

The background of the slide features a dark blue-grey color with a faint, stylized graphic of DNA double helices and molecular structures. The helices are rendered in a lighter shade of blue, creating a sense of depth and scientific context. The overall aesthetic is clean and professional, typical of a scientific presentation.

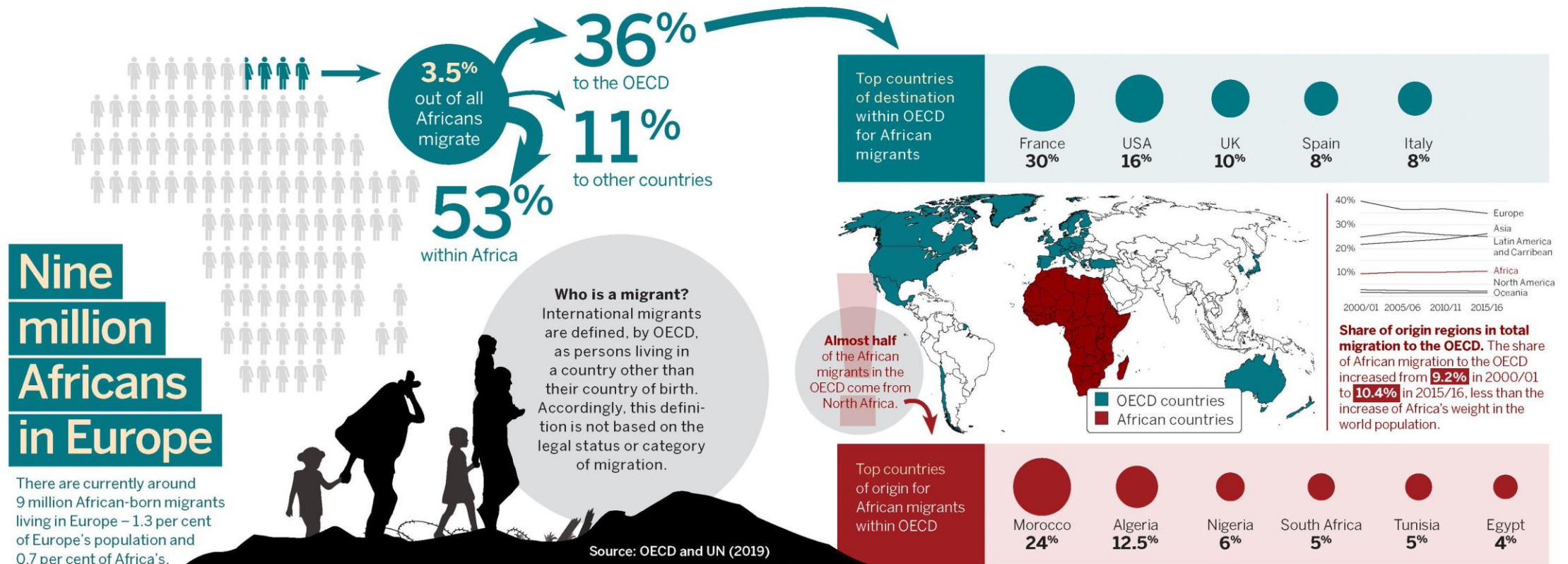
# Epigenetics of cardiometabolic diseases among transitioning African populations

Felix P Chilunga, MD, PhD

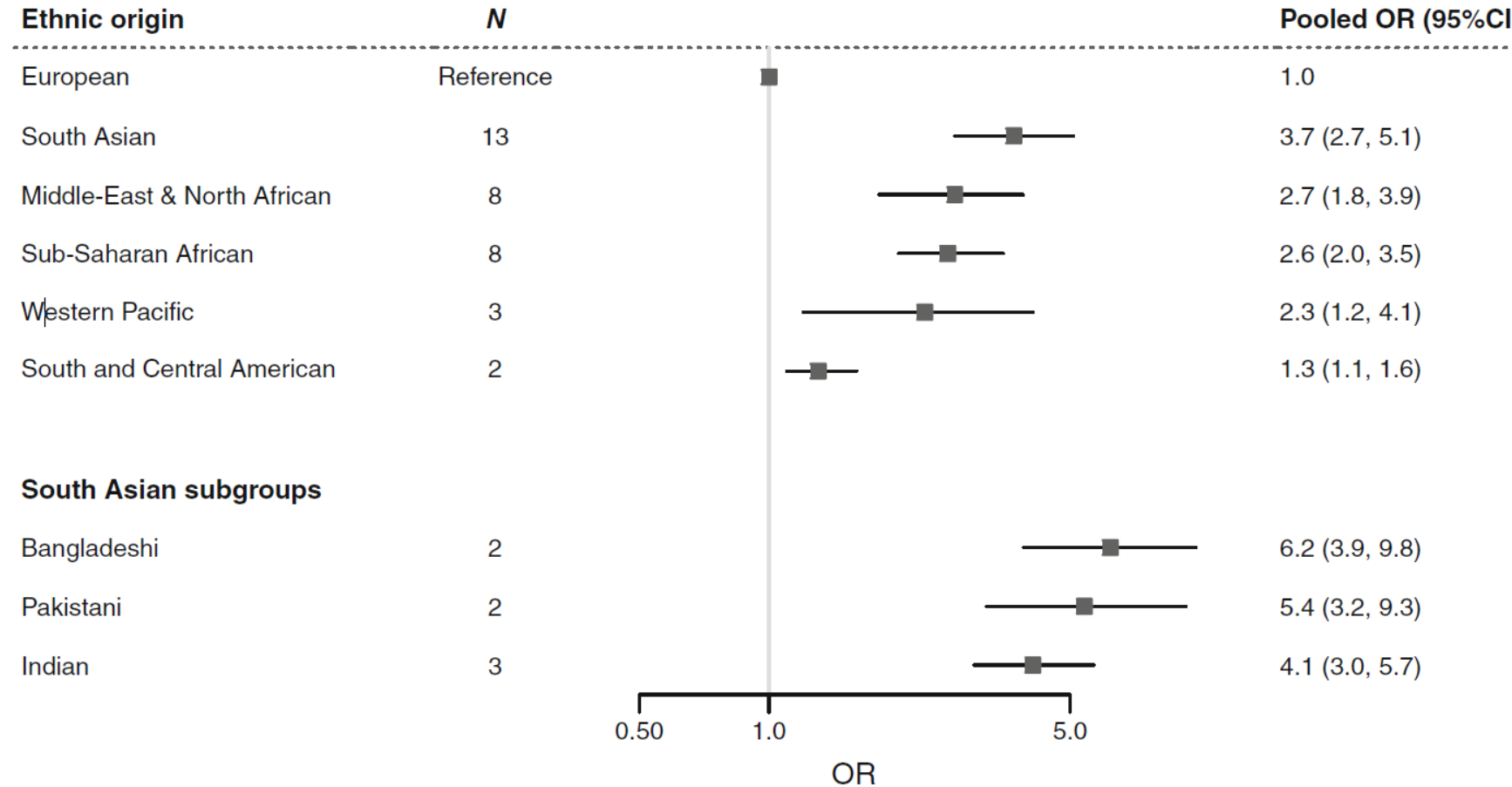
Assistant Professor (Global Health)

Amsterdam UMC (The Netherlands)

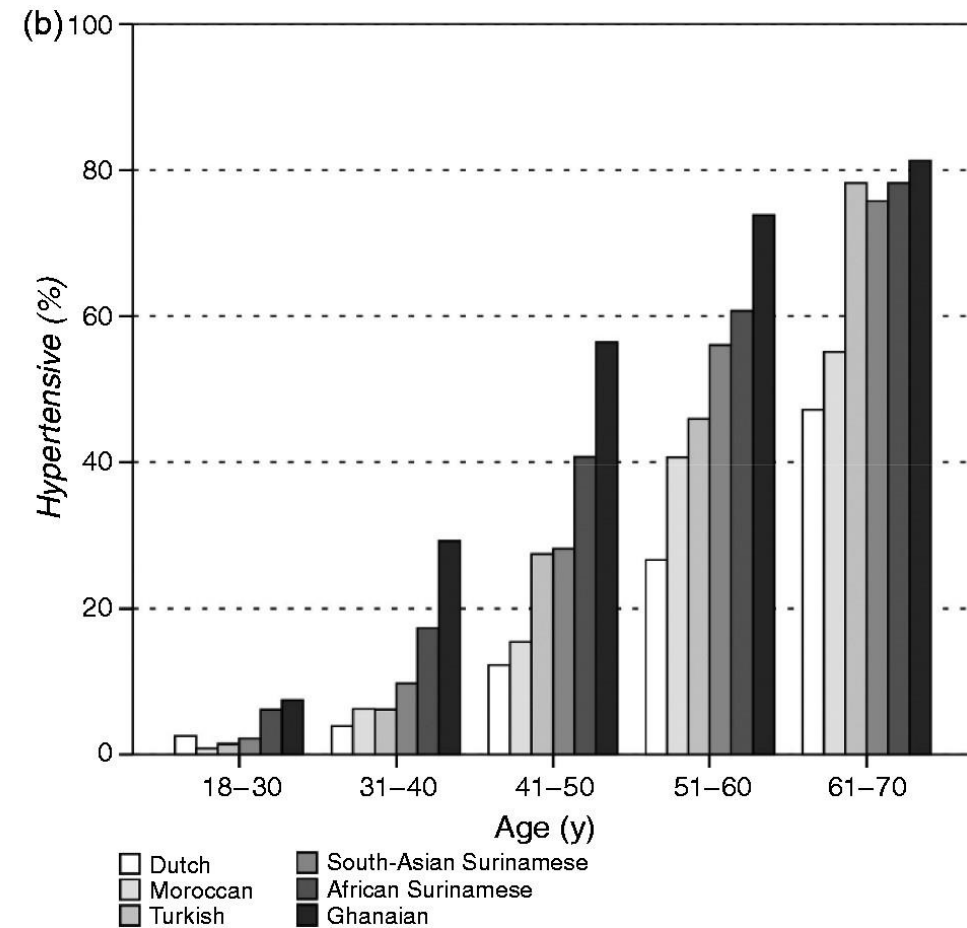
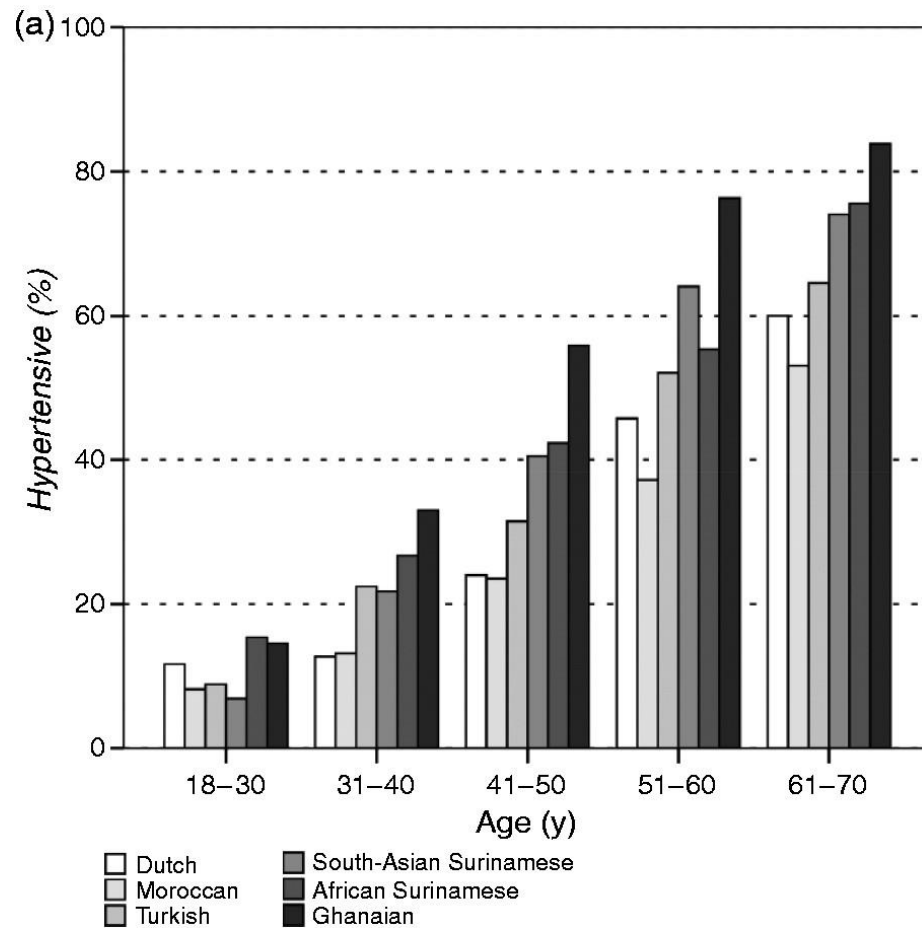
# International migration among Africans



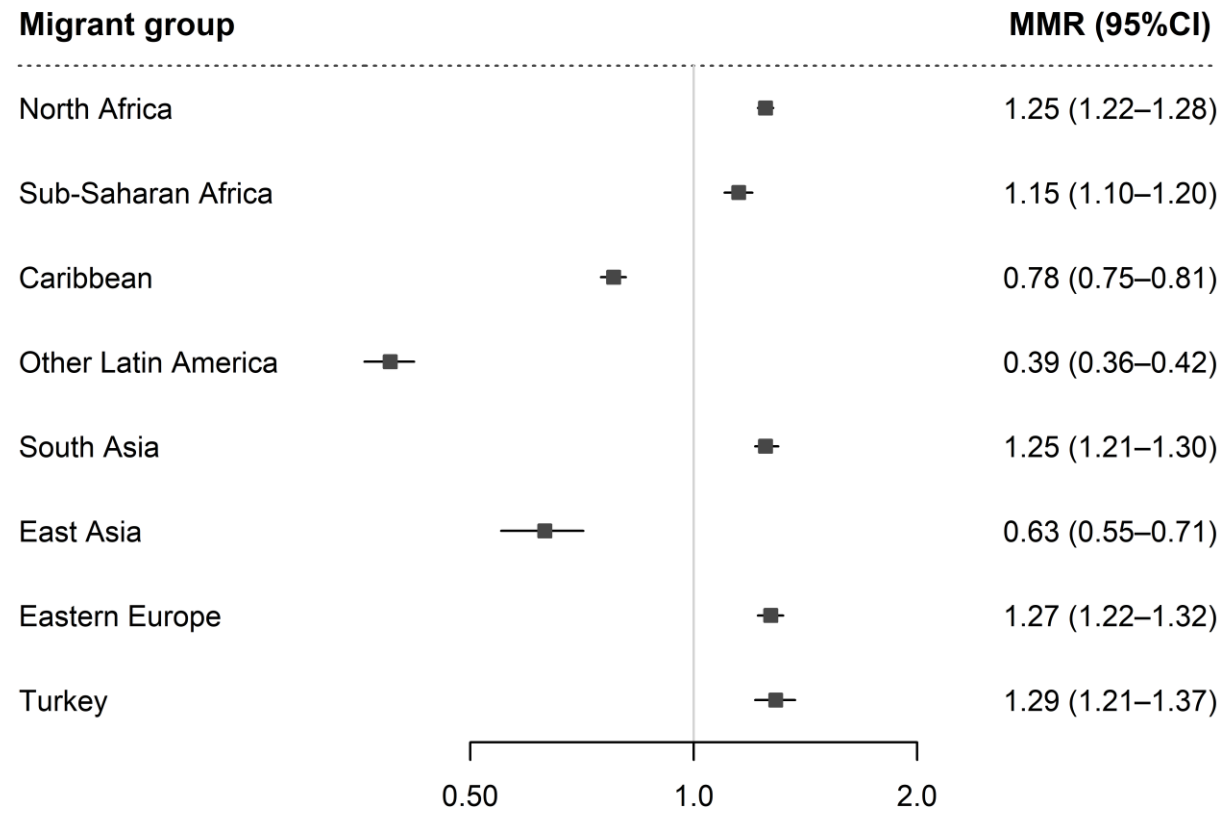
# Type 2 diabetes among migrants in western Europe



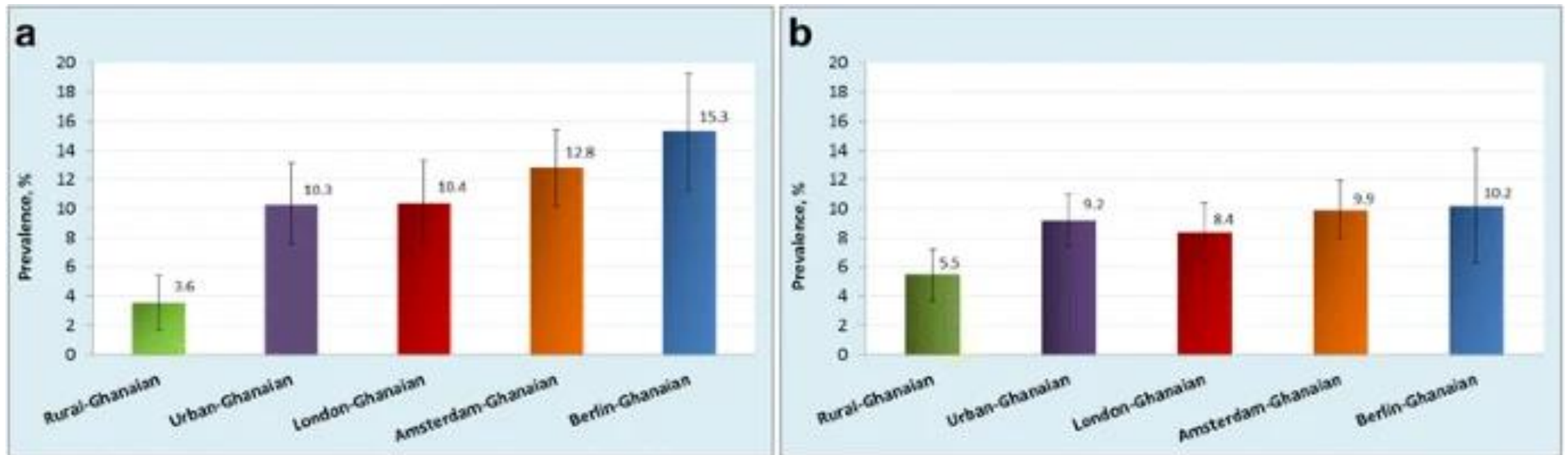
# Hypertension among migrants in western Europe



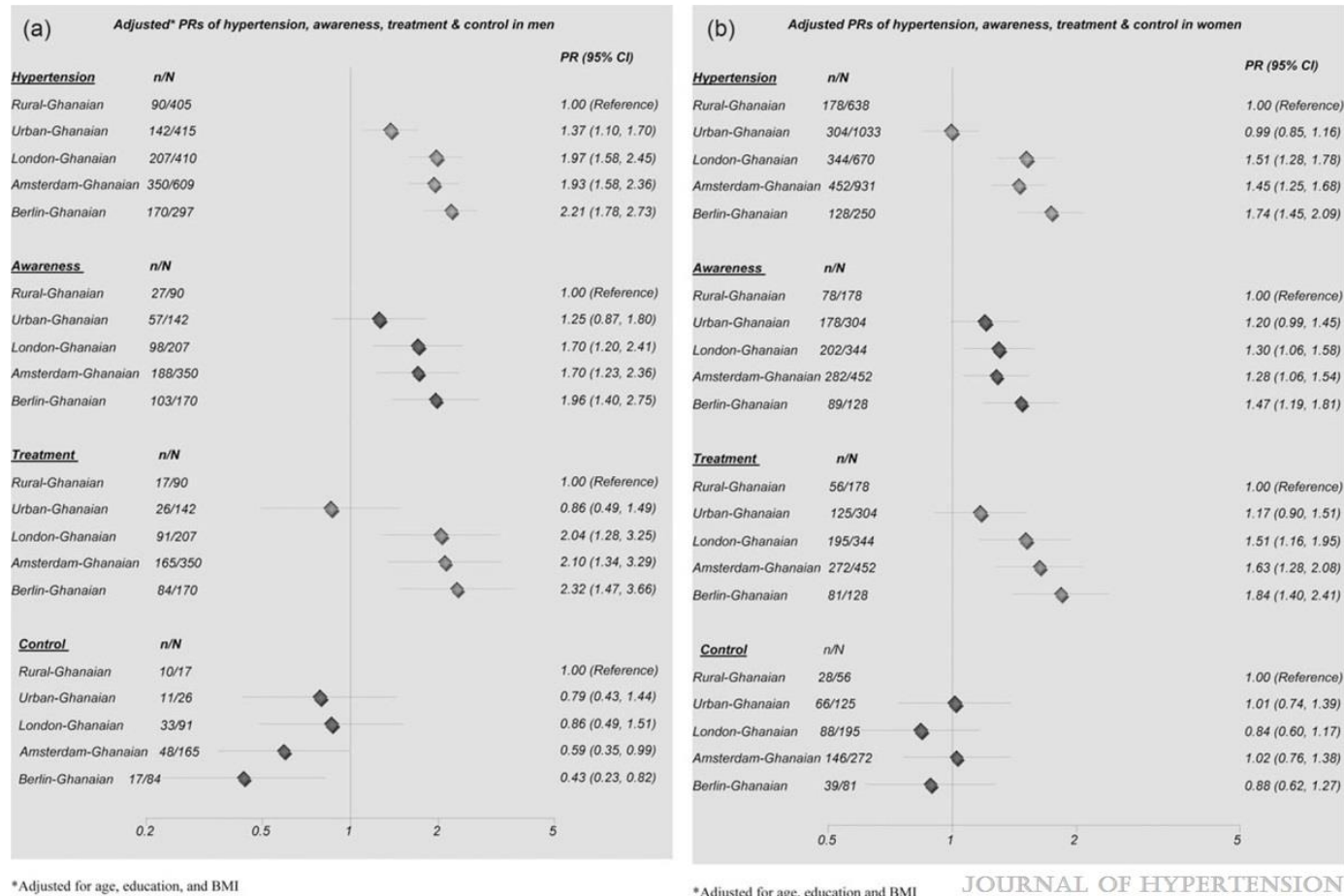
# Cardiovascular disease mortality among migrants in western Europe



# Type 2 diabetes compared to home populations



# Hypertension compared to home populations



# Attributed to changes in lifestyle factors



Tobacco smoking



Unhealthy diet



Physical inactivity



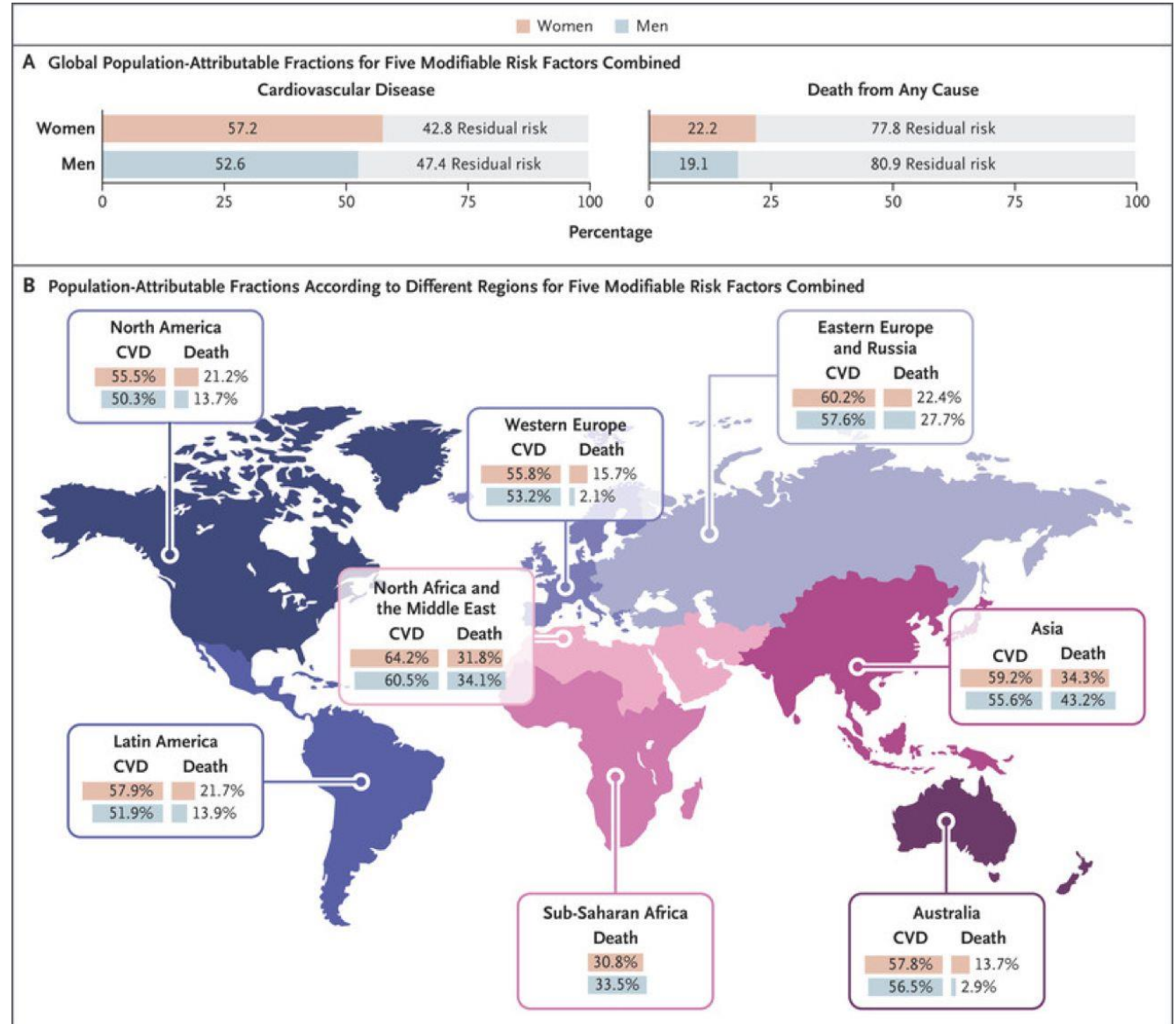
Heavy alcohol  
consumption



Cardiometabolic  
diseases still  
prevalent even  
after adjusting  
for these  
lifestyle factors



CVD  
attributable  
to lifestyle  
factors



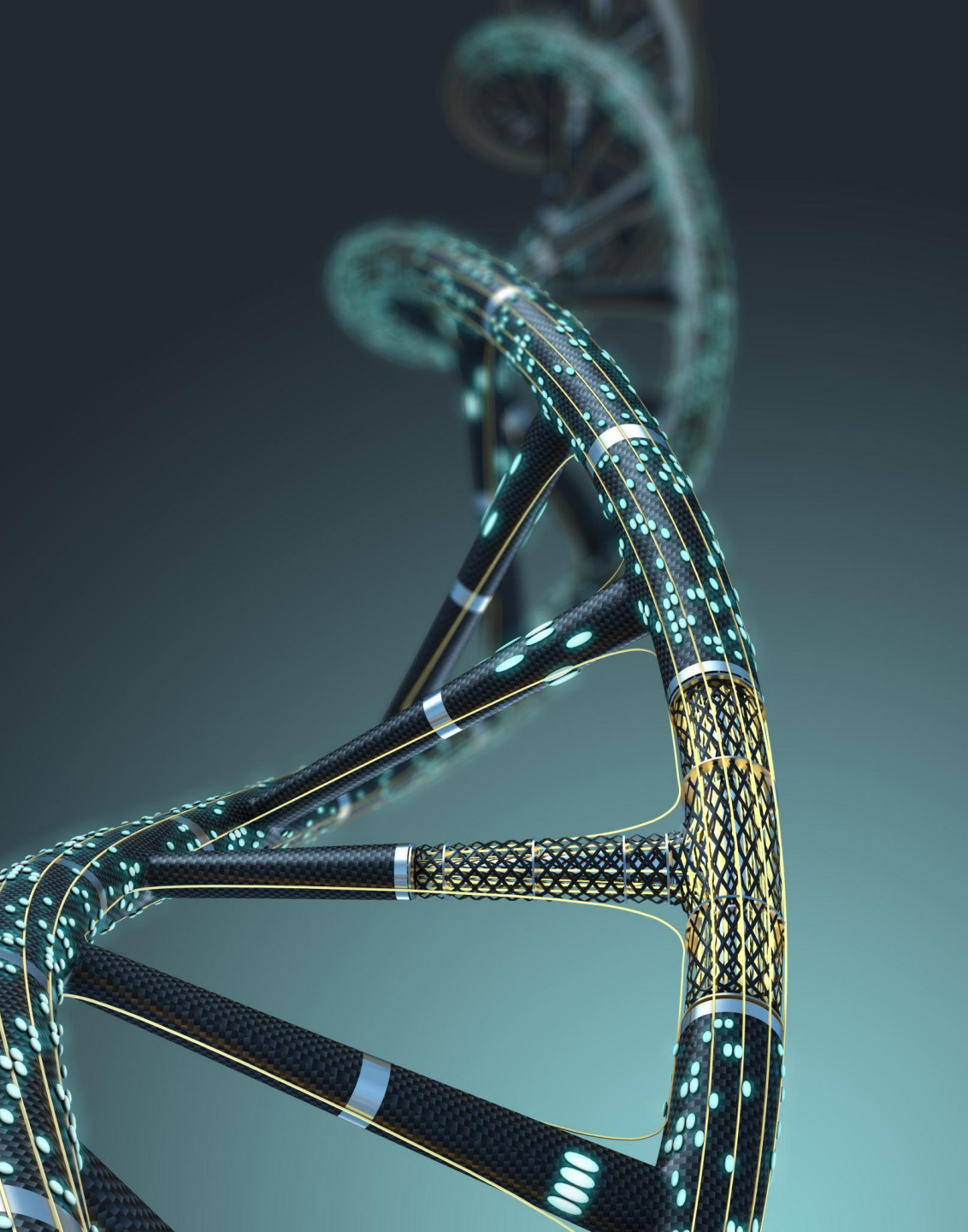
# Missing explanations







Epigenetics could be a  
potential mechanism



# Epigenetics

- Heritable changes in gene expression without changes to the underlying DNA sequence
  - DNA Methylation
  - Histone modifications
  - Noncoding RNAs
- Influenced by both the underlying genome and the environmental
  - Plausible in the context of migration



# From this environment



<https://www.nibio.no/nyheter/healthy-food-for-africa>

<https://freedomfund.org/blog/raising-awareness-of-safer-migration-for-at-risk-women/>

<https://theconversation.com/green-spaces-are-good-for-people-but-in-south-africa-many-cannot-access-them-203791>



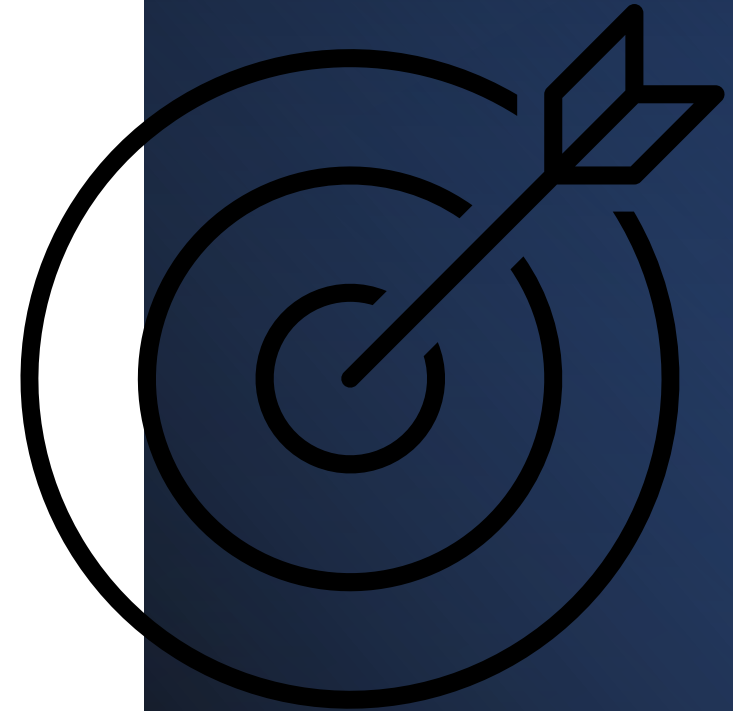


To the Europe (a huge environmental change)

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# Research aim

- assessed for DNAm differences between Ghanaian migrants living in European compared to those who stayed behind in Ghana







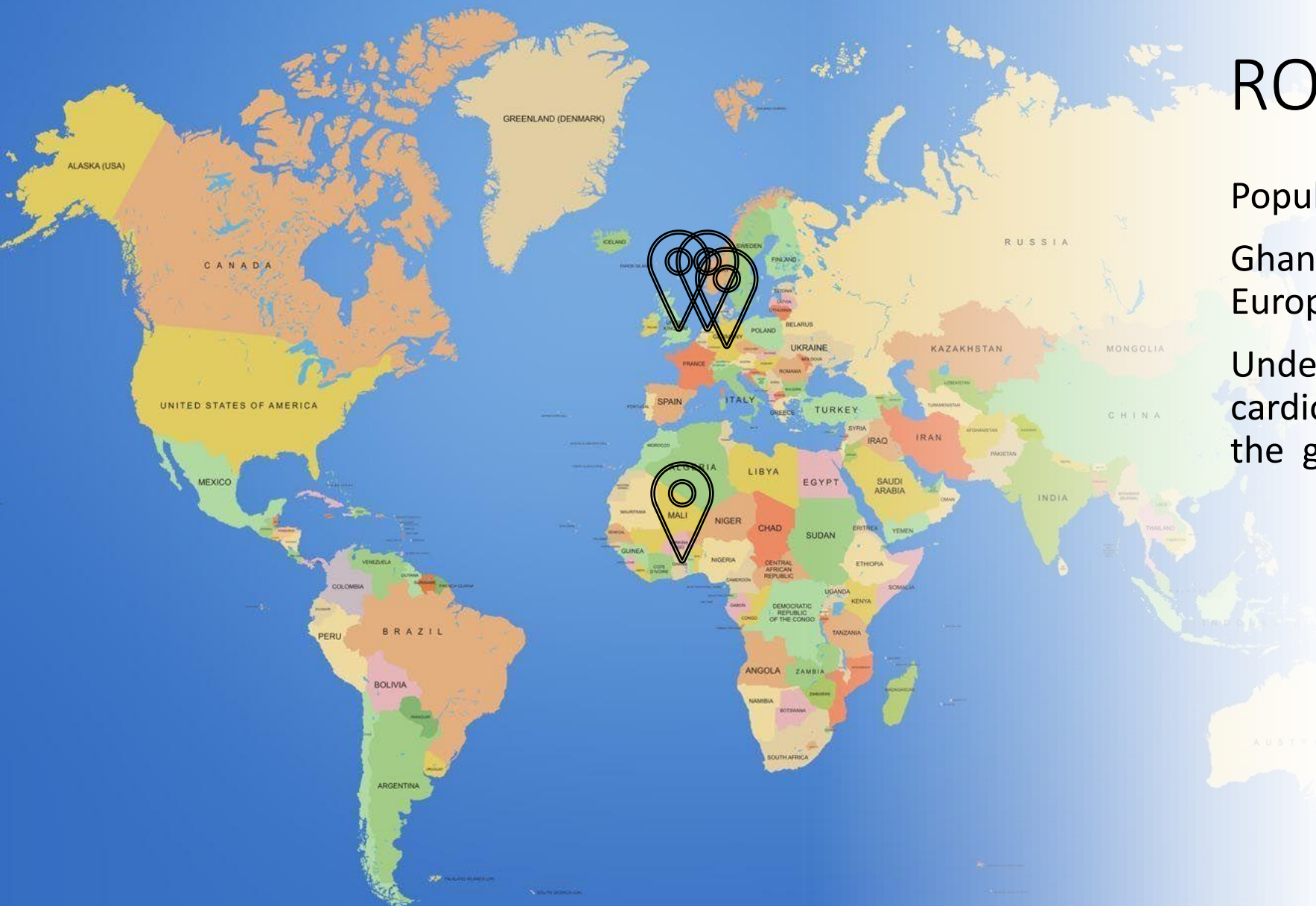
# Methodology

# RODAM study

Population based

Ghanaians in Ghana + Ghanaians in Europe

Understand the interactions of  
cardiometabolic phenotypes with  
the genome and epigenome







# The experiment

- DNA extracted from blood samples and processed
- Placed on a chip to measure methylation at 450,000 genome sites



Removed external sources of variation to make sure result was accurate

- Removed outliers
- Checked that the sex profile by DNA methylation matches the reported sex by participant
- Controlled for bias that can result from measurements e.g., type of chip, place on the chip
- Removed DNA methylation sites on the X and Y chromosome
- Removed DNA methylation sites directly under a genetic variation
- Controlled for amount and type of cells in each blood sample





# Statistical analyses

- Compared mean methylation in migrant's vs non-migrants at the 429,000 genome sites that were left after controlling for external variation

The background features a dark blue-grey gradient with several semi-transparent, stylized DNA double helix structures. These helices are intertwined and vary in size and orientation, creating a sense of depth and complexity. Scattered throughout the scene are numerous small, light-grey spheres, some of which are attached to the DNA strands, suggesting a molecular or biological context.

# Results and interpretation

# Participant inclusion and characteristics

**Table 1. Baseline characteristics of participants.**

	All participants (n = 712)	Migrants <sup>†</sup> (n = 365)	Non-migrants <sup>‡</sup> (n = 347)	p-value
<b>Demographics, n (%)</b>				
Mean age, SD	51.09 (9.86)	49.89 (9.74)	52.36 (9.84)	<0.001
Sex (Female)	409 (57.36)	166 (45.42)	243 (70.00)	<0.001
<b>Location</b>				
Rural Ghana	104 (14.61)		104 (29.97)	
Urban Ghana	243 (34.13)		243 (70.03)	
Ghanaians in Europe	365 (51.26)	365 (100)		

# Differentially methylated positions

No	CpG ID	Chromosome	Position <sup>†</sup>	Gene name <sup>†</sup>	Feature <sup>†</sup>	Relation to Island <sup>†</sup>	Delta $\beta$ value	p-value	FDR
1	cg16411857	16	57023191	NLR5	TSS1500 <sup>‡</sup>	Island	0.021	$4.34 \times 10^{-10}$	0.000
2	cg15706807	8	58106598	IMPAD1	TSS200	Island	-0.045	$9.46 \times 10^{-10}$	0.000
3	cg07839457	16	57023022	NLR5	TSS1500	N_Shore	0.040	$1.29 \times 10^{-8}$	0.002
4	cg07295964	5	175223982	CPLX2	5'UTR	Island	0.009	$7.74 \times 10^{-8}$	0.008
5	cg03024619	3	71803308	GPR27	1stExon	Island	0.008	$3.60 \times 10^{-7}$	0.031
6	cg13273540	3	176850227	TBL1XR1	5'UTR <sup>§</sup>	OpenSea	0.016	$4.90 \times 10^{-7}$	0.031
7	cg16861076	8	11421594	BLK	Body	Island	-0.029	$5.13 \times 10^{-7}$	0.031
8	cg01787285	1	2162682	SKI	Body	S_Shore	0.018	$6.43 \times 10^{-7}$	0.033
9	cg15723874	1	156457945	MEF2D	5'UTR	OpenSea	0.013	$6.82 \times 10^{-7}$	0.033
10	cg01088410	5	170739179	TLX3	Body	Island	0.006	$8.35 \times 10^{-7}$	0.036
11	cg10333808	12	22487459	ST8SIA1	5'UTR	Island	0.005	$1.26 \times 10^{-6}$	0.045
12	cg22895601	14	21131621	ANG	TSS1500	OpenSea	0.002	$1.31 \times 10^{-6}$	0.045
13	cg13985485	1	239550283	CHRM3	Body	Island	-0.025	$1.35 \times 10^{-6}$	0.045

<sup>†</sup> Annotation were performed via IlluminaHumanMethylation450kanno.ilmn12.hg19. *Homo sapiens* (human) genome assembly GRCh37 (hg19). Hansen KD (2016) IlluminaHumanMethylation450kanno.ilmn12.hg19: Annotation for Illumina's 450k methylation arrays. R package version 0.6.0.

<sup>‡</sup> TSS1500 (the region from TSS to – 1500 nucleotides upstream of TSS).

<sup>§</sup> 5'UTR (the region of an mRNA that is directly upstream from the initiation codon).

FDR: False discovery rate; TSS: Transcription start site.



# Differentially methylated positions

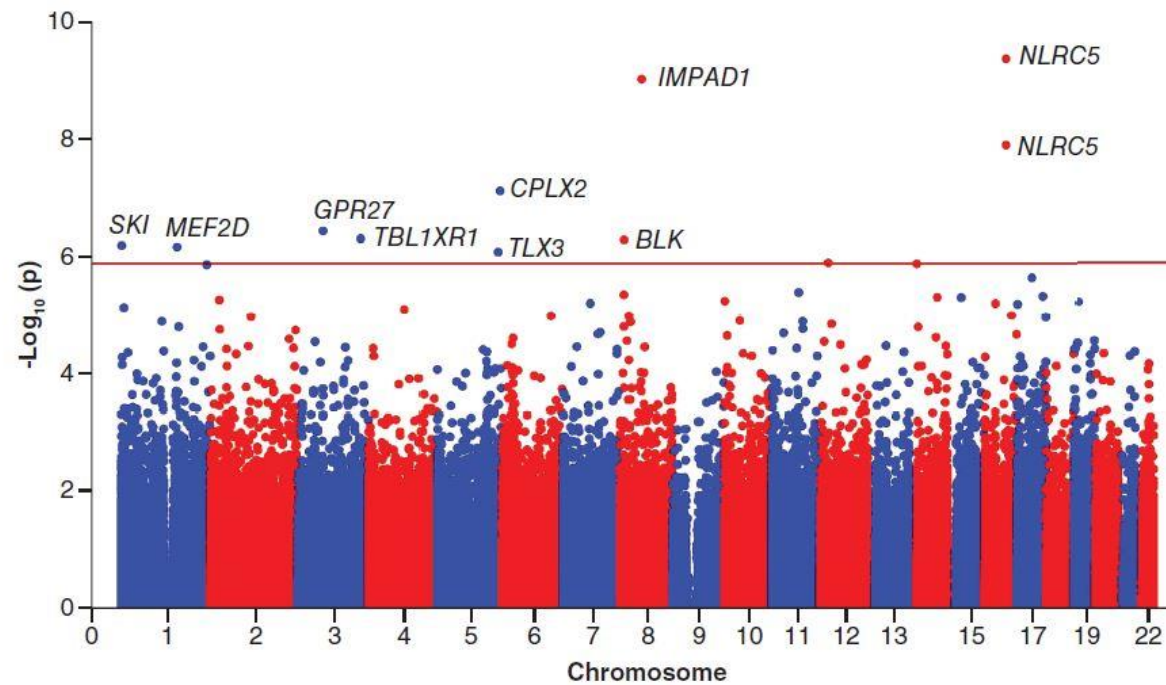
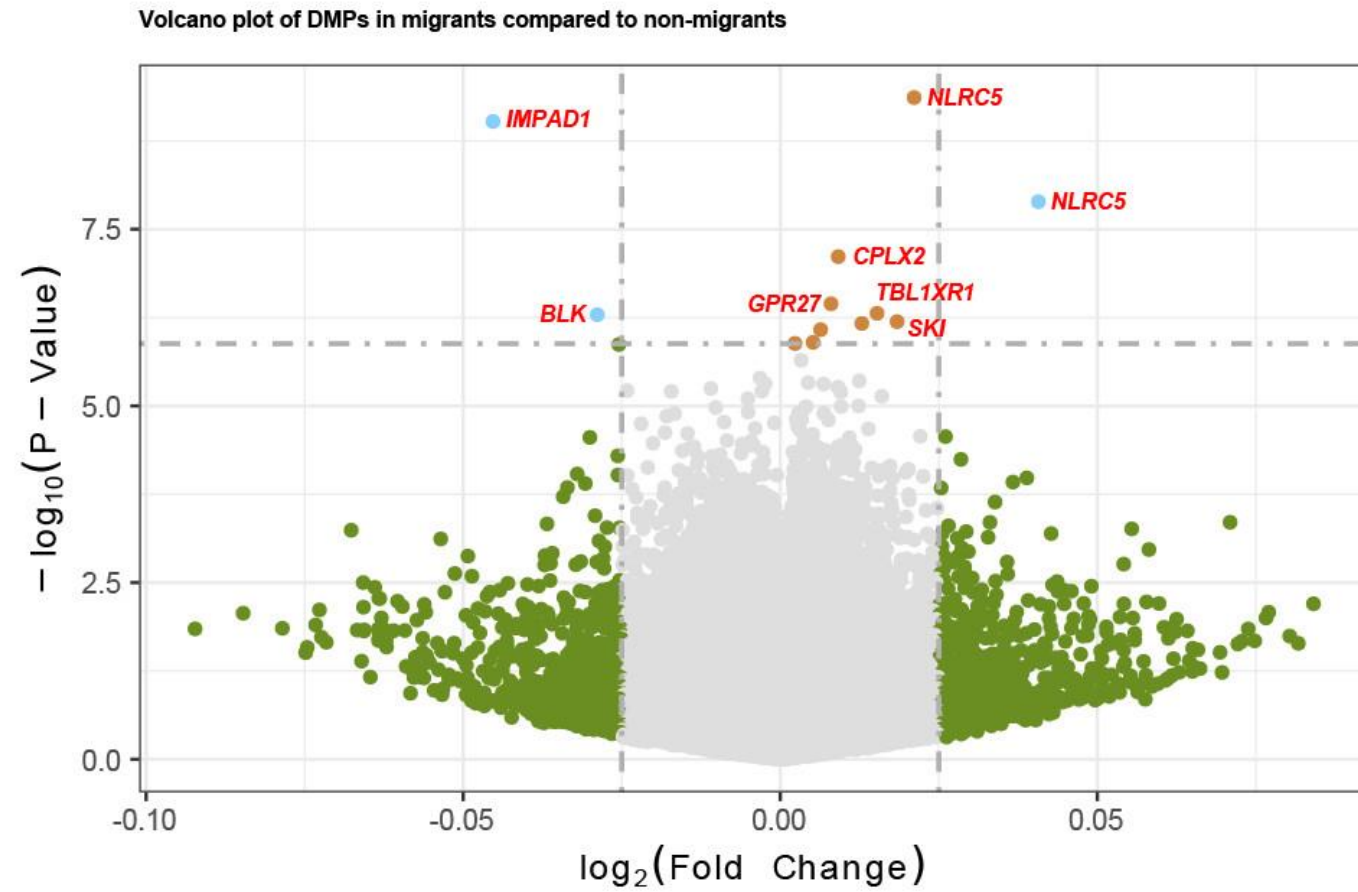


Figure 1. Manhattan plot of differentially methylated positions associated with migration from low- and middle-income countries to high-income countries. All 429,459 CpG sites are presented according to the p-value in the epigenome-wide association study, as well as by chromosomal annotation. Red line is the demarcation line for statistically significant differentially methylated positions at  $p < 1.1 \times 10^{-7}$ .

# Effect sizes



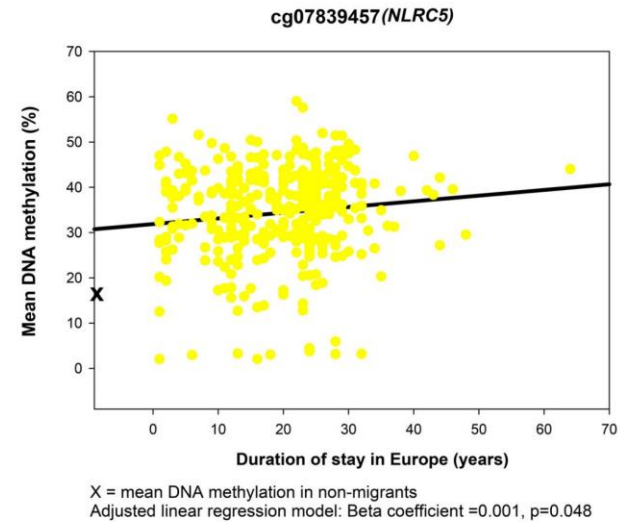
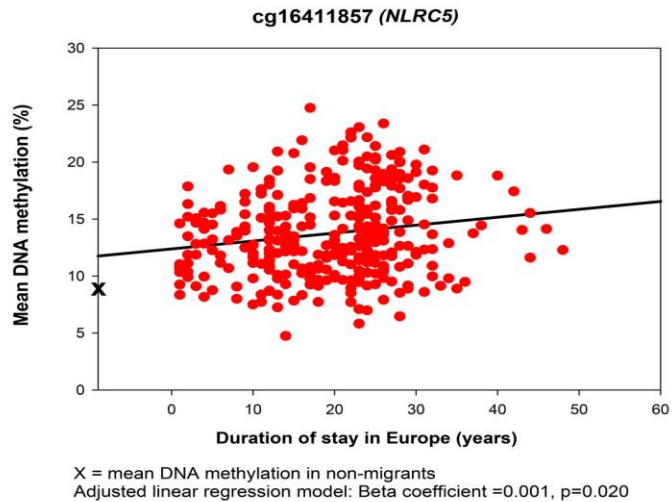
# SNP influences

No	CpG ID	Chromosome	Position <sup>1</sup>	Gene Annotation	Presence of underlying genomic variation ?
<b>1</b>	cg16411857	16	57023191	<i>NLRC5</i>	<b>Yes</b>
<b>2</b>	cg15706807	8	58106598	<i>IMPAD1</i>	<b>Yes</b>
<b>3</b>	cg07839457	16	57023022	<i>NLRC5</i>	<b>Yes</b>
<b>4</b>	cg07295964	5	175223982	<i>CPLX2</i>	No
<b>5</b>	cg03024619	3	71803308	<i>EIF4E3</i>	No
<b>6</b>	cg13273540	3	176850227	<i>TBL1XR1</i>	<b>Yes</b>
<b>7</b>	cg16861076	8	11421594	<i>BLK</i>	<b>Yes</b>
<b>8</b>	cg01787285	1	2162682	<i>SKI</i>	<b>Yes</b>
<b>9</b>	cg15723874	1	156457945	<i>MEF2D</i>	No
<b>10</b>	cg01088410	5	170739179	<i>TLX3</i>	No
<b>11</b>	cg10333808	12	22487459	<i>ST8SIA1</i>	No
<b>12</b>	cg22895601	14	21131621	<i>ANG</i>	No
<b>13</b>	cg13985485	1	239550283	<i>CHRM3</i>	No

# Biological assessment

CpG ID	Gene Annotation	Gene function	Associated traits GWAS catalog	Associated traits EWAS catalog
<b>cg07295964</b>	CPLX2	Regulates neurotransmitter release at synapses	Vascular endothelial function	BMI
<b>cg03024619</b>	EIF4E3	Plays a role in translation initiation	Type 2 diabetes, HDL cholesterol	Type 2 diabetes
<b>cg15723874</b>	MEF2D	Controls muscle and nervous system development, synaptic plasticity, and memory.	Diastolic blood pressure	Type 2 diabetes
<b>cg01088410</b>	TLX3	Aids in the development of T cells in the immune system.	Body mass index, HDL cholesterol	HDL cholesterol
<b>cg10333808</b>	ST8SIA1	Adds sialic acid residues to glycoproteins and glycolipids	Coronary artery calcification	Type 2 diabetes, HDL cholesterol
<b>cg22895601</b>	ANG	Promotes the formation of new blood vessels (angiogenesis)	Blood vessel formation and endothelium repair	Body mass index
<b>cg13985485</b>	CHRM3	Mediates effects of acetylcholine in the central nervous system	Hypertension	Type 2 diabetes

# Duration of stay in urban Area among migrants



# NLCR5 also an interesting gene



**Function:** transcriptional regulator of MHC class I antigen presentation in the immune response

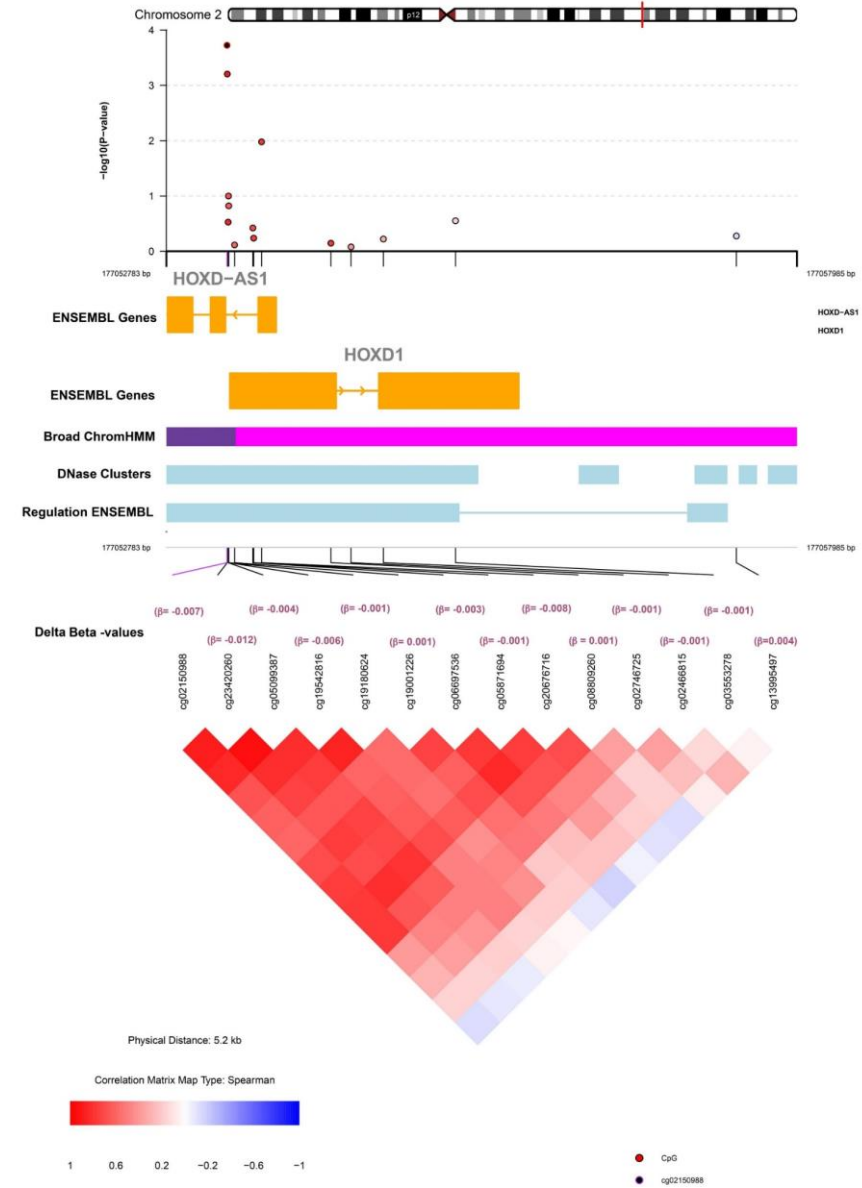


**Associated traits GWAS catalog:** All lipids, metabolic syndrome, coronary artery disease

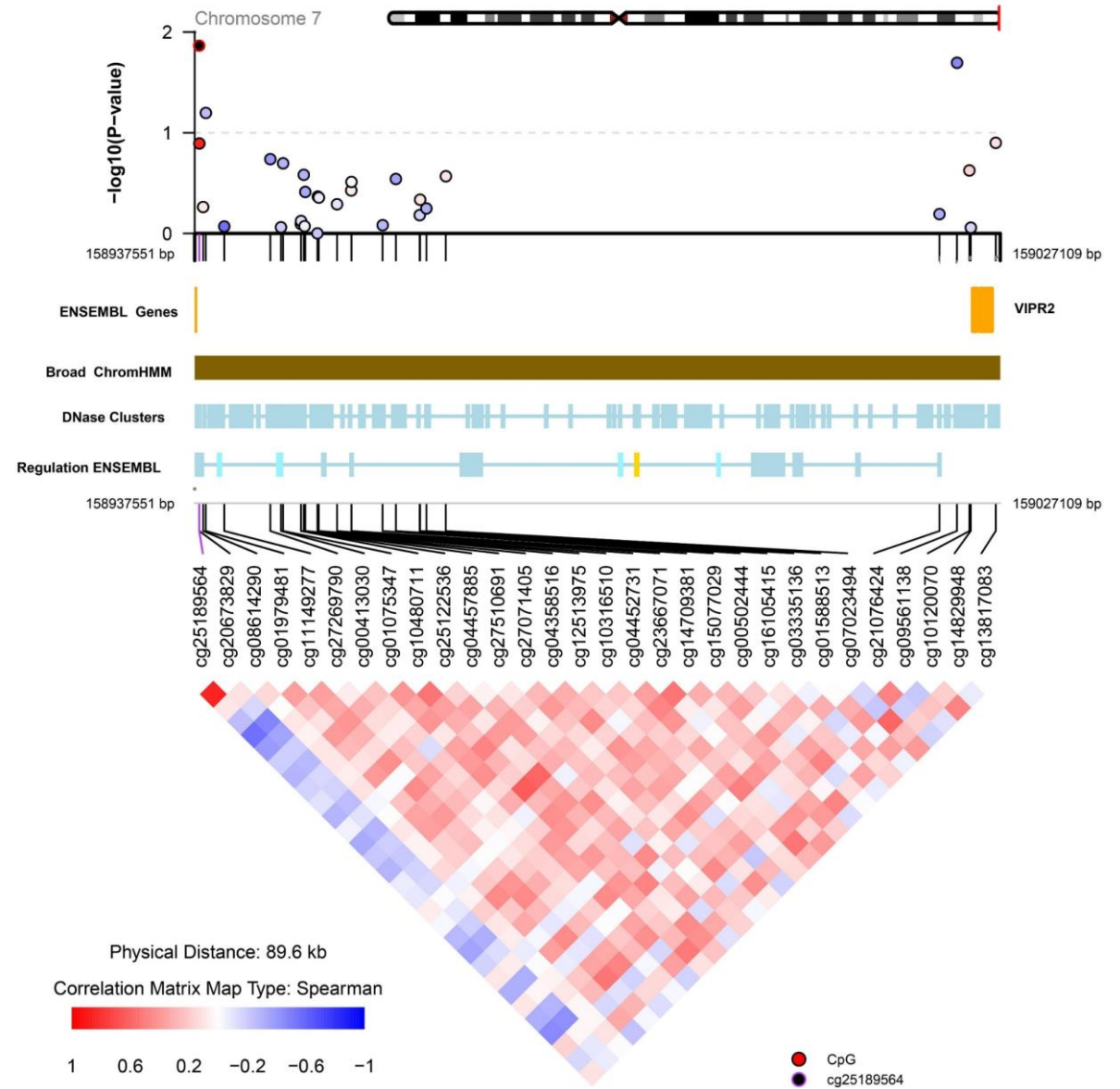


**Associated traits EWAS catalog:** All cholesterol, type 2 diabetes

# Differentially methylated region 1

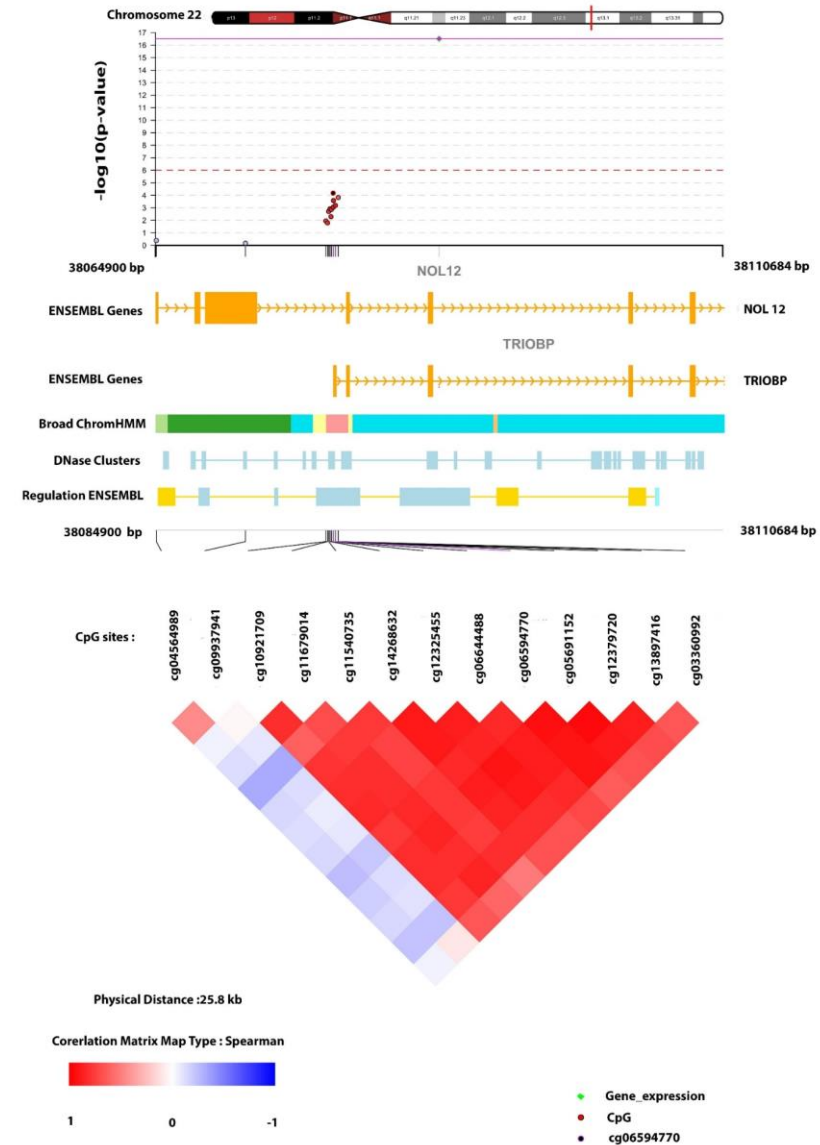


# Differentially methylated region 2





# Differentially methylated region 3



# Biological assessment

GENE NAME	GENE FUNCTION	ASSOCIATED TRAITS IN GWAS CATALOG	ASSOCIATED TRAITS IN EWAS CATALOG
HOXD1	embryonic development, particularly in the patterning and differentiation of the spinal cord and vertebral column	Systolic blood pressure, diastolic blood pressure, stroke, type 2 diabetes	none
VIPR2	encodes a receptor for vasoactive intestinal peptide (VIP), playing a role in various physiological processes including neurotransmission, immune response modulation, and smooth muscle relaxation.	Diastolic blood pressure, ischemic stroke	type 2 diabetes
TRIOBP	associated with the development and maintenance of sensory hair cells in the inner ear, contributing to auditory function and balance	Type 2 diabetes, blood pressure, BMI, cholesterol	type 2 diabetes

# Summary

We performed the first EWAS on migration and in a homogenous group of Ghanaians

We found seven DMPs and three DMRs associated with migration

Two CpG sites in NLRC5 are differentially methylated with duration of stay in Europe

All CpG sites/genes have been related to cardiometabolic diseases in previous studies

DNAm might play a role in the rising burden of cardiometabolic diseases among migrants

# Clinical and public health implications

- Still in early phase
  - Points to an opportunity to possibly develop novel biomarkers of cardiometabolic diseases in migrants
  - DNA methylation changes are reversible, could also provide opportunity to modify these changes or monitor intervention progress over time



# Future perspectives

- Longitudinal studies to validate the causal contribution of the identified DMPs and DMR
  - Currently working on it
- Further assessment as novel biomarkers of cardiometabolic diseases in migrants
  - Replication in other populations



# Contributors and more reading

## Research Article

For reprint orders, please contact: [reprints@futuremedicine.com](mailto:reprints@futuremedicine.com)

## Epigenomics



### DNA methylation as the link between migration and the major noncommunicable diseases: the RODAM study

Felix P Chilunga<sup>\*1</sup> , Peter Henneman<sup>2</sup> , Andrea Venema<sup>2</sup>, Karlijn AC Meeks<sup>3</sup> , Juan R Gonzalez<sup>4</sup> , Carlos Ruiz-Arenas<sup>4</sup> , Ana Requena-Méndez<sup>4,5</sup> , Erik Beune<sup>1</sup> , Joachim Spranger<sup>6</sup> , Liam Smeeth<sup>7</sup> , Silver Bahendeka<sup>8</sup> , Ellis Owusu-Dabo<sup>9</sup> , Kerstin Klipstein-Grobusch<sup>10,11</sup> , Adebawale Adeyemo<sup>3</sup> , Marcel MAM Mannens<sup>2</sup>  & Charles Agyemang<sup>1</sup> 

<sup>1</sup>Department of Public Health, Amsterdam Public Health Research Institute, Amsterdam University Medical Centers, University of Amsterdam, 1105 AZ Amsterdam, The Netherlands

<sup>2</sup>Department of Clinical Genetics, Amsterdam Reproduction & Development Research Institute, Amsterdam University Medical Centers, University of Amsterdam, 1105 AZ Amsterdam, The Netherlands

<sup>3</sup>Center for Research on Genomics & Global Health, National Human Genome Research Institute, National Institutes of Health, Bethesda, MD 20894, USA

<sup>4</sup>Barcelona Institute for Global Health (ISGlobal, University of Barcelona), 08003 Barcelona, Spain

<sup>5</sup>Department of Global Public Health, Karolinska Institutet, SE-171 77 Stockholm, Sweden

<sup>6</sup>Department of Endocrinology, Diabetes & Metabolism, Charité-Universitätsmedizin Berlin, 10117 Berlin, Germany

<sup>7</sup>Department of Non-communicable Disease Epidemiology, London School of Hygiene & Tropical Medicine, London, 1E 7HT, UK

<sup>8</sup>Department of Medicine, MKPGMS-Uganda Martyrs University, 8H33+5M Kampala, Uganda

<sup>9</sup>School of Public Health, Kwame Nkrumah University of Science & Technology, MCFH+R9 Kumasi, Ghana

<sup>10</sup>Julius Global Health, Julius Center for Health Sciences & Primary Care, University Medical Center Utrecht, Utrecht University, 3584 CX Utrecht, The Netherlands

<sup>11</sup>Division of Epidemiology and Biostatistics, School of Public Health, University of the Witwatersrand, 2193 Johannesburg, South Africa

\*Author for correspondence: [f.p.chilunga@amsterdammc.nl](mailto:f.p.chilunga@amsterdammc.nl)



Funding



**European Research Council**





A hand is shown clicking a computer mouse on a light-colored wooden desk. To the right of the hand is a large, three-dimensional '@' symbol made of cardboard. The background is softly blurred, showing a white wall and a window with light coming through. A thin orange horizontal line is positioned below the text.

# Know more

[f.p.chilunga@amsterdamumc.nl](mailto:f.p.chilunga@amsterdamumc.nl)



The background features a dark blue gradient with a faint, stylized DNA double helix structure. Scattered throughout the scene are numerous semi-transparent spheres of varying sizes, some of which appear to be attached to the DNA strands, suggesting a molecular or biological theme.

Thank you