WCE2024 - CHCSA Symposium

Sep 25, 2024

National blood pressure screening in South Africa to address inappropriate use of non-African nomograms

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Sub-theme Lead: Epidemiology and preventive science

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WORLD CONGRESS OF EPIDEMIOLOGY 2024

Conflicts of interest

This work is *partially* based on the research supported by:

- the National Research Foundation (NRF)* of South Africa (Grant Numbers: 99055; 112141),
- the South African Research Chairs Initiative (SARChI) of the Department of Science and Technology and the NRF of South Africa (Unique Identification Number: 86895),
- the South African Medical Research Council (MRC) Self-initiated research programme,
- and the MRC Extramural Research Unit for Hypertension and Cardiovascular Disease.
- Research/Clinical Trials: ExAMIN Youth SA study (Principal Investigator)

Any opinion, findings and conclusions or recommendations expressed in this material are those of the authors and therefore the NRF does not accept any liability in regard thereto.

saMRC advancinglife

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CHCSA Childhood Hypertension Consortium of South Africa

NRF National Research Foundation

Non -Profit Company
Registration #: 2021/787702/08

Non -Profit Organisation
277-116 NPO

Public Benefit Organisation
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Paediatric Specialties
Cardiology, Nephrology, Endocrinology, Physiology, Epidemiology, Nutrition, Biostatistics, Genetics, Biokinetics, Internal Medicine, Global Health

Endorsements
South African Paediatric Association

Southern African Hypertension Society

SAHS Know your blood pressure by

>20
Core Members

14
Institutions

8
Key Opinion Leaders

2
Major Projects

Partnerships
OMRON

SA HEART

WCE WORLD CONGRESS OF EPIDEMIOLOGY 2024

NWU

Our Brand
CHCSA
Childhood Hypertension Consortium of South Africa

In-kind Support
~ R1,15 million

Educational Webinars
THE HEART AND STROKE FOUNDATION SOUTH AFRICA

Aim of the Project

To develop, for the first time, nationally representative paediatric normative reference values for blood pressure by screening children between 5-18 years of age from all provinces in rural, peri-urban (townships) and urban South Africa.

Objectives

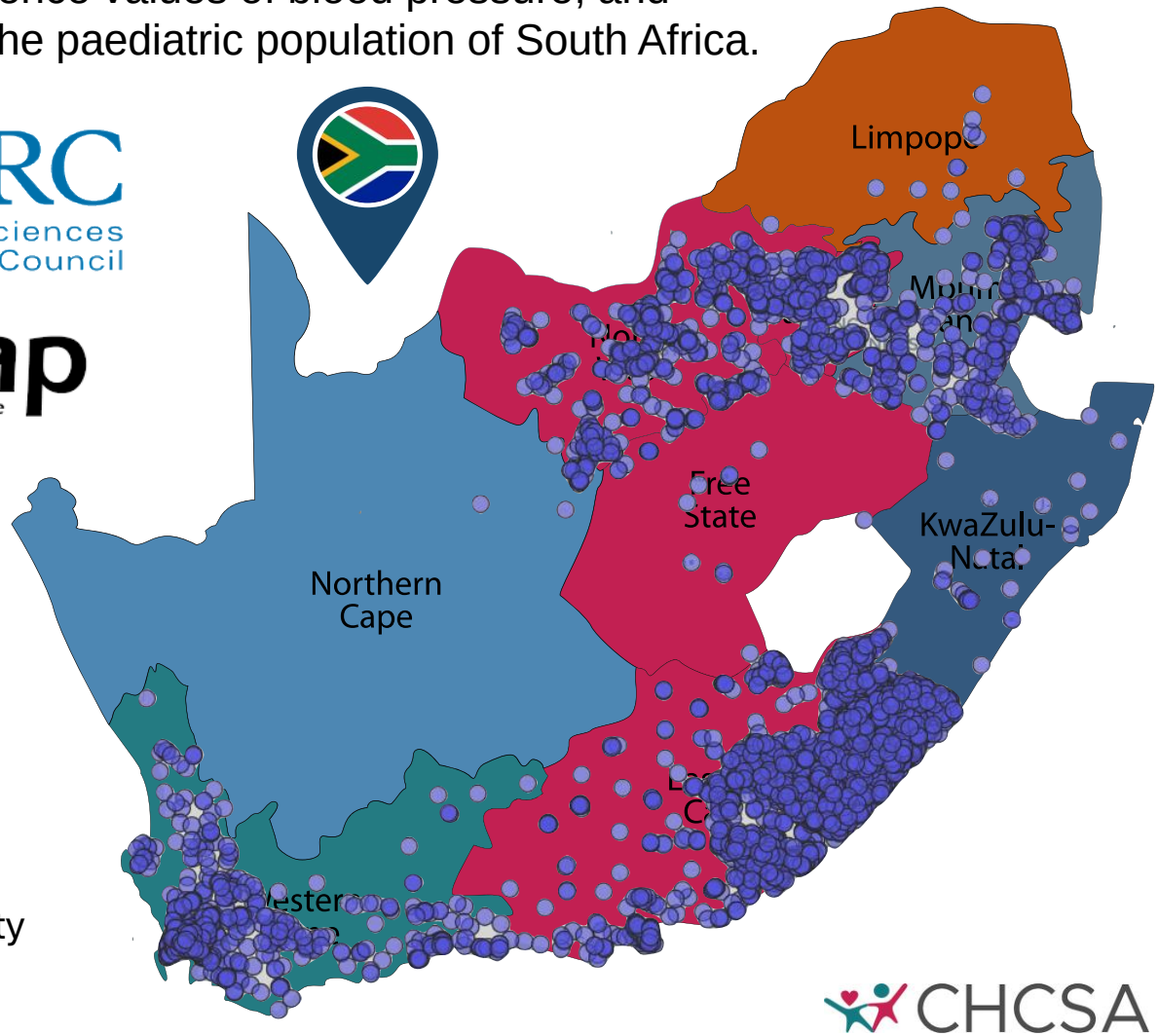
(i) To to development the first nationally representative normal reference values of blood pressure, and
(ii) to develop scientific evidence-based hypertension guidelines in the paediatric population of South Africa.

>22,464

School-aged Children and Adolescents to screen

HSRC Human Sciences Research Council

REDCap Research Electronic Data Capture



United Nations Sustainable Development Goals

- **3** Good Health and Well-being
- **4** Quality Education
- **9** Industry, Innovation and Infrastructure

Study design: This is a multi-stage cluster sampling study with probability proportional to size.

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Why?

JAMA Pediatrics | Original Investigation

Global Prevalence of Hypertension in Children
A Systematic Review and Meta-analysis

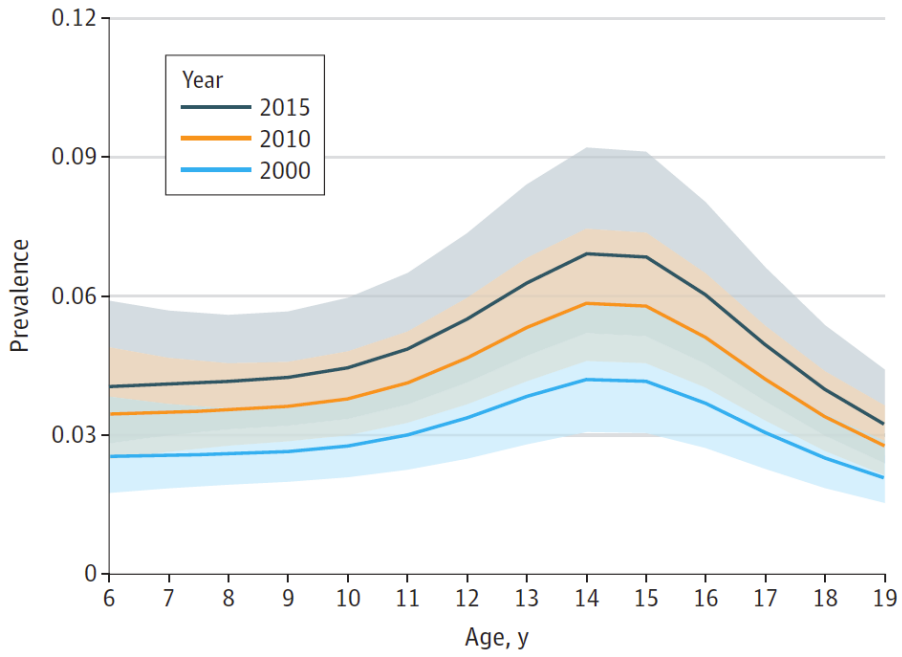
↑77%

Peige Song, PhD; Yan Zhang, MSc; Jinyue Yu, MD; Mingming Zha, MD; Yajie Zhu, PhD; Kazem Rahimi, DM; Igor Rudan, PhD

Table 3. Age-Specific Prevalence of Childhood Hypertension (Measured by Mercury Sphygmomanometer) in 2000, 2010, and 2015 and the Rate of Change From 2000 to 2015 by Age Group

Age, y	Prevalence of Hypertension, % (95% CI)			Relative Rate of Change (1990-2015), %
	2000	2010	2015	
6	2.42 (1.44-4.04)	3.57 (2.35-5.37)	4.32 (2.79-6.63)	78.10
7	2.46 (1.57-3.84)	3.62 (2.56-5.10)	4.38 (3.00-6.36)	78.04
8	2.50 (1.67-3.73)	3.68 (2.73-4.94)	4.45 (3.16-6.23)	77.99
9	2.56 (1.75-3.74)	3.77 (2.84-4.98)	4.56 (3.27-6.34)	77.89
10	2.71 (1.86-3.93)	3.98 (3.00-5.26)	4.82 (3.44-6.71)	77.69
11	3.00 (2.07-4.35)	4.41 (3.34-5.80)	5.33 (3.83-7.37)	77.27
12	3.47 (2.36-5.08)	5.08 (3.84-6.70)	6.13 (4.42-8.45)	76.61
13	4.05 (2.75-5.93)	5.91 (4.46-7.78)	7.12 (5.14-9.76)	75.81
14	4.51 (3.09-6.53)	6.56 (5.00-8.57)	7.89 (5.75-10.75)	75.17
15	4.45 (3.06-6.44)	6.49 (4.94-8.47)	7.80 (5.67-10.65)	75.25
16	3.85 (2.64-5.60)	5.63 (4.28-7.37)	6.79 (4.92-9.29)	76.08
17	3.07 (2.08-4.51)	4.51 (3.40-5.96)	5.44 (3.92-7.52)	77.17
18	2.38 (1.57-3.57)	3.50 (2.58-4.73)	4.23 (2.99-5.96)	78.16
19	1.83 (1.18-2.85)	2.70 (1.92-3.80)	3.28 (2.25-4.77)	78.94

Figure 2. Age-Specific Prevalence of Childhood Hypertension in 2000, 2010, and 2015



Childhood hypertension was based on blood pressure measured by mercury sphygmomanometer. Shaded areas indicate 95% CIs.

JAMA Pediatr. 2019;173(12):1154-1163

MEDICAL PROGRESS
www.jpeds.com • THE JOURNAL OF PEDIATRICS

Primary Hypertension Beginning in Childhood and Risk for Future Cardiovascular Disease

Bonita Falkner, MD[1], and Empar Lurbe, MD[2]
J Pediatr. 2021;238:16-25

Tracking studies

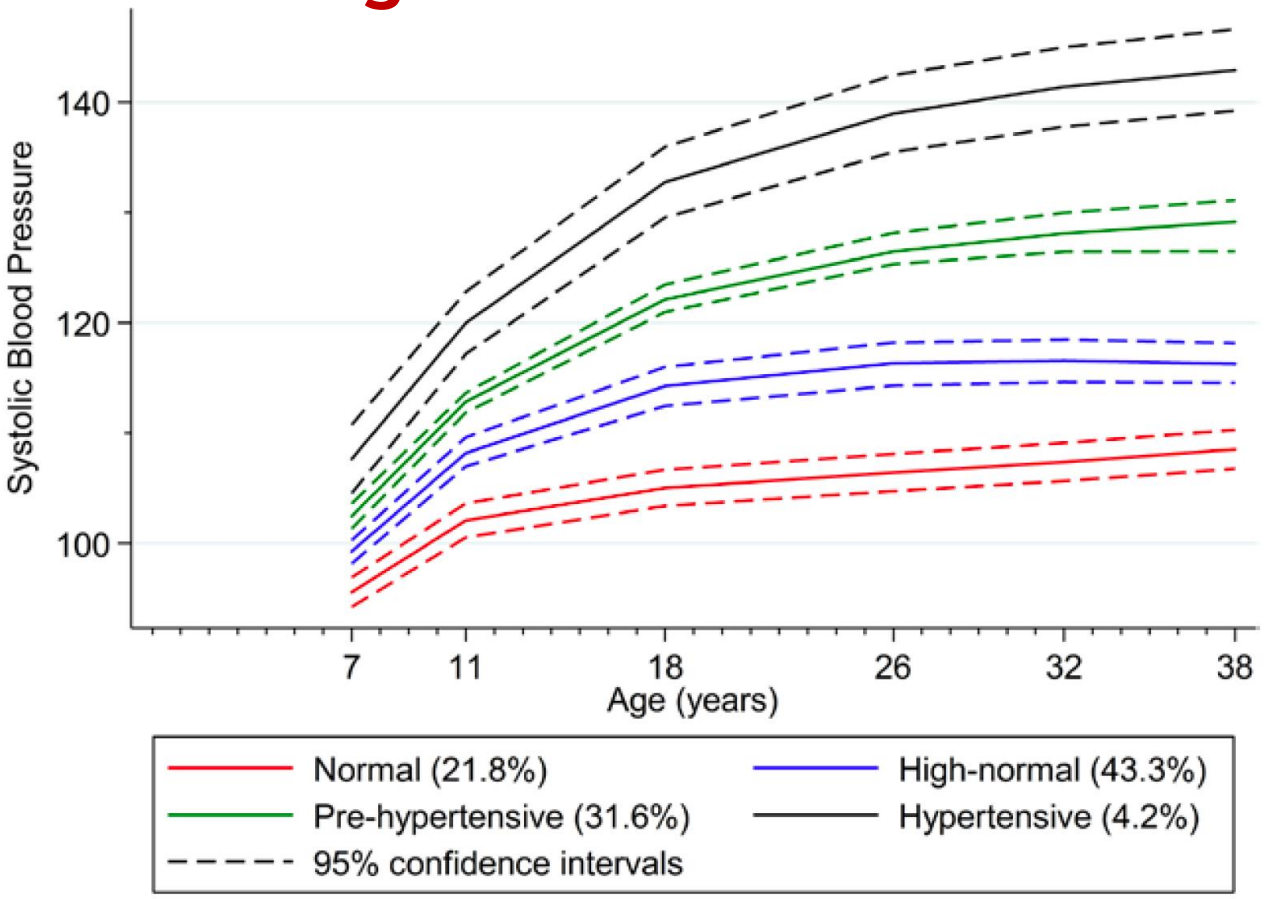
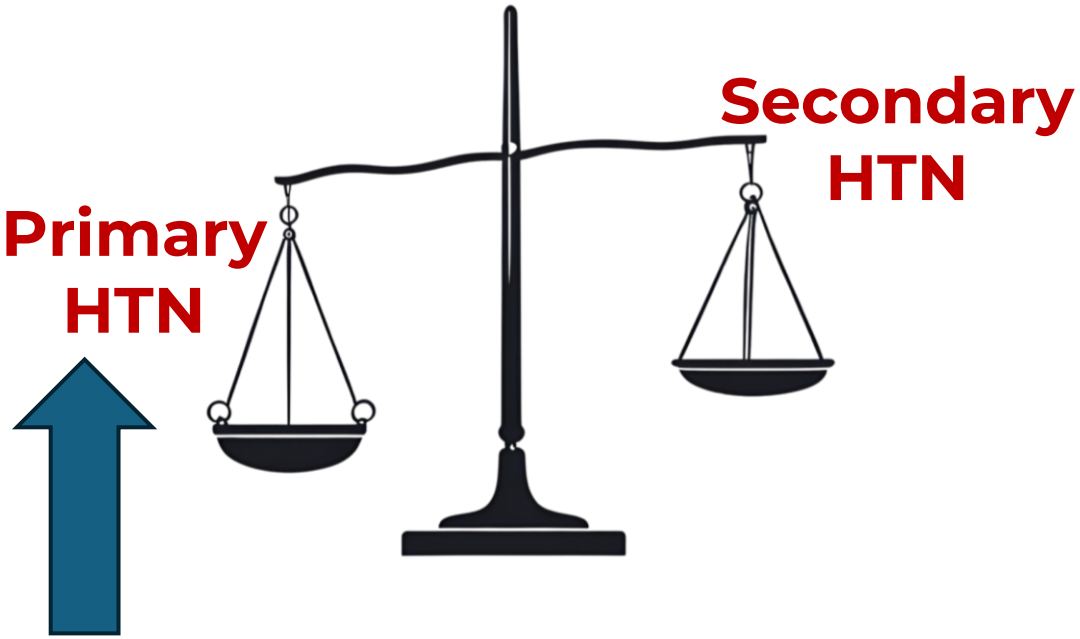
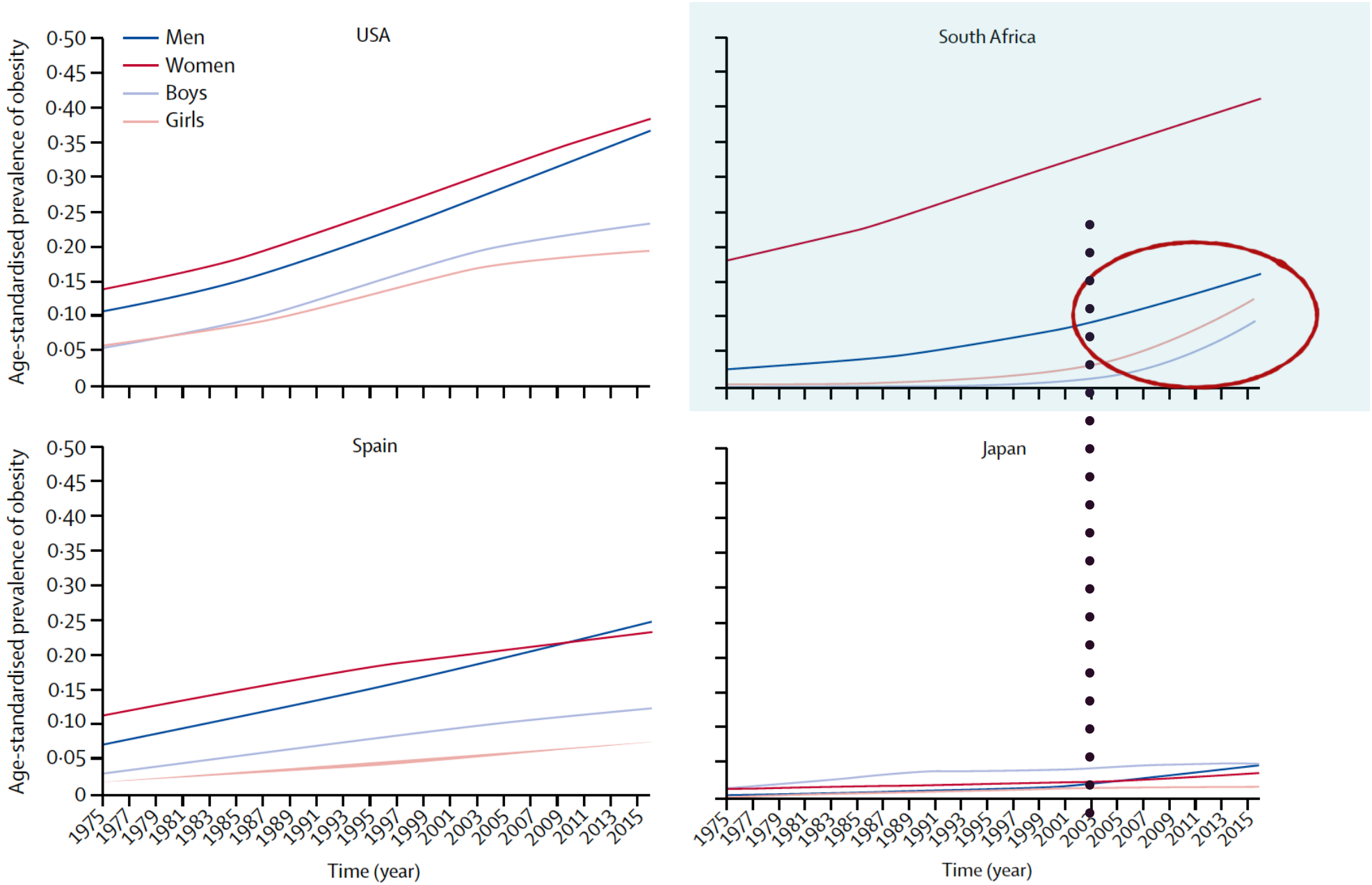


Figure. Plot of predicted trajectory lines with 95% confidence intervals for the 4 blood pressure trajectory groups identified in a general population longitudinal birth cohort.



Theodore RF, et al. Hypertension. 2015;66:1108-1115.

5%



Jaacks et al. Lancet Diabetes Endocrinol, 2019; 7: 231–40

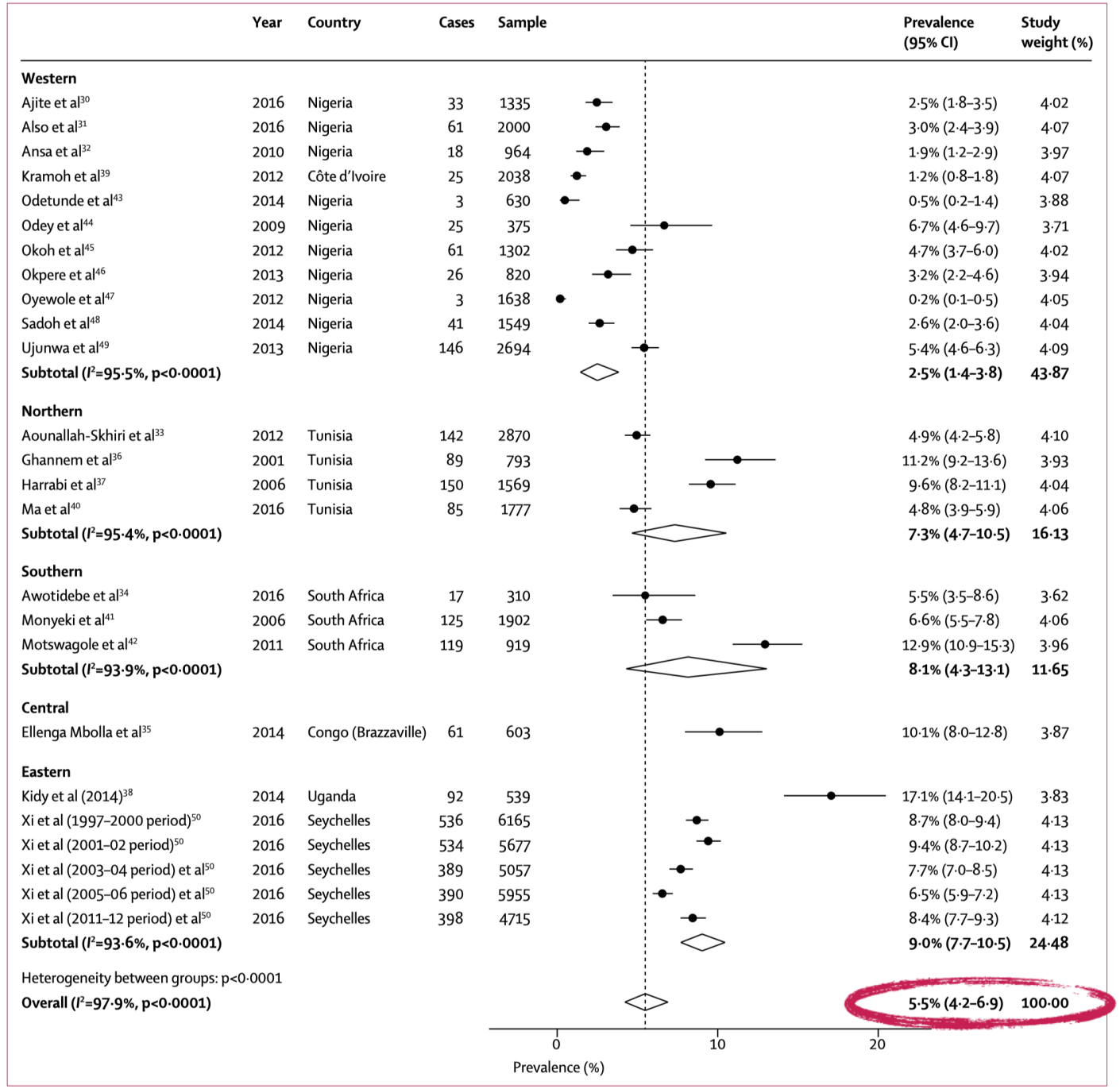
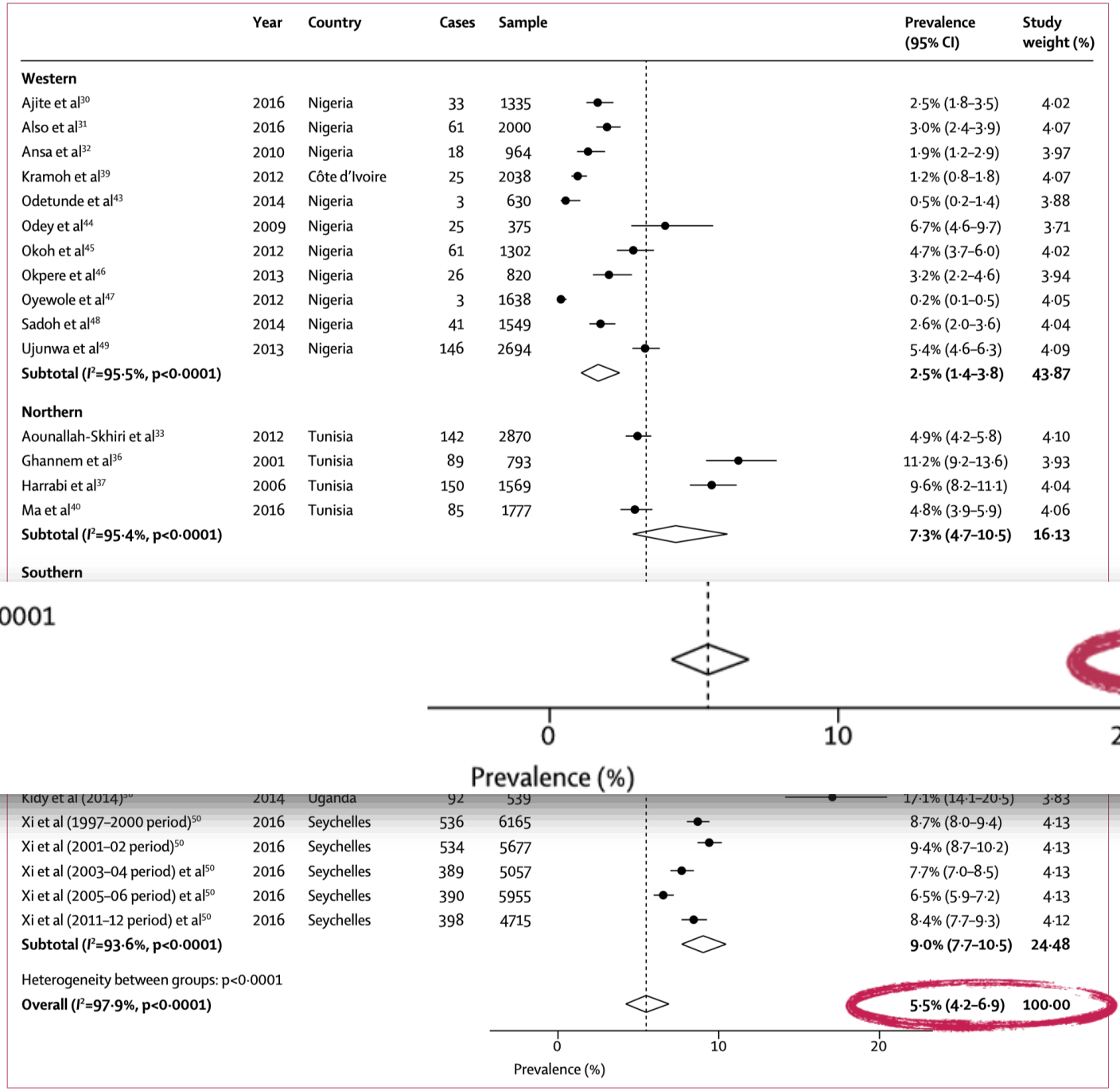


***Figure 2*: Prevalence of elevated blood pressure in children and adolescents by UNSD African regions**
UNSD=United Nations Statistics Division.

Noubiab JJ, et al. Lancet Public Health 2017; 2: e375–86



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Noubiab JJ, et al. Lancet Public Health 2017; 2: e375–86

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Paediatric hypertension in South Africa: An underestimated problem calling for action

Hypertension needs to be detected and managed early in childhood to prevent the associated adverse end-organ changes in later life. Detection of the risk factors underlying elevated BP should therefore start as early as possible. Managing these may be more effective than treatment in reducing the prevalence of hypertension and related health consequences in adulthood. In conclusion, more BP research in SA children is critically needed to provide important epidemiological and aetiological information on paediatric hypertension and its role in the high prevalence of adult hypertension.

Research Paper

Paediatric Hypertension in Africa: A Systematic Review and Meta-Analysis

Simone H. Crouch,[a,†] Larske M. Soepnel,[a,b,*,†] Andrea Kolkenbeck-Ruh,[a] Innocent Maposa,[c] Sanushka Naidoo,[a] Justine Davies,[a,d] Shane A. Norris,[a,e] and Lisa J. Ware,[a,f]

[a]SAMRC/Wits Developmental Pathways for Health Research Unit, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa.
[b]Julius Global Health, Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands.
[c]Division of Epidemiology and Biostatistics, School of Public Health, Faculty of Health Sciences, University of Witwatersrand, Johannesburg, South Africa School of Public Health
[d]Institute of Applied Health Research, University of Birmingham, Birmingham, United Kingdom
[e]School of Health and Human Development, University of Southampton, Southampton, United Kingdom.
[f]DSI-NRF Centre of Excellence in Human Development, University of the Witwatersrand, Johannesburg, South Africa.

Summary

Background The burden of cardiovascular disease (CVD) and hypertension is rapidly increasing in low- and middle-income countries. This is evident not only in adults, but also in children. Recent estimates of prevalence in children are lacking, particularly in Africa. As such, we conducted a systematic review and meta-analysis to provide updated estimates of paediatric hypertension in Africa.

Methods We searched PubMed and EBSCO to identify articles published from January 2017 to November 2020. Studies were assessed for quality. We combined results for meta-analyses using a random effects model (Freeman-Tukey arcsine transformation). Heterogeneity was quantified using the I^2 statistic.

EClinicalMedicine 2021;43: 101229
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https://doi.org/10.101
eclinm.2021.101229

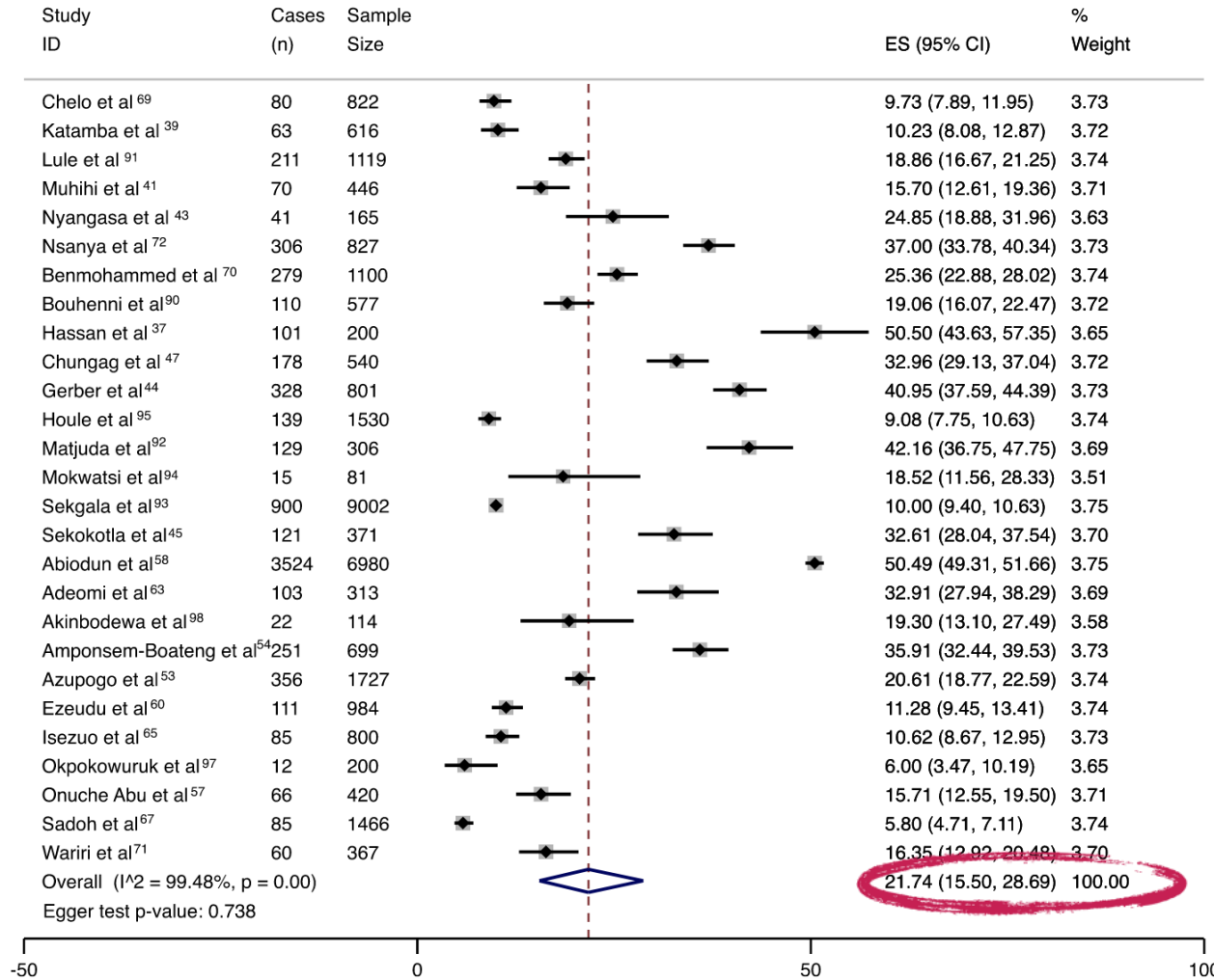

Figure 4. Meta-analysis results in the form of a forest plot for prevalence of combined hypertension and elevated blood pressure with cases (n), sample size, 95% confidence intervals, estimated prevalences and percent weight per included study.
ES= estimated prevalence.

Research Paper

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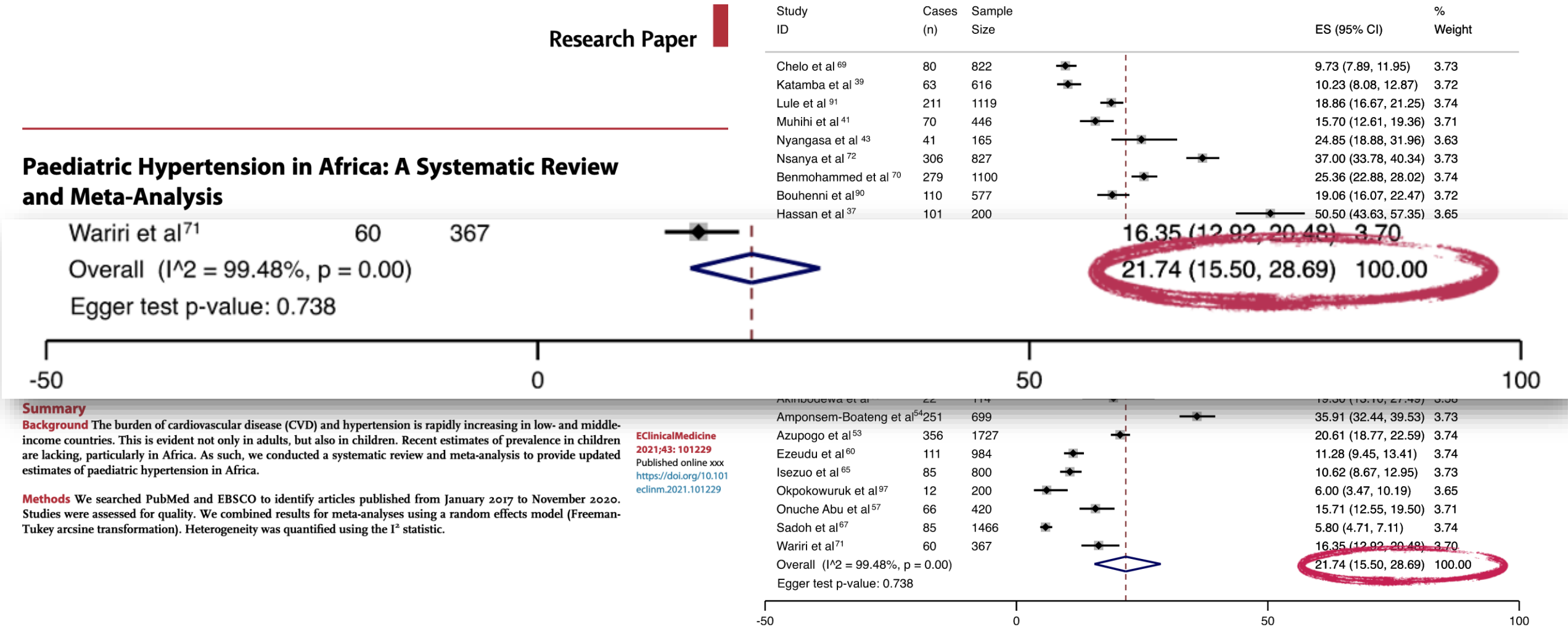

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ES= estimated prevalence.

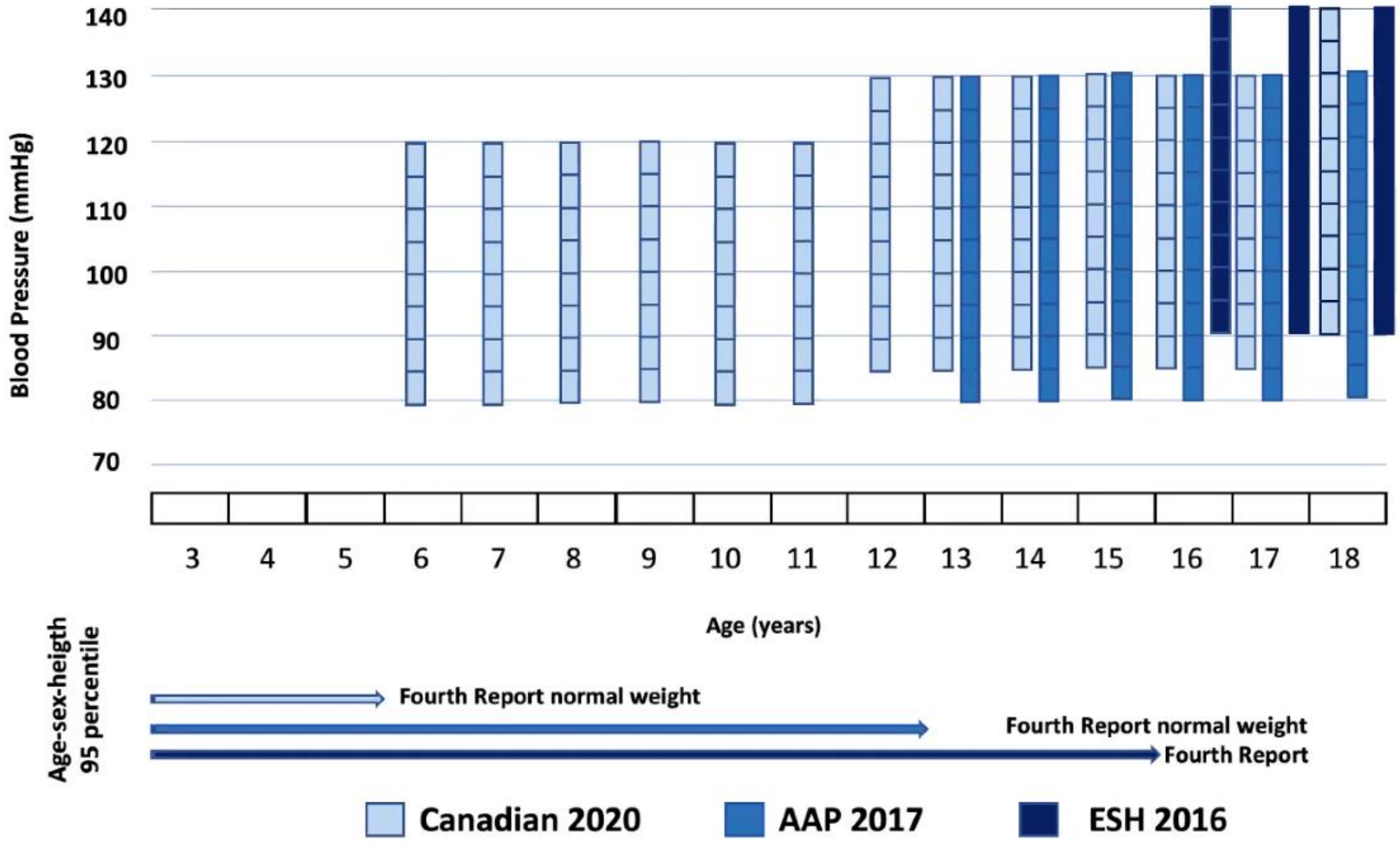
Table 1. Definitions of Childhood Hypertension by Consensus Organizations and National Societies in 2022

Issuing body	Year	Criteria for hypertension*	Comments	Reference
American Academy of Pediatrics	2017	≥95th percentile for age and sex; or ≥130/80, whichever is lower	Adopts static cut points from ACC/AHA guideline starting at 13 y of age; percentiles based on revised, lower normative BP data	Flynn et al[1]
Chinese Hypertension League	2018	≥95th percentile for age and sex	Percentiles based on Chinese-specific normative BP data	Joint Committee for Guideline Revision[2]
European Society of Hypertension	2016	≥95th percentile for age and sex up to age 16 y; ≥140/90 starting at 16 y	Static cut point based on adult thresholds in use at the time; percentiles based on normative BP data from 2004 Fourth Report[4]	Lurbe et al[3]
Hypertension Canada	2020	≥95th percentile for age and sex; or >120/80 for ages 6–11 y, or >130/85 for ages 12–17 y	Static cut points derived from one analysis of the Bogalusa Heart Study[7]	Rabi et al[4]
Japanese Society of Hypertension	2019	≥age-based static cut point ranging from 120/70 in preschool students to 140/85 in high-school students	Screening BP values 10–15 mm Hg higher than those in percentile-based reference charts	Umemura et al[6]

ACC indicates American College of Cardiology; AHA, American Heart Association; BP, blood pressure.
*All require the child's BP to be at or above this level on multiple visits (usually 3) before making a diagnosis of hypertension.

Flynn J. Circulation Research. 2022;130:800–808.

The conundrum of reference BP values



Difficulties to define "normal" values

Graphic expression of the criteria to define HTN according to Guidelines in Children and Adolescents: European Society of Hypertension (ESH 2016) [2], American Academy of Pediatrics (AAP 2017) (3) and Canadian Guidelines (Canadian 2020) [4].

Lurbe & Redon. Hypertension News, 2022; DOI: 10.30824/2204-6

“The pediatric guidelines, including the 2004 National High Blood Pressure Education Program’s (NHBPEP) Fourth Report, offer separate normative values for children of varying ethnic backgrounds (NHBPEP 2004). The samples from which pediatric normative BP values are derived include children from multiple ethnic and race backgrounds. Though height, age, and gender all are accounted for in the determination of pediatric normative BP values, ethnicity is not included as significant factor influencing BP. **This lack of ethnicity specific normative data is likely due to race and ethnicity often being confounded with other known determinants of pediatric BP variability such as body size, sexual development, and socioeconomic status.**”

J.T. Flynn et al. (eds.), Pediatric Hypertension, p.352 https://doi.org/10.1007/978-3-319-31107-4_16

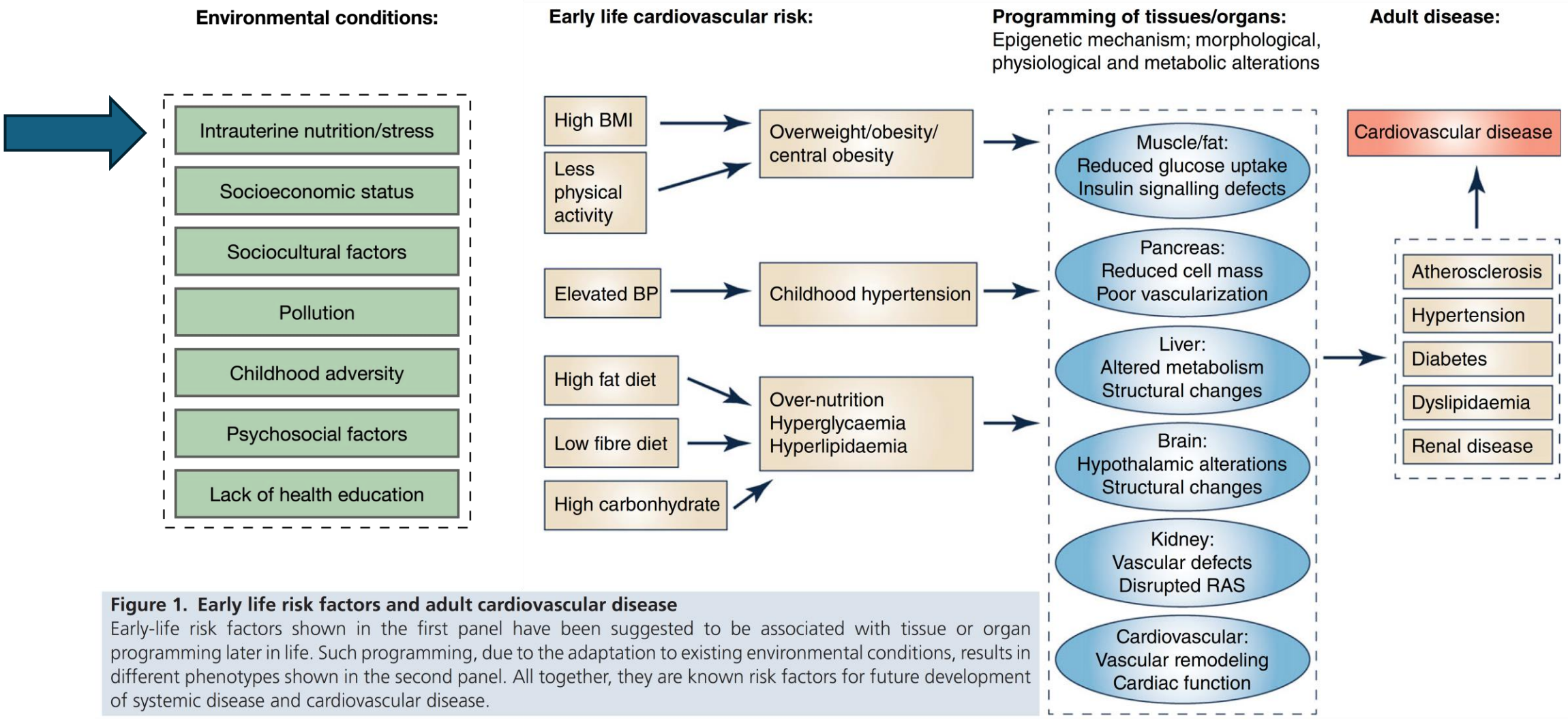


Figure 1. Early life risk factors and adult cardiovascular disease
Early-life risk factors shown in the first panel have been suggested to be associated with tissue or organ programming later in life. Such programming, due to the adaptation to existing environmental conditions, results in different phenotypes shown in the second panel. All together, they are known risk factors for future development of systemic disease and cardiovascular disease.

Adapted from **Li et al. J Physiol 594.8 (2016) pp 2175–2203**

TABLE 2 | Comparison of high blood pressure prevalence among school-aged children in Gqeberha, South Africa, in July 2019 according to the (i) American Academic of Pediatrics, (ii) German guidelines, (iii) a global reference population, and (iv) the *KaziBantu* study population ($N = 897$).

References	Normal blood pressure	Elevated blood pressure	Hypertension stage 1	Hypertension stage 2
Flynn et al. (15)*	555 (61.9%)	85 (9.5%)	181 (20.2%)	76 (8.5%)
Neuhauser et al. (16)†	572 (63.8%)	65 (7.2%)	163 (18.2%)	97 (10.8%)
Xi et al. (17)‡	565 (63.0%)	102 (11.4%)	159 (17.7%)	71 (7.9%)
Müller et al. (21)§	738 (82.3%)	57 (6.4%)	65 (7.2%)	37 (4.1%)

**Normotension: <13 years old: <90th; >13 years old BP < 120/80 mm Hg; elevated BP: <13 years old: ≥90th and <95th or >120/80 mm Hg but <95th; >13 years old: 120/<80 to 129/<80 mm Hg; HTN stage 1: <13 years old: ≥95th and <95th + 12 mm Hg or 130/80–139/89 mm Hg; >13 years old: 130/80 mm Hg to 139/89 mm Hg; HTN stage 2: <13 years old: ≥95th + 12 mm Hg or ≥140/90 mm Hg; >13 years old: ≥140/90 mm Hg.*

† Normotension: <90th; elevated BP: ≥90th and <95th; HTN stage 1: ≥95th and <99.75th; HTN stage 2: ≥99.75th or ≥140/90 mmHg.

‡Normotension: <90th; elevated BP: ≥90th and <95th or >120/80 mm Hg but <95th; HTN stage 1: ≥95th and <99th + 5 mm Hg; HTN stage 2: ≥99th + 5 mm Hg.

§Normotension: <90th; elevated BP: ≥90th and <95th; HTN stage 1: ≥95th and <95th+12 mm Hg; HTN stage 2: ≥95th + 12 mm Hg.

TABLE 2 | Compa ool-aged children in Gqeberha, South Africa, in July 2019 according to the (i) American Academic of Pediatrics, (ii) Gerr d (iv) the *KaziBantu* study population ($N = 897$).

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**Normotension: <1 elevated BP: <13 years old: ≥90th and <95th or >120/80 mm Hg but <95th; >13 years old: 120/<80 to 129/<80 mm Hg; H Hg or 130/80–139/89 mm Hg; >13 years old: 130/80 mm Hg to 139/89 mm Hg; HTN stage 2: <13 years old: ≥95th + 12 mm Hg or ≥140/90 mm Hg; >13 years old: ≥140/90 mm Hg.*

† Normotension: <90th; elevated BP: ≥90th and <95th; HTN stage 1: ≥95th and <99.75th; HTN stage 2: ≥99.75th or ≥140/90 mmHg.

‡Normotension: <90th; elevated BP: ≥90th and <95th or >120/80 mm Hg but <95th; HTN stage 1: ≥95th and <99th + 5 mm Hg; HTN stage 2: ≥99th + 5 mm Hg.

§Normotension: <90th; elevated BP: ≥90th and <95th; HTN stage 1: ≥95th and <95th+12 mm Hg; HTN stage 2: ≥95th + 12 mm Hg.

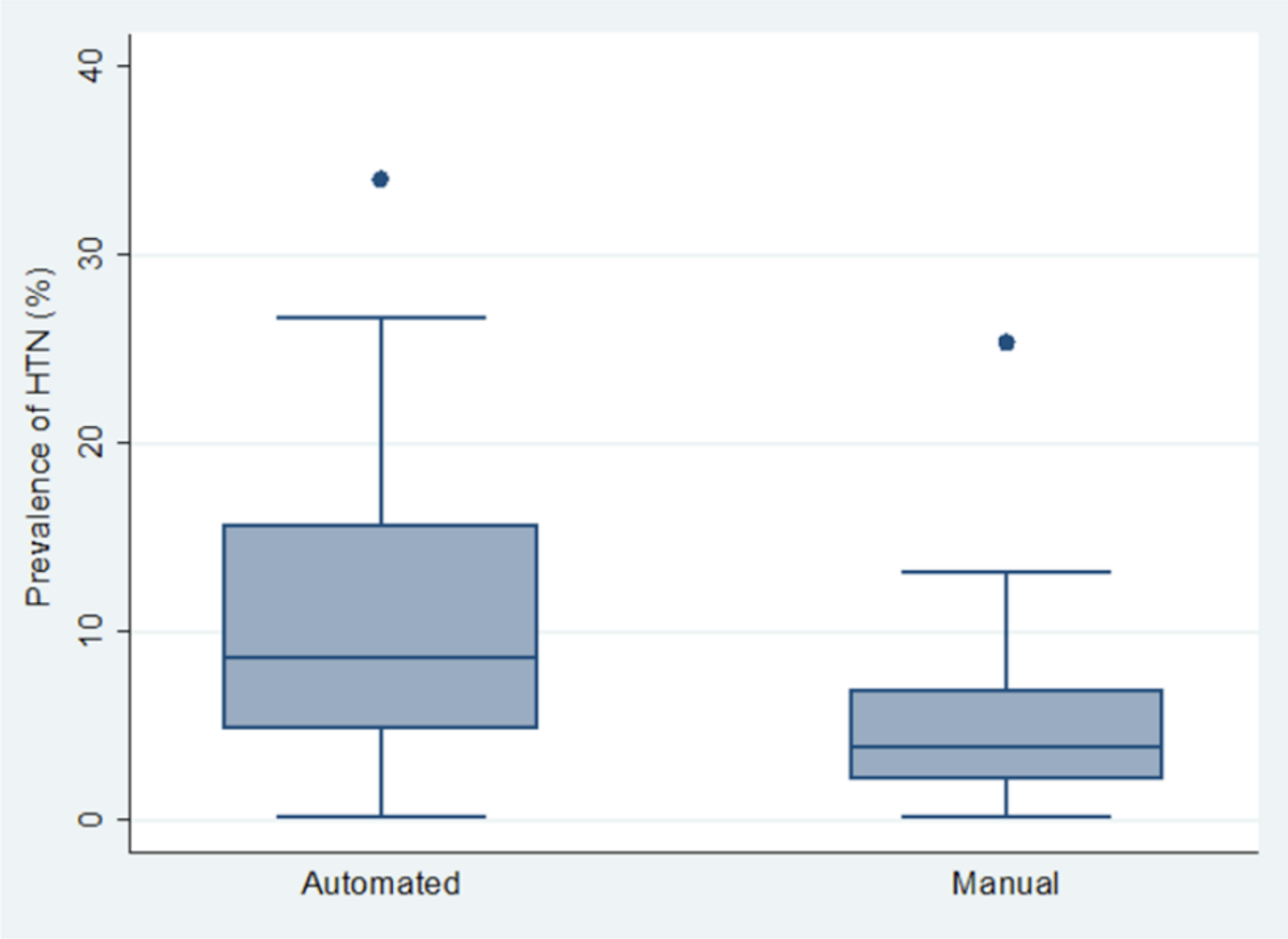


FIGURE 2
Box and whiskers plot showing the distribution of hypertension prevalence across the 2 types of BP measurement device.

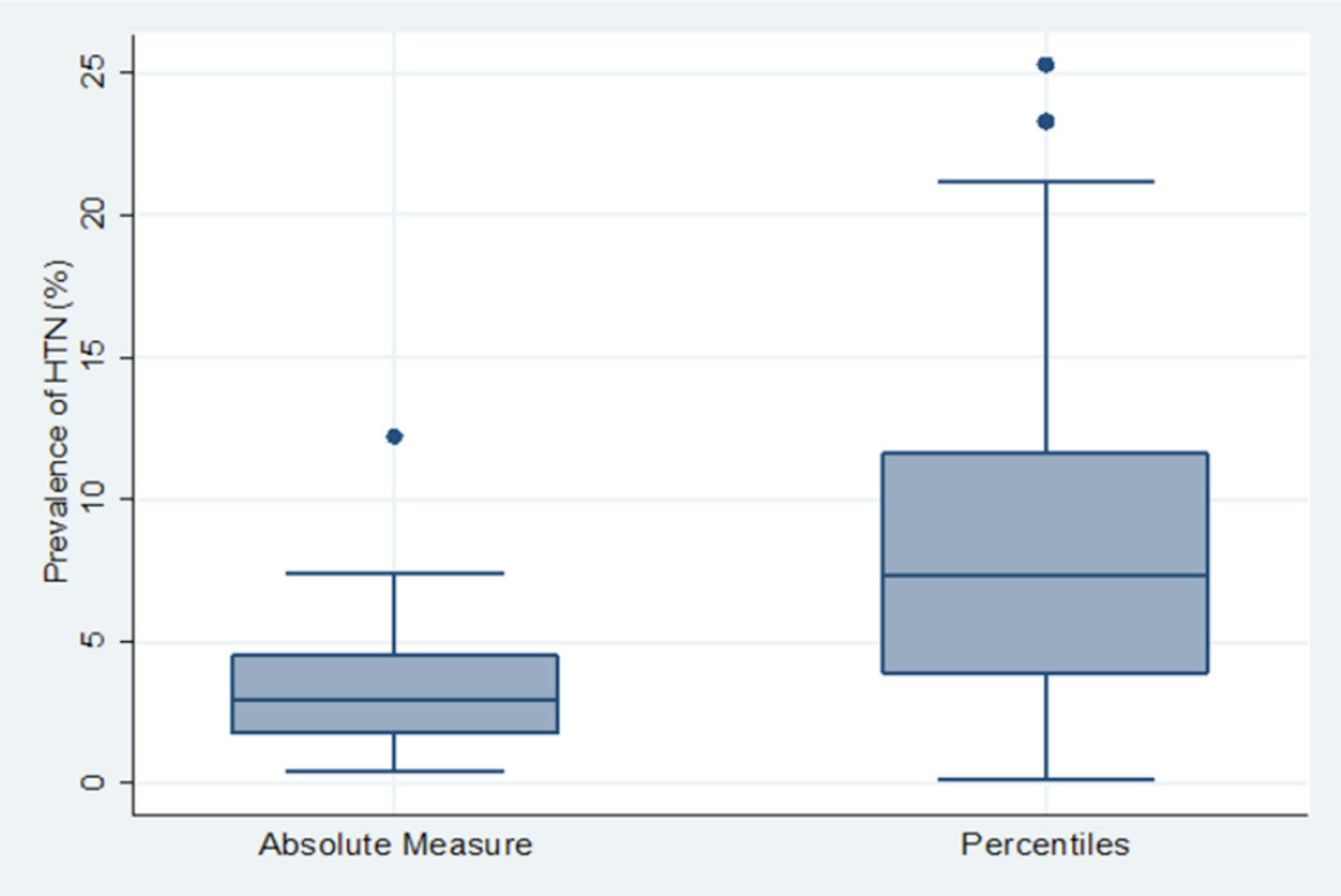


FIGURE 3
Box and whiskers plot showing the distribution of hypertension prevalence across 2 types of hypertension definition.

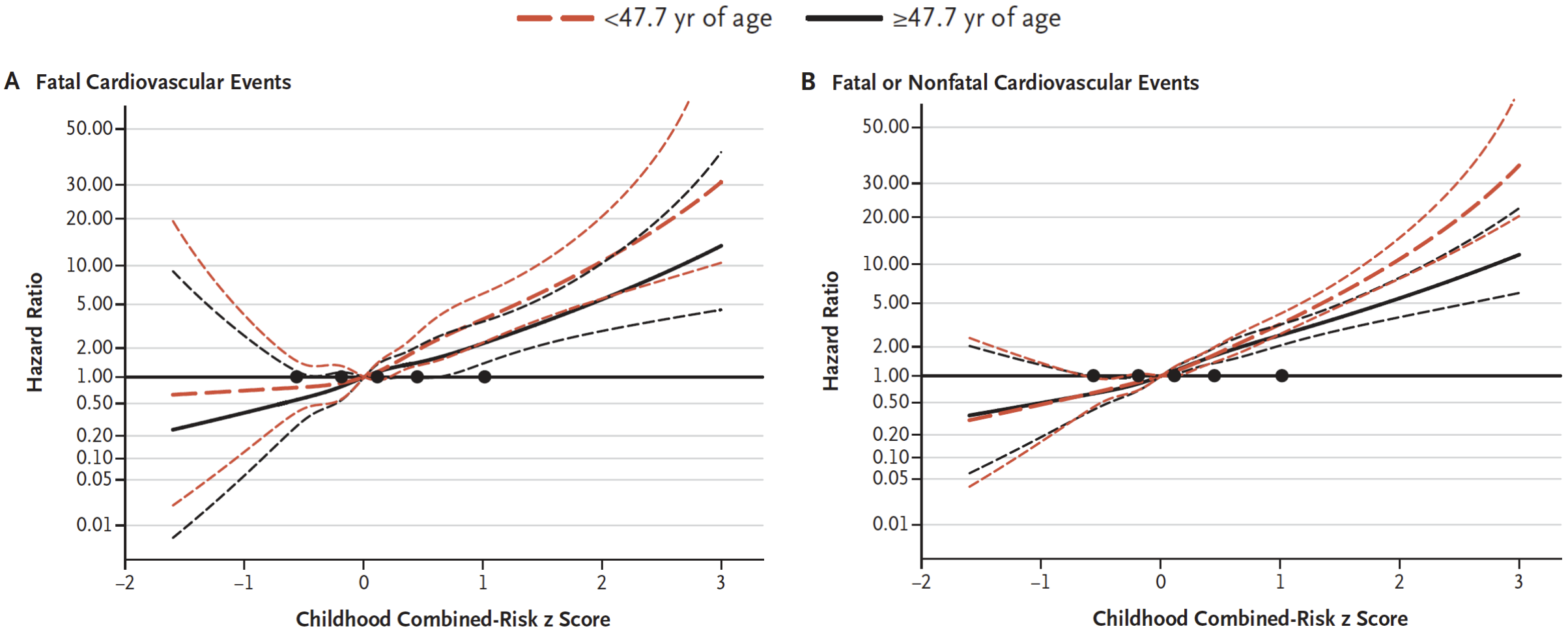


Figure 1. Hazard Ratios for Cardiovascular Events at Younger and Older Ages.

Panel A shows the hazard ratios for fatal cardiovascular events, and Panel B shows the hazard ratios for fatal or nonfatal cardiovascular events. The spline of the hazard ratio is presented on a logarithmic scale across the distribution of the childhood combined-risk z scores, with 95% confidence intervals (shorter dashed lines). Younger age (<47.7 years) includes all the participants, among whom there were 157 fatal events and a mean of 797 fatal or nonfatal events across imputations. The older age group includes only the participants who were followed and had no event or had events at or after 47.7 years of age (a total of 18,352 participants, among whom 162 had a fatal cardiovascular event and 1049 either had a fatal event due to other causes or were not followed past the age of 47.6 years; the 17,141 remaining participants had a mean of 766 fatal or nonfatal events across imputations).

The black circles indicate knots placed at the 5th, 25th, 50th, 75th, and 95th percentiles of the combined-risk z score.

Jacobs et al. N Engl J Med 2022;386:1877-88

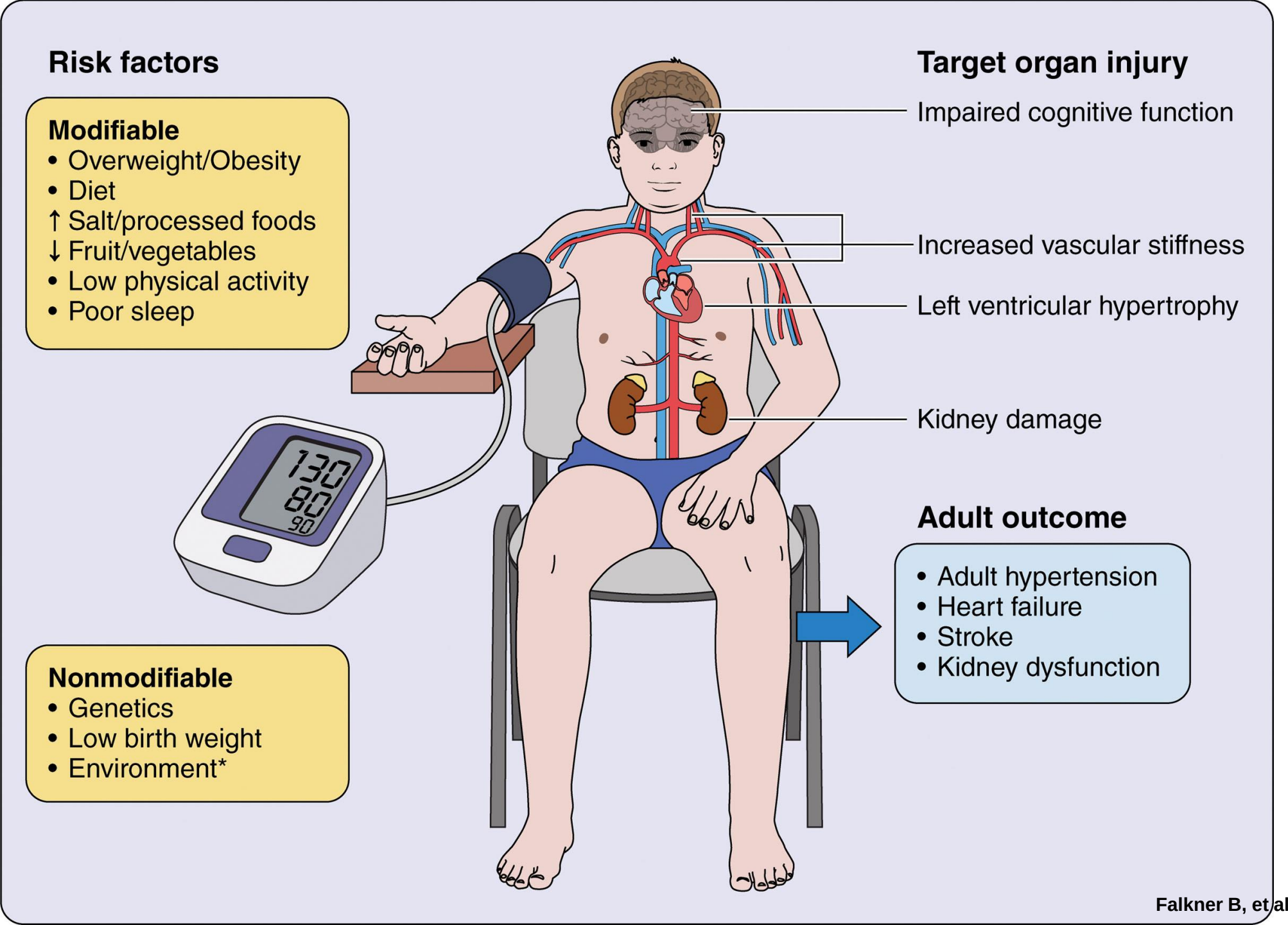


Figure. **Risk factors for high BP in children and adolescents that are modifiable, including improving dietary intake and physical activity and reducing excess adiposity.** Also shown are nonmodifiable risk factors. As shown on the **right**, there is evidence of target organ injury in the heart and blood vessels in youth with primary hypertension. Primary hypertension onset in childhood is associated with adverse cardiovascular disease outcomes in adulthood. *Environment: Many environmental exposures, including excess dietary salt intake and air pollution, that are known to have an adverse effect on blood pressure (BP) in youth and cardiovascular disease in adults are technically modifiable. However, efforts to mitigate these exposures are challenging and require ongoing public health research, advocacy, and policy changes.

Falkner B, et al. Hypertension. 2023; 80(6):e101-e111.

STUDY PROTOCOL
published: 29 April 2020
doi: 10.3389/fped.2020.00212

The Exercise, Arterial Modulation and Nutrition in Youth South Africa Study (ExAMIN Youth SA)

Ruan Kruger[1,2], Makama Andries Monyeki[3], Aletta Elisabeth Schutte[1,2,4], Wayne Smith[1,2], Catharina Martha Cornelia Mels[1,2], Herculina Salomé Kruger[2,5], Anita Elizabeth Pienaar[3], Lebo Francina Gafane-Matemane[1,2], Yolandi Breet[1,2], Leandi Lammertyn[1,2], Gontse Gratitude Mokwatsi[1,2], Ankebé Kruger[3], Elmari Deacon[6] and Henner Hanssen[7]*

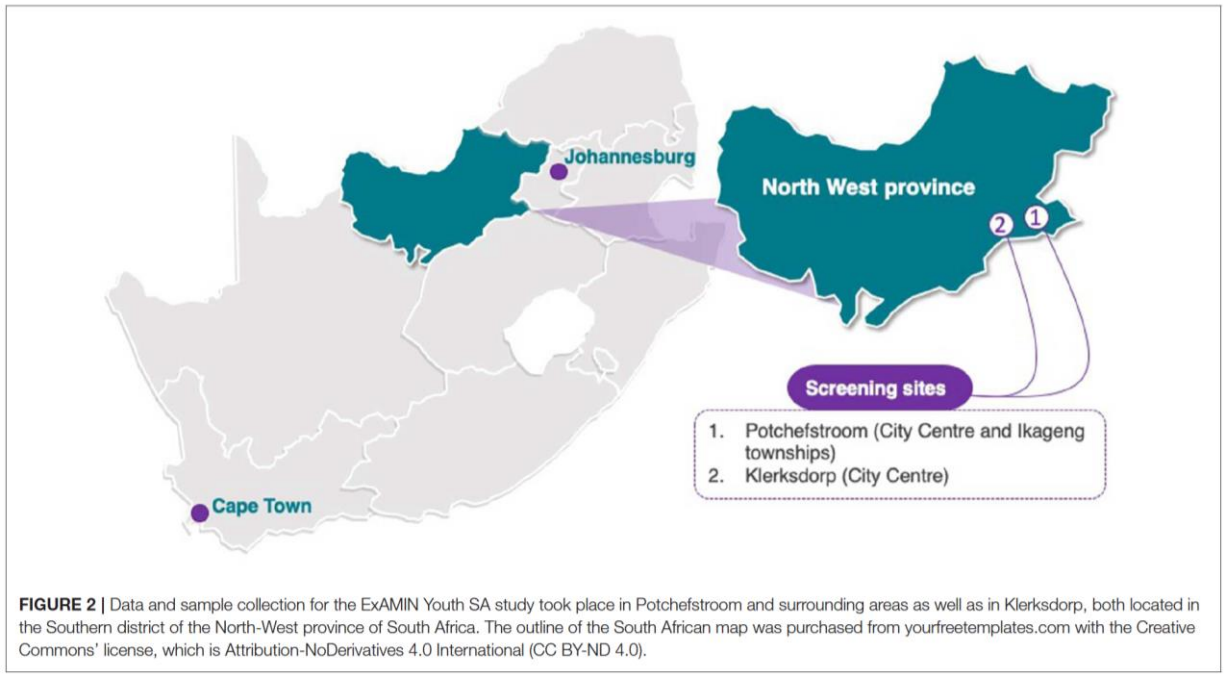


FIGURE 2 | Data and sample collection for the ExAMIN Youth SA study took place in Potchefstroom and surrounding areas as well as in Klerksdorp, both located in the Southern district of the North-West province of South Africa. The outline of the South African map was purchased from yourfreetemplates.com with the Creative Commons' license, which is Attribution-NoDerivatives 4.0 International (CC BY-ND 4.0).

ClinicalTrials.gov Identifier: NCT04056377

ExAMIN Youth SA

The Exercise, Arterial Modulation and Nutrition in Youth South Africa Study

Initial recruitment n=1200

No consent, n=50
Dropouts, illness, n=47

Baseline cohort [2017-2019] **n=1103**

Withdraw, n=60
Unassigned ID, n=3
Wrong age, n=4

Relocated, n=206
Absent, n=27

Follow-up cohort [2021-2022] **n=803**

73% **Successful follow-up rate**

Kruger R, et al., Frontiers Ped 2020; 8: 212

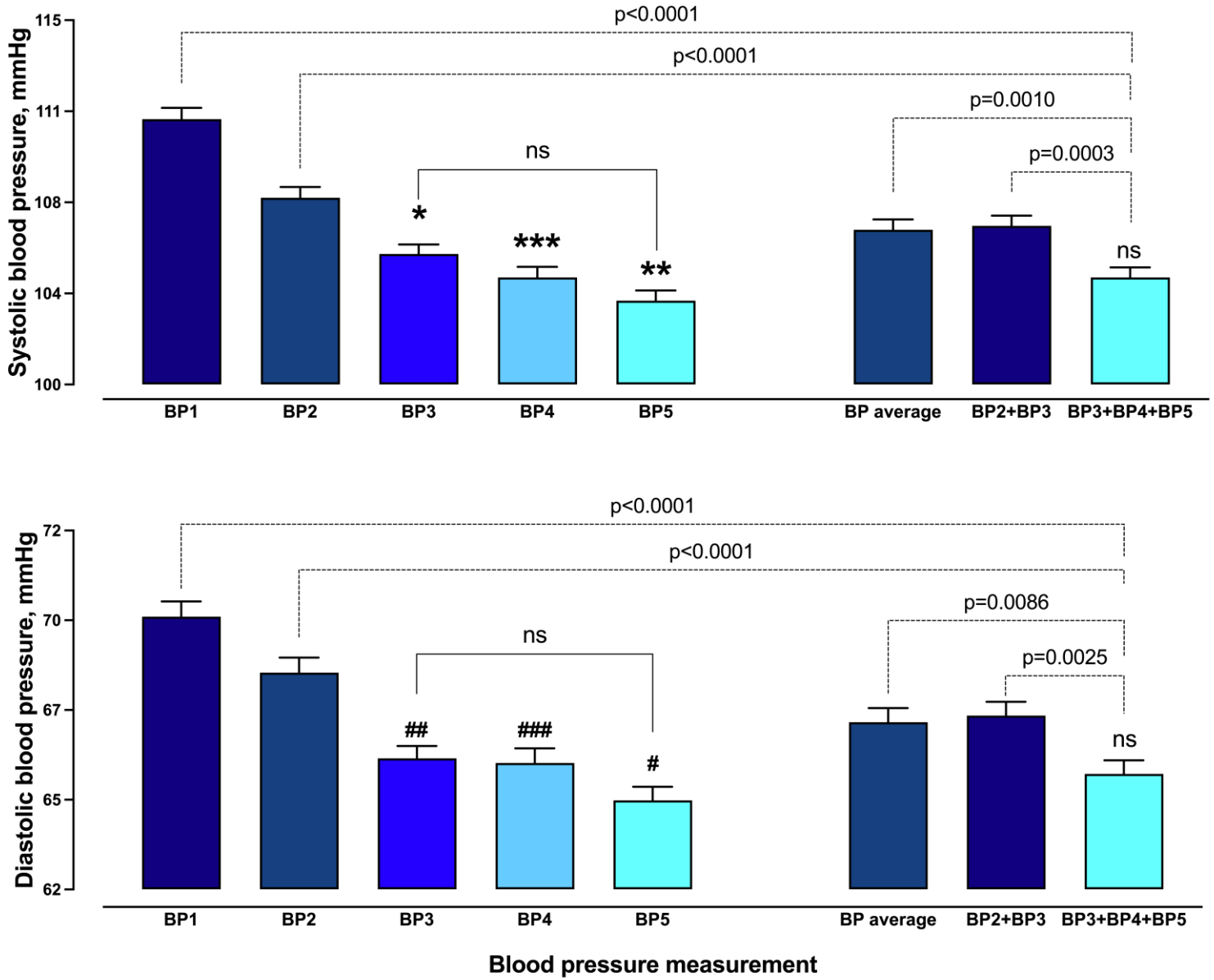
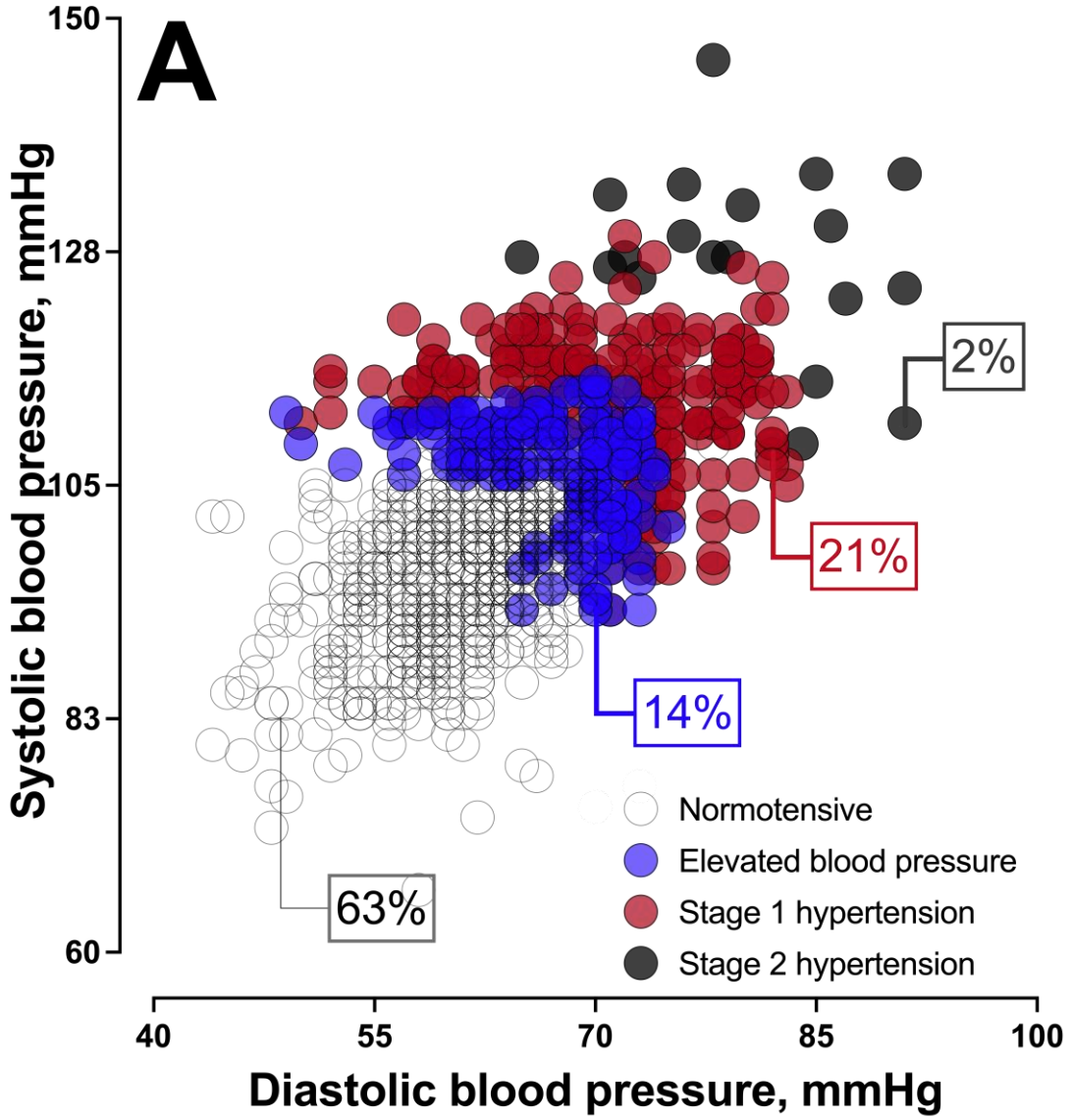


Figure 2. Blood pressure values per interval measurement and estimation of blood pressure average with the least variation. Symbols denote p-values for systolic blood pressure: *p=0.087; **p=0.996; ***p=0.102 and diastolic blood pressure: #p=0.169; ##p=0.399; ###p=0.587 as compared to the average of the three blood pressure measurements with the least variance.

Kruger et al. J Hypertens 39:2190–2199



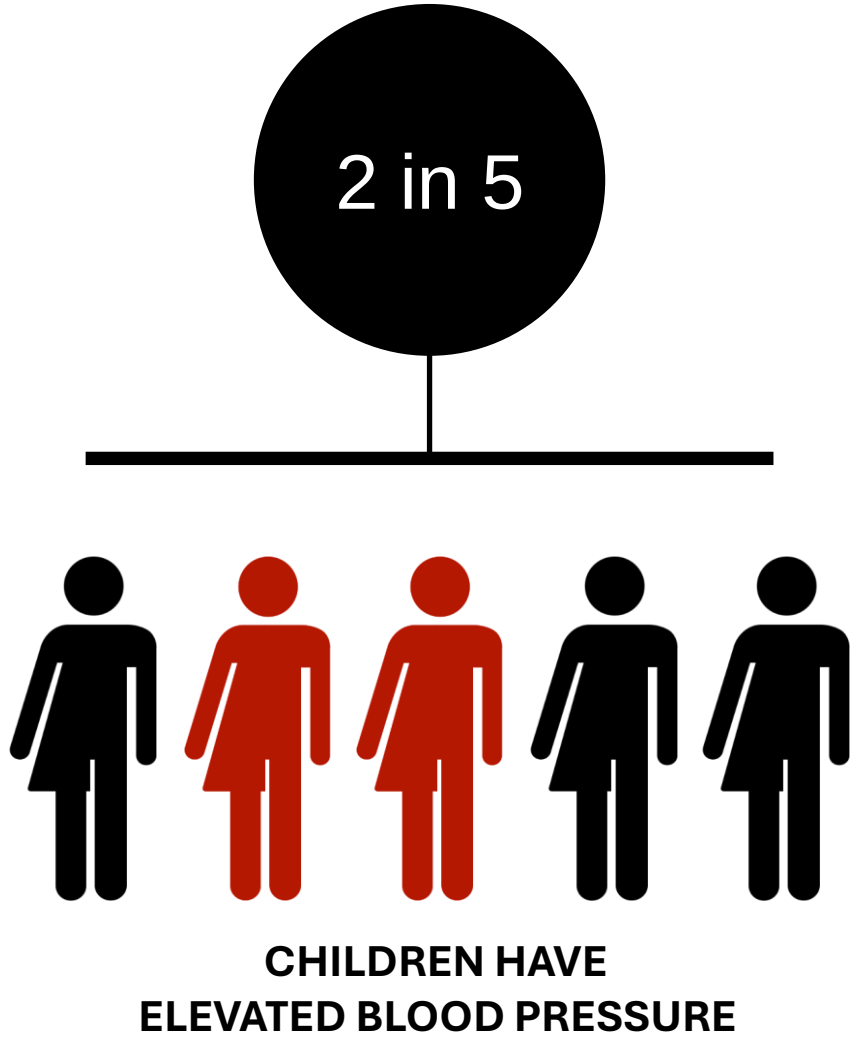
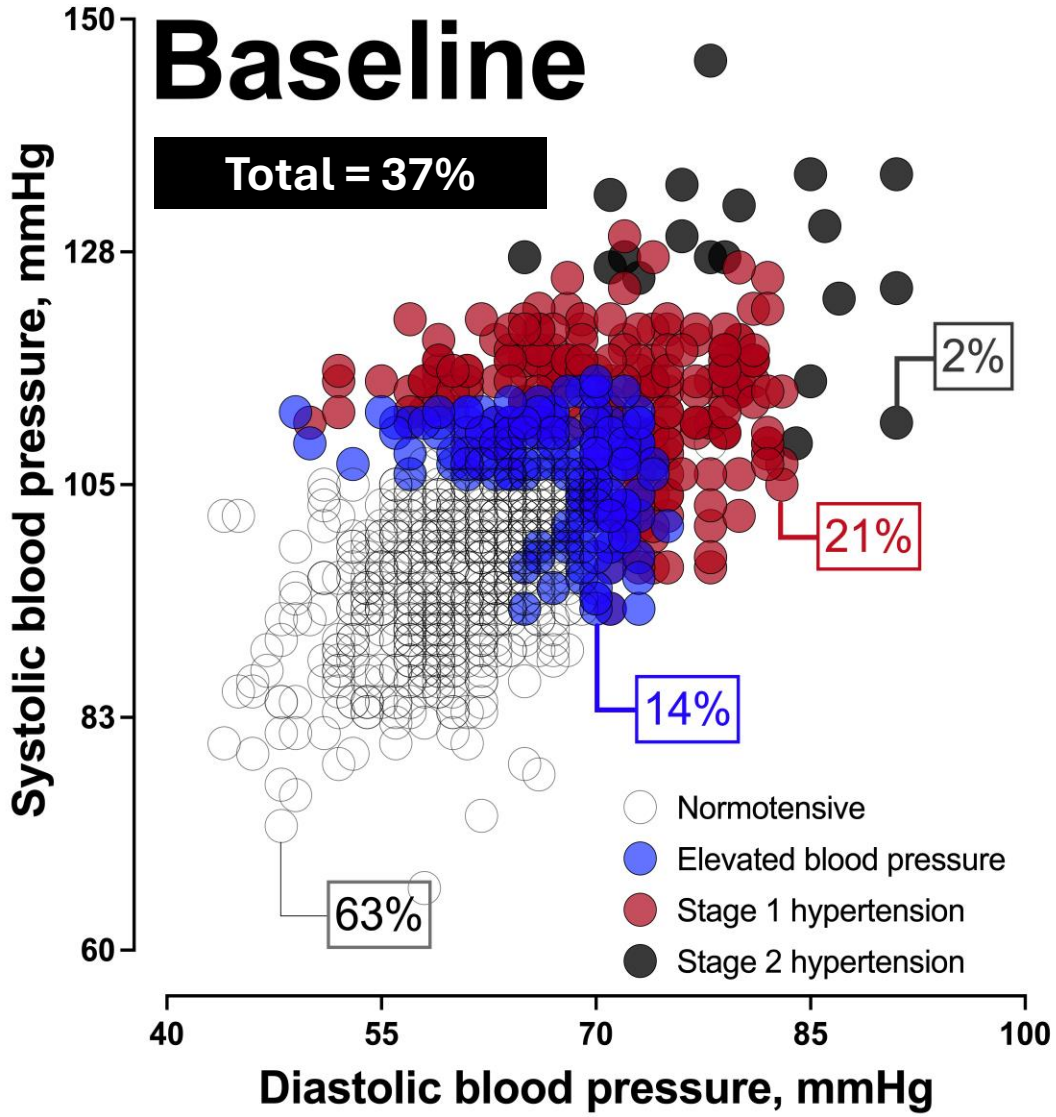
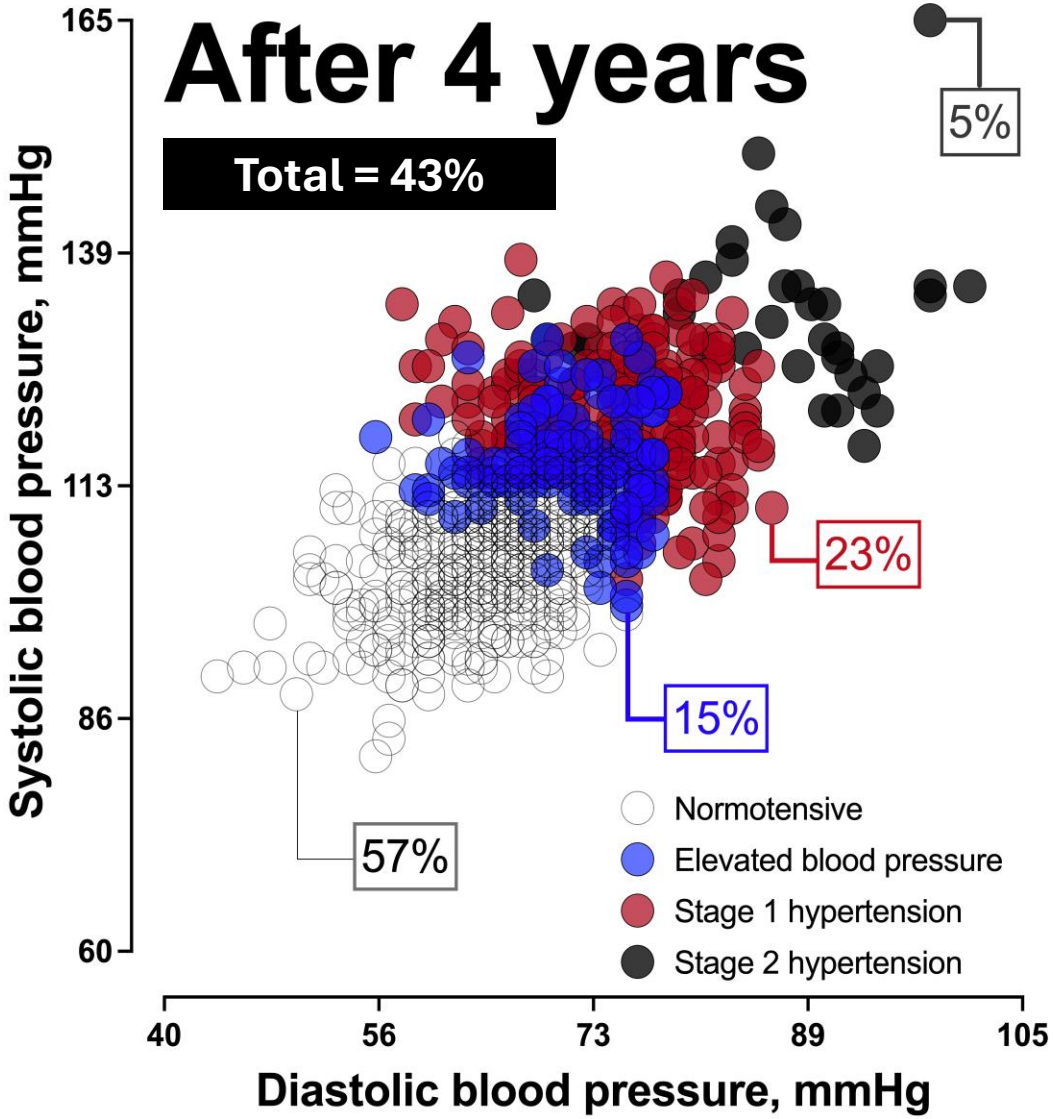
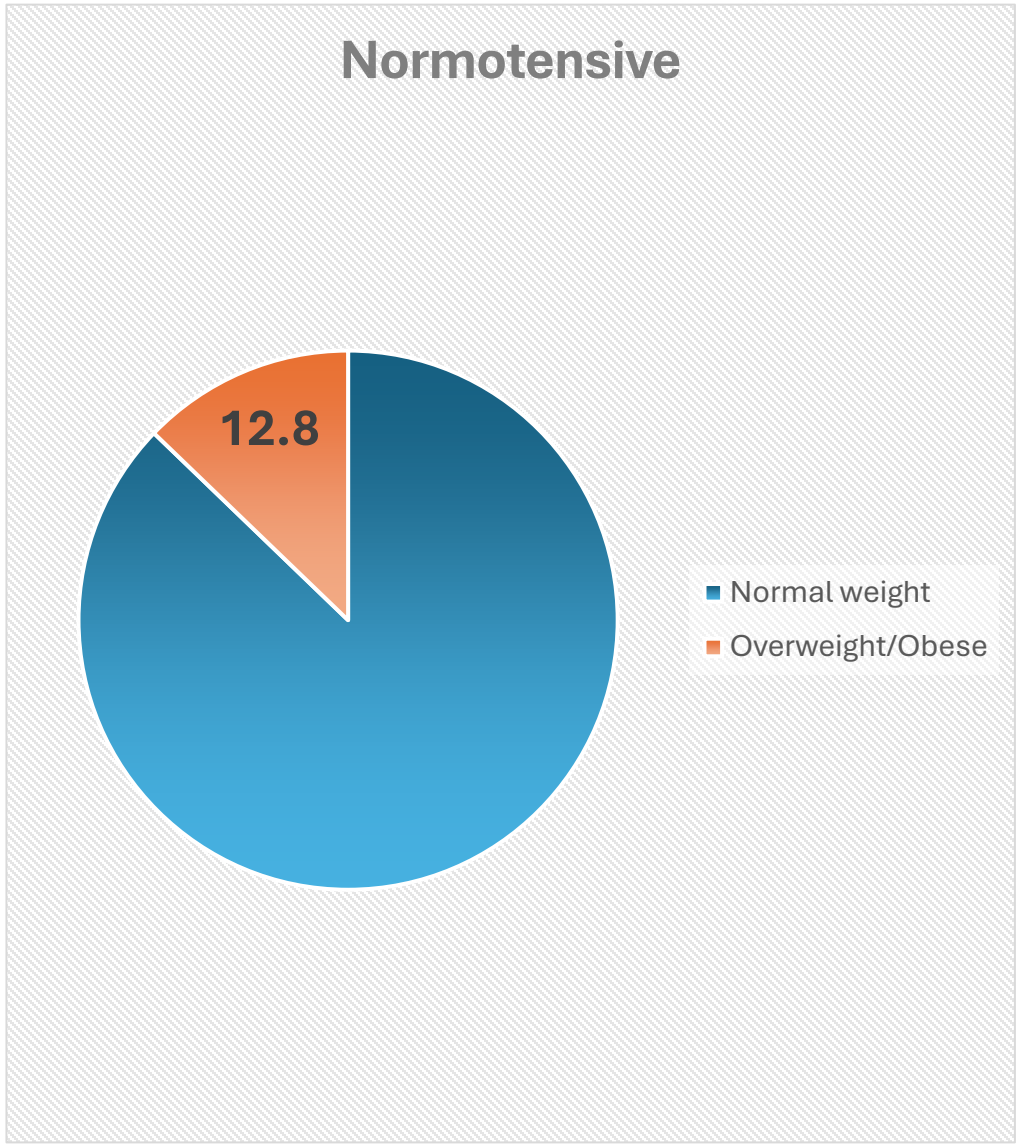


FIGURE 1 (a) Blood pressure distribution and prevalence of hypertension by automated blood pressure measurements in 5–9-year-old children (n=1062) from South Africa.

Kruger et al. J Hypertens 39:2190–2199


Baseline
Total = 37%
Systolic blood pressure, mmHg
150
128
105
83
60
40
55
70
85
100
Diastolic blood pressure, mmHg
2%
21%
14%
63%
Normotensive
Elevated blood pressure
Stage 1 hypertension
Stage 2 hypertension


After 4 years
Total = 43%
Systolic blood pressure, mmHg
165
139
113
86
60
40
56
73
89
105
Diastolic blood pressure, mmHg
5%
23%
15%
57%
Normotensive
Elevated blood pressure
Stage 1 hypertension
Stage 2 hypertension



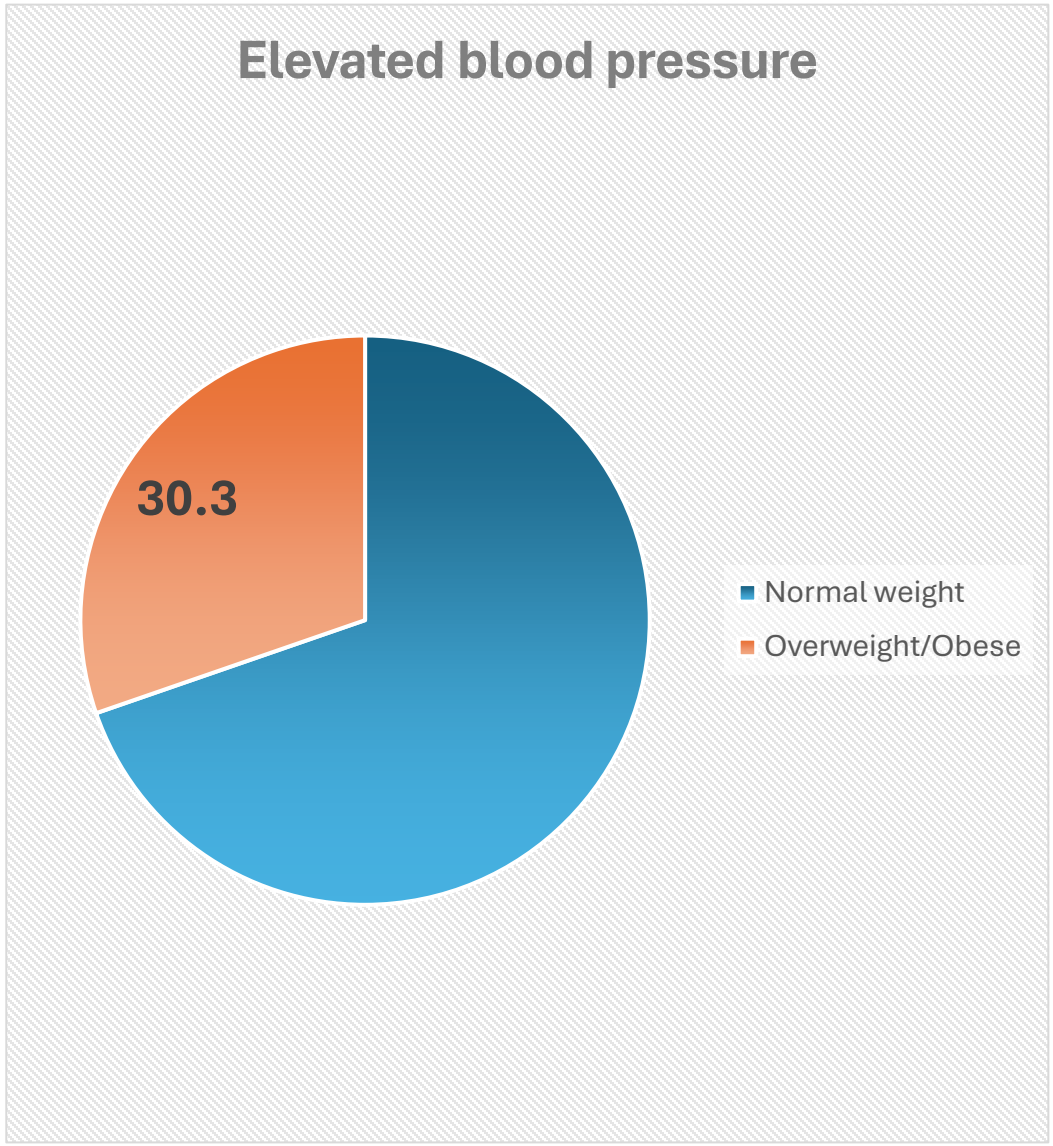


Figure 2. Overweight and obesity prevalence by blood pressure status groups.

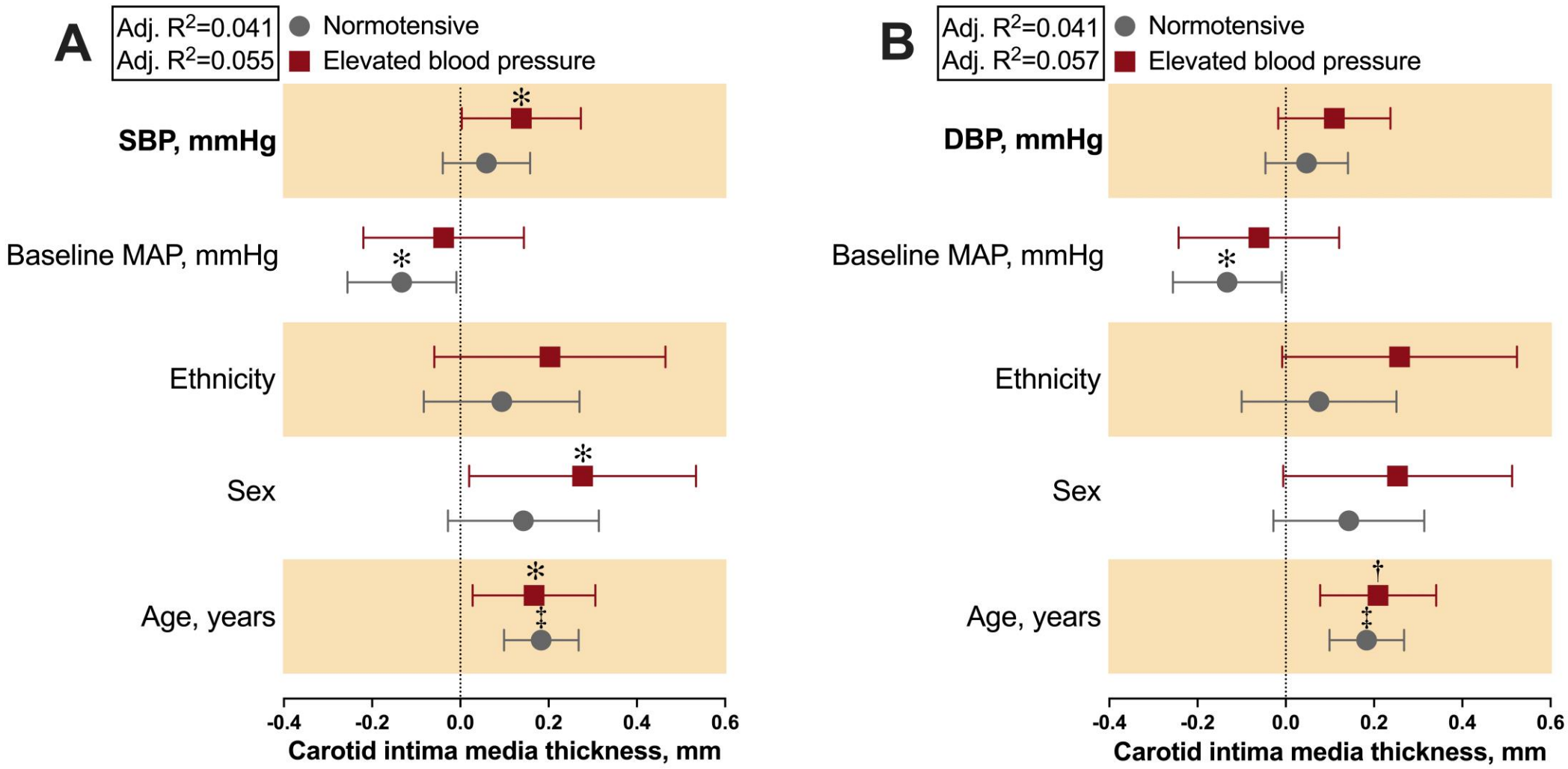


Figure 4. Multiple regression analysis of carotid intima-media thickness with follow-up blood pressure in children stratified by baseline blood pressure status.

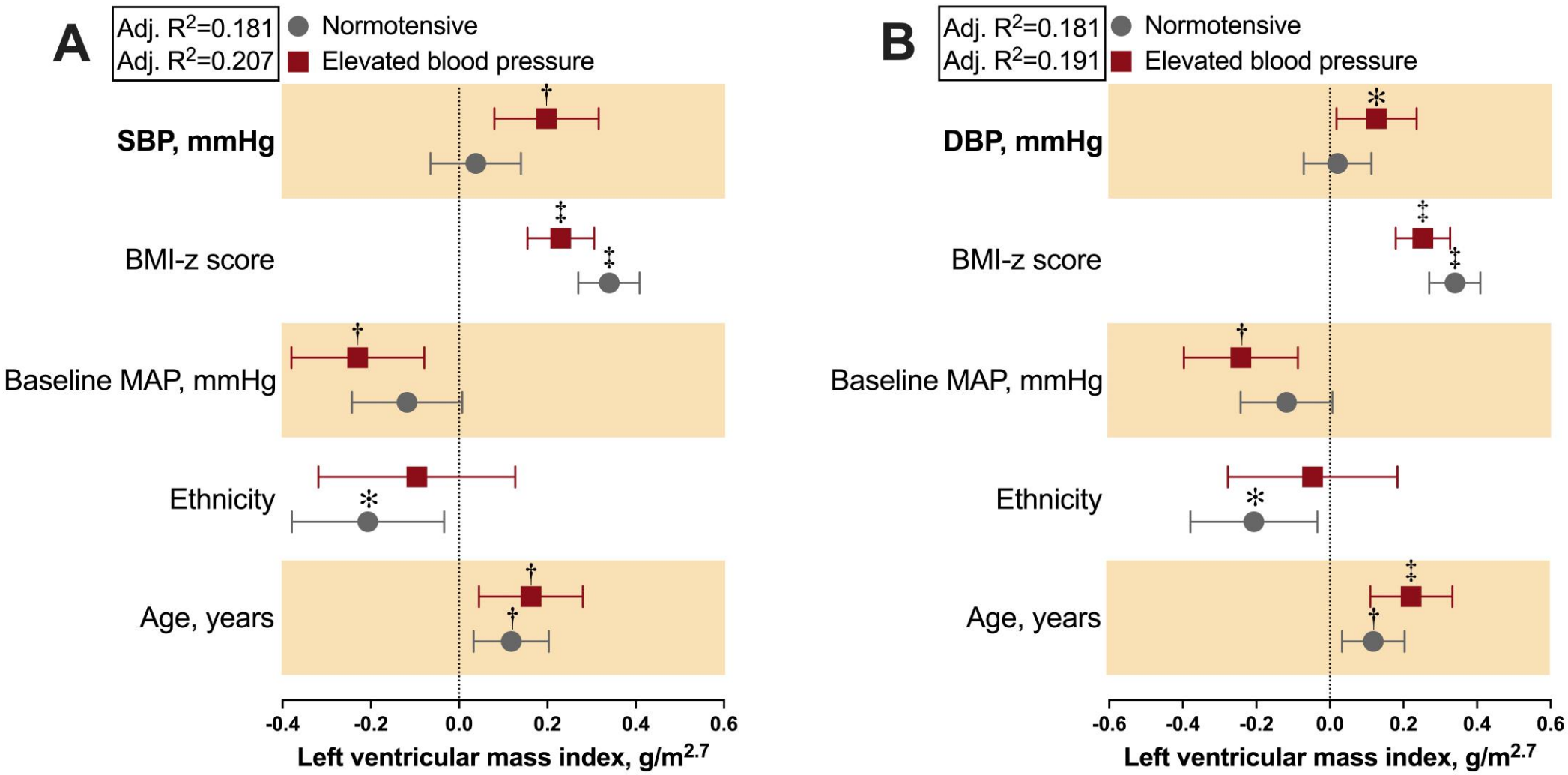


Figure 5. Multiple regression analysis of left ventricular mass index with follow-up blood pressure in children stratified by baseline blood pressure status.

Hypertension in African Children: Neglected or Not existent?

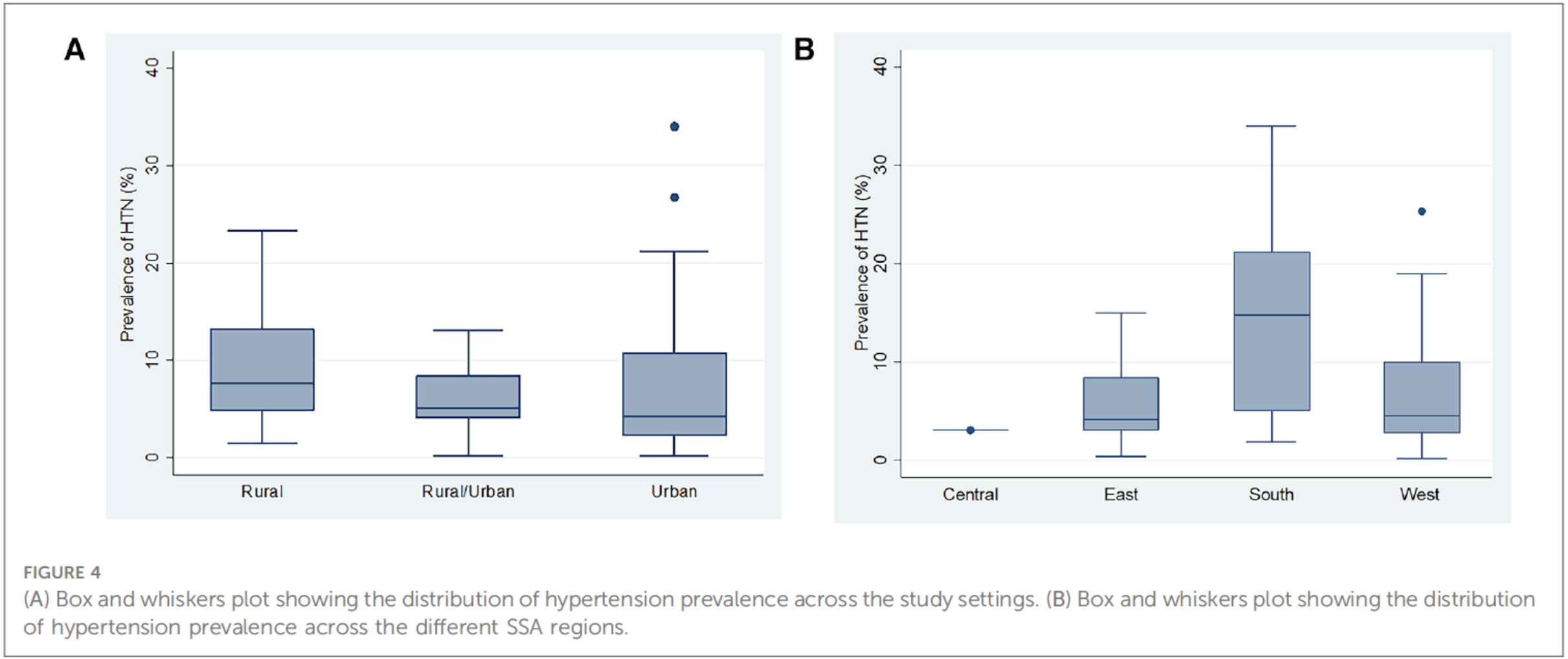


FIGURE 4
(A) Box and whiskers plot showing the distribution of hypertension prevalence across the study settings. (B) Box and whiskers plot showing the distribution of hypertension prevalence across the different SSA regions.

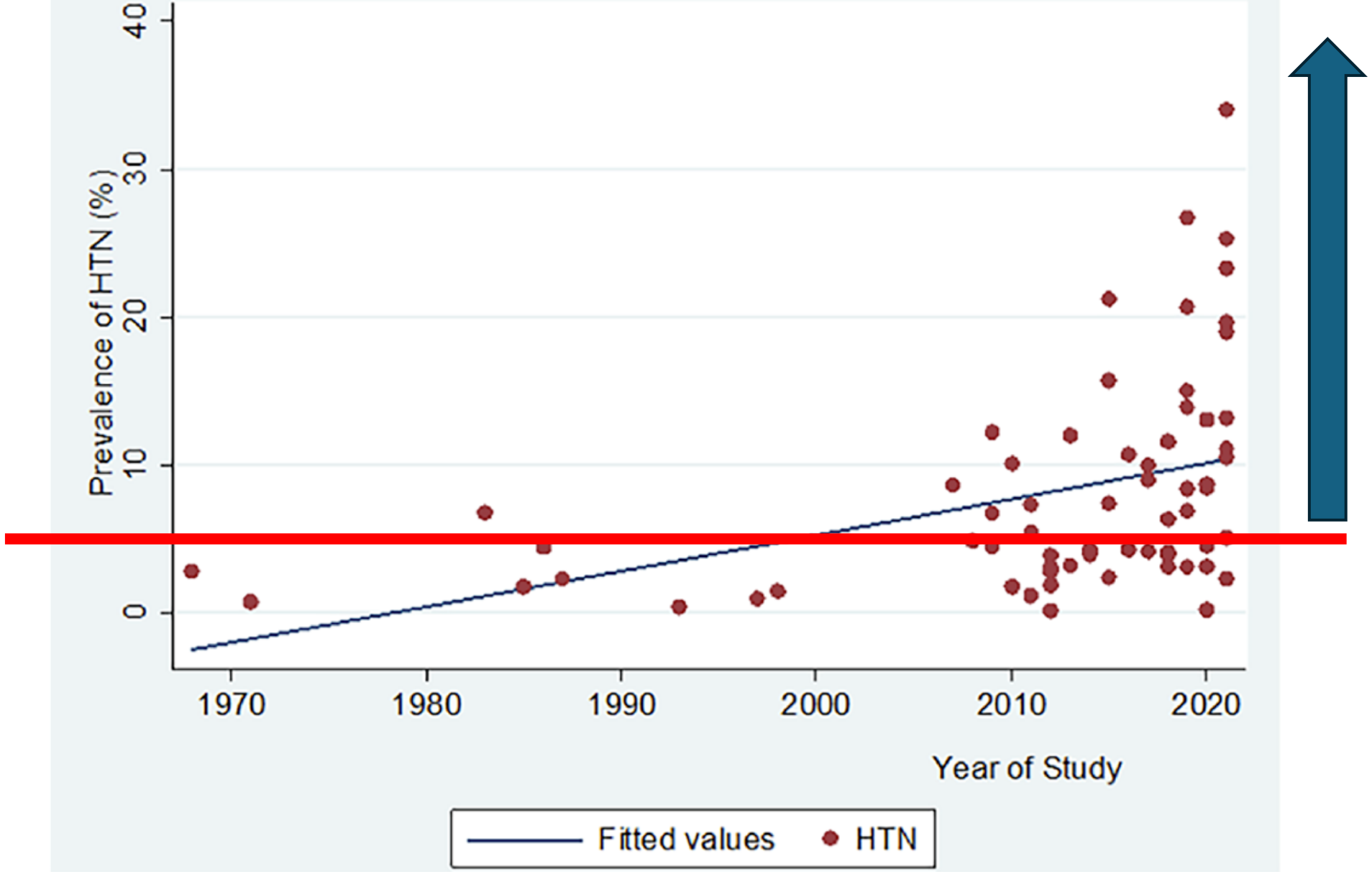
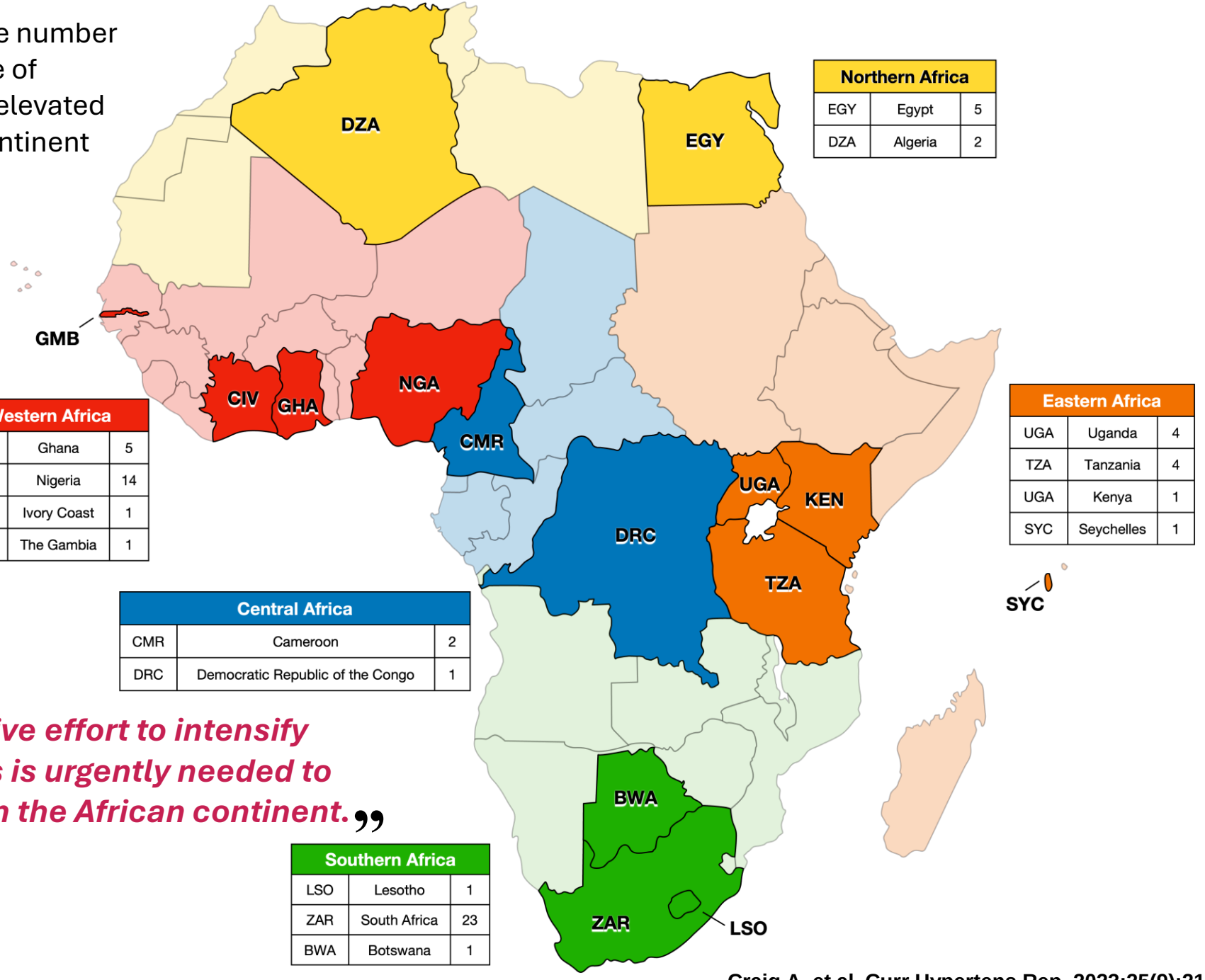


FIGURE 5
Scatter plot showing the relationship between hypertension prevalence and year of study publication. Nsanya MK, et al. 2023; Front. Cardiovasc. Med. 10:1251817

Figure 1. Schematic illustration of the number of studies highlighting the prevalence of hypertension, pre-hypertension and elevated blood pressure across the African continent within the last 5 years



Northern Africa		
EGY	Egypt	5
DZA	Algeria	2

Western Africa		
GHA	Ghana	5
NGA	Nigeria	14
CIV	Ivory Coast	1
GMB	The Gambia	1

Eastern Africa		
UGA	Uganda	4
TZA	Tanzania	4
UGA	Kenya	1
SYC	Seychelles	1

Central Africa		
CMR	Cameroon	2
DRC	Democratic Republic of the Congo	1

Southern Africa		
LSO	Lesotho	1
ZAR	South Africa	23
BWA	Botswana	1

“An Africa-centered collaborative effort to intensify pediatric hypertensive studies is urgently needed to address this knowledge gap on the African continent.”

Craig A, et al. Curr Hypertens Rep. 2023;25(9):211-230

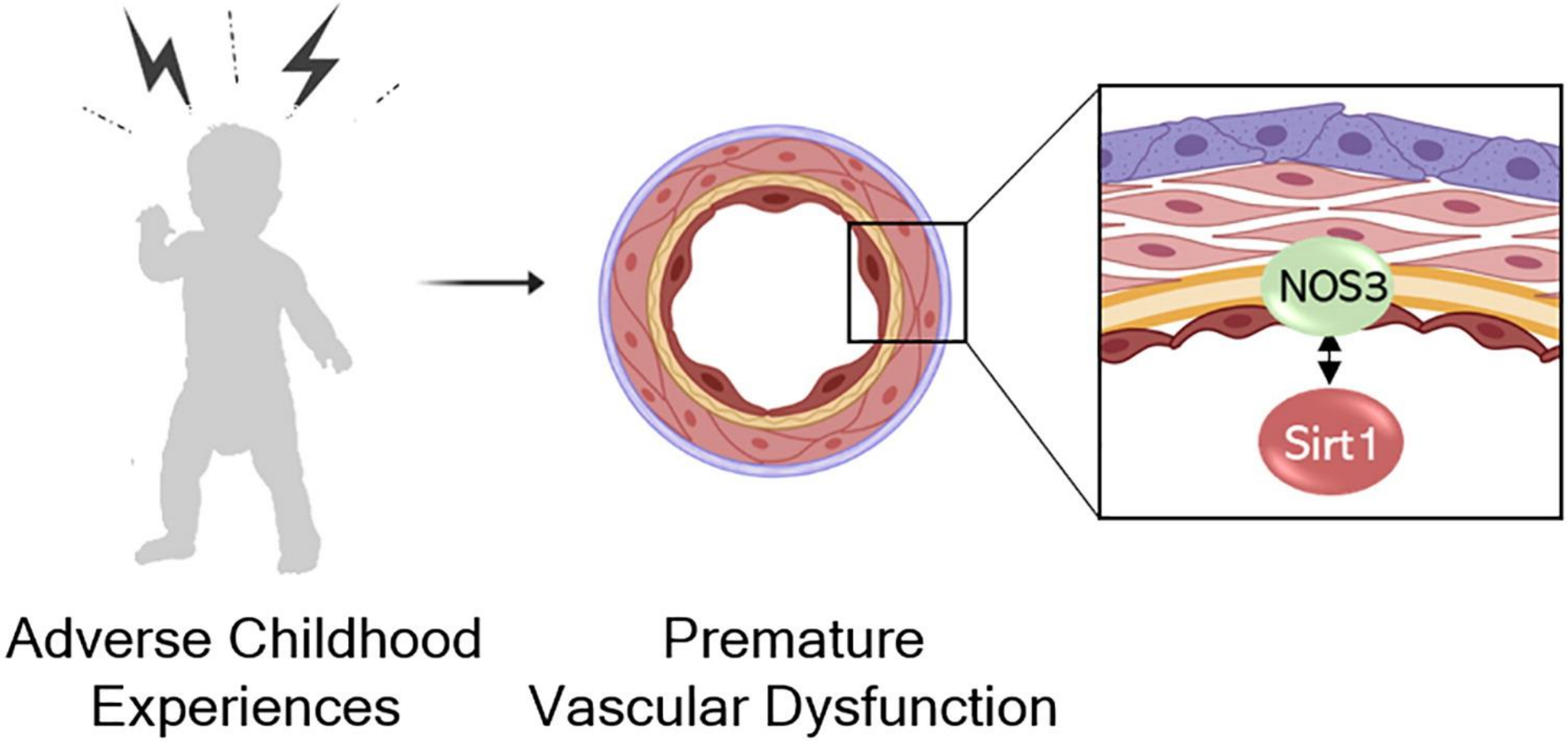


Figure 1. Adverse childhood events and cardiovascular diseases.
Endogenous NO, synthesized from endothelial NO synthase (NOS3), is a key component in preserving endothelial function and maintaining a healthy vasculature. Sirtuin 1 (Sirt1), an NAD+-dependent deacetylase, has an important role in preserving endothelial function by regulating many proteins, including NOS3.

Rodriguez-Miguelez & Pollock. Am J Physiol Heart Circ Physiol321: H577–H579, 2021

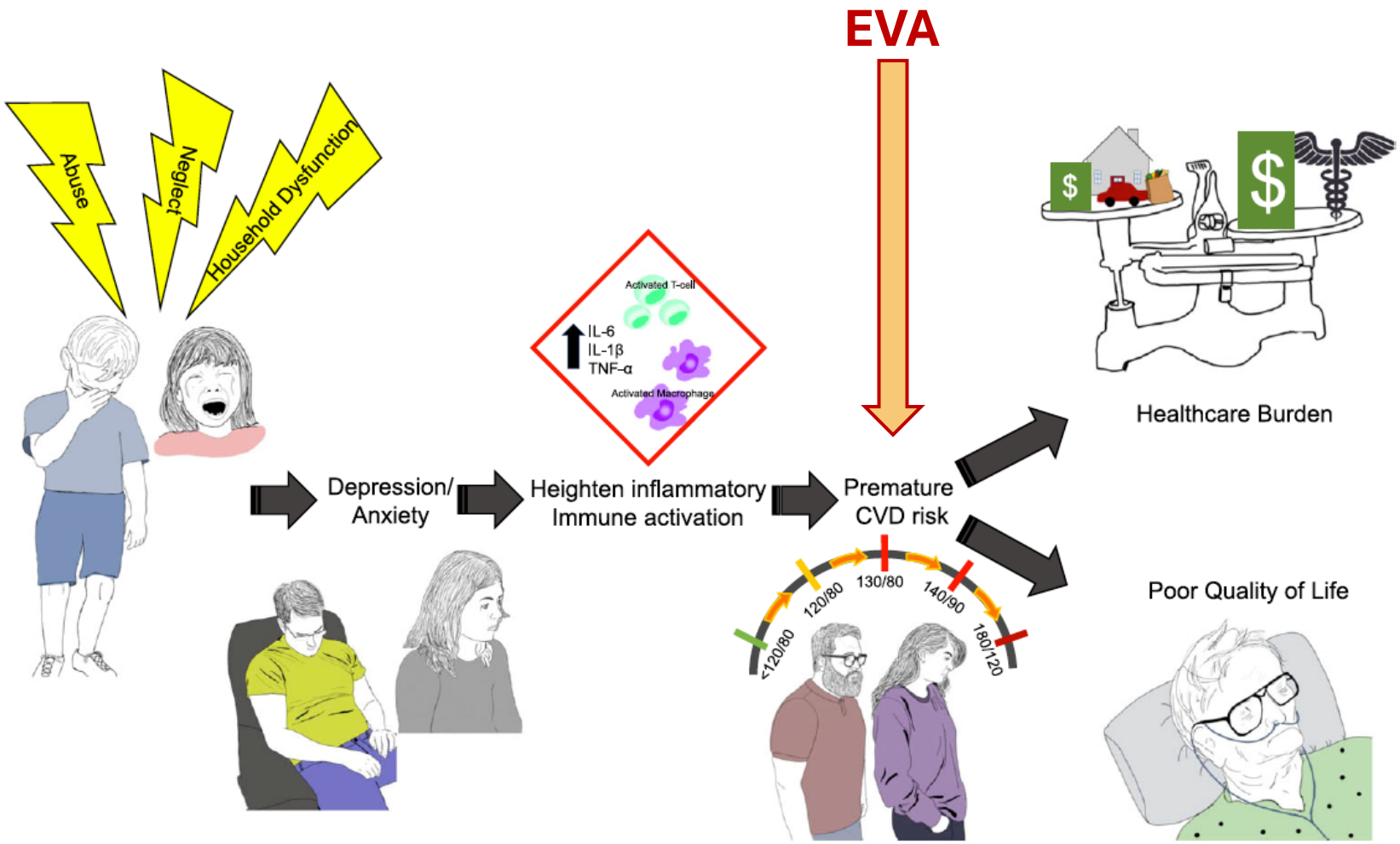


FIGURE 1 ACEs, such as neglect, abuse, and household dysfunction, in humans are associated with increased risk of hypertension and developing CVD. The majority of studies investigating the association of childhood adversity and CVD suggests that detrimental effects of ACEs (depression/anxiety) may induce well-known mechanisms that are involved in the development of hypertension such as inflammation and the associated immune mediators that lead to premature CVD risk and, ultimately, decreased quality of life and increased health burden in adulthood. Acknowledgements to Dr. Kasi McPherson for the elegant artwork presented in this figure

Obi et al. Br J Pharmacol. 2019;176:1932–1950

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1443-9506/21/$36.00
https://doi.org/10.1016/j.hlc.2021.06.516

REVIEW

Vascular Ageing in Youth: A Call to Action

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[i]Hypertension in Africa Research Team (HART); North-West University, Potchefstroom, South Africa
[j]MRC Research Unit for Hypertension and Cardiovascular Disease, North-West University, Potchefstroom, South Africa

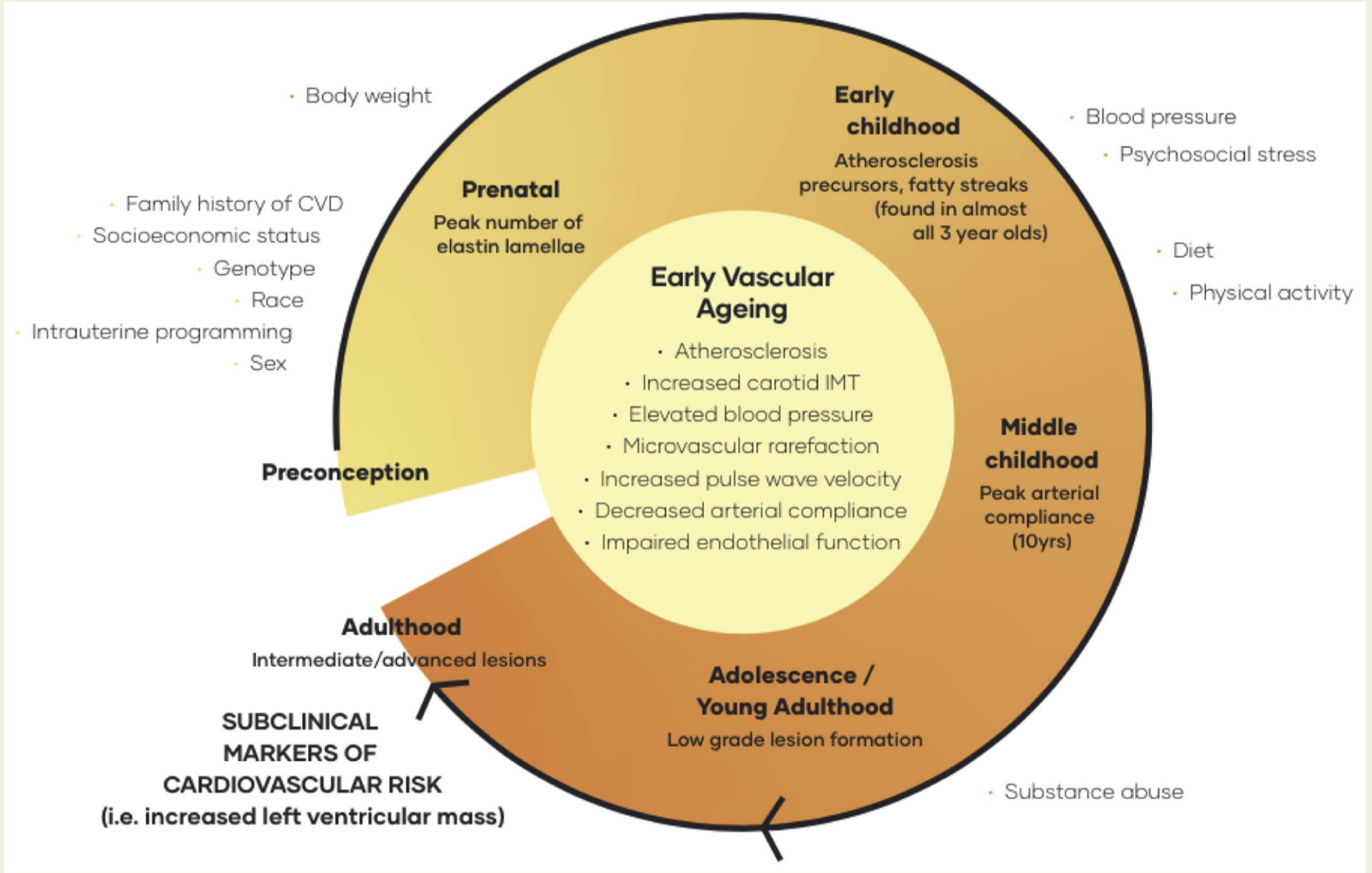
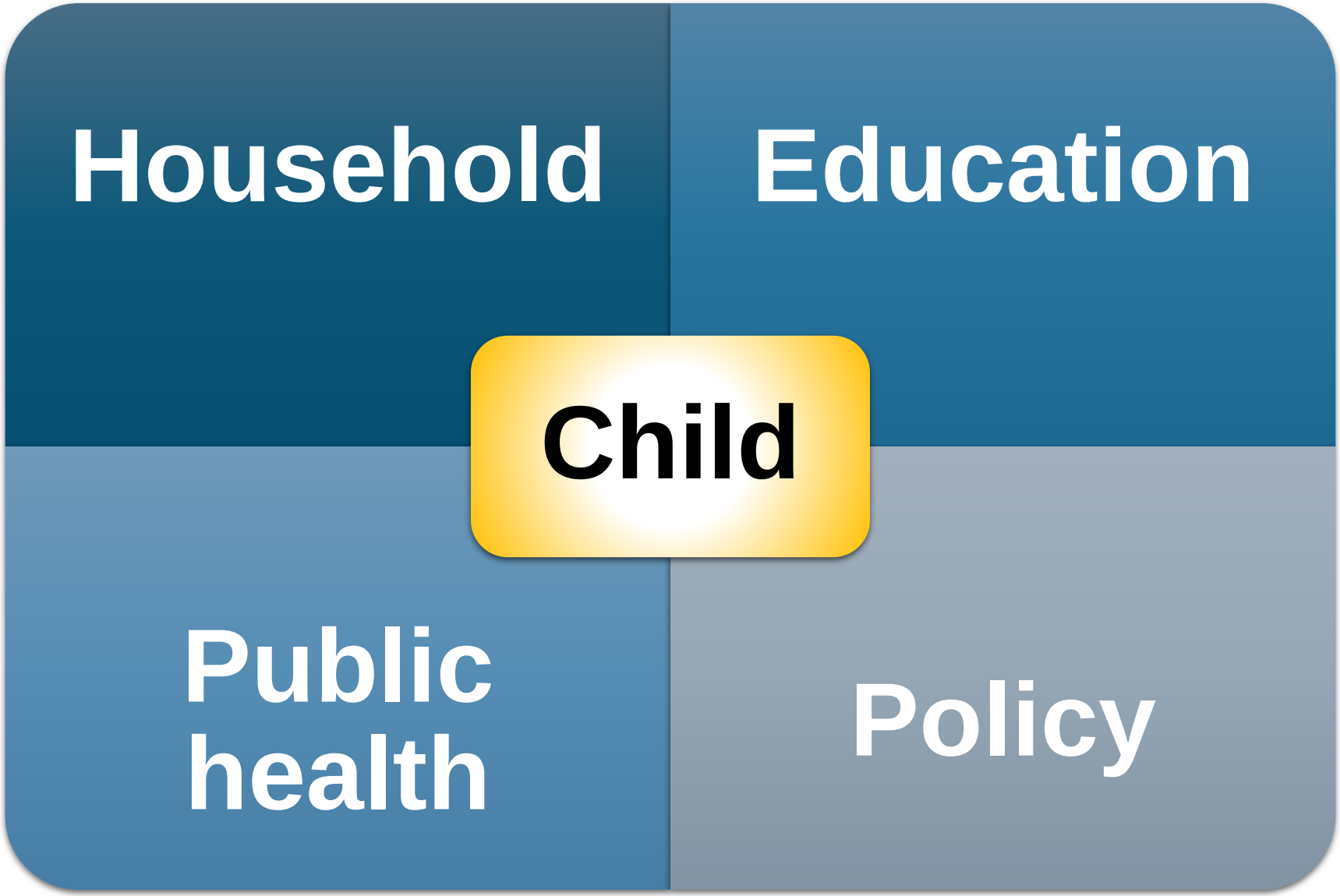


Figure 2 Schematic display of the determinants of early vascular ageing and consequences later in life.

Prevention and Intervention Strategies



Thank you.

ClinicalTrials.gov identifier (NCT number): NCT05982847

IRB approval by the HSRC: REC 4/23/03/22

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