes.

	Previously Known Diabetes			Undiagnosed Diabetes		
	Migrants*	Non-migrants†	*p* value	Migrants*	Non-migrants†	*p* value
	n=286	n=106		n=158	n=100	
CKD-EPI eGFR, mL/min/1.73 m^2	90.7 (±19.0)	87.2 (±21.4)	0.124	91.1 (±19.0)	93.4 (±19.7)	0.361
CKD-EPI eGFR categories			0.180			0.761
G1 and G2	252 (94.0%)	94 (89.5%)		141 (95.9%)	95 (95.0%)	
G3 – G5	16 (6.0%)	11 (10.5%)		6 (4.1%)	5 (5.0%)	
Albuminuria category			<0.001			0.225
A1, normal: <3 mg/mmol	251 (90.0%)	72 (69.9%)		131 (86.2%)	78 (78.0%)	
A2, moderate: 3-30 mg/mmol	23 (8.2%)	28 (27.2%)		18 (11.8%)	18 (18.0%)	
A3, severe: >30 mg/mmol	5 (1.8%)	3 (2.9%)		3 (2.0%)	4 (4.0%)	
Nephropathy	49 (17.1%)	38 (35.8%)	<0.001	39 (24.7%)	28 (28.0%)	0.563
Retinopathy	38 (22.2%)	11 (11.0%)	0.022	-	-	-
ABI	1.21 (±0.11)	1.11 (±0.11)	<0.001	1.19 (±0.10)	1.11 (±0.11)	<0.001
PAD	12 (4.3%)	11 (10.6%)	0.028	3 (1.9%)	12 (12.0%)	0.002
CAD	24 (8.4%)	22 (20.8%)	0.001	13 (8.2%)	16 (16.0%)	0.068
Stroke	10 (3.7%)	8 (7.5%)	0.176	2 (1.4%)	5 (5.3%)	0.120

Values for categorical variables are given as number (percentage); for continuous variables, as mean (±standard deviation) or median (interquartile range).

Definition of abbreviations: ABI, Ankle Brachial Index; ACR, Albumin-creatinine ratio; CKD-EPI, Chronic Kidney Disease - Epidemiology Collaboration; eGFR, estimated glomerular filtration rate; PAD, Peripheral Artery Disease

*Ghanaian residents living in Europe; † Ghanaian residents living in Ghana

Highlights

- African migrants in Europe have higher rates of diabetes than their non-migrants peers.
- Migrants with diabetes had lower rates of nephropathy than non-migrants
- Migrants had lower rates of diabetic macrovascular complications than non-migrants
- Poorer glycemic control could explain the higher complication rates in non-migrants

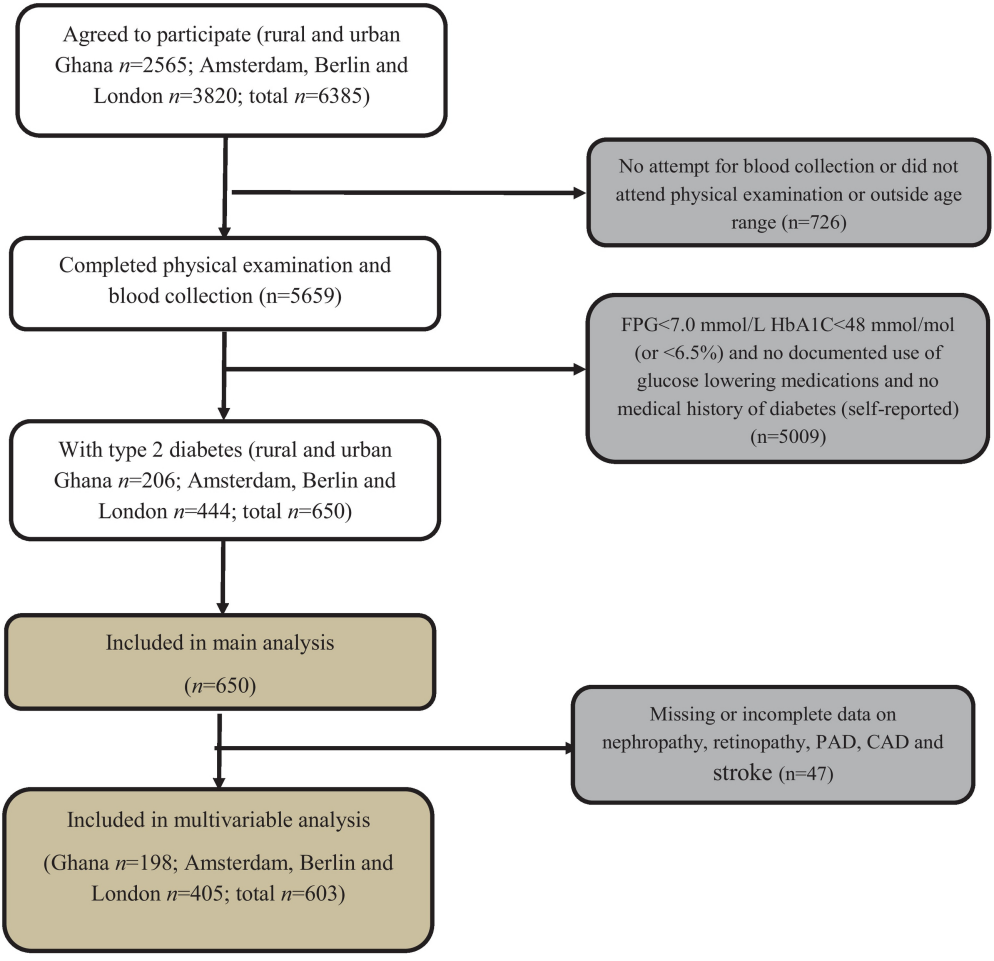
Agreed to participate (rural and urban Ghana n=2565; Amsterdam, Berlin and London n=3820; total n=6385)
No attempt for blood collection or did not attend physical examination or outside age range (n=726)
Completed physical examination and blood collection (n=5659)
FPG<7.0 mmol/L HbA1C<48 mmol/mol (or <6.5%) and no documented use of glucose lowering medications and no medical history of diabetes (self-reported) (n=5009)
With type 2 diabetes (rural and urban Ghana n=206; Amsterdam, Berlin and London n=444; total n=650)
Included in main analysis (n=650)
Missing or incomplete data on nephropathy, retinopathy, PAD, CAD and stroke (n=47)
Included in multivariable analysis (Ghana n=198; Amsterdam, Berlin and London n=405; total n=603)

Figure 1