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Novel Risk Factors for Hypertension in low- and middleincome countries: Building Evidence to Reverse the Burgeoning Epidemic

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A thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the Health Sciences

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Declarations

I am aware of the university's regulations governing plagiarism. This thesis is the work of Mustapha Abba in collaboration with my supervisors, Professor Olalekan A. Uthman, Chidozie Nduka and invited co-authors. This work supports my application for a Doctor of Philosophy Degree at the University of Warwick. The thesis has not been submitted elsewhere for a degree. The author has published three articles and submitted seven manuscripts for publication as a result of this thesis.

Mus Eapha Abba

List of Publications

Published manuscripts

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- Abba M, Nduka C, Anjorin S, Mohamed S, Agogo E, Uthman O.(2022) One Hundred years of hypertension research: A Topic Modelling Study. *JMIR Form Res.* 2022;6(5): e31292 doi: 10.2196/31292.

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- 4. Abba., M.S. Nduka, C.U., Anjorin, S., Mohamed, S.F., Agogo, E. and Uthman O.A., (2022) Geography of Hypertension Research in Africa: An analysis of PubMed Papers.
- 5. Abba., M.S. Nduka, C.U., Anjorin, S., Mohamed, S.F., Agogo, E. and Uthman, O.A., (2022) Citation Classics of The Top 100 Most Cited Hypertension Articles.
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Abstract

Aim

The primary aim of the dissertation was to broaden our understanding of the novel risk factors for hypertension in resource-limited settings.

Methods:

To achieve the dissertation aims, the following innovative analytic methods were used to triangulate the selected novel risk factors: phase 1: bibliometric analyses and topic modelling technique; phase 2: A meta-analysis and decomposition analysis to assess individual-level factors; *Phase 3:* a multilevel analysis propensity score matching to examine contextual compositional risk factors; and *Phase 4:* An ecological study to explore major country-level socioeconomic determinants.

Results:

Phase 1; The percent share of global hypertension research outputs per year increased from 1.7% in 1999 to 5.3% in 2018 in Africa. Country population and gross domestic product were important correlates of hypertension research outputs.

Phase 2: Human immunodeficiency virus and gender-based violence were found to be associated with the risk of having hypertension.

Phase 3: At the contextual level, there was significant variation in the odds of having hypertension across countries and neighbourhoods; and participants exposed to household air pollution (HAP) in Albania were 17% more likely to develop hypertension than those not exposed to HAP. The high blood pressure patterns examined revealed three different patterns of associations: pro-urban, pro-rural and no-difference. The study found significant differences between respondents living in urban and rural areas of South Africa.

Phase 4: For every increase in adult literacy rate, unemployment rate, and percentage of people who live in urban areas, the country's prevalence of hypertension reduces. However, increases in the multidimensional-poverty index and the country's population were found to increase the prevalence of hypertension.

Conclusion

This thesis provides insight into novel risk factors for hypertension, suggesting new preventive targets that can be exploited for public health interventions to reverse the burgeoning epidemic of hypertension in Low- and Middle-income countries.

List of acronyms and abbreviations

AFR	_	African Region
AMR	—	Americas
AOR	_	Adjusted Odds Ratio
B P	—	Blood Pressure
BMI	_	Body Mass Index
C.I.s	_	Confidence Intervals
CIs	_	Credible intervals
СО	_	Carbon monoxide
CVDs	_	Cardiovascular diseases
DALYs	_	Disability-adjusted life-years
DBP	_	Diastolic Blood Pressure
DHS	_	Demographic and Health Surveys
EUR	_	European Region
GBV	_	Gender-based violence
GDP	_	Gross Domestic Product
GNI	_	Gross National Income
НАР	_	Household air pollution
НВР	_	High blood pressure
HDI	_	Human Development Index
HICs	_	High-Income Countries
HIV/AIDS	_	Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome
HTN	_	Hypertension
ICC	_	Intraclass correlation
IMF	_	International Monetary Fund
IPV	_	Interpersonal violence
IQR	_	Inter-quartile ranges
JNC	_	Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure

Kg/m ²	_	Kilogram per metre square
LDA	_	Latent Dirichlet allocation
LMICs	_	Low-and Middle-income countries
MESH	_	Medical Subject Heading mmHg – millimetres of mercury
MOR-	_	Median odds ratio
NCDs	_	Noncommunicable Diseases
NO	_	Nitric oxide
OR	_	Odds Ratio
PLHIVs	_	People living with the human immunodeficiency virus
РМ	_	Particulate matter
РРР	_	Purchasing Power Parity
SBP	_	Systolic Blood Pressure
SSA		sub-Saharan Africa
U.K.	_	United Kingdom
UNDP	_	United Nations Development Programme
UNESCO	_	United Nations Education, Scientific and Cultural Organization
UNGA	_	United Nations General Assembly
USA	_	United States of America
WHO	_	World Health Organisation
WoS –	_	Web of science
YLD	_	Years of healthy life lost due to disability

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1 CHAPTER 1: INTRODUCTION

1.1 OVERVIEW

The burden of non-communicable diseases (NCDs) is growing significantly in low- and middle-income countries (LMICs), resulting in morbidity, mortality, economic loss, diminished quality of life, and poor socioeconomic development (Juma *et al.*, 2019). Deaths from Cardiovascular diseases (CVDs) have been increasing from 12.1 million in 1990, to 18.6 million in 2019 and many disability-adjusted life years (DALYs) have been increasing significantly (Roth *et al.*, 2020). CVDs share modifiable risk factors, including smoking, physical inactivity, and unhealthy diets, which account for most of the global burden of NCDs that drive the epidemiological transition in LMICs (Cappuccio & Miller, 2016; Sarki *et al.*, 2015). Furthermore, NCDs are characterised by their long duration and slow progression (W.H.O, 2018). Even in sub-Saharan Africa (SSA), where infectious diseases remain the most frequent cause of morbidity and mortality, the region still suffers a disproportionately higher percentage of CVD deaths than other geographical regions (Mensah *et al.*, 2015). CVDs extend beyond health to an economic and developmental issue that leads to increased overall poverty and loss of productivity in most resource-limited settings (Gheorghe *et al.*, 2018).

Hypertension is considered the most significant risk factor for cardiovascular disease and the most important preventable cause of mortality (Kearney *et al.*, 2005; Kumar, 2013; Mozaffarian, 2017). Various lifestyle factors were identified, such as excessive alcohol consumption, smoking, physical inactivity, hyperlipidaemia, psychosocial stress, family history of hypertension, and ageing (Forman *et al.*, 2009; Ruan *et al.*, 2018; Zhou *et al.*, 2017). However, other emerging risk factors can also be correlated with hypertension, such as socioeconomic disadvantage (unemployment, low income, and illiteracy), air pollution, noise pollution, insomnia, positive Human Immunodeficiency Virus (HIV) status, intimate partner violence (IPV), etc. (Deaton et al., 2011; Gheorghe et al., 2018; Nduka et al., 2016; Nduka et al., 2015; Sarki et al., 2015). These novel risk factors warrant further exploration, especially in low- and middle-income settings. Furthermore, numerous studies on hypertension cite inefficient health systems (often the results of government underfunding of health promotion and disease surveillance programmes) as a significant contributing factor to the growing hypertension prevalence in LMICs (Addo et al., 2007; Cappuccio & Miller, 2016; Dzudie et al., 2018; Kayima et al., 2013; Thorogood et al., 2019; Tijssen, 2007). It has been observed that hypertension research, interventions, and programmes are usually centred around individual-level socio-demographic issues, even though theories suggest that the distribution and determinants of population health are epistemologically multilevel (Diez-Roux, 2000). Therefore, understanding the research activities and determinants of hypertension beyond individual socio-demographic factors is imperative to facilitate appropriate interventions to minimise the prevalence of hypertension.

This research study has been organised into the following four phases: 1) Evidence harvest and mapping, 2) Individual compositional novel risk factors, 3) Neighbourhood contextual novel risk factors, and 4) societal contextual novel risk factors.

Phase 1: The study analysed the contribution of African countries to hypertensionrelated research over the last two decades by evaluating the characteristics of relevant publications indexed in PubMed. Secondly, the attributes of the top-cited hypertensionrelated publications in the web of science (WoS) were examined. Finally, the study used an algorithm to uncover hidden topics and subtopics from peer reviews of highblood pressure publications. **Phase 2:** HIV and gender-based violence (GBV) were identified and assessed as individual compositional novel risk factors. Moreover, the study examined the contribution of HIV seropositivity to hypertension risk in selected LMICs (Ghana, India, Lesotho, Namibia, and South Africa). Similarly, the association between exposures to GBV and the risk of having hypertension among women in Kyrgyzstan was evaluated.

Phase 3: Neighbourhood contextual novel risk factors were examined at the community level. Firstly, the study analysed the influence of individual-, communityand country-level factors and their association with hypertension in LMICs. Secondly, the study evaluated whether the prevalence of hypertension can be explained by the neighbourhood variations and places of residence. Finally, the impacts of HAP on the risk of having hypertension in LMICs were examined.

Phase 4: The societal contextual novel risk factors were studied. The strength of association between the prevalence of hypertension and eight major socioeconomic factors was determined. These factors include current health expenditure (% of GDP), domestic general government health expenditure per capita, GDP per capita (current US\$), adult literacy rate (% of people ages 15 and above), unemployment, total (% of the total labour force), urban population (% of the total population), multidimensional poverty index, and total population.

Table 1: Overview of the study phases

Phase	<u>Title</u>	Studies	Data Source	<u>Study</u> Design	Outcome [Factors]	<u>Statistical</u> Method	Level of Analysis
1	Evidence harvests and mapping	Geography of Hypertension Research in Africa: An Analysis of PubMed Papers	PubMed, Embase	Bibliometric analysis	Number of publications per country / reported novel factors	Poisson regression models	Country-level study-level analysis
		Citation Classics of The Top 100 Most Cited Hypertension Articles	Web of science			Descriptive statistics	
		One Hundred years of research on Hypertension: Machine Learning Classifications of Topics using Latent Dirichlet allocation (LDA) Model	PubMed, Embase			Latent Dirichlet allocation (LDA) Model	
2	Individual compositional novel risk factors	Gender-Based Violence and The Risk of Having hypertension in Low- And Middle-Income Countries Association between HIV and hypertension in low- and middle- income countries: a tale of three settings (Manuscript submitted for publication)	Demographic and Health Survey	Cross- sectional	Hypertension [HIV status, gender-based violence]	Odds ratios were computed Decomposition analysis using logistic regression	Individual- level analysis
3	Neighbourhood contextual novel risk factors	Influence of contextual socioeconomic position on hypertension risk in low-and middle-income countries: disentangling context from the composition. BMC public health, 21(1), pp.1-13. High blood pressure patterns in rural and urban areas in low- and middle-income countries: a meta- analysis of demographic and health surveys Urbanicity and high blood pressure in a resource-limited setting: a propensity score	Demographic and Health Survey	Cross- sectional	Hypertension [place of residence, indoor air pollution, neighbour socioeconomic status]	Multilevel analysis Odds ratios Meta-analysis Propensity Score Matching	Individual- level analysis and community- level
4	Societal contextual novel risk factors	matching Household air pollution and high blood pressure: a secondary analysis of the 2016 Albania Demographic Health and Survey dataset Socioeconomic Determinants of Hypertension: Ecological Analysis of 53 Countries Low- and Middle-Income Countries (Manuscript Submitted for Publication)	WHO, global health observatory data	Ecological	Prevalence of Hypertension [gross domestic product, illiteracy rate, intensity of deprivation, expenditure on health and income inequality]	Correlation and multivariable linear regression	Country-level

1.2 BACKGROUND

Hypertension (HTN), also known as high blood pressure (HBP), is a condition in which the blood vessels like arteries persistently undergo elevated blood pressure that causes the heart to work too hard, leading to complicated heart conditions (Ridwanah et al., 2021; W.H.O, 2013). Therefore, HBP and its repercussions have been identified as a worldwide public health concern (Chow & Gupta, 2019; Roth et al., 2020). It is considered the most crucial risk factor for CVDs like stroke and coronary heart disease. Moreover, many studies have reported that it is the most ostensible and significant preventable cause of mortality (Kearney et al., 2005; Kumar, 2013; Mills et al., 2020; Mozaffarian, 2017). Hypertension remains a public health problem in low- and middle-income countries (LMICs) (Campbell et al., 2015; Mozaffarian, 2017; Tuoyire & Ayetey, 2019). The prevalence of hypertension has increased significantly during the past decade (Geldsetzer et al., 2019). For instance, between 1990 and 2020, hypertension was estimated to have risen by 120% in women and 137% in men in LMICs, causing 10.4 million deaths per year (Ridwanah et al., 2021). The highest prevalence was reported in SSA, Central Asia, and Eastern Europe (W.H.O, 2013), and these regions consist of countries included in the LMICs (Zhou et al., 2017). Similarly, the Non-communicable Disease Risk Factor Collaboration study (NCD-RisC), comprising more than 19 million participants worldwide over four decades, reveals that the number of adults with hypertension had increased from 594 million in 1975 to 1.13 billion in 2015, resulting in 9.4 million deaths. These deaths represent 12.8% of total global deaths (NCD-RisC, 2016). Moreover, hypertension has caused 57 million people to suffer from Disability Adjusted Lost Years (DALYs), which is 3.7% of all DALYs (Craig et al., 2018; W.H.O, 2009; Zhou et al., 2017). In South Africa, hypertension complications such as stroke and ischemic heart diseases were identified as the second and fourth significant causes of death (Pillay-van Wyk et al., 2016).

An extensive study conducted in 2013 by the World Health Organisation (WHO) reported that the burden of hypertension is the highest in the African region, with 46% of adults aged 25 years and above being hypertensive. As depicted in Figure 1, these numbers are followed by Eastern Mediterranean (EMR) and European (EUR) regions, with a prevalence slightly above 40%. The lowest prevalence of 35% was reported in the Americas region. According to the WHO, the hypertension prevalence in most regions is projected to increase by 30% by 2025 (W.H.O, 2013). The increasing percentage is expected to be the same for both male and female populations (Appelman et al., 2015).



Figure 1: Prevalence of hypertension in WHO regions (Source WHO, 2013).

According to the United Nations Education, Scientific and Cultural Organization (UNESCO) Institute for Statistics, all SSA countries invest less than 1% of their GDP in research and development (R&D) (UNESCO, 2018). Hence, it is no surprise why the best available scientific evidence does not inform healthcare decisions in many SSA countries. That is why the region continues to withstand the worst of the burden of major public health problems, notably hypertension (W.H.O, 2013). The SSA countries produce about 2% of the global research output and remain the least represented region among the world's most significant contributors to high-quality research (Confraria & Wang, 2020), although there has been a steady increase in the volume of published research originating from LMICs (Devos & Menard,

2019; Uthman *et al.*, 2015). However, there are potential disparities in the quantity and quality of hypertension research outputs across country income groups (Oh & Galis, 2014).

Evidence shows that an individual's health can be determined by the environment in which they live, work, and age (W.H.O, 2013) and many studies reported that HBP is a preventable disease associated directly with lifestyle habits (Cuschieri *et al.*, 2017). SSA is considered the world's fastest urbanising region, with 40% of Africans living in urban areas (Mathenge *et al.*, 2010; Saghir & Santoro, 2018). This transformation comes with epidemiological transition, diet modification, socioeconomic status variations, urbanisation, population ageing, and behavioural risk factors such as cigarette smoking, alcohol consumption and physical inactivity (Berry *et al.*, 2017; Sarki *et al.*, 2015; W.H.O, 2013).

The disparity in socio-demographic characteristics between rural and urban people has also been demonstrated to influence the health outcomes of individuals (Al Kibria *et al.*, 2019; Hasan *et al.*, 2021). Several previous studies have established that the prevalence of hypertension varies according to the place of residence (Chowdhury *et al.*, 2016; Harshfield *et al.*, 2015; Rahman *et al.*, 2017; Tareque *et al.*, 2015). Bernabe-Ortiz *et al.* studied Peru migrants and found that participants from rural areas were more than three times more likely to develop hypertension than participants from urban areas (RR:3.58, 95% CI:1.42 to 9.06) after a five-year follow-up period (Bernabe-Ortiz *et al.*, 2017). Hypertension is untreated primarily in rural areas due to lack of awareness, limited access to healthcare facilities, and high cost of treatment (Al Kibria *et al.*, 2019). However, some research studies have revealed higher hypertension in urban areas. For example, Rahman *et al.* (2017) suggested that urban dwellers consume more calories and adopt inactive lifestyle patterns contributing to obesity, a risk factor for hypertension. Hence, it is essential to note that socio-demographic characteristics and place of

residence play a significant role in the prevalence of hypertension in both LMICs and High-Income Countries (HICs). Therefore, it is imperative to stratify and comprehend factors contributing to the differences in the overall prevalence of hypertension between rural and urban regions to improve existing strategies for preventing hypertension.

Numerous studies have linked environmental factors with the development of hypertension in LMICs (Apte & Salvi, 2016; Arku *et al.*, 2018; Giorgini *et al.*, 2016). The studies revealed that the environment could influence an individual's health outcome; for example, a good and secure environment will improve one's quality of life (Apte & Salvi, 2016). However, due to enormous growth in globalisation and industrialisation, the work environment (or home) has become a source of air pollutants that significantly affect the health and wellbeing of individuals, particularly in LMICs (Mecaj & Llano, 2016). For instance, the automotive industry and the establishment of various other factories have significantly contributed to air pollution, especially in cities where most of the population resides. Consequently, this development has influenced the emergence of different diseases that pose high risks to life (Mecaj & Llano, 2016). Therefore, protecting the environment and maintaining clean air quality is the responsibility of every individual.

Clean air is regarded as one of the essential human health and wellbeing requirements (Juginović *et al.*, 2021). However, in 2016, more than 90% of the world population was exposed to poor air quality levels that exceeded the World Health Organization (WHO) Air Quality Guideline limits (W.H.O, 2018a). According to a study by Rafaj et al., air pollution is the fourth most significant overall risk factor for human health globally, followed by high blood pressure, dietary risks, and smoking (Rafaj *et al.*, 2018). It has been associated with three of the leading causes of death worldwide, with significant shares in air-pollution-related

mortality: stroke (26%), ischemic heart disease (20.2%), and primary cancer of the trachea, bronchus, and lungs (19%) (Lackland & Weber, 2015; W.H.O, 2020). Air pollution is linked to 7 million deaths globally, and more than 100 million patients annually suffer from disability-adjusted life years (DALYs) (W.H.O, 2020).

HAP is mainly generated by inefficient household combustion for cooking, heating, and burning solid biomass (*e.g.*, wood, cow dung, charcoal, and crop residues), common in most LMICs (Gordon *et al.*, 2014). A research study by Giorgini *et al.* reported that an elevated level of delicate particulate matter (PM 2.5) is an emerging hypertension risk factor (Giorgini *et al.*, 2016; Ibrahim, 2018).

House air pollutants such as CO and PM are classified to be hazardous, resulting in morbidity and mortality (Woolley *et al.*, 2021). Similarly, the combustion of solid fuels increases the risk of developing cardiovascular diseases, including hypertension and other heart diseases, especially in LMICs (Mohapatra *et al.*, 2018; Qiu *et al.*, 2019). In 2010, HAP from solid fuels accounted for 3.5 million deaths and 4.3% of global disability-adjusted life years (Giorgini *et al.*, 2016). An estimated 3 billion people globally are exposed to HAP from cooking with solid fuels. Most deaths result from using harmful fuels (Arku *et al.*, 2018; Lee *et al.*, 2020). The inhalation of several air pollutants causes acute autonomic imbalance and promotes the release of pro-oxidative, inflammatory, and haemodynamically-active mediators into the systemic circulation (Giorgini *et al.*, 2016). Consequently, numerous adverse responses, including elevated blood pressure, can instigate other cardiovascular-related disorders such as myocardial infarction, stroke, heart failure exacerbation, arrhythmia, and cardiovascularrelated deaths (Deng *et al.*, 2020; Lee *et al.*, 2020; Woolley *et al.*, 2021). Higher PM and blood pressure levels are exclusively linked to premature morbidity and mortality. The biological interconnection between these two risk factors and air pollution causes a significant threat to global public health (Giorgini *et al.*, 2016).

Hypertension contributes to premature mortality in LMICs. People in most countries are exposed to multiple disease burdens with a high prevalence of infectious diseases such as HIV/AIDS (Kandala *et al.*, 2013). Hypertension and HIV are major global health priorities (Haldane et al., 2018), and hypertension is increasingly common among people living with the human immunodeficiency virus (PLHIVs) in low-resource settings (Hing *et al.*, 2019). Moreover, some studies suggested that HIV-positive adults could have a higher prevalence of hypertension than HIV-negative adults (Gazzaruso *et al.*, 2003; Nüesch *et al.*, 2013; Peck *et al.*, 2014; Ryscavage *et al.*, 2017; Seaberg *et al.*, 2005; Xu *et al.*, 2017). The chronic inflammatory effects of HIV and the endothelial damaging effects of antiretroviral drugs have been identified as plausible mechanisms of this association (Nduka *et al.*, 2016). However, some research studies suggested that HIV-positive persons may be more likely to be heavy drinkers (Galvan *et al.*, 2002) and consume more dietary fat (Joy *et al.*, 2007) than HIV-negative individuals, increasing their lifestyle related risks for hypertension more than HIV infection itself.

GBV, especially Intimate Partner Violence (IPV) against women, is a significant public health problem influencing the quality of life of women globally (Zegenhagen *et al.*, 2019). It is described as the most prevalent human rights violation globally (Cruz & Klinger, 2016). GBV is a dehumanising, pervasive and oppressive form of violence. The United Nations Universal Declaration of Human rights stipulates that "*All human beings are born free and equal in dignity and rights*" and "*everyone has the right to life, liberty and security of person*" (UNGA, 1948). Despite the international commitment to achieve gender equality, one in three women experiences physical or sexual violence during their lifetime, mainly by an intimate partner, especially in LMICs (UNGA, 2017). A recent WHO study has reported that women who experience violence are more likely to face physical, sexual, reproductive and mental health consequences (World Health Organisation, 2021). The global prevalence of IPV is estimated at 30% (Zegenhagen *et al.*, 2019). Moreover, the prevalence varies between and within regions and countries and even between neighbourhoods (Heise & Kotsadam, 2015).

IPV against women remains the most significant component of gender-based violence (Ahinkorah, 2021). Southern Asia and SSA regions have the highest prevalence rates of IPV against women aged 15-49, ranging from 33% to 51% (W.H.O, 2021). Similarly, it is widespread in the Kyrgyzstan Republic and other South Asian countries. This could be due to the increase in incidences of bride kidnapping (ala *kachu*), a traditional practice conducted by people in Kyrgyzstan (Chowdhury, 2020; Cooper-Cunningham, 2016). IPV is a serious health problem linked to women's numerous social and health consequences (Chernyak, 2020). Sumner *et al.* have reported that women who have been abused are more likely to have high depression and post-traumatic stress levels, and both these risk factors can cause hypertension (Sumner *et al.*, 2016).

In a significant research study, Wet-Billings & Godongwana studied young women (15-34 years old) and found that 68% of the women experienced physical IPV, among which 41% of the population developed hypertension (Wet-Billings & Godongwana, 2021). The odds of having hypertension increase if women experience physical or sexual violence. Feder and Howarth established that interpersonal violence contributed 8% of the total disease burden in women aged 15-44 years (3% in all women), and was the leading contributor to mortality, disability and illness ahead of higher-profile risk factors such as HBP in Australia (Feder & Howarth, 2014). GBV has adverse health consequences, but little is known about its association with hypertension in LMICs, where the burden of hypertension is equally high and

underreported (Clark *et al.*, 2016). Therefore, it is imperative to evaluate the association between GBV and hypertension among women in resource-limited settings.

The correlations between high blood pressure, income level, wealth, employment status and place of residence have been well determined (Abba et al., 2021; Cois & Ehrlich, 2014; Gupta et al., 2017). Other individual-level factors such as ethnicity, education level and unhealthy lifestyles have also received much attention (Grotto et al., 2008; Leng et al., 2015). Several research studies have established that societal and economic factors are linked to the prevalence and management of hypertension (Cuschieri et al., 2017; Ridwanah et al., 2021). Most LMICs encounter financial or human resource challenges in dealing with hypertension (Angkurawaranon et al., 2016) as the financial implication of accessing treatment can reduce the quality of life (Andrade et al., 2014), productivity in the workplace (Grotto et al., 2008) and be a significant economic burden (Ridwanah et al., 2021). The high incidence of hypertension and the elevated treatment costs can impact GDP and inflation rates, affecting both emerging and high-income countries (Anyabolu et al., 2017; Ridwanah et al., 2021). Moreover, health has many determinants beyond the health sector that are less evident than proximate predictors (Schell et al., 2007). The Human Development Index (HDI) can reflect a country's standard of living, population health, and literacy rates, which are critical benchmarks for its socioeconomic status (Zeng et al., 2020). These determinants have a profound impact on the scale and profile of hypertension. However, few studies were conducted to explore the association among these socioeconomic determinants of population health at the country level (Cuschieri et al., 2017; Gheorghe et al., 2018; Sokolov-Mladenović et al., 2016).

Several studies have suggested that increased spending in the health sector, donor financing and redistribution of national budgets will improve the health of individuals in LMICs (Lu *et al.*, 2010; Wierzejska *et al.*, 2020; Zeng *et al.*, 2020). Similarly, some recent reviews have

shown that more investment in the health system can reduce the prevalence of hypertension (Krzysztoszek *et al.*, 2014; Wierzejska *et al.*, 2020). Influential international organisations have advocated for dedicating more resources to the health sector to reduce the prevalence of hypertension (Cois & Ehrlich, 2014; Zeng *et al.*, 2020). The burden of hypertension can be reduced indirectly by improving the socioeconomic determinants of population health, improving education, housing, gender equality and human rights (Zeng *et al.*, 2020). The significance of the underlying socioeconomic variables is less evident (Schell *et al.*, 2007). The degree to which various socioeconomic factors influence hypertension is unclear. Furthermore, the relative importance of improved education, health services and economic inequity may also vary among various countries. Hence, advanced countries' best practices and strategies can be exploited in other countries undergoing an epidemiological transition from infectious to chronic diseases.

Inefficient health systems and reduced government expenditure on health promotion interventions may explain the high prevalence of hypertension in many African countries (Cappuccio & Miller, 2016; Dzudie *et al.*, 2018; Tijssen, 2007). Nonetheless, we cannot rule out the potential consequences of poor scientific dissemination and reduced government expenditure on R&D in these countries (Woolston, 2019). There has been significant growth in global hypertension research activities (Devos & Menard, 2019). Growing worries about the worldwide epidemic of hypertension and the need to offer information to policymakers and decision-makers for better prevention, treatment, and control have contributed to this growth (Carey *et al.*, 2018). Hypertension-related diseases, such as stroke and ischemic heart disease, are the leading causes of death worldwide (W.H.O, 2013). As a result, evidence-based prevention, early detection, and long-term control methods that reduce mortality and improve quality of life are imperative. Many urban areas lack adequate infrastructure to mitigate the

impending risks associated with urbanisation (Saghir & Santoro, 2018). Furthermore, the health care system in most LMICs is overburdened due to growing demands from hypertension and other cardiovascular disorders and an increasing burden of infectious diseases (Mills *et al.,* 2020). Hence, due to these reasons, the prevalence of hypertension in LMICs is predicted to rise if appropriate intervention measures are not adopted across diverse strata in their societies. In most LMICs, inefficient healthcare systems, poverty and reduced government expenditures on health promotion interventions were highlighted as limiting choices for healthy lifestyles, nutritious foods, recreational physical activities and timely access to healthcare (Addo *et al.,* 2007; Cappuccio & Miller, 2016; Dzudie *et al.,* 2018; Kayima *et al.,* 2013).

1.2.1 Risk Factors for Hypertension

The following are some of the well-established risk factors associated with the high prevalence of hypertension: Lifestyle factors, environmental factors, ageing population, psychosocial stress and comorbidities (Andrade *et al.*, 2014; Appelman *et al.*, 2015; Forman *et al.*, 2009; Ghadieh & Saab, 2015). These factors have been elaborated in detail as follows:

1.2.2 Non-modifiable risk factors

1.2.2.1 Ageing Population

Several studies conducted in LMICs have consistently ascertained that hypertension prevalence increases with age (Kumar, 2013; Sun, 2015), from 12.6% (aged 35-39) to 58.4% (70-74 aged) (Lewington *et al.*, 2016). Ageing is a continuous and progressive process that reduces physiological function across all human body organs. Consequently, it increases the chances of infection and disease elevating mortality risk (Buford, 2016).

1.2.2.2 Genetic factors

The role of hereditary and genetic factors in influencing blood pressure risk of hypertension is well established (Franceschini *et al.*, 2011). Blood regulation is a complex process and multiple

genes are likely to affect blood pressure modulated by the environmental contexts, such as diet, physical activities, psychosocial factors and ageing (Franceschini *et al.*, 2013). However, identifying genes that contribute to the distribution of blood pressure in populations and underlying biology remains a challenge to environmental factors and genetic factors account for the regulation of blood pressure and its control. Understanding genetic factors may help in recognising those at risk and help in their treatment. Discovering hypertension susceptibility genes would help identify those at risk for developing the disease before expressing clinical symptoms (Sarkar & Singh, 2015).

1.2.2.3 Sex

The association between sex and hypertension has been evaluated by Chowdhury et al. (2016) in a cross-sectional study conducted in Bangladesh involving 7,839 participants (3,964 women & 3,875 men) aged 35 years and older. This extensive study revealed that the prevalence of hypertension is higher in women (32%) than in men (20.3%). However, some studies argue that the prevalence of hypertension is generally similar in both sexes and is projected to increase with population growth and ageing in both genders (Sarki *et al.*, 2015). Future studies should examine the mechanisms responsible for the observed gender differences to improve understanding of CVD aetiology.

1.2.3 Modifiable risk factors

1.2.3.1 Lifestyle Factors

Lifestyle factors increase the risk of having hypertension in most LMICs. These factors include smoking, physical inactivity, an unhealthy diet and alcohol consumption.

The side effects of smoking have been significantly highlighted by (Kannel & Higgins, 1990). It is well-established that cigarette smoking is a dominant risk factor for CVD, particularly myocardial infarction, stroke and sudden death (Narkiewicz, 2005; Virdis *et al.*, 2010). Smoke quitting is the single most effective lifestyle measure for preventing many CVDs (Hitchman & Fong, 2011; Virdis *et al.*, 2010). A 2011 study by Hitchman & Fong reported that smoking was responsible for approximately 6 million deaths per year and five million deaths could be attributable to direct smokers, while 600,000 to indirect (Hitchman & Fong, 2011). Smoking contributes to accelerating the age-related stiffening of the arterial walls, thereby increasing the risk of having hypertension (Saladini *et al.*, 2016). Despite the pressor effects of smoking, several epidemiological studies fail to confirm an independent link between smoking and hypertension (Narkiewicz, 2005).

The devastating effects of heavy alcohol consumption have long been recognised (Roerecke & Rehm, 2014). However, recently, the potential benefits of drinking red wine have been suggested. The association of alcohol consumption with chronic disease is considered complex; an example of such complexity is the lower risk of CVD among moderate but not heavy drinkers (Costanzo *et al.*, 2011). High alcohol consumption increases CVD risk by decreasing myocardial contractility and inducing arrhythmias and dilated cardiomyopathy, resulting in progressive cardiovascular dysfunction and structural damage (Fernandez-Sola, 2015). Excessive alcohol consumption enhances the risk of hypertension and enormous global diseases and economic burden despite the beneficial associations of low alcohol consumption with ischemic heart disease (Roerecke *et al.*, 2017).

Other behavioural causes of hypertension include salt intake, low dietary potassium, low consumption of fruits and high alcohol and fats consumption (Campbell *et al., 2015*). A healthy diet plays an essential role in maintaining blood pressure and improving overall health. Adherence to a safe dietary way of life and lifestyle factors are associated with lower self-reported hypertension (Forman *et al., 2009*). Undoubtedly, embracing low-risk nutritional and lifestyle factors significantly reduces hypertension among young women. Therefore, it is

important to integrate healthcare professionals with dieticians in providing care for hypertensive patients.

Physical inactivity is a significant risk cardiovascular risk factor. It is responsible for premature mortality and several non-communicable diseases (NCDs) (Katzmarzyk *et al.*, 2022). The relative burden is more evident in HICs; however, the most significant number of people (absolute burden) affected by physical inactivity live in middle-income countries, given the size of their populations. Physical activity reduces the prevalence of hypertension by decreasing total peripheral resistance and improving endothelium dependant relaxation, primarily mediated by a significant increase in vascular nitric oxide (NO) production (Katzmarzyk *et al.*, 2022). Furthermore, different exercises of various intensity levels had other effects on hypertension. In a recent study, Dun et al. have suggested that residents should be encouraged to engage in various physical activities and maintain a healthy weight to improve their quality of life (Dun *et al.*, 2021).

1.2.3.2 Obesity and other Comorbidities

The correlation between hypertension and other comorbidities such as excess body weight, kidney disease, diabetes maleates and HIV/AIDS has long been studied (Fahme *et al.*, 2018; Kannel *et al.*, 1967; Long & Dagogo-Jack, 2011; Wong *et al.*, 2007). Framingham's research study revealed that weight gain is associated with increased blood pressure. Similarly, studies suggest that hypertension could be common among HIV-infected adults (Fahme *et al.*, 2018), and the antiretroviral drugs might suppress the immune system exposing PLHIVs to other diseases (Nduka *et al.*, 2015; Xu *et al.*, 2017).

1.2.3.3 Environmental Factors

Urbanisation is associated with an increased prevalence of NCDs risk behaviours rising rapidly. More than 50% of the global population lived in cities in 2010, a proportion expected

to reach 60% in 2030 and 70% in 2050 (Juma *et al.*, 2019). SSA is considered the world's fastest urbanising region, with 40% of Africans living in urban areas (Mathenge *et al.*, 2010; Saghir & Santoro, 2018). This shift comes with epidemiological transition, diet modification, socioeconomic status change, population ageing and behavioural risk factors such as cigarette and alcohol use and physical inactivity (Berry *et al.*, 2017; Sarki *et al.*, 2015). Rapid unorganised urbanisation has increased in Nepal in recent years, which resulted in population growth, and increased longevity that drives the epidemiological and nutritional transition in the country (Mehata *et al.*, 2021). Another critical factor of urbanisation is that it causes loss of green space due to overcrowding and pollution (Schutte *et al.*, 2021). Access to greenness was significantly associated with lower odds of hypertension OR: 0.63 (95% CI:0.41-0.95) (Boakye *et al.*, 2021). Crowded housing, poverty, reduced spaces for exercise, increased fast food, alcohol and drug consumption, industrial and traffic noise are some of the significant challenges of urbanisation contributing to hypertension (Fan *et al.*, 2022; Yousaf *et al.*, 2016).

1.2.3.4 Psychosocial factors

There is growing interest in the impact of psychosocial and lifestyle factors on CVDs (Qian *et al.*, 2021). Psychosocial risk factor plays a significant role in the development and progression of CVDs (Medina-Inojosa *et al.*, 2019). Acute stress, chronic stress, depression, anxiety, and low social support are critical risk factors that cause hypertension by elevating blood pressure (Albus *et al.*, 2019). High stress is significantly associated with hypertension. A study by Bhelkar and colleagues indicated that participants with increased stress levels had 2.52 times higher chances of becoming hypertensive than participants without any stress (Bhelkar *et al.*, 2018). In a community-based cohort study of blacks by Spruill et al., higher perceived stress over time was associated with an increased risk of having hypertension (Spruill *et al.*, 2019). Therefore, evaluating stress levels over time and intervening when high perceived stress may reduce hypertension risk. Furthermore, lack of social support is associated with loneliness, and

it is a significant factor for hypertension in single men and women. The effect is comparable to heavy smoking (Hamam *et al.*, 2020; Xia & Li, 2018). There is significant co-occurrence of hypertension with anxiety, depression, and chronic pain, which may lead to undertreatment of hypertension. Physicians treating patients with hypertension should be aware of the role played by anxiety, depression, and chronic pain in treatment efficacy and compliance with poor medication adherence (Dyussenova *et al.*, 2018).

1.2.4 Characteristics of LMICs

The world bank group classification of countries is adopted for analytical purposes. In the 2019 classifications, countries with a gross national income (GNI) per capita of \$995 or less in 2017 are referred to as low-income countries. Moreover, countries are referred to as lower-middle-income countries (LMICs) if they have a GNI per capita between \$996 and \$3,895; upper-middle-income countries are those with a GNI per capita between \$3,896 and \$12,055; high-income economies are those with a GNI per capita of \$12,056 or more (World Bank, 2020). Low and middle-income countries have different backgrounds in terms of resources, demography, history, culture and politics; however, they still share some common characteristics, such as relatively low income per capita and low level of total savings, endowed with rich natural resources, higher dependency on exports and revenue from primary commodities (Carlsen, 2013). In addition, resource limited settings have become increasingly heterogeneous with extreme inequalities and a significant share of the population living in rural areas and primarily employed in agriculture (Alonso *et al.*, 2015).

The World Bank reports that nearly 84% of the world population lives in LMICs, which produce 26% of the world's output. The countries account for 20% of the world population but make up 1.5% of the world's statistically research outputs. In 2015, about 50% of the global extremely poor people lived in some of the most populous countries in South Asia and Sub-Saharan Africa: Bangladesh, Nigeria, Democratic Republic of Congo, India, and Ethiopia

(WorldBank, 2020). Most LMICs are recognised as being in the phase of health transition driven by globalisation and sedentary lifestyle transformation of adopting unhealthy eating and smoking (Raza *et al.*, 2004). Hence, this explains the increasing prevalence of NCDs such as CVDs, cancer, diabetes, etc. The main strength of all developing countries is the availability of human resources; however, authorities need to mobilise these resources by redistributing responsibility, and rewarding good governance and discipline.

1.2.5 Conceptual framework

The design of this thesis was conceptualised based on the socio-ecological model framework **(Figure 2)** from the Centre for Disease Control and Prevention (CDCP) (C.D.C.P, 2022). The model helps to understand the complex factors associated with the prevalence of hypertension. The model incorporates the complicated interaction between various individual, community, and societal factors. The overlapping concentric cycles in Figure 1 allow us to comprehend how factors at one level influence factors at other levels. Furthermore, the diagram illustrates the complex interplay between various factors often depicted as being related to one another in a nested or hierarchical manner.



Figure 2: The Social-Ecological Model: A Framework for Prevention

At the innermost layer (first level 1), individual-level factors identify biological factors (commodities such as HIV), personal history factors (*e.g.*, age, sex, genetics), behavioural

Adapted from the Centres for Disease Control and Prevention (CDC), The Social Ecological Model: A Framework for Prevention, https://www.cdc.gov/violenceprevention/about/social-ecologicalmodel.html (accessed April 2022).

factors (Gender-based violence) and socioeconomic status (wealth attainment, educational levels, skills, *etc.*), and lifestyle factors (such as physical inactivity, alcohol consumption, *etc.*) are mainly described at this level. The middle layers describe relationship and community-level factors; an individual's relationship with the community/environment is described at this level. This research study has incorporated HAP, neighbourhood socioeconomic disadvantage index, and net of individual-level socioeconomic position and place of residence as contextual factors. In the fourth and outermost level, broad societal factors such as gross domestic product, health expenditure, education and policies in society are examined.

1.3 RATIONALE FOR THE STUDY

In addition to the unfinished infectious diseases agenda, low- and middle-income countries (LMICs) now deal with a double-epidemic of infectious diseases and CVDs. The widespread inability to respond to this double epidemic in a coordinated and integrated manner remains challenging, which undermines response measures to infectious and CVDs. As discussed in the previous section, hypertension is the single most preventable risk factor for CVD and a primary cause of death worldwide. Early detection and treatment of hypertension are critical for preventing CVD and related complications and information about novel risk factors for hypertension is essential to design effective care and initiatives to control hypertension in resource-constrained contexts. It is well known that smoking status, alcohol use, and body mass index (BMI) are linked to hypertension risk. Indeed, there is limited evidence of novel risk factors for having hypertension. Given the importance of novel and emerging risk factors.
1.4 AIM, RESEARCH QUESTIONS, AND OBJECTIVES

1.4.1 Aim

The primary aim of this research study was to broaden our understanding of the novel risk factors for hypertension in low- and middle-income countries (LMICs).

1.4.2 Research questions

- I. What are the number and characteristics of hypertension research publications in Africa?
- II. What is the number of citation classics in hypertension research globally?
- III. What are the emerging topics on hypertension globally?
- IV. What is the probability of people with HIV having hypertension than HIV-negative individuals?
- V. What is the probability of having hypertension among women exposed to gender-based violence compared to unexposed women?
- VI. What is evidence of neighbourhood clustering in the risk of hypertension?
- VII. What is the impact of HAP on the risk of having hypertension?
- VIII. Do people living in rural areas to urban areas have a higher probability of having hypertension than de jure residents?
- IX. What is the probability of having hypertension among individuals living in rural areas compared to individuals living in urban areas of South Africa?
- X. What is the correlation between a country's prevalence of hypertension and societal factors?

1.4.3 Objectives

This research was conducted in four different phases, corresponding to ten objectives:

Phase 1: Evidence harvest and mapping

- I. To assess the growth in hypertension research publications in Africa.
- II. To evaluate the citation classics, international collaboration, author productivity, emerging topics, and the mapping of frequent terms in hypertension research globally.

III. To examine the emerging patterns and trends in hypertension-related publications globally

Phase 2: Individual compositional novel risk factors

- IV. To examine the contribution of HIV seropositivity on the risk of hypertension.
- V. To determine whether exposure to gender-based violence is independently associated with the risk of HIV.

Phase 3: Neighbourhood contextual novel risk factors

- VI. To examine whether the risk of hypertension is significantly associated with the neighbourhood socioeconomic disadvantage index, net of individual-level socioeconomic position, and determine whether there is a significant neighbourhood variation in hypertension risk.
- VII. To examine the association between HAP and blood pressure in resource-limited settings.
- VIII. To examine whether neighbourhood variation in the prevalence of hypertension can be explained by place of residence.
- IX. To examine whether respondents living in urban areas are more likely to develop hypertension than those living in rural areas of South Africa,

Phase 4: Societal contextual novel risk factors

X. To assess the strength of association between hypertension prevalence and major socioeconomic determinants measured at the country level [*i.e.*, current health expenditure, (% of GDP), domestic general government health expenditure per capita, GDP per capita (current US\$), adult literacy rate (% of people ages 15 and above), unemployment, (% of the total labour force), urban population (% of the total population), multidimensional poverty index., etc.].

S/N	Research questions	Objective	Study chapter	
1	What are the number and characteristics of hypertension research publications in Africa?	To assess the growth in hypertension research publications in Africa	Study I	
2	What is the number of citation classics in hypertension research globally?	To evaluate the citation classics, international collaboration, author productivity, emerging topics, and the mapping of frequent terms in hypertension research globally	Study II	
3	What are the emerging topics on hypertension globally?	To examine the emerging patterns and trends in hypertension-related publications globally	Study III	
4	What is the probability of people who have HIV having hypertension than HIV-negative individuals?	To examine the contribution of HIV seropositivity on the risk of hypertension.	Study IV	
5	What is the probability of having hypertension among women exposed to gender-based violence compared to unexposed women?	To determine whether exposure to gender-based violence is independently associated with the risk of HIV.	Study V	
6	What is evidence of neighbourhood clustering in the risk of hypertension?	To examine whether the risk of hypertension is significantly associated with the neighbourhood socioeconomic disadvantage index, net of individual-level socioeconomic position, and to determine whether there is a significant neighbourhood variation in hypertension risk.	Study VI	
7	What is the impact of household air pollution on the risk of having hypertension??	I. To examine the association between household air pollution and blood pressure in resource-limited settings.	Study VII	

Table 2: Research questions and study chapters

8	Do people living in rural areas to urban areas have a	I. To examine whether neighbourhood	Study VIII
	higher probability of having hypertension than de	variation in the prevalence of hypertension	
	jure residents	can be explained by place of residence.	
9	What is the probability of having hypertension	What is the probability of having hypertension	Study IX
	among individuals living in rural areas compared to	among individuals living in rural areas compared	
	individuals living in urban areas of South Africa?	to individuals living in urban areas of South	
		Africa?	
10	What is the correlation between a country's	To assess the strength of association between	Study X
	prevalence of hypertension and societal factors?	hypertension prevalence and five major	
		socioeconomic factors measured at the country-	
		level (<i>i.e.</i> , gross domestic product, illiteracy rate,	
		human development index, expenditure on	
		health, and income inequality, etc.).	

HIV: Human Immunodeficiency Virus

1.5 THESIS ORGANISATION

This thesis is organised into six chapters, beginning with a general overview of noncommunicable diseases, CVDs, and hypertension. The epidemiology and risk factors of hypertension, rationale, aims, and objectives are presented in Chapter 1. The study methodology, data sources, statistical analysis, and definitions of variables and determinants are discussed in chapter 2. The result of phase one (evidence harvests and mapping) is presented in chapter 3. In chapter 4, the findings of the contribution of the HIV, and GBV on hypertension risk as individual compositional risk factors are presented. In chapter 5, the result of the community and societal contextual compositional novel risk factors are presented. In chapter 6, the main findings, policy implications, implications for further research, strength, and limitation of the studies are discussed.

2 CHAPTER 2: MATERIALS AND METHODS

2.1 INTRODUCTION:

This chapter presents the data sources, definitions of variables, statistical analysis for the evidence harvest mapping studies, individual compositional risk factors, and the community and societal contextual risk factors. The bibliometric, multi-level analysis, propensity score matching analysis, and odds ratios (ORs) are discussed here.

2.2 **BIBLIOMETRIC DATA SOURCES**

2.2.1 Study I

Hypertension research publications (Data) from African countries were sourced from the PubMed database. These articles included published work from 1 January 1999 to 31 December 2018. Medical Subject Heading (MeSH) terms and keywords were used for the search, which included: "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR ("high"[All Fields] AND "blood"[All Fields] AND "pressure"[All Fields]) OR "high blood pressure"[All Fields]. The "advanced-search" 'option and used "publication date" and "affiliation"" were selected as field names to limit the search by year of publication for each country. However, no restrictions on language or study design were applied. Alternative country names to avoid missing any relevant articles in the database search strategy were added: for example, Cote d'Ivoire and Ivory coast; Swaziland and Swaziland; Cape Verde and Cabo Verde. Data on each country's GDP and population were obtained from the World database. To accredit an article to countries, the method of absolute country counting was adopted. Each country contributing to an article received one paper credit based on the lead author's correspondence or reprint address (Egghe *et al.*, 2000).

2.2.2 Study II

Data were sourced from the Web of Science (<u>http://thomsonreuters.com/web-of-science/</u>) database from inception to 31 December 2018. The hypertension-related articles were retrieved using MeSH keywords, *i.e.*, "hypertension", "high blood pressure", "elevated blood pressure", "hypertensive", and "hypertens". Subsequently, the publications were sorted by the number of citations. To ensure that relevant articles were included in this research study, publications were scrutinised to ensure that only articles focusing on hypertension research were included. For example, veterinary studies, zoology, and plantations were excluded from this research study.

2.2.3 Study III

Data were retrieved from the PubMed database to obtain the records of all hypertension articles published in the last 100 years using the following search string: "("hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR ("high"[All Fields] AND "blood"[All Fields] AND "pressure"[All Fields]) OR "high blood pressure"[All Fields]). Subsequently, the title and abstract of each article were extracted and combined into a single string.



2.3 INDIVIDUAL-LEVEL DATA & CONTEXTUAL DATA SOURCES

Figure 3: Multi-Level Data Structure

Figure 3 describes the multi-level data structure for the individual and contextual data from Demographic and Health Surveys (DHS). The surveys provide information for a wide range of monitoring and impact evaluation indicators in population, nutrition, health, and other vital characteristics. The surveys have large sample sizes (usually between 5,000 and 30,000 households) and are traditionally conducted after every five years to allow comparisons over time. The sample generally represents the national, residential (urban or rural), and regional levels. The surveys utilise a stratified two-stage cluster design. Enumeration areas (EA) are drawn from a census file during the first stage. In each EA selected, the second stage involves drawing a sample of households from an updated list of households. These surveys are typically implemented by the national statistical office in a country, with the data collection process usually taking between 5 to 6 months.

This analysis has utilised cross-sectional data from the most recent DHS survey in twelve countries, as presented in Table 1. The selection of countries is based on the availability of blood pressure measurements. The following countries with up-to-date data on hypertension in

the DHS were selected, Albania, South Africa, Bangladesh, Benin Republic, Ghana, Haiti, India, Kyrgyzstan, Lesotho, Namibia, Nepal, Tajikistan. These countries are spread across the various global regions, including sub-Saharan and North Africa, South, West, and Central Asia, North and South America, the Caribbean, and North and Eastern Europe.

Table 3: Summary	y table	presenting	some DHS	characteristics	of selected	countries
-	/					

				DHS characteristics		
S/N	Country	Population '000	Income category	Households	Women	Men
1	Albania	2926	Upper middle income	15823	10861	6142
2	Bangladesh	162,952	Lower middle income	19457	20107	N/A
3	Benin Republic	10872	Low-income countries	14156	15928	7595
4	Ghana	28207	Lower middle income	11835	9396	4388
5	Haiti	10847	Low income	13405	14371	9795
6	India	1324171	Lower middle income	601509	699686	112122
7	Kyrgyzstan	5956	Lower middle income	8040	8208	2413
8	Lesotho	2202	Lower middle income	9402	6621	2931
9	Namibia	2480	Upper middle income	9849	9176	4481
10	Nepal	28983	Low income	11040	12862	4063
11	South Africa	56015	Upper middle income	11083	8514	3618
12	Tajikistan	8735	Lower middle income	7843	10718	N/A

Sources: Worldbank 2018 report & DHS available online accessed on the 28th of April 2020 from <u>https://data.worldbank.org/indicator/NY.GDP.PCAP.KD.ZG</u>

2.3.1 Community-level data sources

The study utilised the term neighbourhood to describe clustering within the same geographical living environment. Neighbourhoods were selected based on sharing a standard primary sample unit within the DHS data. The sampling frame for identifying the primary sample unit in the DHS is usually the most recent census. The unit of analysis was chosen for the following two reasons. First, the primary sample unit is the most consistent measure of the neighbourhood across all the surveys (Griffiths *et al.*, 2004), and thus the most appropriate identifier of the

neighbourhood for this cross-region comparison. Second, for most of the DHS conducted, the sample size per cluster meets the optimum size with a tolerable precision loss (Kravdal, 2006).

2.3.2 Societal-level data source

The HIV prevalence data was sourced from the WHO global health observatory database to measure population health. It is a repository gateway to the health-related statistics for its 194member states. It provides access to over 1000 indicators on priority health to priority health topics, including mortality and disease burden, HIV/AIDS, TB, malaria, neglected diseases, epidemic-prone diseases, health systems, environmental health water and sanitation, NCDs and risk factors, violence and injuries and equity among others. The UNDP publishes the multidimensional poverty index across three dimensions, and ten indicators, which include health (child mortality & nutrition), education (years of schooling and number of enrolment), living standards (Water, Sanitation, electricity, cooking fuel, and floor asset)

Current health expenditure (% of GDP), domestic general government health expenditure per capita, GDP per capita (current US\$), adult literacy rate (% of people ages 15 and above), unemployment (% of the total labour force), urban population (% of the total population), multidimensional poverty index and total population were extracted from the World Development Indicators database (Bank, 2020; WorldBank, 2020).

2.4 VARIABLES

2.4.1 Hypertension

The study's primary outcome was the collection of hypertension data from DHS. It included all the respondents who had a systolic blood pressure > 140mmHg or diastolic blood pressure > 90mmHg or those taking anti-hypertensive drugs. The blood pressure readings were taken three times at the interval of 10 minutes with small, medium, and large cuff sizes depending

on the cuff size of the respondent. Subsequently, an average value of the second, and third measurements was used for the categorisation (Chobanian, 2006).

2.4.2 Country prevalence of hypertension

The percentage of people with hypertension.

2.4.3 Individual Novel risk factors (HIV status and gender-based violence)2.4.3.1 HIV status

For HIV testing in DHS, blood spots were acquired on filter paper from a finger prick and transported to a research facility for testing. As a laboratory protocol, an initial enzyme-linked immunosorbent assay (ELISA) test was conducted for participants found to be positive. A retest was done, and 5–10 % of those found to be negative had a second ELISA test. For those with discordant results on the two ELISA tests, another ELISA test was conducted, or a Western Blot was performed. The HIV test results were anonymously linked to individual questionnaire information. All the ethical and confidentiality issues were addressed according to the standards (Urio *et al.*, 2015).

2.4.3.2 Gender-based violence

GBV and IPV against women (spousal physical, sexual, and emotional abuse) were assessed. A modified and previously validated version of the Conflict Tactic Scale was used for the assessment. GBV is defined as exposure to one or several of the following experiences ever enacted by a spouse or partner (Straus & Douglas, 2004). For this research study, physical abuse was measured using six variables: spouse ever pushed, shook, or threw something; spouse ever slapped; spouse ever punched with a fist or something harmful; spouse ever kicked or dragged; spouse ever tried to strangle or burn, and spouse ever threatened with knife/gun or other weapons. Furthermore, the sexual abuse was quantified using two variables: forced sexual intercourse and other sexual acts when undesired. Finally, the emotional abuse was measured using three variables: the spouse ever humiliated her in public, the spouse ever threatened her with harm, and the spouse ever insulted or made their partner feel bad.

2.4.4 Community Level

2.4.4.1 Indoor air pollution

Exposure to HAP was grouped into two categories in this research analysis based on exposure to cooking smoke: "clean fuels," including electricity, liquid petroleum gas (LPG), natural gas, and biogas, and "polluting fuels," including kerosene, coal/lignite, charcoal, wood, straw/shrubs/grass, and animal dung.

2.4.4.2 Place of residence

The migration variable was generated using variables on the current place of residence, and earlier place of residence as reported by the respondents. Respondents' information was utilised to construct the following six migration streams: urban non-migrants (urban 'permanent' residence, did not migrate recently), rural non-migrants (rural 'permanent' residence, did not migrate recently), rural-urban (recently migrated from rural area to urban area), rural-rural (recently migrated from one rural area to another rural area), urban-urban (recently migrated from one urban area to another urban area), and urban-rural (recently migrated from urban area).

2.4.4.3 Neighbourhood-level factors

The neighbourhood is defined as respondents clustering within the same geographical area based on sharing a common primary sample unit within the data. The sampling frame for identifying the primary sample unit in the DHS was drawn from the most recent census. The primary sample unit is the most reliable and suitable identifier of neighbourhood quantification across all surveys (Griffiths *et al.*, 2004; Kravdal, 2006). Additionally, the sample size per cluster met the optimum size, with a tolerable degree of precision loss across the DHS. Moreover, this research study classified neighbourhood socioeconomic disadvantage as a community-level variable. Respondents who had no education (illiterate), were unemployed, were rural residents, and lived below the poverty level, especially those with an asset index below 20% in the lowest quintile, were included in estimating the neighbourhood socioeconomic disadvantage. Subsequently, a standardised score with a mean of 0 and a standard deviation of 1 from this index was generated, indicating that greater scores depict a lower socioeconomic position (SEP). To achieve nonlinear effects, we divided the resulting scores into five quintiles to generate easily interpretable results by decision-makers. Moreover, we derived community-level variables using non-self means or proportions to avoid overlapping measures between the two levels of analysis. Finally, we assigned a value representing the average for all other respondents, excluding those within the cluster.

2.4.5 Country-level factor

The United Nations Development Programme's human development index (HDI) was included as the country-level factor and was categorised into three (low, moderate, and high) levels. The HDI, also known as the intensity of deprivation, is the average percentage of deprivation experienced by people in multidimensional poverty. Like the wealth index, the intensity of deprivation was computed using a principal component based on household deprivation data concerning education, health and living standards at the country level.

2.4.6 Socioeconomic Determinants

The following country-level socioeconomic factors included in the analysis have been considered development markers. These factors include current health expenditure (% of GDP), domestic general government health expenditure per capita, GDP per capita (current US\$), adult literacy rate (% of people ages 15 and above), unemployment (% of the total labour force), urban population (% of the total population), multidimensional poverty index and total population

2.4.7 Covariates

The following covariates were included in the analysis: gender of the respondent (male versus female), respondents' age in completed years (18 - 24, 25 - 34, 35 - 44 or 45 – and above), educational level (no education, primary, secondary, and tertiary); marital status (never married versus ever married), occupation (working or not working), drinking of alcohol, body mass index (BMI), and cigarette smoking. Data on household income and expenditure was missing from the DHS; instead of a wealth index, a proxy indicator for the socioeconomic position was used.

DHS wealth index is an index of economic status for each household that was constructed using principal components analysis (PCA) based on the following household variables: number of rooms per house, ownership of a car, motorcycle, bicycle, fridge, television, and telephone as well as any kind of heating device. From these criteria, the DHS wealth index was segregated into five categories (poorest, poorer, middle, richer, and richest), and was calculated by PCA.

2.5 STATISTICAL ANALYSIS

2.5.1 Study I

Total hypertension research has been defined as the total number of articles indexed in PubMed from 1999 to 2018. The weighted comparison among countries was obtained by calculating the ratio of the number of publications for each country to the population of that country.

To analyse trends in hypertension research output over the period under study, Poisson regression (PR) model was fitted using total hypertension research outputs as an outcome variable and year as a predictor:

$$\ln(\mathbf{p}) = \mathbf{a} + (\boldsymbol{\beta} * \mathbf{t})$$

Where *p* is the number of articles per year, *ln* denotes the natural logarithm, *a* is the intercept, β is the trend, and *t* is the year given as 0 for 1999, 1 for 2000, 2 for 2001, until 2018).

This model also allows for the estimation of time trends across individual calendar years to obtain the average annual percentage change (AAPC) of hypertension research output derived using the following formula:

$$\mathbf{AAPC} = 100 * (\exp{(\beta)} - 1)$$

Where the study was unable to estimate time trends in research output over the entire 20-year period from 1999 to 2018, AAPC over the following 5-year interval periods: period 1 (1999 – 2003); period 2 (2004 – 2008); period 3 (2009 – 2013); period 4 (2014 – 2018) (Uthman *et al.*, 2015) was calculated.

The percent relative growth for each country was calculated as follows:

Percent relative growth =
$$\left(\frac{(\text{number of publications in 2018-Number of Publications in 1998})}{(\text{Number of publications in 1998})}\right) * 100$$

The percent share per year of global research output was calculated as follows:

Percent share of global research output =
$$\left(\frac{(\text{number of articles from all African countries})}{(\text{Total number of articles indexed in PubMed})}\right) * 100$$

Pearson's correlation analysis was used to examine the associations of hypertension research output with the population and GDP of respective African countries. These variables were transformed to their natural logarithm to linearise associations. Moreover, Pearson correlation analysis was also used to compare absolute numbers of published articles between the different WHO Africa regions (Eastern Africa, Middle Africa, Northern Africa, Southern Africa, and Western Africa) during the period under study. The data were processed and analysed using R software (Version 4.2.1, by R core Team, Vienna, Austria).

2.5.2 Study II

This study identified 100 most cited articles (T100) and selected these articles for further descriptive analysis. We included articles with hypertension as the outcome of interest. Subsequently, the data were further evaluated to assess the number and patterns of citations,

country of origin, trend and year of publication, author, number of publications, study design, research category, journal impact factor, country of origin, and collaborating institutions. Additionally, the bibliometric analyses were also performed according to the following parameters: citation number, authorship, source (*i.e.*, Journal), country of origin, institutions, and frequently referenced topics.

2.5.3 Study III

Phase 1: Pre-processing

In the pre-processing phase, to create a document term matrix, each article was tokenised (divided) into a list of terms (words). The text was filtered to exclude common keywords with no analytical significance (prepositions, articles, and pronouns), punctuations, and digits. Following that, stemming was conducted, which is the process of deleting frequent word ends (*i.e.*, "compression," "compressed," and "compressing" are converted to "compress"). The frequency of each word was normalised using the frequency of the most frequently used word in all articles that year, and a scale of 1 to 100 was produced (1 being most frequently used, 100 being least frequently used). The goal of normalisation techniques like stemming and lemmatisation is to reduce inflectional forms and sometimes derivationally related forms of a word to a common base form.

Phase II: Topic extraction

The pre-processed document-term matrix was then subjected to Latent Dirichlet allocation (LDA), a hierarchical Bayesian algorithm and one of the most common topic modelling approaches. It identifies theme subjects by looking for keywords that frequently appear together in a document. Subsequently, the model utilises the associations between terms to define two things: (1) themes, each characterised by a distribution of words, and (2) documents as a distribution of topics. Therefore, LDA is well suited to assessing articles covering a wide range of topics. Using a collapsed Gibbs sampler set to run for 5000 iterations, model

parameters were provided to uncover 50 themes with high interpretability (Dirichlet hyperparameters: [alpha] = 0.02; [eta] = 0.02). Next, after the model fitting was completed, topic numbers were allocated.

The probability distribution of words in each topic was visualised and utilised to create word clouds during the next step. The top 15 most likely terms in each topic were then put into a word cloud, with greater font size and darker colour indicating higher probability.

Topic popularity and dynamics were evaluated by dividing the total number of abstracts in each year by the cumulative sum of articles belonging to each topic, yielding a percentage of subjects in each year. The most prevalent themes in each article were also determined by assessing subject popularity by article. Using simple linear regression and Cochran-Armitage-Trend-Testing, a trend analysis was performed to identify themes with growing ("hot") or decreasing ("cold") popularity over time.

Phase III: Topic-based sentiment analysis

The first step in sentiment analysis was to align the pre-processed text with the NRC valence classification (*e.g.*, positive, or negative). The NRC Emotion Lexicon (Mohammad & Turney, 2010) is a database that indexes the valence and emotion of over 4,000 frequently used English lemmas. Most words in the NRC vocabulary have been classified as positive or negative. The overall positive and negative valence for each item was computed by summing the counts of positive and negative terms. The ratios were calculated by dividing the number of positive words in each article by the total number of nonstop words and vice versa for negative words (scores ranging from 0 neutral to 1 highest). The final score was expressed as a percentage of positive or negative words compared to other significant words in the article.

2.5.4 Study IV

Descriptive statistics, univariable analysis, and Blinder-Oaxaca decomposition approaches, using logistic regressions, were all utilised in this study. To depict the distribution of respondents by the significant factors, the study employed descriptive statistics. Absolute numbers (percentages) were used to express the results. Similarly, means (standard deviation) were used for categorical and continuous variables. Moreover, the risk difference in hypertension risk between the two groups (HIV positive vs HIV negative) was computed. In this case, a risk difference greater than 0 suggests that hypertension is prevalent among people living with HIV (pro-HIV inequality). Conversely, a negative risk difference indicates that hypertension is prevalent among HIV negative participants (pro-non-HIV inequality). Finally, the logistic regression method was adopted using the pooled cross-sectional data to conduct the Blinder-Oaxaca decomposition analysis.

The Blinder-Oaxaca decomposition is a counterfactual method assuming that people living with HIV have the same characteristics as their HIV-negative counterparts (Blinder). The Blinder-Oaxaca method decomposes the difference in an outcome variable between two groups into two components (Blinder, 1973). The first component is the "explained" element of the gap, which incorporates differences in the distributions of these groups' measurable attributes (known as "compositional" or "endowments"). We can quantify the disparity between the "advantaged" and "disadvantaged" groups using this method due to specific and measurable qualities variations. The second component is the "unexplained" or structural component, representing the disparity between the two groups due to variances in regression coefficients and unmeasured variables (Blinder; Blinder, 1973).

2.5.5 Study V

In the descriptive statistics, the distribution of respondents by the key variables was expressed as percentages. The study utilised Pearson's chi-squared test for analysing contingency tables. All cases in the DHS data were given weights to adjust for differences in the probability of selection and non-response. Individual weights were employed for descriptive statistics in this research study. The OR for the prevalence of hypertension between respondents not exposed to GBV and respondents exposed to GBV was computed. The OR value of more than 1 suggests hypertension prevalence estimates are more prevalent among respondents exposed to GBV. Conversely, an OR value of less than 1 indicates that the hypertension prevalence estimates are more prevalent among respondents exposed to GBV/IPV. In addition to estimating the association between GBV and hypertension for all participants, the association was stratified by the overall sample; the association was also categorised by various participants' ages, genders, literacy levels, occupation, BMI category, and place of residence.

2.5.6 Study VI

Descriptive data analyses

This cross-sectional study was performed with a survey, and the data obtained were analysed using descriptive statistics. Moreover, the distribution of respondents stratified by key variables was expressed as percentages.

Modelling approaches

Multivariable multi-level logistic regression models were utilised to analyse the associations between individual compositional and contextual factors associated with hypertension. Moreover, a multi-level logistic regression model was created for the binary hypertension risk for all respondents at level 1, respondents living in a neighbourhood at level 2, and respondents living in a country at level 3; five models were created as follows:

- The first model was an empty or unconditional model without any explanatory variables to decompose the variance between the country and neighbourhood levels.
- The second model contained only individual-level factors.
- The third model included only neighbourhood-level factors.
- The fourth model incorporated only country-level factors.
- The fifth model simultaneously controlled for individual-, neighbourhood- and country-level factors (full model).

Fixed effects (measures of association)

The measures of the association are reported as ORs with 95% confidence interval intervals (CIs). The measures of association (ORs) with 95% confidence interval (95% CI) are summarised rather than 95% confidence intervals (95% CI) using Bayesian statistical inference, which provides probability distributions.

Random effects (measures of variation)

The likely contextual effects were measured using the intraclass correlation (ICC) and median odds ratio (MOR). The similarity between respondents in the same neighbourhood and within the same country was measured using the ICC, which signifies the percentage of the total variance in the probability of hypertension related to the neighbourhood- and country-level factors, *i.e.*, a measure of clustering of the odds of hypertension in the same neighbourhood and country. Hence, the ICC by the linear threshold latent variable method was calculated (Snijders & Bosker, 2011), and neighbourhood effects in terms of the odds were reported (Merlo *et al.*, 2006). On the other hand, the MOR measures neighbourhood or country variance as an OR and estimates the probability of hypertension attributed to the second or third level (neighbourhood or country context). When the MOR value equals 1 (one), it indicates no neighbourhood or country variance. When the MOR value is higher, the contextual effects are more relevant for understanding the odds of having hypertension.

Model fit and specifications

The study checked for multi-collinearity among the explanatory variables by examining the variance inflation factor (VIF) (Tu *et al.*, 2005). All diagonal elements in the variance-covariance (τ) matrix for correlations are between -1 and 1, and diagonal elements for any elements are close to zero. However, none of the test results provided reasons for concern because they were within the acceptable ranges. Thus, the models provided robust and valid results. For this analysis, *MLwinN* software (version 2.31, University of Bristol) was utilised.

2.5.7 Study VII

In this study, the analytical approach included descriptive as well as bivariable and multivariable analyses. The descriptive statistics demonstrate the distribution of respondents by the key variables. These values are expressed as absolute numbers (percentages) and means (standard deviation) for categorical and continuous variables. In this study, individual weights were used for descriptive statistics. The OR value for the prevalence of hypertension between respondents exposed to clean fuels and respondents exposed to polluted fuel was computed. An OR value of more significant than 1 suggested hypertension prevalence estimates was more prevalent among respondents exposed to polluting fuels.

On the other hand, an OR value of less than 1 indicated that the hypertension prevalence estimates were higher among respondents exposed to/using bad/polluting fuels indicating the association between indoor air pollution and hypertension for all participants. The association was stratified by age, sex, educational attainment, occupation, BMI category, and the place of residence of the participants. The association between indoor air pollution and hypertension was equally examined. Next, bivariable analyses were employed to evaluate the association between each variable and high blood pressure. Contingency tables were analysed using the Pearson χ^2 test or Fisher exact test. Multivariable logistic regression analyses were used to examine the net effects of the explanatory variables on the dependent variables. For multivariable analyses, HAP and other control variables listed above that were significant in the bivariable study (p < 0.05) were included in the regression model in a single block to control possible confounding factors. The magnitude and direction of association were expressed in the adjusted ORs, and significant levels were defined as p-values. Regression diagnostics were utilised to judge the goodness-of-fit of the model. They included the tolerance test for multicollinearity, its reciprocal variance inflation factors (VIFs), the presence of outliers and estimates of the adjusted R square of the regression model. In addition, the Hosmer-Lemeshow

goodness-of-fit test was utilised. None of the results of the tests provided any cause for concern. Thus, the models provided robust and valid results. The significance tests were two-tailed, and statistical significance was defined at the alpha level of 0.05. For all these analyses, Stata software (Version 17, StataCorp, Texas, USA).

2.5.8 Study VIII

Descriptive statistics

• The participants' background characteristics were summarised by their place of residence at the time of the survey. Categorical variables were reported with numbers and percentages, while continuous variables were reported with median and range. The weighted percentage with a 95% confidence interval (CI) was computed to obtain the prevalence of hypertension by place of residence in the sample.

Meta-Analysis

Next, crude odds ratios (CORs) were obtained for all study factors. The ORs and the 95% CI for the association between place of residence and the risk of having hypertension for each country were calculated. The DerSimonian-Laird method (random-effects model) was used to compute the pooled OR across 12 countries. The random-effects model is conservative as it assumes variation exists across studies (countries in this context). To examine if the observed variability in effect size of the included countries was within the expected range and if they shared a common population effect size, the homogeneity of the results through Cochran's Q test, where the quantity I² describes the percentage variation across countries that have heterogeneity, were evaluated. Hence, the heterogeneity values from 0% to 100% represented none to the highest level of heterogeneity.

After calculating pooled estimates for all countries, the following country-level variables: illiteracy rate, unemployment rate, poverty rate, survey sample size, and survey year were stratified for the analysis. A series of meta-regression studies were conducted for each country

component given above to account for variations in the effect of explanatory factors on the outcome. All tests were two-sided, and a significance level of 0.05 was utilised. The analysis was performed using Stata 17 software (Stata Corp, College Station, TX, USA).

Sub-group analyses

The differential effects of various explanatory factors were assessed on the pooled estimates by conducting subgroup analyses using the DerSimonian-Laird method. The factors considered in the subgroup analyses included: age, sex of the participants, smoking, obesity, marital status, air pollution, education attainment, media access, money problem, health insurance, and wealth status.

2.5.9 Study IX

Crude rural-urban differences in hypertension prevalence:

The OR for the prevalence of hypertension between populations in rural and urban regions was computed. Any OR greater than 1 suggested hypertension prevalence estimates were higher among respondents living in the urban areas. Conversely, an OR value of less than 1 indicated that the hypertension prevalence estimates were higher among rural residents.

Propensity score-adjusted rural-urban differences in hypertension prevalence:

The baseline characteristics of the respondents and estimated standardised differences for all variables before and after matching were examined. A standardised difference of 10% or more suggests an imbalance. The propensity score method was utilised to account for all measured differences in baseline characteristics between respondents living in urban and rural areas. The propensity score approach was used to control all observed confounding factors that might influence assignment and outcome. The study constructed a sample of patients balanced on covariates and risk factors (listed above).

Moreover, propensity scores using logistic regression were constructed. Subsequently, each respondent was matched with health insurance with the closest propensity score using the

nearest neighbour algorithm with no replacement. The average treatment effect on hypertension, which quantifies the impact of living in urban areas, was calculated. Next, the probability ratio of having hypertension in urban and rural residents in the propensity scorematched cohort was calculated. All data were analysed using Stata software (Version 17, StataCorp, Texas USA). Finally, the null hypothesis was tested against a two-sided alternative hypothesis at a significance level of 5%.

2.5.10 Study X

After the initial selection of variables, a three-step procedure was performed to investigate the relative significance of the following factors: current health expenditure (% of GDP), domestic general government health expenditure per capita, GDP per capita (current US\$), adult literacy rate (% of people ages 15 and above), unemployment (% of the total labour force), urban population (% of the total population), multidimensional poverty index.

1. A visual analysis of scatter plots of hypertension versus each predictor variable was followed by pair-wise Pearson correlation analyses.

2. Linear regression analyses were performed to examine all possible combinations of the eight predictor variables, using adjusted R^2 to measure model strength. The relative importance of each variable was evaluated by its partial correlation.

3. Residual analysis revealed outliers and generated hypotheses for better models.

4. To investigate effect modification by country's income level (World Bank income classifications), a separate model was fitted for low-, lower-middle- and upper-middle-income countries. The R statistical package (Version 4.2.1, R Core Team, Vienna Austria) was used for all these statistical analyses

2.6 SUMMARY CHAPTER

This chapter defined the statistical methods, variables, and data sources for all the ten objectives of the study. Phase 1: Bibliometric analyses were deployed to examine the hypertension research trends using Poisson regression, citation classics and the latent Dirichlet allocation model. Phase 2: The odd ratios and decomposition analysis were performed at the individual level. Phase 3: Multivariable multilevel logistic regression analysis was deployed, a meta-analytical approach, propensity score-matching, and odd ratios were computed. Phase 4: an ecological study, a correlation, and linear regression analysis, were discussed.

The findings of the bibliometric analysis, citation classics, and topic modelling technique are discussed in the next chapter. The aim was to synthesise the existing evidence and the hypertension research productivity globally.

3 CHAPTER 3: EVIDENCE HARVEST AND MAPPING

3.1 INTRODUCTION

In this chapter, findings from three bibliometric analyses are presented. The hypertension research productivity in Africa, citation classics of 100 most cited hypertension research articles and 100 years of hypertension research were assessed to measure the impact of research outputs and productivity in low- and middle-income countries.

3.2 Study I: Geography of Hypertension Research in Africa: A Bibliometric analysis of trends in Publications Indexed in the PubMed Database

The study articulates data from **11,634** articles across **57** countries in WHO Africa Region indexed in PubMed between 1999 and 2018 (**Annex 1**). Figure 4 maps the volume of hypertension research publications across African countries. The data shows that South Africa (2533 articles), Nigeria (1621 articles), and Egypt (1561 articles) contributed most significantly to hypertension in Africa from 1998 to 2018. In contrast, Sao & Tome, Mayotte, Liberia, Guinea Bissau, Burundi, and Comoros are among the countries with the least contribution to hypertension, with fewer than ten publications.



Figure 4: Mapping hypertension research output in Africa (1999 to 2018)

Table 4 shows the difference in publications in the top-ten African countries with the highest contribution to hypertension research from 1999 to 2018. A substantial increase in published articles from most African countries was noticed throughout the period. Analyses of the AACP also confirmed a statistically significant net increase in hypertension research output from most of the top-ranking countries, with the most significant improvements coming from Ethiopia (25.1%, 95% CI 21.4 to 29.1), Ghana (22.3%, 95% CI 19.6 to 25.2), and Cameroon (20.1%, 95% CI 17.2 to 23.2). Compared to the other African countries, Guinea produced high hypertension research output. However, an overall decline in research output in the country between 1999 and 2018 can be observed (relative growth = -39.4 per year; AACP = -3.3%, 95% CI -4.9 to -1.7).

Table 3: Publication statistics of hypertension research contributions from top-ranking African countries between 1998 and 2018

Country	Total publications	Number of publications in 1999	Number of publications in 2018	Relative growth	AAPC % (95% CI)	Global research output share (%)
	2522	42	222	(70.1	12.8	0.65
South Africa	2533	43	332	6/2.1	(11.9 - 13.7) 10.7	0.41
Nigeria	1621	26	150	476.9	(9.7 - 11.8)	0.41
C					17.7	0.40
Egypt	1561	15	242	1513.3	(16.5 to 19.0)	
					-3.3	0.12
Guinea	459	33	20	39.4	(-4.9 to -1.7)	
					10.5	0.11
Tunisia	436	3	35	1066.7	(8.5 - 12.5)	
					22.3	0.11
Ghana	420	2	74	3600.00	(19.6 to 25.2)	
					14.3	0.11
Swaziland	419	7	50	614.3	(12.1-16.5)	
					20.1	0.08
Cameroon	327	4	50	1150.0	(17.2 to 23.2)	0.0 7
	270		21		13.4	0.07
Morocco	279	4	31	6/5.0	(10.8 - 16.2)	0.07
E41. i.a. i.a	267	2	57	1000.0	23.1	0.07
Ethiopia	207	3	57	1800.0	(21.4-29.1)	

CI: Confidence interval

Figure 4 illustrates the relationship of hypertension research output with the population of each country in Africa. Countries with the highest population, such as Nigeria, Egypt, and South Africa, produced significantly higher numbers of publications than the smaller countries such as Seychelles, Cape Verde, and Sao Tome and Principe. However, exceptions can be observed. Swaziland ranks in the top 10 African countries with a high number of publications, although it is a relatively smaller country.

After adjusting the size, Seychelles, Swaziland, and Cape Verde were among the top-ranked countries with the highest median number of publications per million population each year, compared to relatively large countries such as South Africa, Nigeria, and Egypt (Figure 5).



Figure 5: Scatter Plot showing the relationship between total PubMed publications and resident population in different African Countries

AGO-Angola, BDI-Burundi, BEN-Benin Republic, BFA-Burkina Faso, BWA-Botswana, CAF-Central African Republic CIV-CoteD'Ivoireeeee, CMR-Cameroon, the COD-Democratic Republic of the Congo, COG-Republic of the Congo, CPV-Cape Verde, DJI-Djibouti, DZA-Algeria, EGY-Egypt, ERI-Eritrea, ESH-Western Sahara, ETH-Ethiopia, GAB-Gabon, GHA-Ghana, GIN-Guinea, GMB-Gambia, GNB-Guinea Bissau, GNQ-Equatorial Guinea, KEN-Kenya, LBR-Liberia, LBY-Libya, LSO-Lesotho, MAR-Morocco, MDG-Madagascar, MLI-Mali, MOZ-Mozambique, MRT-Mauritania, MUS-Mauritius, MWI-Malawi, MYT-Mayotte, NAM-Namibia, NER-Niger, NGA-Nigeria, REU-Reunion, RWA-Rwanda, SDN-Sudan, SEN-Senegal, SHN-Saint Helena, SLE-Sierra Leone, SOM-Somalia, STP-Sao Tome and Principe, SWZ-Swaziland, SYC-Seychelles, TCD-Chad, TGO-Togo, TUN-Tunisia, TZA-Tanzania, UGA-Uganda, ZAF-South Africa, ZMB-Zambia, ZWE-Zimbabwe



Figure 6: Box-and-Whisker plots showing top-ranked countries by the median number of publications per year (1999 to 2018) after adjusting for population size



Figure 7: Correlation Between Number of Publications and Country's GDP

Figure 6 illustrates a significant positive correlation between the number of PubMed publications and the country's GDP (Pearson correlation r = 0.60, p <.001). Whereas **Figure 7** demonstrates the relationship of GDP with the number of PubMed publications, it can be depicted from figure 7 those wealthier African countries such as Nigeria, South Africa, and Egypt produced considerably higher publications than relatively emerging countries. However, after plotting countries' GDP by the median number of publications per year, Swaziland and Cape Verde were among the top-ranked countries compared to relatively large countries such as South Africa, Nigeria, and Egypt (**Figure 9**).



Figure 8: Scatter plot of the association between total PubMed publications and gross domestic product (GDP) for different African countries

AGO-Angola, BDI-Burundi, BEN-Benin Republic, BFA-Burkina Faso, BWA-Botswana, CAF-Central African Republic CIV-Cote D'Ivoire, CMR-Cameroon, the COD-Democratic Republic of the Congo, COG-Republic of the Congo, CPV-Cape Verde, DJI-Djibouti, DZA-Algeria, EGY-Egypt, ERI-Eritrea, ESH-Western Sahara, ETH-Ethiopia, GAB-Gabon, GHA-Ghana, GIN-Guinea, GMB-Gambia, GNB-Guinea Bissau, GNQ-Equatorial Guinea, KEN-Kenya, LBR-Liberia, LBY-Libya, LSO-Lesotho, MAR-Morocco, MDG-Madagascar, MLI-Mali, MOZ-Mozambique, MRT-Mauritania, MUS-Mauritius, MWI-Malawi, MYT-Mayotte, NAM-Namibia, NER-Niger, NGA-Nigeria, REU-Reunion, RWA-Rwanda, SDN-Sudan, SEN-Senegal, SHN-Saint Helena, SLE-Sierra Leone, SOM-Somalia, STP-Sao Tome and Principe, SWZ-Swaziland, SYC-Seychelles, TCD-Chad, TGO-Togo, TUN-Tunisia, TZA-Tanzania, UGA-Uganda, ZAF-South Africa, ZMB-Zambia, ZWE-Zimbabwe



Figure 9: Box-and-Whisker plots showing top-ranked countries by the median number of publications per year (1998 to 2018) after adjusting for country GDP

Figure 11 shows the relative countries' ranking for hypertension research output in Africa throughout the period under study. South Africa consistently produced the highest number of hypertension research publications from 1999 to 2018. Similarly, Nigeria, Egypt, and Swaziland remained among the top-ranked countries for hypertension research in Africa. Sao Tome and Principe, Liberia, and Guinea Bissau consistently generated the lowest number of research outputs throughout the study period. Some countries like Guinea, Senegal and Zimbabwe experienced an enormous decline in hypertension research output from 1999 to 2018. These countries had previously remained in the top ten African countries in this category from 1999 to 2002, then lost their positions. Conversely, Ghana, Uganda, Cameroun, Tunisia, Kenya, Cape Verde, Ethiopia, and Morocco showed continuous improvements in hypertension research output from 1999 to 2018.



Relative Rank of Hypertension Research in Africa, 1999 - 2018

Figure 10: Relative country ranking for hypertension research output in Africa from 1999 to 2018.

Figure 12 shows regional trends in hypertension research outputs between 1999 and 2018. Hypertension research publications originated mainly from South African countries. However, there has been a sharp increase in hypertension research output in all 5 African regions.



Figure 11: Depicts trends in Africa's sub-regional hypertension articles output indexed by PubMed (1999-2018).

Figure 13 presents the proportion of global hypertension research outputs throughout Africa from 1998 to 2018. Overall, there has been a net increase in Africa's contribution to international hypertension research from 1.7% in 1999 to 5.3% in 2018.

georegion

Eastern Africa Middle Africa Northern Africa Southern Africa



Figure 12: Percentage contributions of the African region to global hypertension research output from 1999 to 2018.
3.3 STUDY II CITATION CLASSICS: TOP 100 MOST CITED ARTICLES ON HYPERTENSION INDEXED IN THE WEB OF SCIENCE

In terms of the number of citations, the top 100 cited articles on hypertension were retrieved from the Web of Science in descending order (**Table 5**). The number of citations ranged from 2307 for Wright et al. (A Randomised Trial of Intensive versus Standard Blood-Pressure Control 2015), which was ranked as the 100th cited paper, to 12,555 citations for Chobian et al. (The Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure) with average per year of 697.5. The retrieved articles received 377,628 citations, with an average number of 3776.8 citations per article. The oldest article was published in 1987 by Ferrannini et al. (Insulin Resistance in essential-Hypertension). The article received 2309 citations and was published in the New England Journal of Medicine (NEJM).

S/N	Author	Title	Source	TC*
1	Chobanian A.V Roccella, E.J. (Reprint Author)	The Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, And Treatment of High Blood Pressure - The Jnc 7 Report	JAMA-Journal of the American Medical Association	12,555
2		A More Accurate Method to Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation	Annals of Internal Medicine	10,893
3	Levey A.S, Chobanian A.V, Roccella, E.J. (Reprint Author)	Seventh Report of The Joint National Committee on Prevention, Detection, Evaluation, And Treatment of High Blood Pressure	Hypertension	8,354
4	(Bevacizumab Plus Irinotecan, Fluorouracil, And Leucovorin for Metastatic Colorectal Cancer	New England Journal of Medicine	7,419
5	Hurwitz H	Free Radicals and Antioxidants in Normal Physiological Functions and Human Disease	International Journal of Biochemistry \& Cell	6,895
6		Chronic Kidney Disease and The Risks of Death, Cardiovascular Events, And Hospitalisation	New England Journal of Medicine	6,882
7	Go A.S	Harmonising the Metabolic Syndrome, A Joint Interim Statement of The International Diabetes Federation Task Force on Epidemiology and Prevention, National Heart, Lung, And Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, And International Association for The Study of Obscitu	Circulation	6,444
8	Alberti Kolvilvi,	Effects of An Angiotensin-Converting-Enzyme Inhibitor, Ramipril, On Cardiovascular Events in High-Risk Patients	New England Journal of Medicine	6,148
9	Yusuf S,	Effect of Potentially Modifiable Risk Factors Associated with Myocardial Infarction In 52 Countries (The Interheart Study): Case- Control Study	Lancet	6,042
	Vueuf S			

Table 4: Summary of top-cited articles

10	V: 66	A Comparative Risk Assessment of Burden of Disease and Injury Attributable To 67 Risk Factors and Risk Factor Clusters In 21 Regions, 1990-2010: A Systematic Analysis for The Global Burden	Lancet	6,012
11	Lim S.S,	of Disease Study 2010 Prediction of Coronary Heart Disease Using Risk Factor Categories	Circulation	5,901
12	wilson Pwr,	Age-Specific Relevance of Usual Blood Pressure to Vascular Mortality: A Meta-Analysis of Individual Data for One Million Adults In 61 Prospective Studies	Lancet	5,680
13	Lewington S, Pitt B 1999	The Effect of Spironolactone on Morbidity and Mortality in Patients with Severe Heart Failure	New England Journal of Medicine	5,469
14	1 m B, 1999,	Inference of Population Structure Using Multilocus Genotype Data: Linked Loci and Correlated Allele Frequencies	Genetics	5,319
	Falush D,			
15	Stearne M. R	Tight Blood Pressure Control and Risk of Macrovascular and Microvascular Complications in Type 2 Diabetes: Ukpds 38	BMI-British Medical Journal	4,940
16		Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012	Critical Care Medicine	4,812
17	Dellinger R. P	Physical-Activity and Public-Health - A Recommendation from The Centres-For-Disease-Control-And-Prevention and The American-	Jama-Journal of The American Medical	4,772
18	Pate R.R,	Atrial-Fibrillation as An Independent Risk Factor for Stroke - The Framingham-Study	Stroke	4,724
19	woll r. A	Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy	New England Journal of Medicine	4,563
	Brenner B.M			
20	Hoffman S. M	Mortality from Coronary Heart Disease in Subjects with Type 2 Diabetes and Nondiabetic Subjects with And Without Prior	New England Journal of Medicine	4,510
21		Prevalence of The Metabolic Syndrome Among Us Adults - Findings from The Third National Health and Nutrition Examination Survey	JAMA-Journal of The American Medical Association	4,447
22	Ford E. S Singer M, Deutschman, Cs (Reprint Author)	The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)	Jama-Journal of The American Medical	4,287
23	Natl High Blood Pressure Educ Prog NHBPEP, 2004, Paediatrics	The Fourth Report on The Diagnosis, Evaluation, And Treatment of High Blood Pressure in Children and Adolescents	Paediatrics	4,224
24	Kearney PM, He, J (Reprint Author)	Global Burden of Hypertension: Analysis of Worldwide Data	Lancet	4,202
25	Autior),	The Effect of Angiotensin-Converting Enzyme-Inhibition on Diabetic Nephropathy	New England Journal of Medicine	4,130
26	Lewis E.J,	10-Vegr Follow-Un of Intensive Chugose Control in Type 2 Disketer	New England Journal of	4 060
20	Holmon D D	10- Tear Follow-Op of Intensive Officose Control in Type 2 Diabetes	Medicine	4,000
27	noiman k.k,	Effects of Intensive Blood-Pressure Lowering and Low-Dose Aspirin in Patients with Hypertension: Principal Results of The Hypertension Optimal Treatment (Hot) Randomised Trial	Lancet	4,055
	Hansson L,			
28		Guidelines for The Management, Of Adults with Hospital-Acquired, Ventilator-Associated, And Healthcare-Associated Pneumonia	American Journal of Respiratory and Critical Care Medicine	3,942
29	[Anonymous] A,	Mechanisms of TGF-Beta Signalling from Cell Membrane to The	Cell	3,929
30	Sni YU,	Bariatric Surgery: A Systematic Review and Meta-Analysis	Jama-Journal of The American Medical	3,869
31	Buchwald H,	2013 Esh/Esa Guidalines for the management of Artorial	Association	3 961
51	Mancia G.	Hypertension the Task Force for The Management of Arterial Hypertension of The European Society Of hypertension (Esh) and The European Society Of cardiology (Esc)	Journal of Hypertension	3,804

32		Collaborative Overview of Randomised Trials of Antiplatelet Therapy .1. Prevention of Death, Myocardial-Infarction, And Stroke by Prolonged Antiplatelet Therapy in Various Categories of Patients	BMJ-British Medical Journal	3,780
33	Altman R,	Renoprotective Effect of The Angiotensin-Receptor Antagonist Irbesartan in Patients with Nephropathy Due to Type 2 Diabetes	New England Journal of Medicine	3,757
34	Lewis E.J,	2014 Evidence-Based Guideline for The Management of High Blood	Jama-Journal of The	3,739
	Invert D.A.	Pressure in Adults: Report from The Panel Members Appointed to The Eighth Joint National Committee (JNC 8) (Vol 311, Pg 507, 2014)	American Medical Association	
35	Furberg C.D, Wright, Jt (Reprint Author),	Major Outcomes in High-Risk Hypertensive Patients Randomised to Angiotensin-Converting Enzyme Inhibitor or Calcium Channel Blocker Vs Diuretic - The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (Allhat)	Jama-Journal of The American Medical Association	3,693
36	DallaffD	Cardiovascular Morbidity and Mortality in The Losartan Intervention for Endpoint Reduction in Hypertension Study (Life): A Randomised	Lancet	3,687
37	Escudier B.	Sorafenib In Advanced Clear-Cell Renal-Cell Carcinoma	New England Journal of Medicine	3,639
38	Lucia Ai	Atherosclerosis	Nature	3,625
39	Lusis Aj,	Global Strategy for The Diagnosis, Management, And Prevention of Chronic Obstructive Pulmonary Disease - Gold Executive Summary	American Journal of Respiratory and Critical	3,622
40	Rabe KI,	Insulin Resistance - A Multifaceted Syndrome Responsible for NIDDM, Obesity, Hypertension, Dyslipidaemia, And Atherosclerotic	Care Medicine Diabetes Care	3,574
41	Defronzo Ra,	Cardiovascular-Disease Carotid-Artery Intima and Media Thickness as A Risk Factor for Myocardial Infarction and Stroke in Older Adults	New England Journal of Medicine	3,515
42	O'leary Dh,	Expert Consensus Document on Arterial Stiffness: Methodological	European Heart Journal	3,508
	Laurent S,	Issues and Clinical Applications	-	
43	Mcewen Bs,	Protective and Damaging Effects of Stress Mediators	New England Journal of Medicine	3,468
44		for Men Screened in The Multiple Risk Factor Intervention Trial	Diabetes Care	3,459
45	Stamler J,	Heart Disease and Stroke Statistics-2017 Update A Report from The American Heart Association	Circulation	3,363
46	Benjamin Ej,	1999 World Health Organization International Society of Hypertension Guidelines for The Management of Hypertension	Journal of Hypertension	3,303
	Chalmers J,		_	
47	Macmahon S.	Blood-Pressure, Stroke, And Coronary Heart-Disease .1. Prolonged Differences in Blood-Pressure - Prospective Observational Studies Corrected for The Regression Dilution Bias	Lancet	3,301
48	, ,	Dietary Antioxidant Flavonoids and Risk of Coronary Heart-Disease - The Zutphen Elderly Study	Lancet	3,268
49	Hertog Mgl,	The Metabolic Syndrome and Total and Cardiovascular Disease Mortality in Middle-Aged Men	Jama-Journal of The American Medical Association	3,235
50	Lakka Hm,	2007 Esh-Esc Practice Guidelines for The Management of Arterial Hypertension - Esh-Esc Task Force on The Management of Arterial	Journal of Hypertension	3,220
51	Mancia G,	Hypertension Validation of Clinical Classification Schemes for Predicting Stroke - Results from The National Registry of Atrial Fibrillation	Jama-Journal of The American Medical	3,178
52	Gage Bf,	Prevalence of Chronic Kidney Disease in The United States	Jama-Journal of The American Medical	3,165
53	Coresh J,	Blood-Pressure, Stroke, And Coronary Heart-Disease .2. Short-Term	Association Lancet	3,147
		in Their Epidemiologic Context		
54	Collins R,	Health Benefits of Physical Activity: The Evidence	Canadian Medical Association Journal	3,145
	Warburton Der,			

55	Appel Lj, Kaiser Permanente Ctr Hlth RES, Portland	A Clinical Trial of The Effects of Dietary Patterns on Blood Pressure	New England Journal of Medicine	3,145
56	Dellinger Pn	Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Sentic Shock: 2008	Critical Care Medicine	3,129
57	Denniger Kp,	Effects of Conjugated, Equine Oestrogen in Postmenopausal Women with Hysterectomy - The Women's Health Initiative Randomized	Jama-Journal of The American Medical	3,076
58	Anderson Gl,	Controlled Trial Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor- Based Approach the Euro Heart Survey on Atrial Fibrillation	Association Chest	3,069
59	Lip Gyh,	Impotence and Its Medical and Psychosocial Correlates - Results of	Journal of Urology	3,063
60	Feldman Ha,	The Massachusetts Male Aging Study Cardiovascular Morbidity and Mortality Associated with The Metabolic Syndrome	Diabetes Care	3,056
61	Isomaa B,	Insulin Signalling and The Regulation of Glucose and Lipid Metabolism	Nature	3,053
62	Saltiel Ar,	General Cardiovascular Risk Profile for Use in Primary Care - The Framingham Heart Study	Circulation	3,047
63	D'Agostino Rb,	Liver Fibrosis	Journal of Clinical Investigation	3,043
64	Bataller R,	National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, And Stratification	Annals of Internal Medicine	2,981
65	Levey As,	The Disease Burden Associated with Overweight and Obesity	Jama-Journal of The American Medical	2,953
66	Must A,	Prospective Study of The Association Between Sleep-Disordered Breathing and Hypertension	Association New England Journal of Medicine	2,950
67	Peppard Pe, Mancia G, Zanchetti, A (Reprint Author).	2003 European Society of Hypertension - European Society of Cardiology Guidelines for The Management of Arterial Hypertension	Journal of Hypertension	2,949
68	Benjamin Fi	Impact of Atrial Fibrillation on The Risk of Death	Circulation	2,882
69	Conroy Rm, Graham, Im (Reprint Author)	Estimation of Ten-Year Risk of Fatal Cardiovascular Disease in Europe: The Score Project	European Heart Journal	2,841
70	Carmeliet P,	Angiogenesis in Health and Disease	Nature Medicine	2,830
71	Charlson M.	Validation of A Combined Comorbidity Index	Journal of Clinical Epidemiology	2,815
72	, 	The Sixth Report of The Joint National Committee on Prevention, Detection, Evaluation, And Treatment of High Blood Pressure	Archives of Internal Medicine	2,806
73	Black Hr, Amer Diabet Assoc	Standards of Medical Care in Diabetes-2014	Diabetes Care	2,775
74	Trut,	Effects on Blood Pressure of Reduced Dietary Sodium and The Dietary Approaches to Stop Hypertension (Dash) Diet.	New England Journal of Medicine	2,736
75	Sacks Fm, 2001,	Prevalence of Obesity, Diabetes, And Obesity-Related Health Risk Factors, 2001	Jama-Journal of The American Medical	2,727
76	Mokdad Ah, Gaede P, Pedersen, O (Reprint Author)	Multifactorial Intervention and Cardiovascular Disease in Patients with Type 2 Diabetes	Association New England Journal of Medicine	2,709
77	Kamath Ps, Kim, Wr (Reprint	A Model to Predict Survival in Patients with End-Stage Liver Disease	Hepatology	2,697
78	Dimmeler S, Zeiher, Am (Reprint Author).	Activation of Nitric Oxide Synthase in Endothelial Cells by AKT- Dependent Phosphorylation	Nature	2,678
79	"	Long-Term Cardiovascular Outcomes in Men with Obstructive Sleep Apnoea-Hypopnoea with or Without Treatment with Continuous Positive Airway Pressure: An Observational Study	Lancet	2,675

Marin Jm,

80	Sjostrom L,	Lifestyle, Diabetes, And Cardiovascular Risk Factors 10 Years After Bariatric Surgery	New England Journal of Medicine	2,670
81	Haslam Dw	Obesity	Lancet	2,665
82	Trashani D,	Predicting Obesity in Young Adulthood from Childhood and Parental Obesity	New England Journal of Medicine	2,651
83	Whitaker Rc, Cai H, Harrison, Dg (Reprint Author)	Endothelial Dysfunction in Cardiovascular Diseases - The Role of Oxidant Stress	Circulation Research	2,635
84	Laurent S.	Aortic Stiffness Is an Independent Predictor of All-Cause and Cardiovascular Mortality in Hypertensive Patients	Hypertension	2,599
85		Global Mortality, Disability, And the Contribution of Risk Factors: Global Burden of Disease Study	Lancet	2,583
86	Murray Cjl,	A Comparison of Rate Control and Rhythm Control in Patients with Atrial Fibrillation	New England Journal of Medicine	2,571
87	Wyse Dg, Malliani A	Cardiovascular Neural Regulation Explored in The Frequency-	Circulation	2,565
88	Sever Ps.	Prevention of Coronary and Stroke Events with Atorvastatin in Hypertensive Patients Who Have Average or Lower-Than-Average Cholesterol Concentrations, In the Anglo-Scandinavian Cardiac Outcomes Trial-Lipid Lowering Arm (Ascot-LLA): A Multicentre Randomised Controlled Trial	Lancet	2,562
	Poulter, Nr (Reprint Author),			
89		Comparison Of C-Reactive Protein and Low-Density Lipoprotein Cholesterol Levels in The Prediction of First Cardiovascular Events.	New England Journal of Medicine	2,478
90	Ridker Pm, Katz A, Quon, Mj (Reprint Author)	Quantitative Insulin Sensitivity Check Index: A Simple, Accurate Method for Assessing Insulin Sensitivity in Humans	Journal of Clinical Endocrinology \& Metabolism	2,462
91	Autior),	Abiraterone And Increased Survival in Metastatic Prostate Cancer	New England Journal of Medicine	2,444
92	De Bono Js,	Primary Prevention of Cardiovascular Disease with Atorvastatin in Type 2 Diabetes in The Collaborative Atorvastatin Diabetes Study (Cards): Multicentre Randomised Placebo-Controlled Trial	Lancet	2,436
	Colhoun Hm,			
93	V T	Epidemiology of Obstructive Sleep Apnoea - A Population Health Perspective	American Journal of Respiratory and Critical	2,425
94	Maynard Se, Karumanchi, Sa	Excess Placental Soluble FMS-Like Tyrosine Kinase 1 (Sflt1) May Contribute to Endothelial Dysfunction, Hypertension, And Proteinuria in Preeclampsia	Journal of Clinical Investigation	2,414
95	(Reprint Author),	Association Between Multiple Cardiovascular Risk Factors and Atherosclerosis in Children and Young Adults	New England Journal of Medicine	2,371
96	Owan Te, Redfield, Mm	Trends in Prevalence and Outcome of Heart Failure with Preserved Ejection Fraction	New England Journal of Medicine	2,363
97	(Reprint Author), Marshall D, Nord Sah Publ Hith	Meta-Analysis of How Well Measures of Bone Mineral Density Predict Occurrence of Osteoporotic Fractures	British Medical Journal	2,362
98	Dalonzo Ge,	Survival in Patients with Primary Pulmonary-Hypertension - Results from A National Perspective Registry	Annals of Internal Medicine	2,337
99	Ferrannini E,	Insulin Resistance in Essential-Hypertension	New England Journal of Medicine	2,309
100	Wright Jt,	A Randomised Trial of Intensive Versus Standard Blood-Pressure Control	New England Journal of Medicine	2,307

*TC: Total citation

Several eligible studies regarding hypertension research were published between 1987 and 2017. They primarily entailed research into fatal (cardiovascular and all-cause mortality) and

non-fatal complications of hypertension, including coronary heart disease and stroke. Articles were published across 29 journals (impact factor ranged from 2.9 to 79.3), including The New England Journal of Medicine (25%) and Lancet (14%). The Journal of the American Medical Association (13%) accounts for more than half of the published Top 100 cited publications on hypertension **(Table 6)**.

Sources	Articles	Impact	Times Cited/no	h-index	m-index	Pub
		factor	Citation			year-
						start
New England Journal	25	79.258	91264		0.74	
of Medicine				25	0., 1	1987
Lancet	14	53.254	52315	14	0.452	1990
Jama-Journal of The	13	5.325	55696			
American Medical					0.500	
Association				13		1995
Circulation	6	18.88	24202	6	0.200	1991
Diabetes Care	4	6.823	12864	4	0.133	1991
Journal of	3	19.384	13336		0.182	
Hypertension				3	0.110_	1999
American Journal of	3	13.397	9989			
Respiratory and Critical					0.158	
Care Medicine				3		2002
Annals of Internal	3	23.425	16211		0.100	
Medicine				3	0.100	1991
Nature	3	6.823	9356	3	0.136	1999
BMJ-British Medical	2	15.211	8720		0.074	
Journal				3	0.071	1994
Critical Care Medicine	2	6.63	7941	2	0.154	2008
European Heart Journal	2	2.872	6349	2	0.111	2003
Hypertension	2	41.577	10953	2	0.100	2001
Journal of Clinical	1	15.239	5457		0.111	
Investigation				2	0.111	2003
Archives of Internal	1	6.78	2806		0.042	
Medicine		(2015)		1	0.042	1997
British Medical Journal	1		2362	1	0.040	1996
Canadian Medical	1	1.21	3145		0.067	
Association Journal		(2015)		1	0.007	2006
	1	20.785	3929		0.056	
Cell		(2016)		1	0.050	2003
Chest	1	6.21	3069	1	0.091	2010
Circulation Research	1	2.363	2635	1	0.048	2000
Genetics	1	7.652	5319	1	0.056	2003
Hepatology	1	14.079	2697	1	0.050	2001
International Journal of			6895			
Biochemistry \& Cell					0.071	
Biology						2007
Journal of Clinical	1	3.247	2462			
Endocrinology \&					0.048	
Metabolism				1		2000

Table 5: Summary of source impact

Journal of Clinical Epidemiology	1	4.245	2815	1	0.037	1994
Journal of Urology	1	5.157 (2016)	3063	1	0.037	1994
Nature Medicine	1	32.621	2830	1	0.056	2003
Paediatrics	1		4224	1	0.059	2004
Stroke	1	6.239	4724	1	0.033	1991

The United State of America (USA) had the highest number (54) of hypertension research articles with the most significant number of citations (n= 207808), followed by the United Kingdom with 11 articles (citation=45824), Italy with 3 articles (citation=14907) and Canada with 3 articles (citation = 15335) (**Figure 14**).



Most Cited Countries

Figure 13: Most Cited Countries

The findings also revealed that the USA had 39 Single Country Publications (SCP) (Publications where all the contributing authors are affiliated with the same country) and 15 Multiple Country Publications (MCP) (Publications where the contributing authors are

affiliated with more than one country which, in turn, represents inter-country collaboration) (Figure 15).



SCP: Single Publication Country Publication

MCP: Multiple Country Publication

Most of the publications on hypertension research were published by institutions in the USA. Harvard University had the highest number of publications (n=15), followed by Boston University (n = 14) and Brigham Women's Hospital (n = 13). Globally, The University of Milan, Italy (n=6), the University Hospital U.K. (n=6), and Sahlgrens University Hospital, Sweden (n=5), were among the top productive institutions (Figure 16). In essence, all the 100 articles were published in high-income countries. More than half of the worldwide articles in hypertension-related journals were published in the USA. It can be observed in Table 7 that more than 50% of the studies are conducted in the USA and U.K.

Most Relevant Affiliations



*UNIV: University * HOSP: Hospital

Figure 15: Most Relevant Affiliations

Table 6: List of countries with the highest number of publications

			Average		Single	Multi-	
Company	Autialaa	Total Citations	Article	Davaantaga	Country Dublication	Country Dublic	MCP Datia
Country	Articles	Citations		Percentage	Publication	Public	
USA United	54	207808	2848 4166	58.1	39	15	0.38
Kingdom	11	45824	1100	11.8	4	7	0.6
Italy	5	14907	2981	5.4	2	3	0.6
Sweden	4	12774	3194	4.3	1	3	0.8
Canada	3	15335	5112	3.2	3	0	0.0
France	3	9746	3249	3.2	1	2	0.7
Germany	2	7997	3998	2.2	1	1	0.5
Ireland	2	5277	2638	2.2	1	1	0.5
Netherlands	2	6890	3445	2.2	1	1	0.5
Australia	1	3303	3303	1.1	1	0	0.0
Belgium	1	2830	2830	1.1	1	0	0.0
Denmark	1	2709	2709	1.1	1	0	0.0
Finland	1	3056	3056	1.1	0	1	1.0
Israel	1	2414	2414	1.1	1	0	0.0
Slovakia	1	6895	6895	1.1	0	1	1.0
Spain	1	2675	2675	1.1	1	0	0.0

MCP: Multiple Country Publication

Figure 17 shows a visualisation of the most frequently referenced topics. Coronary heart disease and blood pressure were the most referenced topics.



Figure 16: Most Frequently Referenced Topics

Figure 18 provides the list of the top 20 of the most productive and active authors in the field of research. Oparil. S had the highest number of publications (6 articles), citation, and h-index.

It also indicates that 93% of the top-cited articles were co-authored, while 7% were singleauthored publications.



Most Relevant Authors

Figure 17: Most Relevant Authors

The findings revealed that the previously published articles contain more citations than the recent ones, which appears to be a limitation. To adjust this, the number of citations was divided by the number of years since publications to determine a citation rate/mean citation per year, as listed in **Table 8**. The citation rates for the top 10 articles ranged from 3363 for Benjamin et al. (Heart disease and Stroke Statistics-2017 Update A Report from the American Heart Association) to 693.8 for the American Diabetic Association (Standard of Medical Care in Diabetes-2014). Benjamin et al.'s article had a total citation of 3363 and ranked as the 68th top-cited article. In contrast, Chobian et al.'s article that received the most significant number of citations had a lower citation rate of 837.

S/N	Authors	Title	Total Citation	Publication	No of Years Since Publication	Citation Rate (Per Veer)
5/11	Authors	The	Citation	year	Fublication	rear)
1	Benjamin et al.	Heart Disease and Stroke Statistics-2017 Update A Report from The American Heart Association	3363	2017	1	3363.0
2	Singer M;	The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) A Comparative Risk Assessment of Burden of Disease and Injury Attributable To 67 Risk Factors and Risk Factor Clusters In 21 Regions	4287	2016	2	2143.5
3	Lim et al	1990-2010: A Systematic Analysis for The Global Burden of Disease Study 2010	6012	2012	6	1002.0
4	Dellinger Rp;	International Guidelines for Management of Severe Sepsis and Septic Shock: 2012	4812	2013	5	962.4
5	James Da	2014 Evidence-Based Guideline for The Management of High Blood Pressure in Adults: Report from The Panel Members Appointed To The Eighth Joint National Committee (Jnc 8) (Vol 311, Pg 507, 2014)	3730	2014	Α	034 8
5	Chobanian	The Seventh Report of The Joint National Committee on Prevention, Detection Evaluation And Treatment of	5759	2014	т	75- .0
6	A.V;	High Blood Pressure - The Jnc 7 Report	12555	2003	15	837.0
7	Mancia G;	2013 Esh/Esc Guidelines for The Management of Arterial Hypertension the Task Force for The Management of Arterial Hypertension of The European Society of Hypertension (Esh) And the European Society of Cardiology (Esc)	3864	2013	5	772.8
8	Wright J. T	A Randomised Trial of Intensive Versus Standard Blood-Pressure Control Harmonising The Metabolic Syndrome, A Joint Interim Statement of The International Diabetes Federation Task	2307	2015	3	769.0
		National Heart, Lung, And Blood Institute, American Heart Association, World Heart Federation, International Atherosclerosis Society, And International Association for The Study				
9	Alberti Amer	of Obesity	6444	2009	9	716.0
10	Diabet Assoc Ada	Standards Of Medical Care in Diabetes- 2014	2775	2014	4	693.8

Table 7: Top 10 Articles with Highest Citation Rate

3.1 STUDY III: ONE HUNDRED YEARS OF RESEARCH ON HYPERTENSION: MACHINE LEARNING CLASSIFICATIONS OF TOPICS

A total of 581,750 articles on hypertension research were indexed between 1900 and 2018 in PubMed. As shown in **Figure 19**.



Figure 18: Trends in the number of hypertension research indexed in PubMed (1900 to 2018).

The number of publications has been increasing exponentially over the period. The studied period was divided into three stages: the first stage ranged from 1900 to 1940 (average publication: 7 per year), the second stage ranged from 1941 to 1990 (3,000 per year), and the third stage ranged from 1991 to 2018 (15,000 per year). From 1991 to 2018, hypertension publications rapidly increased, accounting for almost 75% of the entire research (434,487/ 581,750; 74.7%). **Table 9** contains three columns consisting of topic names and 15 keywords inside the topics and their probabilities. It manually attached a label that best captures the semantics of the words.

Classification and topic	Keywords	%
name		
Pre-clinical studies		
Topic 5: Human Proteome	cell, protein, human, activit, tissue, express, use, study, factor, show, membrane, model, peptide antibody, tumor	4.0
Topic 9: Biochemical	plasma, method, use, concentr, sampl, determin, liquid, detect, extract, chromatographi, acid, human, metabolit, pharmacokinet, serum	5.6
Topic 11: Plasma renin activity	plasma, hypertens, effect, level, increas, signific, activ, renin, concentr, blood, urinari, calcium, excret, serum, decreas	4.7
Topic 12: Animal model	rat, hypertens, increas, activ, receptor, vascular, effect, express, oxid, shr, inhibit, respons, mice, role, cell	6.5
Topic 17: Physiology	brain, respons, sympathet, rate, increas, activ, heart, effect, pressur, group, control, nerv, hypotens, system, signific	3.4
Topic 20: Genetics	gene, hypertens, associ, genet, polymorph, studi, genotyp, famili, mutat, allel, signific, variant, control, analysi, phenotyp	2.1
Epidemiology		
Topic 1: Risk factors	risk, age, studi, associ, factor, hypertens, preval, women, blood, vear, men, among, level, cholesterol, high	6.5
Topic 2: Evidence review	diseas, hypertens, use, clinic, care, review, health, medic, manag, cardiovascular, patient, prevent, includ, studi, treatment	10.1
Topic 3: blood pressure measurement	pressur, blood, measur, flow, arteri, exercis, mmhg, hypertens, increas, mean, chang, use, differ, signific, studi	5.8
Topic 13: Correlation studies	hypertens, patient, group, arteri, signific, systol, pressur, function, diastol, age, subject, correl, index, left, studi	3.8
Topic 16: Diets	diet, intak, blood, sodium, dietari, salt, group, pressur, effect, vitamin, hypertens, weight, increas, high, acid	2.5
Complications	······································	
Topic 4: Cardiopulmonary	group, transplant, oxygen, patient, lung, acut, increas, dialysi, iniuri, level, ventil, signific, high, pulmonari, respiratori	3.0
Topic 6: Hypertrophic cardiomyopathy	cardiac, heart, ventricular, left, myocardi, coronari, failur, hypertrophi, right, arteri, increas, atrial, group, infarct, function	3.2
Topic 7: chronic kidney disease	renal, kidney, arteri, diseas, patient, function, portal, chronic, caus, children, stenosi, adren, treatment, case, progress	5.3
Topic 8: Metabolic syndrome	metabol, diabet, syndrom, insulin, obes, glucos, level, type, associ, resist, sleep, patient, increas, met, serum	3.4
Topic 14: Cardiopulmonary	pulmonari, patient, hypertens, arteri, diseas, pah, lung, sever, heart clinic right valy transplant associ vascular	4.4
Topic 15: Maternal heart disease	women, pregnanc, hypertens, matern, gestat, infant, birth, fetal, preeclampsia deliveri neonat studi pregnant outcom group	2.5
Topic 19: Major Cardiovascular	patient, risk, diseas, factor, associ, diabet, studi, stroke, age,	7.0
Treatment	year, mortal, coronari, cardiovascular, mold, use	
Topic 10: Antihypertensive	nations treatment hypertens affect therein drug group blood	70
Topic 10. Anunypertensive	pressur, studi, antihypertens, trial, control, combin, signific	1.9
Topic 18: Heart surgery	patient, case, hypertens, surgeri, present, complic, report, surgic, portal, clinic, year, postop, vein, one, intracrani	8.5

Table 8: Topic classification and keywords on hypertension

Most of the uncovered topics can be grouped into four categories (i.e., Preclinical, Epidemiology, Complications, and Treatment-related Studies). 'Animal Model', topic 12, is the most prevalent topic in the 'Pre-Clinical Studies' category. It contains salient words like

'rat', 'inhibit', 'mice', and 'cell'. Whereas topic 2, 'Evidence Review', best suits the category of 'Risk Factors Studies'. It contains salient words like 'disease', 'review', and 'prevent'. Topic 19 'Major Cardiovascular Events' lies best in the 'Complications Studies' category. It contains salient words like 'stroke', 'coronary', and 'mortal'. Topic 18, 'Antihypertensive' and topic 18, 'Heart surgery', are categorised into 'Pharmacotherapy' and 'Interventional Cardiology' studies.

Figure 20 shows clustering topics where topics are connected based on the similarity of topic probability distributions over the documents. The topics that were more likely included in the same articles had a high level of similarity in the distribution of topics over the documents. Hence these topics were paired or clustered together. Several interesting clusters can be observed in the figure above. For instance, topic 5 'Human Proteome', topic 9 'Physiology' and topic 20 'Genetic' are paired, which means all these articles emphasise the Pathophysiology of Hypertension.

Another example is topic 11, 'Plasma Renin Activity, topic 7, 'Chronic Kidney Disease', and topic 18, 'Heart Surgery', were often discussed in the same articles. It is important to note that topic 15, 'Maternal Heart Disease', is the only topic not connected to other topics. This is because topic 15 is not usually discussed in the same article with other topics.



Figure 19: Clustering Topics

Figure 20 shows the temporal dynamics of the distributions of all topics. It demonstrates how the population of each topic has changed relative to other topics over time. The interpretation

of these trends is speculative. However, three categories of interest were identified: 'Increasingly Hot' (topics 1, 2, 12, and 19), 'Decreasingly Cold' (topics 3, 7, 10, 11, 17, and 18), and 'Infrequently Published' (topics 4, 5, 6, 8, 9, 13, 14, 15, 16 and 20). Topic 2, 'Evidence Review' and topic 19, 'Major Cardiovascular events', are the key 'hot topics. Most cardiopulmonary disease subtopics show slight variation over time and only make a small contribution in terms of proportions.



Figure 20: Dynamics and trends of the topics

Article sentiment analysis

The highest proportion of articles was framed with a negative valency (71.2%), followed by positive (20.6%) and neutral valences (8.2%). Yearly sentiment trends with hypertension articles are shown in **Figure 22**.



Figure 21: Dynamics and trends of the article valency

Negative sentiments articles decreased slightly between 1980 and 2000. At the same time, both positive and neutral sentiments articles increased to some extent over the same period. The top 20 frequently used positive and negative words are shown in **Figure 23**.



Figure 22: Top 20 negative and positive words

'Risk', 'chronic', 'syndrome', 'failure', and 'severe' were the more common negative sentiments words. Whereas 'healthy', 'effective', 'positive', 'survive', and 'improved' were the more common positive sentiments words.

3.2 CHAPTER SUMMARY

The reviews measure the contribution of African countries to global hypertension research, citation analysis, publication counts, journal rankings and emerging topics in hypertension research. The findings provide evidence on the impact of research outputs and identify new emerging areas of research and high impact journals. Bibliometric analysis was chosen to assess the research productivity across the selected low- and middle-income countries and to understand the pattern and trend of hypertension research to guide strategic decisions by academic managers and policymakers.

The following chapter identifies HIV and GBV as individual compositional novel risk factors based on the literature review. The risk factors are discussed in the next chapter.

4 CHAPTER 4: INDIVIDUAL COMPOSITIONAL NOVEL RISK FACTORS

4.1 INTRODUCTION

This chapter examines the contribution of the HIV and gender-based violence on hypertension risk at the individual level. HIV is a biological risk factor, while GBV is preventable risk factor. Therefore, Public health education and raising awareness interventions at this level are expected to promote attitudes and behaviour change, invariably improving health outcomes.

4.2 STUDY IV: ASSOCIATION BETWEEN HIV AND HYPERTENSION IN LOW-AND MIDDLE-INCOME COUNTRIES: A TALE OF THREE SETTINGS

The sample and survey characteristics, including the list of countries, years of data collection, and survey characteristics, are presented in **Table 10.** A total of 812,910 participants drawn from five countries from low- and middle-income countries participating in the DHS surveys between 2013 and 2016 were as included in the analysis. Table 10 presents the descriptive statistics for the final pooled sample. The median number of neighbourhoods sampled was 546, ranging from 399 in Lesotho to 28,408 in India. The respondents included in the analysis ranged from 3,630 in Namibia to 781,117 in India. The human development index was low for all the countries except South Africa.

Table 10: Table 9: Summary	of pooled sample characteristics	of the Demographic and Health
Surveys data in selected low-	and middle-income countries	

Country	Survey year	Number of Neighbourhoods	Sample Size	Human Development Index	Hypertension (%)
Ghana	2014	427	13,741	Low	13.5

India	2015	28408	781,117	Low	16.5
Lesotho	2014	399	6,076	Low	19.5
Namibia	2013	546	3,630	Low	46.2
	2016	710	0.246	TT' 1	10
South	2016	718	8,346	High	48
Africa					

Association between HIV and hypertension risk

Figure 24 shows the rate of hypertension among those living with HIV and HIV-negative participants. Among people living with HIV, hypertension ranged from 13.5% in Ghana to 48.5% in South Africa. Hypertension ranged from 13.8% in Ghana to 48.0% in South Africa and Namibia among HIV-negative participants.



Figure 23: Risk difference (RD) between people living HIV and HIV negative in hypertension risk by countries

Figure 24 also shows the risk difference (a measure of inequality) in hypertension between HIV and HIV-negative participants. Out of the five countries included in this analysis, one country (India) showed pro-HIV inequality (i.e., hypertension is prevalent among the people living with HIV), Namibia showed pro-non-HIV inequality (i.e., hypertension is prevalent

among HIV negative participants) and remaining three countries showed no statistically significant inequality. In India, 120 of 484 (24.8%) people living with HIV were hypertensive compared with 38,763 of 221,011 (17.5%) HIV-negative participants. In Namibia, 264 of 694 (38.0%) people living with HIV were hypertensive compared with 1323 of 2759 (48.0%) HIV-negative participants.

Decomposition of HIV-Related Inequality in Hypertension Risk

Figure 25 shows the detailed decomposition of the part of the inequality caused by the compositional effects of the determinants. The critical factors responsible for the disparity differed across the two countries. In India, the participants' age following obesity was the most important factor explaining the differential in hypertension risk. In Namibia, the most significant contribution to the inequality in hypertension was obesity, followed by the participant's age and HAP.



Figure 24: Contributions of differences in the distribution of 'compositional effect' of the determinants of hypertension risk to the total gap between people living with HIV and HIV negative participants.

4.3 STUDY V: GENDER-BASED VIOLENCE AND THE RISK OF HAVING HYPERTENSION. A SECONDARY ANALYSIS OF THE KYRGYZSTAN DEMOGRAPHIC HEALTH AND SURVEY

The characteristics of the participants are summarised in **Table 11**. The prevalence of hypertension was 10.3%. The number of respondents with blood pressure sampled in the Kyrgyzstan Republic included in the analysis was 100% females 4,793, and most of the respondents belonged to 25-34 years age group (39.08%). In comparison, 13.2% of the respondents belong to the 45-54 years age group. Most of the respondents had secondary or higher education (99.7%) while less than 0.02% had no education, and only 0.25% had primary education. About 18.1% and 19.49% of the respondents in the Kyrgyzstan Republic belonged to the richest and richer wealth quintile, respectively. Around 62% cumulatively belonged to the poorest, poorer middle wealth quintile and 33.8% of the respondents belong to the working class, while 66.2% reported not working. Approximately 69.2% of the participants live in rural areas, while 30.8% live in urban areas. Of the respondents, 31.7% and 14.0% were overweight and obese, respectively. Respondents exposed to GBV/IPV in the Kyrgyzstan Republic were 23.6% more likely to develop hypertension than respondents not exposed to GBV.

The percentage of individuals with hypertension was significantly higher among the 35-44 years age group. Approximately, 40.0% of respondents, in this age group, reported to be hypertensive and were exposed to gender-based violence. The prevalence was lower among participants aged 15-24 years (0.05%), followed by those aged 25 to 34 years (22.5%). Respondents with primary or no education were more likely to be exposed to GBV. The prevalence of hypertension was significantly higher amongst all respondents with secondary and higher education. The burden of hypertension was higher among the poorest households than among respondents from the wealthiest families (24.6% versus 15.7%), p<0.0001). The prevalence of hypertension was higher among respondents who were not working (61.5%) than respondents in the working class (38.0%). Additionally, the prevalence was higher among rural

residents exposed to GBV than urban residents exposed to GBV (73.0% versus 27.0%). Overweight (38.4%) and obese (32.0%) respondents exposed to GBV were more likely to be hypertensive than average weight (28.3%), and underweight (1.14%) respondents exposed to GBV.

	Number	Percentage	Normotensive Percentage	Hypertensive Percentage	p-value
			%	%	
Sex					< 0.001
Female	4,793	100.0	87.0	13.0%	
Education					< 0.001
No education	1	0.02	100	0.0	
Primary	12	0.25	91.6	8.33	
Secondary+	4,780	99.73	87.0%	12.9	
Wealth	,				< 0.001
Poorest	998	20.82	84.7	15.3	
Poorer	991	20.68	85.0	15.0	
Middle	1,002	20.91	88.5	11.5	
Richer	934	19.49	88.5	11.5	
Richest	868	18.11	88.7	11.3	
Not working					< 0.001
Working	1.617	33.83	85.4	14.6	
Not working	3,163	66.17	88.0	12.0	
Body Mass Index					< 0.001
Underweight	188	3.96	96.3	3.72	
Normal weight	2.383	50.24	92.7	7.30	
Overweight	1.505	31.73	83.9	15.6	
Obese	667	14.06	70.4	29.5	
Place of Residence				_,	< 0.001
Rural	3.317	69.21	86.3	13.6	
Urban	1,476	30.79	88.6	11.4	
Ago of households					<0.001
15 to 24	850	17 73	06.2	2.8	\0.001
15.0024	1 873	30.08	90.2 02 5	5.0 7 5	
25 to 34	1,075	20.06	92.5	17.1	
15 to 51	1, 4 30 634	29.90 12.22	68.0	32.0	
+0 00 0+	034	13.23	00.0	52.0	

Table 10: Summary of Sample Characteristics of Survey Data in the Kyrgyzstan Republic

Association between Gender-based Violence and hypertension

The measure of association between GBV and hypertension is summarised in **Figure 26**. Participants exposed to GBV were 24% more likely to have hypertension than those not exposed to GBV (COR = 1.24, 95% CI 1.03 to 1.48), such that 621 (13%) of the total sample of 4,793 were hypertensive. Out of the 1,401 exposed to GBV, 206 (14.7%) had hypertension, while 415 (12.2%) were not exposed to GBV but were hypertensive. When stratified by education, place of residence, and work status, participants who were not working and exposed to GBV were 45% more likely to develop hypertension than those not working and not exposed to GBV (OR=1.45, 95% (1.15-1.81). In addition, rural residents exposed to GBV were 29% more likely to have hypertension than those not exposed to GBV (OR = 1.29, 95% CI 1.04 to 1.59).



Figure 25: Association between exposure to GBV and hypertension risk

Figure 27 describes the age trajectories of hypertension among participants exposed to genderbased violence and participants not exposed to GBV. The odds of experiencing a higher prevalence of hypertension among those exposed to GBV increase with increasing age. The difference was more pronounced after 45 to 80 years of age.



Figure 26: Age trajectories of hypertension among participants exposed to gender-based violence Vs participants not exposed to GBV.

4.4 CHAPTER SUMMARY

In this chapter variations among HIV-positive and negative individuals across LMICs regarding hypertension risks was found. The study also found GBV a problem in the Kyrgyzstan republic. Community and societal contextual risk factors will be examined in the next chapter using a multi-level analysis and ecological analysis to understand hypertension risk factors beyond the individual-level factors. The study will have a high translational potential and may provide insight into novel risk factors for hypertension and suggest new preventive targets that can be exploited for public health interventions.

5 CHAPTER 5: COMMUNITY AND SOCIETAL CONTEXTUAL NOVEL RISK FACTORS

5.1 INTRODUCTION

In this chapter, both community and societal contextual risk factors are presented. A multilevel, secondary data analysis, meta-analysis, and ecological techniques are chosen to examine the community and country-level factors. This is to identify and understand the neighbourhood contextual risk factors of hypertension. The influence of socioeconomic position, HAP, ruralurban disparity, urbanicity and socioeconomic determinants of health are discussed in detail:

5.2 STUDY VI: INFLUENCE OF CONTEXTUAL SOCIOECONOMIC POSITION ON HYPERTENSION RISK IN LOW- AND MIDDLE-INCOME COUNTRIES: DISENTANGLING CONTEXT FROM COMPOSITION

The list of countries, years of data collection, and survey characteristics are presented in **Table 12.** The median number of neighbourhoods sampled was 498, ranging from 316 in the Kyrgyz Republic to 28,408 in India. The number of respondents included in the analysis ranged from 3,630 in Namibia to 781,117 in India. The prevalence of hypertension ranged from 10.3% in the Kyrgyz Republic to 52.2% in Haiti.

Table 11:	Description of	Demographic	and Health	Surveys	data in	low- and	d middle	-income
countries	, 2011 to 2018							

Country	Survey year	Number Neighbourhoods	of	Sample Size	Human Development Index	Hypertension (%)
Albania	2018	715		20846	High	29.9
Bangladesh	2011	600		7887	Low	29.4
Benin	2018	555		6700	Low	22.2
Ghana	2014	427		13741	Low	13.5
Haiti	2017	450		4615	Low	52.2
India	2015	28408		781117	Low	16.5
Kyrgyz Republic	2012	316		10487	High	10.3

Lesotho	2014	399	6076	Low	19.5
Namibia	2013	546	3630	Low	46.2
Nepal	2016	383	14823	Low	22.4
South Africa	2016	718	8346	High	48
Tajikistan	2017	366	10657	High	12.1

The descriptive statistics for the final pooled sample are presented in **Table 13**. For this analysis, the data of 888,925 respondents (Level 1) nested within 33,883 neighbourhoods (Level 2) from 12 countries (Level 3) in LMICs. Most of the respondents were female (84%), had secondary or higher education (61%), and were currently married (70%). One in five respondents did not have access to a newspaper, television, or radio. A relatively equal number of respondents were exposed to indoor air pollution. Approximately 15% of the respondents had health insurance, and a few respondents reported that they had problems getting money for treatment. Only about 3% of the respondents reported a history of cigarette smoking. The percentage of individuals with hypertension was higher among males than females (21.2% versus 16.8%, p<0.0001). Respondents from wealthier households had a significantly higher prevalence of hypertension than those from poorer families (20.4% versus 14.1%, p<0.0001). Respondents who were average weight (15.0%) and underweight (9.5%, p<0.0001). The prevalence of current smoking was significantly higher among smokers than non-smokers (23.1% versus 16.9%, p<0.0001).

Table 12: Summary of pooled sample characteristics of the Demographic and Health	Surveys
data in low- and middle-income countries, 2011 to 2018	

			Normotensive	Hypertensive	
	Number	Percentage	Percentage	Percentage	
			%	%	p-value
Sex					< 0.001
Male	143171	16.1	78.8	21.3	
Female	745754	83.9	83.2	16.8	
Education					< 0.001

No education	216545	24.4	80.4	19.6	
Primary	130884	14.8	79.0	21.0	
Secondarv+	539716	60.8	84.1	15.9	
Wealth					< 0.001
Poorer	287855	33.3	85.9	14.1	
Middle	287852	33 3	82.7	173	
Richer	287853	33.3	79.6	20.5	
Marital status	207035	55.5	19.0	20.5	<0.001
Never married	222530	25.9	92.3	77	0.001
Currently married	603679	70.2	79.8	20.2	
Previously married	3/120	10.2	77.0	20.2	
Rody Mass Index	54129	 0	/ 4. /	25.5	<0.001
Underweight	178086	20.4	90.5	0.5	<0.001
Normal weight	518077	20. 4 50.5	90.3	9.5	
Overweight	121977	15 1	83.0 70.0	13.0	
Obere	131073	5.0	70.0	30.0	
	43372	5.0	57.5	42.0	<0.001
Access to media	202765	22.0	05.5	14.0	<0.001
0	202765	22.8	85.5	14.6	
1	325536	36.6	82.0	18.0	
2	305967	34.4	81.8	18.3	
3	54657	6.2	78.0	22.0	
Indoor air pollution					<0.001
Low	444874	50.1	80.9	19.1	
High	444049	50.0	84.0	16.0	
Have any health					< 0.001
insurance					
No	754999	84.9	82.8	17.2	
Yes	133926	15.1	81.3	18.7	
Problem getting the					< 0.001
money needed for					
treatment					
No	534161	73.7	83.6	16.4	
Yes	191145	26.4	82.8	17.2	
Cigarette smoking					< 0.001
No	821951	97.1	83.1	16.9	
Yes	24669	2.9	76.9	23.1	
Neighbourhood					< 0.001
disadvantage					
Least	296341	33.3	79.5	20.5	
Moderate	296308	33.3	82.1	179	
Higher	296276	33 3	85.8	14.2	
Human developme	ent	0010	0010	1	< 0.001
index					01001
Low	396577	44.6	82.1	18.0	
Moderate	442012	49 7	83.6	16.0	
High	50336	57	75.0	25.0	
	50550	5.1	73.0	23.0	

Measures of associations (fixed effects)

The results of the different models are shown in **Table 14.** In the fully adjusted model, the effects of the individual-, neighbourhood- and country-level factors were controlled for, and the findings showed that for every 10-year increase in the age of the respondents, the odds of having hypertension increased by 74% (AOR = 1.74, 95% CI 1.73 to 1.76). The odds of having

hypertension increased with increasing educational attainment and wealth index. Respondents with secondary or higher education were 4% more likely to have hypertension than those with no education (OR = 1.04, 95% CI 1.02 to 1.06). Similarly, respondents from wealthier households were 8% more likely to have hypertension (OR = 1.08, 95% CI 1.05 to 1.12). Respondents who were currently (OR = 1.35, 95% CI 1.32 to 1.38) or ever married (OR = 1.37, 95% CI 1.32 to 1.42) were 35% and 37% more likely to have hypertension than those who were never married, respectively. Respondents overweight (OR = 1.72, 95% CI 1.69 to 1.75) and obese (OR = 2.67, 95% CI 2.60 to 2.74) were almost two and three times more likely to have hypertension than those with average body weight. Respondents who reported money problems with assessing care were 8% more likely to have hypertension (OR = 1.08, 95% CI 1.08, 95% CI 1.06 to 1.09) than those who do not have money problems. Respondents who smoked cigarettes were 13% more likely to have hypertension than those who did not smoke cigarettes (OR = 1.13, 95% CI 1.04 to 1.23). Respondents living in the least deprived areas were 14% more likely to have hypertension than those from the most deprived areas (OR = 1.14, 95% CI 1.10 to 1.17).

Measures of variations (random effects)

The study observed a significant variation in the odds of hypertension across the countries ($\sigma^2 = 1.65, 95\%$ CI 1.11 to 2.48) and across the neighbourhoods ($\sigma^2 = 1.34, 95\%$ CI 1.33 to 1.35). **Table 14** shows the results for Model 1 (unconditional model). The intra-country and intra-neighbourhood correlation coefficients indicate that 26.3% and 47.6% of the variance in the odds of hypertension could be attributed to country- and neighbourhood-level factors, respectively. The median MOR results also confirmed that neighbourhood and societal contextual phenomena influence the individual risk of having hypertension. The results from the full model (Model 5) show that if a respondent moved to another country or another neighbourhood with a higher probability of hypertension, the median increase in their odds of

hypertension would be 2.83-fold (95% CI 2.62 to 3.07) and 4.04-fold (95% CI 3.98 to 4.08),

respectively.

Table 13: Individual compositional and contextual factors associated with hypertension identified by multivariable multi-level logistic regression models, Demographic and Health Surveys data, 2011-2018.

	Model 1 OR (95%	a % CI)	Model 2 OR (959	/o CI)	Model 3 OR (95	° % CrI)	Model 4 OR (959	d % CI)	Model 5 OR (959	e ⁄6 CI)
Fixed effect Individual-level factors										
Male (vs female)					0.95***	[0.94,0.97]	0.95***	[0.93,0.97]		
Age per 10 years			1.74***	[1.73,1.76]	1.88***	[1.87,1.89]	1.90***	[1.89,1.91]	1.74***	[1.73,1.76]
Education										
attainment										
No education			***						***	
Primary			1.09***	[1.06,1.11]					1.08	[1.05,1.10]
Secondary or			1.05	[1.03,1.07]					1.04	[1.02,1.06]
Wealth index										
Poorer										
Middle			1.10***	[1.08,1.12]					1.08***	[1.05,1.10]
Richer			1.11***	[1.08,1.14]					1.08***	[1.05,1.12]
Marital status										
Never married										
Currently			1.35***	[1.32,1.38]					1.35***	[1.32,1.38]
married			1 27***	[1 22 1 42]					1 27***	[1 22 1 42]
Ever married Body mass index			1.37	[1.32,1.42]					1.57	[1.32,1.42]
Underweight			0.79***	[0 77 0 80]					0.79***	[0,77,0,80]
Normal weight			0172	[0177,0100]					0172	[0177,0100]
Overweight			1.72***	[1.69,1.75]					1.72***	[1.69,1.75]
Obese			2.67***	[2.60,2.74]					2.67***	[2.60,2.74]
Media access			1.02**	[1.00,1.03]					1.01^{*}	[1.00,1.02]
Indoor air			0.99	[0.97,1.01]					0.99	[0.97,1.01]
pollution			1.00	[0 00 1 02]					1.00	[0.09.1.02]
Money problem			1.00	[0.99, 1.02]					1.00	[0.98,1.02]
Cigarette smoker			1.14**	[1.05,1.24]					1.13**	[1.04,1.23]
Neighbourhood-				[]						[]
level factors										
Neighbourhood advantage										
Least										
Moderate					1.47***	[1.44,1.51]			1.10***	[1.06,1.14]
Higher					1.32***	[1.30,1.36]			1.14***	[1.10,1.17]
Country-level factors										
Human development index										
Low										
Moderate							0.77	[0.44,1.34]	1.34	[0.63,2.85]
High							0.54	[0.24,1.21]	0.96	[0.37,2.51]
Random effects										
Variance (95 CrI)	1.65*	[1 11 2 48]	1.20*	[1 02 1 41]	1.16*	[1 03 1 30]	1.13*	[1 02 1 24]	1 19*	[1 02 1 38]
VPC (%, 95%	26.3	[19.40.34.80]	18.8	[16.50.21.30]	19.3	[17.60.21.10]	17.5	[16.20.18.80]	1.17	[15.90.20.20]
CrI)		[]		[]		[]	- /	[]		[]
MOR (95% CrI)	3.41	[2.73,4.49]	2.84	[2.62,3.10]	2.79	[2.63,2.97]	2.76	[2.62,2.89]	2.83	[2.62,3.07]
Explained variation (%)		[.,.]	27.3	[8.10,43.10]	29.7	[7.20,47.60]	31.5	[8.10,50.00]	27.9	[8.10,44.40]
Neighbourhood- level										

Variance (95 CrI)	1.34***	[1.33,1.35]	1.90***	[1.87,1.93]	1.56***	[1.54,1.57]	2.03***	[2.00,2.06]	2.14***	[2.10,2.17]
VPC (%, 95%										
CrI)	47.6	[42.60,53.80]	48.5	[46.70,50.40]	45.2	[43.80,46.60]	49	[47.80,50.10]	50.3	[48.70,51.90]
MOR (95% CrI)	3.02	[3.00,3.03]	3.72	[3.69,3.76]	3.29	[3.27,3.30]	3.89	[3.85,3.93]	4.04	[3.98,4.08]
Explained				[-40.60, -		[-15.80, -		[-50.40, -		[-57.90, -
variation (%)		[.,.]	-41.8	43.00]	-16.4	16.30]	-51.5	52.60]	-59.7	60.70]
^a Model 1 – empty null mode model 2 – adjusted for model 3 – adjusted for model 4 – adjusted for model 5 – adjusted for OR – odds ratio, CI –	l, baseline mo only indiv neighbour only coun the indivio - confiden	del without any explana idual-level factor: hood-level factor: try-level factors lual neighbourhoo ce interval, MOR	ttory variables s od-, and co – median o	(unconditional model) untry-level factor odds ratio, VPC -	rs (full mo	del) partition coefficie	ent.			

* p < 0.05, ** p < 0.01, *** p < 0.001

5.3 STUDY VII: HOUSEHOLD AIR POLLUTION AND HIGH BLOOD PRESSURE: A SECONDARY ANALYSIS OF THE 2016 ALBANIA DEMOGRAPHIC HEALTH AND SURVEY

Sample Characteristics

The characteristics of the participants are summarised in **Table 15**. The prevalence of hypertension was 29.9%, and the number of respondents with blood pressure sampled in Albania included in the analysis was 20,846. Many of the respondents were females (71.3%); in comparison, 28.9% of the respondents were males. More than half of the respondents had secondary or higher education (53%), while 47% either had no education or primary school education only. Most of the respondents belonged to the 45–54 age group (25%).

In comparison, 13% of the respondents belonged to the 55–64 age group. About 28% of the respondents in Albania belonged to the poorest wealth quintile, while 11% belonged to the wealthiest quintile. A total of 59.1% of the respondents were not working, while 40.8% reported working. Approximately 40% of the respondents had a normal weight, while 57% were overweight or obese. About 54% of the participants lived in rural areas, while 45% lived in urban areas. Respondents exposed to HAP (bad fuel) in Albania were 16.5% more likely to develop hypertension than respondents not exposed to house air pollution or respondents who used clean energy.

The percentage of individuals with hypertension was higher among females exposed to/using bad fuel than males (20.8% versus 9%, p < 0.0001). Respondents with primary school education or no education were more likely to be exposed to indoor air pollution. The prevalence of hypertension was significantly higher in those with no education or primary school education than in respondents with higher education (16.9% versus 12.9%, p < 0.0001). The prevalence of hypertension was significantly higher among the older age groups of 35 years and above. Approximately 12% of the 45–54-year-old respondents were hypertensive, while the prevalence was the lowest among 15–24-year-olds (1.4%). The level of hypertension was higher among the poorest households than among the wealthiest families (9.2% versus 3.0%, p < 0.0001). The prevalence of hypertension was higher among respondents who were not working (17.0%) than respondents who did work (12.0%). Respondents who were overweight (11.8%) and obese (11.5%) were significantly more likely to be hypertensive than those who had an average weight (6.4%) and were underweight (0.18% p < 0.0001).

		Normotensive Hypertensive		p-value
Number	Percentage	Percentage	Percentage	
		%	%	
				< 0.001
5,988	28.7	68.6	31.4	
14,858	71.3	70.7	29.2	
				< 0.001
190	0.9	70.5	29.5	
9,593	46.0	64.0	36.1	
11,054	53.1	75.6	24.4	
				< 0.001
5,828	28.0	66.7	33.2	
5,027	24.1	68.7	31.2	
4,075	19.6	71.0	28.9	
3,526	16.9	72.8	27.2	
2,390	11.5	75.6	24.3	
				< 0.001
8,515	40.8	27.9	12.9	
12,331	59.1	71.4	16.9	
				< 0.001
503	7.4	91.6	7.35	
8,252	40.3	84.0	16.0	
7,166	35.0	66.3	33.7	
4,519	22.1	47.9	52.0	
				< 0.001
11, 303	54.2	68.3	31.7	
9,543	45.7	72.2	27.8	
				<0.001
4.511	21.6	93.5	6.51	0.001
4.082	19.6	87.0	13.0	
4.091	19.6	73.5	26.5	
5,257	25.2	53.2	46.7	
2,905	13.9	36.0	63.9	
	Number 5,988 14,858 190 9,593 11,054 5,828 5,027 4,075 3,526 2,390 8,515 12,331 503 8,252 7,166 4,519 11, 303 9,543 4,511 4,082 4,091 5,257 2,905	NumberPercentage5,98828.714,85871.31900.99,59346.011,05453.15,82828.05,02724.14,07519.63,52616.92,39011.58,51540.812,33159.15037.48,25240.37,16635.04,51922.111, 30354.29,54345.74,51121.64,09119.65,25725.22,90513.9	NumberPercentageNormotensive Percentage5,98828.768.614,85871.370.71900.970.59,59346.064.011,05453.175.65,82828.066.75,02724.168.74,07519.671.03,52616.972.82,39011.575.68,51540.827.912,33159.171.45037.491.68,25240.384.07,16635.066.34,51922.147.911, 30354.268.39,54345.772.24,51121.693.54,09119.673.55,25725.253.22,90513.936.0	NumberPercentageNormotensiveHypertensive Percentage9%% $5,988$ 28.768.631.414,85871.370.729.21900.970.529.59,59346.064.036.111,05453.175.624.45,82828.066.733.25,02724.168.731.24,07519.671.028.93,52616.972.827.22,39011.575.624.38,51540.827.912.912,33159.171.416.95037.491.67.358,25240.384.016.07,16635.066.333.74,51922.147.952.011, 30354.268.331.79,54345.772.227.84,51121.693.56.514,08219.687.013.04,09119.673.526.55,25725.253.246.72,90513.936.063.9

Table 14: Summary	v of Sam	ole Chara	acteristics	of S	Survey	Data in	1 Albania
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Association between HAP and Hypertension

The measure of association between house air pollution and hypertension is summarised in **Figure 28 and Table 16.** In the adjusted analysis, participants exposed to HAP were 17% more likely to have hypertension compared to those not exposed to indoor air pollution (COR = 1.17, 95% CI 1.10 to 1.24), such that 2310 of the 4906 (32.0%) individuals exposed to HAP had hypertension. In comparison, 3917 of the 9699 (28.8%) individuals not exposed to HAP had hypertension. When stratified by the sex of the participants, the association was only significant among women, such that women exposed to HAP were 22% more likely to have had hypertension than women not exposed to HAP (OR = 1.22, 95% CI 1.13 to 1.31). In addition, the association was only significant among rural residents. Rural residents exposed to HAP were 12% more likely to have had hypertension than those not exposed to HAP (OR = 1.12, 95% CI 1.04 to 1.22). The association was more significant among participants aged 25 to 54 years.

After controlling for other potential confounding variables in the adjusted analyses, the association between hypertension and HAP remained statistically significant (OR = 1.09, 95% CI 1.01 to 1.19). The following traditional risk factors remained statistically substantial: women were 20% less likely to be hypertensive (OR = 0.80, 95% CI 0.74 to 0.86); participants with primary school education were 21% more likely to be hypertensive (OR = 1.21, 95% CI 0.12 to 1.30) than those with secondary school or higher education; overweight and obese respondents were more likely to be hypertensive, and the odds of hypertension increased with increasing age.

	Unadjusted OR (95% CI)	Adjusted Association	
		OR (95% CI)	
Household air pollution			
Clean vs. unclean	1.17 (1.10 to 1.24)	1.09 (1.01 to 1.19)	
Sex			
Female vs. male	0.90 (0.84 to 0.96)	0.80 (0.74 to 0.86)	
Education			
No education	1 29 (0 94 to 1 77)	1.20(0.84 to 1.71)	
Primary	1.25 (0.5 + 10 + 1.77) 1.75 (1.65 to 1.86)	1.20(0.01001.71) 1.21(1.12 to 1.30)	
Secondarv+	1 (reference)	1 (reference)	
5		· · · · ·	
Wealth			
Poorest	1.54 (1.39 to 1.72)	1.51 (1.29 to 1.76)	
Poorer	1.41 (1.26 to 1.58)	1.33 (1.16 to 1.53)	
Middle	1.27 (1.13 to 1.42)	1.21 (1.06 to 1.39)	
Richer	1.16 (1.03 to 1.31)	1.13 (0.99 to 1.31)	
Richest	1 (reference)	1 (reference)	
Not Working			
Not working vs. working	0.87 (0.82 to 0.92)	1.02 (0.95 to 1.10)	
BMI			
Underweight	0.42 (0.30 to 0.59)	0.84 (0.59 to 1.21)	
Normal weight	1 (reference)	1 (reference)	
Overweight	2.77 (2.47 to 2.88)	1.50 (1.38 to 1.64)	
Obese	5.70 (5.24 to 6.19)	2.67 (2.42 to 2.93)	
Place of Residence			
Rural vs. urban	1.20 (1.13 to 1.28)	1.07 (0.98 to 1.16)	
Age of Households			
15 to 24	1 (reference)	1 (reference)	
25 to 34	2 15 (1 86 to 2 50)	1.78(1.52 to 2.09)	
35 to 44	5.17 (4.5 to 5 93)	3.72(3.20 to 4.32)	
45 to 54	12.60 (11.07 to 14.36)	8.40(7.27 to 9.69)	
55 to 64	25.49 (22.15 to 29.33)	16.86 (14.47 to 19.64)	

Table 15: Unadjusted and adjusted odds ratios of the association between high blood pressure, indoor air pollution, and selected factors.


Figure 27: Association between exposure to HAP and hypertension risk.

5.4 STUDY VIII: RURAL-URBAN DISPARITIES IN HYPERTENSION BURDEN IN LOW- AND MIDDLE-INCOME COUNTRIES: A TALE OF DIFFERENT ASSOCIATIONS

The study characteristics are presented in **Table 17.** Across 12 countries stratified by place of residence and hypertension status, 888,925 participants were included. The countries, year of data collection, and the characteristics of the survey are presented. The surveys were conducted between 2011 and 2018. The median number of neighbourhoods sampled was 498, ranging from 316 in the Kyrgyz Republic to 28,408 in India. The number of respondents included in the analysis was 3,630 in Namibia, and as many as 781 117 in India. The prevalence of hypertension ranged from 10.3% in the Kyrgyz Republic to 52.2% in Haiti. Of the total sample, 68.9% were rural dwellers (612,050), while 31.1% (276, 050) were urban dwellers. The percentage of hypertensive individuals was higher among urban dwellers than rural dwellers (16.4% vs 20.1%.). The proportions of females were higher than males in both rural and urban areas 16.1% (143,171) of the sample were males, while 83.9% (745,754) were females.

Country	Survey year	Number of neighbourhoods	Sample Size	Human Development Index	HTN (%)	Rural	Urban	Total	% Rural	% Urban
Albania	2018	715	20846	High	29.9	11,303	9,543	20,846	54.2	45.7
Bangladesh	2011	600	7887	Low	29.4	5,298	2,589	7,887	67.1	32.8
Benin	2018	555	6700	Low	22.2	3,710	2,990	6,700	55.3	44.6
Ghana	2014	427	13741	Low	13.5	7,113	6,628	13,741	51.7	48.2
Haiti	2017	450	4615	Low	52.2	3,176	1,439	4,615	68.8	31.1
India	2015	28408	781117	Low	16.5	552,437	228,680	781,117	70.7	29.2
Kyrgyz Republic	2012	316	10487	High	10.3	7,137	3,350	10,487	68.0	31.9
Lesotho	2014	399	6076	Low	19.5	4,135	1,941	6,076	68.0	31.9

Table 16: Description of Demographic and Health Surveys data in low- and middle-income countries, 2011 to 2018

						612,050	276,875	888,925		
Tajikistan	2017	366	10657	High	12.1	6,481	4,176	10,657	60.8	39.1
South Africa	2016	718	8346	High	48	3,918	4,428	8,346	46.9	53.0
Nepal	2016	383	14823	Low	22.4	5,434	9,389	14,823	36.6	63.3
Namibia	2013	546	3630	Low	46.2	1,908	1,722	3,630	52.5	47.4

HTN: hypertension

Patterns of rural-urban differential in the burden of hypertension

Figure 29 shows three different patterns of associations, namely pro-urban, pro-rural, and nodifference. In eight countries (Bangladesh, Benin, Ghana, India, Lesotho, Namibia, Nepal, and South Africa), urban residents were 39% more likely to be hypertensive than the rural residents (pooled OR = 1.39, 95% CI 1.26 to 1.54). However, the association was pro-rural in three countries (Albania, Kyrgyz Republic, and Tajikistan). Such participants living in urban areas were 18% less likely to have hypertension than those living in rural areas (pooled OR = 0.82, 95% CI 0.78 to 0.87). The association was similar in Haiti, and there was no statistically significantly different in the burden of hypertension between those living in rural and urban areas.

	Urba	n area	Rura	al area		Odds ra	tio	Weight
Study	Hypertensive	Normotensive	Hypertensive	Normotensive	•	with 95%	5 CI	(%)
Pro-Urban								
Bangladesh	917	1,398	1,672	3,900			1.69]	8.36
Benin	764	724	2,226	2,986		1.42 [1.26,	1.59]	8.27
Ghana	1,128	727	5,500	6,386		———————————————————————————————————————	1.99]	8.37
India	43,188	86,001	185,492	466,436		1.26 [1.25,	1.28]	8.67
Lesotho	428	758	1,513	3,377		1.26 [1.10,	1.44]	8.15
Namibia	894	782	828	1,126		——— 1.55 [1.36,	1.77]	8.16
Nepal	2,211	1,112	7,178	4,322			1.30]	8.47
SouthAfrica	2,244	1,762	2,184	2,156		-1.26 [1.15,	1.37]	8.45
Heterogeneity: τ ²	= 0.02, l ² = 92.	52%, H² = 13.36				1.39 [1.26,	1.54]	
Test of $\theta_i = \theta_j$: Q(7) = 74.97, p = 0	0.00						
Pro-rural					_			
Albania	2,651	3,578	6,892	7,725	- • -	0.83 [0.78,	0.88]	8.56
KyrgyzRepublic	303	777	3,047	6,360		0.81 [0.71,	0.94]	8.10
Tajikistan	448	843	3,728	5,638	•	0.80 [0.71,	0.91]	8.23
Heterogeneity: τ ²	$I = 0.00, I^2 = 0.00$	0%, H² = 1.00			•	0.82 [0.78,	0.87]	
Test of $\theta_i = \theta_j$: Q(2)	2) = 0.26, p = 0.	88						
No difference								
Haiti	740	1,667	699	1,509	•		1.09]	8.21
Heterogeneity: τ ²	$= 0.00, I^2 = .\%,$	H ² = .			-	0.96 [0.85,	1.09]	
Test of $\theta_i = \theta_i$: Q(0) = 0.00, p = .						-	
Overall						1.18 [1.02,	1.38]	
Heterogeneity: τ ²	= 0.07, l ² = 98.0	09%, H² = 52.41						
Test of $\theta_i = \theta_j$: Q(11) = 367.90, p	= 0.00		Rural more hy	pertensive	Urban more hypertensive		
Test of group diffe	erences: Q _b (2) =	86.72, p = 0.00						
				C).71	1.99		
Bandom-effects B	EMI model							

Figure 28: Patterns of rural-urban disparities in the burden of hypertension

Factors explaining the rural-urban differentials in hypertension burden

When the analyses were stratified by country's illiteracy rates, the study found that respondents living in urban areas were more likely to be hypertension in countries with moderate and high poverty rates than those living in rural areas (**Figure 30**). However, the analyses were stratified by the country's unemployment rates. The study found that in countries with low and moderate unemployment rates, respondents living in urban areas were more likely to be hypertension than those living in rural areas (**Figure 31**). However, for those from countries with high and moderate unemployment rates, respondents living in urban areas were less likely to be hypertension than those living in rural areas (**Figure 31**). However, for those from countries with high and moderate unemployment rates, respondents living in urban areas were less likely to be hypertension than those living in rural areas (**Figure 32**). The association did not differ significantly by country's poverty rate (Fig 33 **eFigure 1**), survey year (Fig 33 **eFigure 2**), and survey sample size (Fig 34 **efigure 3**). As shown in **Table 18**, most countries' variations in

rural-urban disparities could be explained by the country's unemployment rates followed by survey year and illiteracy rate.

	Urba	n area	Rura	l area		Odds ra	atio	Weight
Study	Hypertensive	Normotensive	Hypertensive	Normotensive		with 95%	6 CI	(%)
Low								
Albania	2,651	3,578	6,892	7,725	- • -	0.83 [0.78	, 0.88]	8.56
KyrgyzRepublic	303	777	3,047	6,360	•	0.81 [0.71	0.94]	8.10
Lesotho	428	758	1,513	3,377		1.26 [1.10	, 1.44]	8.15
Namibia	894	782	828	1,126			, 1.77]	8.16
SouthAfrica	2,244	1,762	2,184	2,156			, 1.37]	8.45
Tajikistan	448	843	3,728	5,638	•	0.80 [0.71	, 0.91]	8.23
Heterogeneity: τ ²	= 0.08, I ² = 96.6	63%, H² = 29.65				1.05 [0.83	, 1.32]	
Test of $\theta_i = \theta_j$: Q(§	5) = 139.42, p =	0.00						
Medium								
Ghana	1,128	727	5,500	6,386		———————————————————————————————————————	, 1.99]	8.37
Haiti	740	1,667	699	1,509	•	0.96 [0.85	, 1.09]	8.21
India	43,188	86,001	185,492	466,436		1.26 [1.25	, 1.28]	8.67
Nepal	2,211	1,112	7,178	4,322		1.20 [1.10	, 1.30]	8.47
Heterogeneity: τ ²	= 0.06, I ² = 98.0	04%, H² = 51.11				1.27 [0.99	, 1.64]	
Test of $\theta_i = \theta_j$: Q(3)	3) = 68.97, p = 0	0.00						
High								
Bangladesh	917	1,398	1,672	3,900			, 1.69]	8.36
Benin	764	724	2,226	2,986			, 1.59]	8.27
Heterogeneity: τ ²	$= 0.00, I^2 = 0.00$	0%, $H^2 = 1.00$				1.48 [1.37	, 1.60]	
Test of $\theta_i = \theta_j$: Q(1) = 0.99, p = 0.	32						
Overall						1.18 [1.02	, 1.38]	
Heterogeneity: τ ²	$= 0.07, I^2 = 98.0$	$09\%, H^2 = 52.41$						
Test of $\theta_i = \theta_j$: Q(11) = 367.90, p :	= 0.00		Rural more hyp	pertensive	Urban more hypertensive		
Test of group diffe	erences: Q _b (2) =	8.58, p = 0.01						
				0.	71	1.99		
•								

Figure 29: Rural-urban disparities in the burden of hypertension by country's illiteracy rate

	Urban area		Rura	l area		Odds ratio	Weight
Study	Hypertensive	Normotensive	Hypertensive	Normotensive		with 95% CI	(%)
Low							
Bangladesh	917	1,398	1,672	3,900			8.36
Benin	764	724	2,226	2,986			8.27
India	43,188	86,001	185,492	466,436		1.26 [1.25, 1.28]	8.67
Lesotho	428	758	1,513	3,377		1.26 [1.10, 1.44]	8.15
Heterogeneity: τ ²	= 0.01, l ² = 79.9	99%, H ² = 5.00				1.36 [1.23, 1.49]	
Test of $\theta_i = \theta_j$: Q(3)	3) = 17.16, p = 0	0.00					
Medium							
Ghana	1,128	727	5,500	6,386		———————————————————————————————————————	8.37
Namibia	894	782	828	1,126		——————————————————————————————————————	8.16
SouthAfrica	2,244	1,762	2,184	2,156			8.45
Heterogeneity: τ ²	= 0.03, l ² = 91.7	72%, H² = 12.08				1.52 [1.23, 1.87]	
Test of $\theta_i = \theta_j$: Q(2)	2) = 29.15, p = 0	0.00					
High							
Albania	2,651	3,578	6,892	7,725	- • -	0.83 [0.78, 0.88]	8.56
KyrgyzRepublic	303	777	3,047	6,360	•	0.81 [0.71, 0.94]	8.10
Tajikistan	448	843	3,728	5,638	•	0.80 [0.71, 0.91]	8.23
Heterogeneity: τ ²	= 0.00, l ² = 0.00	0%, H ² = 1.00			•	0.82 [0.78, 0.87]	
Test of $\theta_i = \theta_j$: Q(2)	2) = 0.26, p = 0.	88					
Overall						1.21 [1.01, 1.45]	
Heterogeneity: τ ²	= 0.08, l ² = 98.3	35%, H ² = 60.75					
Test of $\theta_i = \theta_j$: Q(9) = 350.24, p = 0.00				Rural more hy	pertensive	Urban more hypertensive	
Test of group diffe	erences: Q,(2) =	D					
				o	.71	1.99	

Figure 30: Rural-urban disparities in the burden of hypertension by country's unemployment rate

	Urban area		Rura	l area			Odds ratio	Weight
Study	Hypertensive	Normotensive	Hypertensive	Normotensive		1	with 95% CI	(%)
Low								
Bangladesh	917	1,398	1,672	3,900			1.53 [1.38, 1.69]	8.36
KyrgyzRepublic	303	777	3,047	6,360	•		0.81 [0.71, 0.94]	8.10
Nepal	2,211	1,112	7,178	4,322			1.20 [1.10, 1.30]	8.47
SouthAfrica	2,244	1,762	2,184	2,156			1.26 [1.15, 1.37]	8.45
Heterogeneity: τ ²	$= 0.06, I^2 = 96.2$	26%, H ² = 26.73					1.17 [0.91, 1.51]	
Test of $\theta_i = \theta_j$: Q(3)	3) = 52.17, p = 0	0.00						
Medium								
Albania	2,651	3,578	6,892	7,725			0.83 [0.78, 0.88]	8.56
Ghana	1,128	727	5,500	6,386			- 1.80 [1.63, 1.99]	8.37
India	43,188	86,001	185,492	466,436		•	1.26 [1.25, 1.28]	8.67
Lesotho	428	758	1,513	3,377			1.26 [1.10, 1.44]	8.15
Namibia	894	782	828	1,126			1.55 [1.36, 1.77]	8.16
Heterogeneity: τ ²	$= 0.08, I^2 = 98.7$	70%, H ² = 76.77					1.30 [1.00, 1.68]	
Test of $\theta_i = \theta_j$: Q(4)	4) = 243.97, p =	0.00						
High								
Benin	764	724	2,226	2,986			1.42 [1.26, 1.59]	8.27
Haiti	740	1,667	699	1,509	- •	—	0.96 [0.85, 1.09]	8.21
Tajikistan	448	843	3,728	5,638	•		0.80 [0.71, 0.91]	8.23
Heterogeneity: τ ²	$= 0.08, I^2 = 95.5$	50%, H ² = 22.24					1.03 [0.74, 1.43]	
Test of $\theta_i = \theta_j$: Q(2)	2) = 46.20, p = 0	0.00						
Overall							1.18 [1.02, 1.38]	
Heterogeneity: τ ²	= 0.07, I ² = 98.0	09%, H ² = 52.41						
Test of $\theta_i = \theta_j$: Q(11) = 367.90, p = 0.00				Rural more hyp	pertensive	Urban more hyper	ensive	
Test of group differences: $Q_{h}(2) = 1.17$, p = 0.56								
	$a_{\rm b}(z) = a_{\rm b}(z) = a_{\rm b}(z)$			0.	71	1.99		

Figure 31: Rural-urban disparities in the burden of hypertension by country's poverty rate

	Urba	n area	Rura	l area			Odds ratio	Weight	
Study	Hypertensive	Normotensive	Hypertensive	Normotensive			with 95% CI	(%)	
2011 to 2014									
Bangladesh	917	1,398	1,672	3,900			1.53 [1.38, 1.69]	8.36	
Ghana	1,128	727	5,500	6,386			- 1.80 [1.63, 1.99]	8.37	
KyrgyzRepublic	303	777	3,047	6,360	•		0.81 [0.71, 0.94]	8.10	
Lesotho	428	758	1,513	3,377			1.26 [1.10, 1.44]	8.15	
Namibia	894	782	828	1,126		•	1.55 [1.36, 1.77]	8.16	
Heterogeneity: τ ²	= 0.09, I ² = 96.0	09%, H ² = 25.60					1.35 [1.03, 1.76]		
Test of $\theta_i = \theta_j$: Q(4)	4) = 89.82, p = 0	0.00							
2015 to 2018									
Albania	2,651	3,578	6,892	7,725	- • -		0.83 [0.78, 0.88]	8.56	
Benin	764	724	2,226	2,986			1.42 [1.26, 1.59]	8.27	
Haiti	740	1,667	699	1,509	•	<u> </u>	0.96 [0.85, 1.09]	8.21	
India	43,188	86,001	185,492	466,436		•	1.26 [1.25, 1.28]	8.67	
Nepal	2,211	1,112	7,178	4,322		-•-	1.20 [1.10, 1.30]	8.47	
SouthAfrica	2,244	1,762	2,184	2,156			1.26 [1.15, 1.37]	8.45	
Tajikistan	448	843	3,728	5,638	•		0.80 [0.71, 0.91]	8.23	
Heterogeneity: τ ²	= 0.05, l ² = 97.7	77%, H ² = 44.78					1.08 [0.92, 1.28]		
Test of $\theta_i = \theta_j$: Q(6)	6) = 250.48, p =	0.00							
Overall							1.18 [1.02, 1.38]		
Heterogeneity: τ ²	= 0.07, l ² = 98.0	09%, H ² = 52.41							
Test of $\theta_i = \theta_j$: Q(11) = 367.90, p = 0.00				Rural more hy	pertensive	Urban more hyperte	ensive		
Test of group differences: $Q_{h}(1) = 1.86$, p = 0.17									
				0.	.71	1.99			

Figure 32: Rural-urban disparities in the burden of hypertension by country's survey year



Figure 33: Rural-urban disparities in the burden of hypertension by country's sample size

Factor	Odds ratio (95% CI)	Heterogeneity explained (%)
Illiteracy rate		9.0
Low	1 (reference)	
Medium	1.21 (0.83 to 1.78)	
High	2.40 (0.87 to 2.28)	
Unemployment rate		81.0
Low	1 (reference)	
Medium	1.11 (0.90 to 1.38)	
High	0.60 (0.48 to 0.75)	
Poverty rate		0.0
Low	1 (reference)	
Medium	1.10 (0.72 to 1.69)	
High	0.88 (0.54 to 1.43)	
Survey year		10.0
2011 to 2014	1 (reference)	
2015 to 2018	0.80 (0.57 to 1.13)	
Sample size		00.0
<10,000	1 (reference)	
10,000 to 20,000	0.83 (0.56 to 1.25)	
>20,000	0.78 (0.47 to 1.29)	

Table 17:	Country-level factors	associated	with rural-urban	disparities	in hypertension
burden					

5.5 STUDY IX: URBANICITY AND HIGH BLOOD PRESSURE IN A RESOURCE-LIMITED SETTING: A PROPENSITY SCORE MATCHING

A total of 8,346 respondents with high blood pressure were included in the analysis. Characteristics of the respondents before and after matching are summarised in **Table 19**. Before matching, there were significant differences between respondents living in urban and rural areas. Respondents living in rural areas were more likely to have only primary education (16.1% versus 9.8%), be living in poorer households (33.4% vs 10.9%), not working (72.4% versus 64.3%), and have access to no media (13.0% versus 4.4%), exposed to indoor air pollution (42.4% versus 9.3%), had a problem getting money for treatment (36.7% versus 19.5%) than those living in urban areas. However, respondents living in urban areas.

	Before ma	tching			After mate	hing		
	Urban	Rural	р-	%	Urban	Rural	р-	%Bias
	(n=4,428)	(n=3,918)	value	Bias	(n=1,631)	(n=1,408)	value	
Age								
25 to 34	32.8	29.3	0.040	7.5	32.8	34.1	0.436	-2.8
35 to 44	24.7	23.0	0.274	4.0	24.7	24.6	0.968	0.1
45 to 54	10.1	10.7	0.628	-1.8	10.1	11.1	0.363	-3.2
Education								
No education								
Primary	9.8	16.1	< 0.001	-18.7	9.8	6.1	< 0.001	10.8
Secondary or higher	88.3	80.9	< 0.001	20.6	88.3	92.9	< 0.001	-12.8
Wealth								
Poorer	10.9	33.4	< 0.001	-56.4	10.9	12.0	0.296	-2.9
Middle	24.4	24.7	0.872	-0.6	24.4	22.1	0.116	5.4
Richer	33.6	5.7	< 0.001	75.0	33.6	38.3	0.006	-12.5
Richest	20.4	1.4	< 0.001	63.8	20.4	17.5	0.040	9.5
Not working	64.3	72.4	< 0.001	-17.5	64.3	66.0	0.321	-3.6
BMI								
Normal weight	33.9	35.8	0.276	-4.0	33.9	31.4	0.135	5.1

Table 18: Summary of the characteristics of the respondents before and after Matching

Overweight	27.2	27.9	0.644	-1.7	27.2	27.0	0.906	0.4
Obese	35.4	31.8	0.039	7.5	35.4	39.2	0.025	-8.1
No media access	4.4	13.0	<0.001	-31.0	4.4	4.1	0.602	1.3
Indoor air	9.3	42.4	<0.001	-81.6	9.3	8.7	0.541	1.5
pollution								
Problem getting	19.5	36.7	<0.001	-39.0	19.5	16.4	< 0.001	7.1
money for								
treatment								
Smoker	7.4	1.4	<0.001	29.5	7.4	6.9	0.541	2.7

Crude rural-urban differences in hypertension prevalence:

The odds of hypertension risk between those living in urban and rural areas for the overall population and by different socioeconomic statuses are shown in **Figures 35**. The prevalence of hypertension was significantly higher among those living in urban than those living in rural areas, such that 2,244 of the 4,428 (50.7%) of the respondents living in urban areas had hypertension. In comparison, 1,762 of 3,918 (45.0%) those living in rural areas had hypertension (OR = 1.26, 95% CI 1.15 to 1.37). The odds of experiencing a higher prevalence of hypertension by place of residence tended to be higher among those with secondary or higher education than those not working, and those with no access to media. **Figure 36** describes the age trajectories of hypertension among those living in urban areas. The odds of experiencing a higher prevalence of hypertension among those living in urban areas increase with increasing age. The difference was more pronounced after 70 years of age.

Propensity score-adjusted rural-urban differences in hypertension prevalence:

Of the 8,346 respondents, we successfully matched 1,631 respondents living in urban areas and 1,408 respondents living in rural areas. The average exposure effect for those living in urban areas using the matched sample was calculated. In this matched sample, those living in urban areas had a hypertension probability of 37.4% compared to 29.3% of those living in rural areas (risk ratio: 1.27, 95% CI 1.15 to 1.41), such as those living in urban areas were 27% more likely to be hypertensive than those living in rural areas.



Figure 34: The odds of hypertension risk between those living in urban and rural areas for the overall population and by different socioeconomic status.



Figure 35: The age trajectories of hypertension among those living in urban and rural areas.

5.6 STUDY X: SOCIOECONOMIC DETERMINANTS OF HYPERTENSION: ECOLOGICAL ANALYSIS OF 53 COUNTRIES LOW- AND MIDDLE-INCOME COUNTRIES

A total of 53 countries from LMICs were included in this analysis. Summary characteristics of variables included in the study are shown in **Table 20.** The median prevalence of agestandardised hypertension was 28.4% across the 53 countries, ranging from 23.2% in Tunisia to 33.4% in Niger (**Figure 37**).



Figure 36: The median prevalence of age-standardised hypertension across countries.

The adult literacy rate ranged from 22.3% in Chad to 95.0% in South Africa. The percentage of unemployed ranged from 0.53% in Niger to 26.3% in Djibouti. The rate of living in urban areas ranged from 12.1% in Burundi to 88.1% in Eritrea.

Country	Raised blood pressure (SBP ≥ 140 OR DBP ≥ 90), age-standardized (%)	Current health expenditure (% of GDP)	Domestic general government health expenditure per capita	GDP per capita (current US\$)	Literacy rate, adult total (% of people ages 15 and above)	Unemployment, total (% of the total labour force)	Urban population (% of the total population)	Multidimensional poverty index	Total population
Angola	29.7	2.6	90.6	4167.0	66.0	7.4	63.4	51.1	27,884,380
Burundi	29.2	6.4	20.4	305.5	68.4	1.6	12.1	74.3	10,160,034
Benin	27.7	2.9	16.9	1076.8	42.4	2.0	45.7	66.8	10,575,962
Burkina Faso	32.6	5.1	25.0	653.3	39.3	4.3	27.5	83.8	18,110,616
Botswana	29.6	5.7	603.2	6402.9	86.8	20.6	67.2	17.2	2,120,716
The Central African Republic	31.2	5.0	3.6	377.4	37.4	5.6	40.3	79.4	4,493,171
Cote d'Ivoire	27.2	3.2	37.4	1972.5	89.9	3.1	49.4	46.1	23,226,148
Cameroon	24.8	3.7	12.4	1382.5	77.1	3.6	54.6	45.3	23,298,376
Congo, Dem. Rep.	28.5	4.0	6.0	497.3	77.0	4.5	42.7	64.5	76,244,532
Congo, Rep.	26.2	2.5	51.9	2447.5	80.3	20.4	65.5	24.3	4,856,093
Comoros	27.9	4.6	12.6	1242.6	58.8	8.1	28.5	37.3	777,435
Cabo Verde	29.5	4.8	190.3	3043.0	86.8	11.8	64.3		524,740
Djibouti	26.8	3.1	77.9	2658.9		26.3	77.4		913,998
Algeria	25.1	7.0	590.8	4177.9	81.4	11.2	70.8	2.1	39,728,020
Egypt, Arab Rep.	25.0	5.3	191.9	3562.9	71.2	13.1	42.8	5.2	92,442,549
Eritrea	29.1	4.5	11.8		76.6	5.8			
Ethiopia	30.3	3.8	16.0	640.5	51.8	2.3	19.4	83.5	100,835,453
Gabon	25.5	2.7	230.1	7384.7	84.7	20.6	88.1	14.8	1,947,690
Ghana	23.7	4.6	83.0	1774.1	79.0	6.8	54.1	30.1	27,849,203
Guinea	30.3	5.8	7.8	769.3	39.6	4.9	35.1	66.2	11,432,096
The Gambia	29.1	3.2	20.6	660.7	50.8	9.5	59.2	41.6	2,085,860
Guinea-Bissau	30.3	8.1	9.4	603.4	45.6	5.9	42.1	67.3	1,737,207
Equatorial Guinea	28.4	2.9	133.3	11283.4	94.4	8.5	70.6		1,168,575

Table 19: Summary of the characteristics of variables included in the study

Kenya	26.7	5.2	70.9	1464.6	81.5	2.8	25.7	38.7	47,878,339
		10.							
Liberia	28.3	6	15.2	721.6	48.3	2.1	49.8	62.9	4,472,229
Libya	23.7			4337.9		19.5	79.3	2.0	6,418,315
Lesotho	29.0	9.0	165.2	1146.1	76.6	23.8	26.9	19.6	2,059,011
Morocco	26.1	5.1	150.1	2875.3	73.8	9.5	60.8	18.6	34,663,608
Madagascar	28.1	5.0	30.8	467.2	76.7	1.8	35.2	69.1	24,234,080
Mali	32.6	4.1	18.7	751.5	30.8	7.7	40.0	68.3	17,438,772
Mozambique	29.1	6.7	23.4	589.9	60.7	3.4	34.4	72.5	27,042,001
Mauritania	31.7	3.7	59.6	1524.1	53.5	10.1	51.1	50.6	4,046,304
Mauritius	25.0	5.7	457.9	9260.4	91.3	7.4	41.0		1,262,605
Malawi	28.9	9.3	27.4	380.6	62.1	5.9	16.3	52.6	16,745,305
Namibia	28.5	10.	447.9	4896.6	91.5	20.9	46.9	38.0	2,314,901
Niger	33.4	5.3	12.7	484.2	35.0	0.5	16.2	90.5	20,001,663
Nigeria	23.9	3.6	32.0	2687.5	62.0	4.3	47.8	46.4	181,137,454
Rwanda	26.7	6.6	38.0	751.1	73.2	1.1	17.0	54.4	11,369,066
Senegal	30.2	4.4	32.0	1219.2	51.9	6.8	45.9	53.2	14,578,450
Sierra Leone	30.3	20	26.2	588.2	43.2	4.7	40.8	57.9	7,171,909
Somalia	32.9			386.4		18.9	43.2		13,797,204
Sao Tome and Principe	25.8	5.3	64.8	1584.8	92.8	13.8	70.2	22.1	199,439
Eswatini	29.8	7.1	259.8	3680.3	88.4	23.3	23.3	19.2	1,104,038
Chad	32.9	4.5	17.5	776.0	22.3	1.1	22.5	85.7	14,110,971
Togo	28.9	5.0	17.8	570.9	66.5	2.2	40.1	37.6	7,323,162
Tunisia	23.2	6.6	365.0	4094.8	79.0	15.2	68.1	0.8	11,179,951
Tanzania	27.3	3.6	28.7	947.9	77.9	2.1	31.6	55.4	51,482,638
Uganda	27.3	5.1	17.2	847.3	76.5	1.9	22.1	55.1	38,225,447
South Africa	26.9	8.8	629.8	6259.8	95.0	25.1	64.8	6.3	55,386,369
Zambia	27.1	4.4	71.7	1338.3	86.7	10.1	41.9	47.9	15,879,370
Zimbabwe	28.2	7.5	41.6	1445.1	88.7	4.8	32.4	25.8	13,814,642
Sudan		7.3	100.4	1329.6	60.7	17.5	33.9	52.3	38,902,948
South Sudan				1119.7	34.5	12.3	18.9	91.9	10,715,657
Median	28.4	5.1	34.7	1286.1	73.5	6.81	6.8	42.4	12,614,650

Minimum	23.2	2.5	3.58	305.6	22.5	0.53	0.5	12.1	199,439
		20.							181,137,454
Maximum	33.4	4	630	11,283.4	95.0	626.3	26.3	88.1	

The pair-wise correlation between hypertension and the eight factors is summarised in Table





Figure 37: The pair-wise correlation between hypertension and the eight factors

Note: A scale from + 1 to -1 is used to calculate the correlation coefficient. Either + 1 or -1 represents a variable's complete connection with another. The correlation is positive when one variable rises as the other rises; it is negative when one variable falls as the other rises. A correlation with zero degree of absence is indicated by 0. The strength of the association, for absolute values of r, 0-0.19 is regarded as very weak, 0.2-0.39 as weak, 0.40-0.59 as moderate, 0.6-0.79 as strong and 0.8-1 as very strong correlation.

Results not statistically significant (p>0.05) are marked with X.

There was a negative statistically significant weak correlation between hypertension prevalence and domestic healthcare expenditure (r = -0.36, 95% CI -0.55 to -0.04), GDP per capita (r = -0.46, 95% CI -0.60 to -0.12) and percentage living in urban areas (r = -0.46, 95% CI -0.66 to -0.21). There was a negative, statistically significant moderate correlation between hypertension prevalence and adult literacy rate (r = -0.56, 95% CI -0.79 to -0.45). As the adult literacy rate increases, the prevalence of hypertension reduces (Figure 39).



Figure 38: The prevalence of hypertension and adult literacy rate

In addition, there was a positive, statistically significant moderate correlation between hypertension prevalence and the multidimensional poverty index (r = 0.70, 95% CI 0.52 to 0.83). The hypertension prevalence increases as the multidimensional poverty index increases (**Figure 40**).



Figure 39: The prevalence of hypertension and the Multidimensional poverty index

The crude and adjusted association between the country's hypertension prevalence and socioeconomic factors is shown in **Table 21.** The multivariable model accounted for 73.2% of the variation in countries' hypertension prevalence estimates. In the adjusted analyses, where all the eight factors were controlled, country literacy rate, unemployment rate, percentage of

living in an urban area, multidimensional poverty index, and total population were statistically significantly associated with the hypertension prevalence. For every 10% increase in adult literacy rate, hypertension prevalence reduced by 5.3%. For every 10% increase in the unemployment rate, the prevalence of hypertension increased by 1.4%. For every 10% increase in people living in urban areas, hypertension reduced by 3.9%. As the country's multidimensional poverty index increases, the country's hypertension prevalence increased by 0.07%. In addition, for each one million increases in the country's population, hypertension reduced by 0.19%.

	Pearson correlation	Unadjusted	Adjusted association
		association	
Current health expenditure (% of			
GDP)	-0.07 (-0.17 to 0.39)	1.00 (-1.42 to 3.42)	-0.27 (-1.78 to 1.24)
Domestic general government			
health expenditure per capita, PPP			
(current international \$)	-0.36 (-0.55 to -0.04)	-0.05 (-0.09 to -0.01)	0.03 (-0.02 to 0.08)
GDP per capita (current US\$)	-0.46 (-0.60 to -0.12)	-0.41 (-0.70 to -0.12)	0.07 (-0.48 to 0.62)
Literacy rate, adult total (% of			
people ages 15 and above)			
	-0.56 (-0.79 to -0.45)	-0.82 (-1.10 to -0.53)	-0.53 (-0.84 to -0.22)
Unemployment, total (% of total			
labour force)	0.18 (-0.45 to 0.08)	-0.70 (-1.67 to 0.27)	1.41 (0.38 to 2.43)
Urban population (% of total			
population)	-0.46 (-0.66 to -0.21)	-0.64 (-0.99 to -0.28)	-0.39 (-0.73 to -0.05)
Multidimensional poverty index	0.59 (0.52 to 0.83)	0.07 (0.05 to 0.09)	0.07 (0.04 to 0.10)
Total population	-0.12 (-0.5 to 0.02	-0.21 (-0.43 to 0.02)	-0.19 (-0.32 to -0.06)

Table 20: The crude and adjusted association between the Country's Hypertension prevalence and socioeconomic factors

GDP: Gross domestic product; US\$: United States Dollar; PPP: Purchasing Power Parity

5.7 CHAPTER SUMMARY

In this chapter, four studies evaluated both community and societal contextual risk factors. The findings revealed that hypertension remains a problem in LMICs. The multilevel study examined the separate and independent association of the novel individual, community and societal risk factors associated with hypertension in LMICs. The study found that HAP, place of residence, and socioeconomic determinants were associated with hypertension at community and societal levels. Therefore, an understanding of determinants of hypertension beyond individual characteristics (i.e., at community- and society levels), and traditional risk factors is necessary to develop appropriate interventions to reduce the epidemic.

The next chapter is the discussion, main findings of the studies, policy implications, implications for further research, and the strengths and limitations of the studies.

6 CHAPTER: DISCUSSION

6.1 MAIN FINDINGS

The first phase of this thesis deployed bibliometric analysis of several hypertension-related publications among African countries, citation classics and machine learning classification of topics. The results depicted that hypertension research output in Africa has improved considerably over the last two decades. This finding is consistent with previous evidence (Confraria & Wang, 2020; Tijssen, 2007; Uthman *et al.*, 2015). However, the results also showed that Africa still contributes less than 6% of the world's overall hypertension research output. The low investment in the educational sector potentially explains the knowledge gaps in hypertension research among SSA and other low- and middle-income countries; (Chow *et al.*, 2013; Kandala *et al.*, 2013). Country population size and GDP were key factors in the determining the degree of hypertension research performed in Africa, where countries such as Egypt (Population = 97.6 million; GDP = 235.4 billion USD), South Africa (Population = 56.7 million; GDP = 349.4 billion USD), and Nigeria (Population = 190.9 million; GDP = 375.8 billion USD) consistently ranked among the most significant contributors to global hypertension research.

On the other hand, comparatively smaller African countries such as Sao Tome & Principe (Population = 97.6 million; GDP = 235.4 billion USD) and Seychelles (Population = 95,843; GDP = 1.5 billion USD) were identified among the lowest contributing countries to the same research. This finding was consistent with earlier analyses of public health research in Africa (Mihai & Reisz, 2017; Uthman & Uthman, 2008). A large number of research and educational institutions in the densely populated countries such as Egypt, Nigeria, and South Africa, explain their higher degree of contribution towards the research (Tijssen, 2007), most probably because such countries have more financial as well as human sources to invest in Research and Development (R&D) sector (UNESCO Institute for Statistics, 2018).

Moreover, such countries are more likely to build international collaborations in research, thereby enhancing the scope of research (Bozeman & Boardman, 2014; Perkmann *et al.*, 2013). However, population size and GDP reflect those smaller countries like Seychelles and Cape Verde lie among the best-ranked nations for hypertension research in Africa. Perhaps, high-quality research will be the opportunity cost of publishing in larger quantities. However, an alternate explanation for this trend may be that other social factors beyond population size and country income become more conducive in research in smaller African countries than in the larger/wealthier nations in the region. These social factors may also explain why hypertension research output in larger African countries has not translated to higher life expectancy compared to smaller countries. For instance, the average life expectancy in smaller African nations like Mauritius (74.8 years), Seychelles (73.3 years), and Cape Verde (73.2 years) are much higher compared to larger countries such as South Africa (63.6 years) and Nigeria (54.2 years) (WHO, 2018). The study observed considerable variability in the number of publications per capita in some countries, such as Seychelles; this could be due to fluctuating GDP per capita over the study period.

Furthermore, this thesis evaluated the top 100 articles with the highest impact on hypertensionrelated topics. Information on the primary source of articles and country of origin that contributed to the most cited article was examined. The study revealed that seventy-one of the one hundred documents assessed were articles, twenty-three were review papers, and five were found to be proceeding papers. The articles were published across twenty-nine journals over 30 years, and the top 100 articles were written in English. Chobanian et al. and Levey et al. published the most popular article, which received the highest number of citations. This findings were consistent with the study of (Oh & Galis, 2014). The guideline by Chobanian and colleagues remains a critical policy document that significantly impacts hypertension research and health planning. The New England Journal of Medicine and Lancet journal were identified as the sources with the highest number of articles and citations. The total number of citations an article receives can be altered with time. For this reason, all results are valid at the specified period of study. The Journal of American Medical Association ranked third amongst all the journals (n=13) total citations of 55,696. The study demonstrates that specialised journals such as Journal of hypertension, diabetic care and circulation were among the top 10. Among the first 20 institutes examined, those in the USA appeared to be the most productive ones. Oparil was the most productive author, with six publications starting from 1997. This finding potentially suggests that much attention is given to chronic diseases. The study identified Harvard (15), Boston (14), Brigham and Women's hospital (9), and John Hopkins University (9) as the top four institutions with the highest number of articles. These findings correspond with another previous study (Oh & Galis, 2014). The United States of America published the highest number of articles. The rapid growth of public and private universities in the USA explains the phenomenon of increasing research publications in such high-income countries (Powell et al., 2017). The study also revealed that frequently referenced topics like fatal (cardiovascular and all-cause mortality) and non-fatal complications of hypertension, including coronary heart disease and blood pressure, were among the common terms retrieved. Perhaps this could be due to high mortality and disability-adjusted lost years caused by these conditions.

An unsupervised text mining methodology was employed to uncover hypertension research topics and their dynamics by examining publications indexed in PubMed during the last century to provide additional information on the evolutionary patterns of hypertension research. The study uncovered that more than half-a-million articles were published on hypertension worldwide between 1900 and 2018. The study revealed that most topics discovered may be divided into four categories (i.e., preclinical, risk factors, complications, and treatment-related studies). The important 'hot' topics include topic 2, ' evidence review', and topic 19 ', major cardiovascular events.' The majority of the cardiopulmonary disease subtopics show little fluctuation over time and contribute a modest share of the total. In the eyes of the researcher, commonly published topics may represent a large body of knowledge, a common disorder, or a low-cost, easy-to-study subject. On the other hand, less often published topics may represent the study of less common hypertension-related diseases and subject matter that is difficult or expensive to research. Pathophysiological research, for instance, can be regarded as unordinary research that necessitates a significant investment of time and resources and collaboration among physicians, biochemists, and physiologists.

Similarly, some genetic disorders may be infrequent and have high unmet demand, posing significant therapy and research obstacles. In the themes, we saw some intriguing clumping. Topics 5 'human proteome,' 9' physiology,' and 20 'genetic' were paired, indicating that these papers were all on hypertension pathophysiology. Topic 11, 'plasma renin activity,' subject 7, 'chronic kidney illness,' and topic 18, 'heart surgery,' were frequently mentioned in the same articles. It's worth noting that topic 15, "maternal heart disease," is the only one that isn't linked to the others because it isn't mentioned in the same article. This work adds to our understanding of hypertension research by helping researchers, journal editors, and donors identify new or ignored trends from established themes and freshly developing trends that can be evaluated in a structured way.

The prevalence of hypertension among people living with HIV in the five resource-limited settings, namely Ghana, India, Lesotho, Namibia, and South Africa, was examined. The results showed a high prevalence of hypertension among people living with HIV/AIDs in LMICs, as

demonstrated by Nduka and Xu (Nduka *et al.*, 2016; Xu *et al.*, 2017). This finding reveals that the number of hypertension victims may increase since more and more people who have HIV are on treatment, increasing the life expectancy. The hypertension risk difference between HIV and HIV negative was measured. India showed pro- HIV inequality (i.e., hypertension is more prevalent among HIV negative participants) while Namibia showed pro-non-HIV inequality. This finding corresponds to the study of Mohammed on 3075 Namibians showing that hypertension prevalent was lower among HIV-positive participants compared to HIV-negative participants (7.2% vs. 38.6%) (Mohamed, 2015).

Supporting pro-HIV inequality, Davies and colleagues' systematic review and meta-analysis revealed the overall global crude risk of prevalent hypertension to be lower among PLHIVs than negative individuals. Subgroup analysis confirmed the prevalence of hypertension to be lower in Africa and other regions (Davis *et al.*, 2021). Benzekr and colleagues also support this finding by estimating the prevalence of hypertension to be higher among the general population (32%) than among PLHIVs (22%) in Senegal. (Benzekri *et al.*, 2018). This research also identified the essential factors responsible for this inequality across the two countries. The age of the participants and obesity were the determining factors for the differential hypertension risk in India.

Meanwhile, obesity, age, and HAP were some of the most significant contributors to the differences in hypertension risk in Namibia. Supporting this finding, Lubega and colleagues identified an increase in age and being overweight as factors independently associated with hypertension among PLHIVs in Uganda. (Lubega *et al.*, 2021).

Furthermore, the study examined the association between GBV and hypertension among women in Kyrgyzstan at the individual level. Individuals exposed to GBV were more likely to

have hypertension than those not exposed, significantly among the rural residents, those with higher education and not working women. Clark and colleagues identified financial burden as a cofounding factor considerably associated with GBV, which substantially increases the risk of hypertension (Clark *et al.*, 2021). This finding is in accordance with the study of Wet-Billings & Godongwana, suggesting a positive association between IPV and hypertension amongst women in South Africa (Wet-Billings & Godongwana, 2021). Women's risk of GBV was associated with husbands' age, education level, place of residence, and low socioeconomic status as predisposing factors, including unemployment which supports the findings of this analysis (Sanjel, 2013). The study found a significant association between non-working individuals and hypertension. The discovery provides suggestive evidence that unemployed/not working participants who were working and exposed to GBV were more likely to develop hypertension than those who were not working as well as are not exposed to GBV.

Poverty contributes to IPV frequently occurring among lower socioeconomic groups. Victims of GBV have less control over their finances, little or no decision-making authority within households and consequently are unable to seek medical health care (Jewkes, 2002). Under this circumstance, it is difficult to prevent CVDs, particularly hypertension. Financial stability is associated with lower acceptance of abuse and other forms of violence. On the other hand, the study found that employed women face a greater risk of abuse in communities with relatively higher acceptance of the culture of wife-beating (Cools & Kotsadam, 2017). The findings underscore the importance of empowering women and creating awareness among individuals with higher education. This is reinforced by Chernyak's (2020) study, indicating that empowerment and experiential characteristics are risk factors for IPV. Household wealth, women's employment, and community education among women increase the likelihood of these women experiencing IPV in the Kyrgyz Republic. These results highlight the importance

of socioeconomic empowerment as a significant factor associated with IPV. The study also indicates that hypertension increases with age. The odds of experiencing a higher prevalence of hypertension among those exposed to GBV increased with age. The difference was more pronounced after 45 to 80 years. These findings agree with Buford, who emphasised that age is a known risk factor for hypertension (Buford, 2016), and with the study of Wet-Billings & Godongwana (2021).

The research employed a multilevel approach to examine hypertension risk in low- and middleincome countries at the contextual level. Like most traditional epidemiological studies that had examined traditional well-established individual-level risk factors, the study found that an increase in age, educational attainment, wealth status, overweight/ obesity, and cigarette smoking were positively associated with increased risk of hypertension. The findings also revealed that differences between neighbourhoods and countries determine hypertension risk. The results showed that hypertension is still relatively high in LMICs. Previous studies revealed high hypertension prevalence in Bangladesh, Nepal, and other LMICs (Kibria *et al.*, 2018: Chowdhury *et al.*, 2016). The increase in the prevalence of hypertension has been linked to rapid urbanisation and unhealthy lifestyle changes, such as the consumption of unhealthy diets that include fast foods, sedentary behaviour, and increased alcohol consumption (Tuofire & Ayetey, 2019).

After adjusting and controlling for the effects of the individual, neighbourhood, and countrylevel factors, the results showed that for every 10-year increase in age, there was an increase in the odds of having hypertension. Researchers have consistently found that hypertension increases with age and environmental factors, sex, education, wealth index, working status and body mass index (BMI) or obesity (Chowdhury *et al.*, 2016: Hassan *et al.*, 2018). The chances of suffering hypertension increase by increasing the different stages of education and wealth. For instance, respondents with secondary or higher education levels were more likely to develop hypertension than those with no education. Similarly, respondents from wealthier households were more likely to have hypertension. Supporting this finding, Kibria et al. (2018), Tareques (2015) & Sanuade et al. (2018) revealed that the prevalence of hypertension was higher in urban individuals and those in higher socioeconomic classes (i.e., the highest wealth quintile) than those respondents from rural areas and the lowest wealth quintile (Kibria *et al.*, 2018; Sanuade *et al.*, 2018; Tareque *et al.*, 2015). The odds of having hypertension in higher socioeconomic classes and urban individuals can be attributed to several behavioural factors, such as unhealthy diet, cigarette use, and alcohol consumption, influenced by residence, wealth status, and level of education (W.H.O, 2009). To address these risk factors, behaviour change programmes should be tailored to wealthier populations and individuals with higher educational attainment to reduce the incidence of hypertension in this group.

Marital status was also found to be a significant independent predictor of hypertension. In LMICs, married respondents had an increased prevalence hypertension than single or reported that being currently married or divorced increased the odds of having hypertension in Ghanaian women (Sanuade *et al.*, 2018; Tuoyire & Ayetey, 2019). This could result from low income or inability to access health care facilities and much stress from daily struggle. The study found that individuals who were overweight and obese were almost two and three times more likely to have hypertension than those with normal body weight. This conclusion is consistent with studies carried out by Harshfield et al. (2015), Rahman et al. (2017), Taraque et al. (2015), Chowdhoury et al. (2016), and Alkibria et al. (2019) & Fottrell et al. (2018). Their studies confirmed that being obese or overweight is a risk factor for hypertension. Rahman and colleagues estimated the prevalence of hypertension to be higher in urban areas than in rural areas (Rahman *et al.*, 2017). People living in urban areas may consume more calories and have sedentary lifestyle patterns that may increase their BMI, increasing their risk of having hypertension. We also noted that individuals who reported financial problems while addressing

their health care problems were at higher risk of having hypertension than those financially stable. The lack of universal health care insurance coverage has been a significant barrier to accessing health care services in most LMICs (Sanuade *et al.*, 2018). The rapid increase in the prevalence of hypertension is due to low and limited projected investment in the health sector. Despite the high number of populations in these regions, only 0.4% of global health spending was in LMICs in 2016 (Mills *et al.*, 2020). Another finding of this study indicated that smoking was a vital determining factor regarding having hypertension. Respondents who smoked cigarettes were more likely to have hypertension than non-smokers. This finding aligns with the study by Saladini et al. (2016) (Saladini *et al.*, 2016). Tobacco smoking is associated with increased arterial wall stiffness, increasing the risk of having hypertension (Asemu *et al.*, 2021).

Another phenomenon that the study found out was that the place of residence played a significant role in determining the health outcome of individuals. Respondents living in the most deprived areas were more likely to be hypertensive than those in the least deprived areas. Chowdhury et al. (2016), Kibra et al. (2018) & Sanuade et al. (2018) noted that place of residents had significant associations with hypertension in rural and urban regions, particularly among older people, wealthier people, females, those with diabetes and overweight individuals. Based on the distributions of these significant factors, it is highly likely that public health awareness campaigns targeted at deprived areas could contribute to controlling hypertension globally. More crucially, the findings add to the body of knowledge by revealing those factors at the contextual level which increase hypertension risk and individual-level determinants. Researchers have recently become more interested in exploring the effects of contextual Socioeconomic Status (SES) on CVD risk variables (Cubbin *et al.*, 2006; Diez-Roux, 2000). Several studies revealed an inverse relationship between blood pressure activity and neighbourhood SES. This suggests that Socio-Economic Status (SES) may be an independent

predictor of blood pressure activity and, thereby, hypertension. (Kapuku *et al.*, 2002; Liu *et al.*, 2013; Matheson *et al.*, 2010). According to Matheson et al. (2008), deprivation in the neighbourhood appears to be a stronger predictor of hypertension among women. Women living in high deprivation areas are 10% more likely to have hypertension than males living in the same areas and women living in the least deprived areas (Matheson *et al.*, 2008). Liu and colleagues also discovered that disadvantaged physical, as well as social environments, can account for between 44 and 53% of the variation in the prevalence of high blood pressure, and that individuals living in disadvantaged physical and socio-economic environments have a significantly higher risk of HBP prevalence (Liu *et al.*, 2013).

The study also found evidence of geographical clustering in the risk of hypertension. Differences between countries and neighbourhoods accounted for approximately 26% and 48% of the variation in hypertension, respectively. Respondents moving to another neighbourhood or country with a comparatively higher risk of hypertension have an increased risk of having hypertension. People from the same community are inherently more similar in terms of their current risk of having hypertension than people from different neighbourhoods, i.e., the contextual phenomenon manifests itself as the clustering of the risk of hypertension within neighbourhoods. Researchers frequently use an ecological perspective to understand the risk of developing a disease (Bronfenbrenner, 2005a; Bronfenbrenner, 2005b; Bronfenbrenner & Ceci, 1994). The disease is viewed as a multidimensional phenomenon including the interaction of individual, family, community, and societal factors in this paradigm. The framework considers many levels of societal factors and their impact on disease. An individual lives in a household unit, which is part of a community that is governed by the policies of a state or national government. Every level of the social hierarchy and restriction can impact an individual's illness risk. The ecological model promotes a complete public health strategy rather than tackling an individual's hypertension risk. Based on these contextual findings, we

might infer that there is some evidence for a possible neighbourhood and country contextual phenomenon shaping a common individual hypertension risk. The study concluded that there exists an association between hypertension and individual, neighbourhood, and country-level factors.

Additionally, this study examined the association between indoor air pollution exposure in LMICs at the community level. In Albania, the respondents exposed to the intense indoor household pollution expressed significant prevalence of hypertension levels compared to those not exposed to such high levels of pollution. The odds of having hypertension increased by 17% among the respondents exposed to indoor air pollution. This study revealed that exposure to HAP caused by burning solid fuels for cooking trigger the blood pressure levels to increase to striking levels. Biomass cooking fuel was associated with greater hypertension risk than the use of cleaner-burning LPG (Apte & Salvi, 2016; Deng *et al.*, 2020; Li *et al.*, 2020). A study conducted by Li et al. found a positive association between increased indoor air pollution and solid fuel use and hypertension risk (Li *et al.*, 2020). This could be due to high dust contents originating from local natural sources and metallurgical combinations (Giorgini *et al.*, 2016). An assessment revealed that dust levels in streets and houses were approximately at the same level as those on roads; due to emission of a considerable amount of PM, also known as Particle Pollution (Lika *et al.*, 2012).

Conversely, Ofori et al. and Fatmi et al. found a negative association between indoor air pollution and hypertension; notably, this inconsistency might have been due to the type of fuel, location, and other confounding factors (Fatmi *et al.*, 2019; Ofori *et al.*, 2018). Overall, this study demonstrated that the percentage of individuals with hypertension was higher among females exposed to HAP than males and those females who used clean fuels for cooking. This finding is consistent with the study carried out by Arku and colleagues (Arku *et al.*, 2018). The results indicated a significant increase in blood pressure among women cooking with solid

fuels, with substantially high blood pressure, particularly among rural women. Supporting this finding, Gordon et al. stated that this gender difference in hypertension levels is most probably because women have a leading role in domestic cooking in more cultures than men (Gordon *et al.*, 2014). Balmes also found more substantial effect estimates for women due to intense daily cooking smoke exposure (Balmes, 2019).

Another significant predictor of exposure to Household Air Pollutant (HAP) in most cultures is socio-economic status. In any context, frequently less expensive fuel options are less efficient fuels, produce more HAP, and are used by people with the most poorly designed homes. In this study, the results demonstrated variations in population exposure to indoor air pollution across socio-economic groups. Respondents with primary school or no education had a significantly higher prevalence of hypertension than respondents with higher education. Additionally, the prevalence of hypertension was higher among respondents in the poorest households than those from the wealthiest households. Supporting this findings, Apte and Salvi reported that the poor socio-economic strata of society in rural settings live in poorly ventilated houses and use bad fuel as a source of energy, which contributes immensely to hypertension risk (Apte & Salvi, 2016). The situation is aggravated by inappropriate infrastructure such as electricity in Albania, making it difficult to use electricity as a source of energy.

In contrast, houses in high-income countries use clean liquefied petroleum gas, natural gas, or electricity for cooking. Many of these houses are well ventilated and have green areas and fitted air conditioners. Furthermore, in Albania, it was found that the prevalence of hypertension was more significant among the respondents who were employed as compared to the ones unemployed. Most workers live in the cities, can afford clean fuel as their energy source, and access good health care. Indoor air pollution has the most significant impact on vulnerable populations due to limited resources to afford clean energy sources and exposure due to underlying health conditions (Ferguson *et al.*, 2020). The prevalence of hypertension was

significantly higher among the older age groups aged 35 and above. Giorgini et al. classified the elderly as vulnerable subjects with slightly higher blood pressure than younger groups following exposure to indoor air pollution (Giorgini *et al.*, 2016).

Similarly, Deng et al. observed that older people exposed to biomass are more likely to develop hypertension in China (Deng *et al.*, 2020). The prevalence was significant among rural residents. Rural residents exposed to HAP were more likely to develop hypertension than those not exposed to HAP. Since most of the population in LMICs live in rural and poor urban areas and mainly use biomass fuel as a source of their energy, they are the most vulnerable to HAP (Abtahi *et al.*, 2017). Other studies reported that the prolonged inhalation of smoke from biomass cooking can increase the prevalence of hypertension (Giorgini *et al.*, 2016).

The previous study established a place of residence to be associated with hypertension. To further understand this concept, there is a need to observe the patterns of rural-urban area disparities in the context of hypertension in LMICs. The analysis demonstrated hypertension to be high across urban and rural areas of most LMICs. As highlighted earlier, this could be because of the ongoing epidemiological and nutritional transition. The prevalence was observed to be higher among urban populations compared to rural residents.

Moreover, hypertension was higher among females than males and the results showed three different patterns (pro-urban, pro-rural and no difference). The following countries were pro urban: Bangladesh, Benin, Ghana, India, Lesotho, Namibia, Nepal, and South Africa. This finding is consistent with the studies of Al Kibria, Appiah, Craig, Desormias, Huang, and Rani (Al Kibria *et al.*, 2019; Appiah *et al.*, 2021; Craig *et al.*, 2018; Desormais *et al.*, 2019; Huang *et al.*, 2019; Rani *et al.*, 2022). Tajikistan, Kyrgyzstan, and Albania were pro-rural, and Haiti showed no significant difference. The analyses were stratified by the country's illiteracy, poverty, and unemployment rates. In countries with moderate and extreme poverty rates and

low and moderate unemployment rates, respondents living in urban areas were more likely to be hypertensive than those living in rural areas, whereas in countries with high or moderate unemployment rates, respondents living in urban areas were less likely to be hypertensive than those living in rural areas.

Unemployment and poverty can cause behavioural and lifestyle risk factors such as smoking, poor diet, alcohol consumption, and lack of exercise (Zagożdżon *et al.*, 2014). Appiah and colleagues found hypertension to be higher among urban women than in their rural counterparts in Ghana (Appiah *et al.*, 2021). The study further suggested that age, wealth quintile, and marital status influenced the likelihood of being hypertensive in Ghana. Age and behavioural factors are essential contributors to hypertension in urban areas. Lifestyle factors such as unhealthy diet, smoking and alcohol consumption have been associated with urban life (Sarki *et al.*, 2015).

Rani and colleagues found hypertension to be higher among male youths living in urban areas in India. The odds of hypertension in urban areas of India were attributed to being overweight and male sex (Rani *et al.*, 2022). Consistent with our findings, Alkibria and colleagues confirm the prevalence to be higher among urban Bangladeshi residents identifying concomitant diabetes, and being overweight as contributing factors (Al Kibria *et al.*, 2019). Similarly, the same pattern was observed in Namibia, Nepal, and Benin Republic (Craig *et al.*, 2018; Desormais *et al.*, 2019; Huang *et al.*, 2019). In Benin and other African countries, the commonness of hypertension levels can be attributed to the low awareness of blood pressure and other comorbidities. Inadequate knowledge of antihypertensive medications plays a crucial role in uncontrolled hypertension. Improving knowledge of hypertension knowledge and its drugs is a critical intervention required in this population. In addition, the high risk of HIV/AIDS in Lesotho contributed to the high incidence of hypertension (Mugomeri *et al.*, *et* 2016). Therefore, the integration of HIV care and hypertension could reduce the prevalence in Lesotho and other countries with the same problem.

The study found two out of the three countries with the pro-rural inequality were in Central Asia (i.e., Tajikistan and Kyrgyzstan). Child marriage is quite common in the region and could be associated with various adverse socio-economic and pregnancy outcomes. The odds of being hypertensive for the young adult women were associated with child death, marital control, and spousal violence being higher among child brides than their peers (Datta & Tiwari, 2022). These findings suggest that child marriage may increase the risk of hypertension among young adult women. In addition to child marriage, obesity and smoking were prevalent among rural inhabitants in Kyrgyzstan. Approximately 26% of the entire male population and less than 1% of the female population smoke (Kontsevaya *et al.*, 2017).

Albania showed a pro-rural pattern. Perhaps this could be a result of the recently implemented innovative primary health care programme termed "Si Je", meaning "how are you". This initiative allows Albanians to receive free yearly basic health examinations at all levels, and the uptake is very high in the urban areas. However, awareness and limited access to primary care and other challenges in the rural areas impede the programme's success and perhaps, explain the high prevalence of hypertension (Sentell *et al.*, 2021). A similar association of high hypertension levels and limited health facilities was identified in Haiti. The reason behind these limited health facilities in Haiti is the catastrophic earthquake of 2010, which destroyed most of the country's infrastructures, particularly that of health care services. (Kenerson, 2014).

South Africa was identified as a pro-urban country; hence this study further examined the pattern of association. The study implied that the overall prevalence of hypertension is high in South Africa because respondents living in urban areas have a higher prevalence of

hypertension than rural residents. As a result, the findings support the growing concern about hypertension as a public health problem in urban regions of Southern Africa. This finding is consistent with other studies conducted in different geographical contexts across the LMICs, e.g., Nepal, Bangladesh, Uganda, and Kenya. The results revealed a positive association between urbanicity and the risk of having hypertension among urban residents than respondents living in rural areas (Al Kibria et al., 2019; Aryal et al., 2015; Chowdhury et al., 2016; Craig et al., 2018; Hasan et al., 2018; Mathenge et al., 2010). In contrast, Ntuli and colleagues discovered that hypertension was more common in rural communities and associated with being married, having a low education level, and elderly (Ntuli et al., 2015). Similarly, Bernabe-Ortiz et al. found that having hypertension was almost four times greater among rural residents relative to their urban counterparts in Peru (Bernabe-Ortiz et al., 2017). Stevn et al. identified rural black people in South Africa to have a significantly lower risk of having hypertension than urban black, coloured and Asians, thus suggesting rural-urban differences (Steyn et al., 2008). The data showed that the odds a higher prevalence of hypertension among those living in urban areas increases with age. Rural residents are more likely to engage in daily household chores and other labour-intensive activities that may keep them physically active, burn more calories and lower BMI (Rahman et al., 2004). The study found that increase in age has a strong link with hypertension. The difference was more pronounced after 70 years of age. This finding is consistent with findings from other studies (Asemu et al., 2021; Chowdhury et al., 2016). That might be due to an increase in systolic blood pressure with age and the reduction in elasticity and other changes in the vascular system ((Ntuli et al., 2015). The study also revealed that the prevalence increased with richer wealth status in rural and urban areas, secondary or higher education, those not working, and those with no access to media. This is in line with the findings of Hassan et al. (2018). The study revealed that being hypertensive in Nepal is positively associated with increasing age, receiving education, and living in urban

areas. Respondents living in rural areas were more likely to have a low level of education, live in poorer households, not working, have no access to media, exposure to indoor air pollution, and have a problem getting money for treatment in urban areas to our findings. The study found that most respondents in urban areas belong to the wealthier class and are educated. As a result, they are more likely to adopt certain lifestyles such as cigarette smoking than those living in rural areas. This finding is in line with another previous study (Kibria et al., 2018). Nepalese residents with higher levels of education had a greater likelihood of having hypertension than those with lower education levels. Numerous researchers have found that the prevalence is significantly associated with older age, gender, education, place of residence, working status, wealth index, and comorbidities (Chowdhury et al., 2016). This observation is supported by sedentary lifestyles combined with junk food consumption, an ageing population, insufficient health system due to lack of funding, poor infrastructure, and lack of equipment, all of which have emerged as an inevitable consequence of urbanisation (Neuman et al., 2013; Rahman et al., 2016). The WHO reported that socio-economic factors influence behavioural risk factors, including education level, wealth status, and place of residence (W.H.O, 2009). On the other hand, some studies indicate that the people having higher education and belonging to the wealthier quintile often demonstrate less or no physical activity leading them to gain weight, which leads to hypertension. Wealth status of the respondents had an association with hypertension in both rural and urban regions in South Africa. Other studies indicated that people of higher socio-economic status follow more sedentary lifestyle patterns and engage in less physical activity than people of lower socio-economic status (Bernabe-Ortiz et al., 2017; Sanuade et al., 2018; Tareque et al., 2015). The odds of having hypertension are higher among people with higher socio-economic status since the wealthier class can afford/purchase more consumable resources with many calories. As a result, they tend to consume more calories,
resulting in being overweight or obese and higher risk of hypertension than people from lower socio-economic status (Al Kibria *et al.*, 2019; Tareque *et al.*, 2015).

The ecological study of geographic variations between the countries also demonstrated a very high widespread of hypertension in LMICs. Moreover, the prevalence has increased considerably in most countries. The adult literacy rate in LMICs was relatively low compared to other high-income countries. South Africa, Mauritius, and Sao Tome had extremely high adult literacy. In contrast, Chad, Guinea, and Burkina Faso had the least adult literacy rate. The study revealed a high percentage of unemployment in most LMICs. Niger, Chad, and Madagascar had the highest unemployment rates, whereas Djibouti, Botswana and Gabon had the lowest unemployment rates. The study also reveals that many people live in urban areas; hence, Gabon, Equatorial Guinea, and Djibouti had the highest number of urban residents, whereas Burundi, Malawi, South Sudan, and Kenya the highest number of rural residents. The results showed that a country's GDP and its domestic health expenditure were correlated with the levels of hypertension in the respective country. Both determinants are common macroeconomic indicators used to measure the standard of living and public health policies (Sposato & Saposnik, 2011). The study also revealed that countries with high GDP and domestic health expenditure have a lower prevalence of hypertension. These findings agree with the study of Gheorghe and colleagues (Gheorghe et al., 2018). The burden of CVDs is higher in lower-income countries with low GDPs and considerably low health expenditures. Symmetrically, CVDs cause significant reductions in GDP, suggesting a reciprocal relationship (Gheorghe et al., 2018). These findings highlight the need for more investment in the health sector to manage the burden of hypertension and other CVDs across limited-resource settings. The research also found the country's multidimensional poverty index and the unemployment rate to be among the determinants of hypertension. Increased multidimensional

poverty index and unemployment rates increased the country's hypertension prevalence. There are several possible explanations for the positive association of the multidimensional poverty index with hypertension. For example, due to the limited access to health care, cardiovascular risk factors are more common in LMICs (Krzysztoszek et al., 2014), and the cost of hypertension care is high, and the expenses increase each year (Krzysztoszek et al., 2014). Another explanation could be that poorer countries allocate a lower proportion of their economic resources to health than wealthier countries. (Sposato & Saposnik, 2011). Inefficient health systems and reduced government expenditure on health promotion interventions may explain the high prevalence of hypertension (Cappuccio, 2004; Dzudie et al., 2018). For instance, populations in most emerging countries still lag in affording even secondary medications and treatments to prevent CVDs. Individuals, households, financial agents, public institutions, government, and society suffer economic repercussions from CVD-related disability. Sadly, the research projects a significant increase in CVDs in future and the burden is expected mainly to be in LMICs due to population growth, ageing, and globalisation (Gheorghe et al., 2018). In LMICs, the economic burden of CVDs on households, health systems, and national incomes could discourage the current poverty-reduction efforts. The societal cost of hypertension is significant because increasing number of hypertension patients will distort the overall productivity, adversely impacting many household finances (Sokolov-Mladenović et al., 2016). Furthermore, according to this study, there also exists a correlation between hypertension prevalence and the adult literacy rate. The result showed that, with the increase in adult literacy, the prevalence of hypertension reduces. People from countries with high literacy rates are more likely to be aware of their hypertension status and seek medical treatment than citizens of countries with low literacy rates. It was found that access to health care was associated with hypertension awareness and management (Lee et al., 2022). The study showed that a place of residence has an association with the prevalence of hypertension. The

result indicated that hypertension reduces as more people live in urban areas. This change could result from urbanicity and economic development (Lee et al., 2022). Living in a city provides access to public health facilities, which enhances the likelihood of hypertensive adults using antihypertensive medications across the economic spectrum. Moreover, access to a public health centres is critical for people with little financial resources, emphasising the value of free or very low-cost medication supplied by a public health centre in achieving blood pressure control (Lee et al., 2022). We also found that the prevalence of hypertension reduces with each one million increases in the country's population. An increase in population is a global challenge being confronted by LMICs. Urban planning also reduces non-communicable diseases while managing rapid urbanisation. It might include encouraging walking, cycling and public transport use, while reducing private motor vehicle use. Therefore, creating safe and secure neighbourhoods, convenient transportation, and healthier households will establish a sustainable living environment and reduce the behavioural risk choices and hypertension levels. (Giles-Corti et al., 2016). The general improvements in overall hypertension care for those with low economic status could perhaps explain the findings. Using antihypertensive medications was linked to having access to public health facilities. Primary health care has been steadily improving, and this expansion appears to have contributed to increasing antihypertensive drug use, which has resulted in better blood pressure control (Lee *et al.*, 2022).

6.2. IMPLICATIONS FOR PRACTICE

This bibliometric analysis provides insight into the historical development of hypertension research. The findings from the study highlight the need for governments of African countries to meet the African Union target of 1% of GDP invested in research and development. Presently, no country in the WHO African region has achieved this target. Publications play a vital role in the scientific process, providing a critical linkage between knowledge production and use. The present data reveal a solid mass of research activities on hypertension. The current

study provides valuable information to researchers and funding societies concerned with implementing research strategies to improve hypertension research.

Additionally, the results of this study delineate a framework for better understanding the situations of current hypertension research and future directions of the research in this field, which could be applied for managing and prioritising future research efforts in hypertension research. This study provides some novel insights useful for policymakers, researchers, and funders interested in advancing the hypertension research agenda. International research collaborations and networks should be encouraged to help prioritise hypertension research, particularly among women. Moreover, this study also provides fundamental data to research scholars and policymakers to help them recognise the bibliometric indicators when conducting hypertension research, while making future policies and funding decisions. Finally, our study showed that bibliometric analysis is an excellent methodological tool to map published literature on a particular subject and pinpoint research gaps.

This study adds to the existing literature by providing information on hypertension in relation to HIV infection. The study established that hypertension is a growing problem in HIV-infected adults. Both conditions have similar needs for chronic care, which present an opportunity to coordinate efforts and achieve synergies to benefit patients in resource-limited settings (Patel *et al.*, 2018). Most LMICs across worldwide are undergoing a rapid transition characterised by a shift from communicable to non-communicable diseases (Gouda *et al.*, 2019; Sarki *et al.*, 2015). People living with HIV currently live longer and are at greater risk of developing non-communicable diseases (Hing *et al.*, 2019). There is no doubt that remarkable success in combating HIV occurred. Still, there is less attention to the steadily emerging problem of chronic diseases in resource-limited settings, which indicates a real need to re-evaluate the health care systems, including screening programmes. HIV treatment is equally important in preventing and managing hypertension among PLHIV (Nash *et al.*, 2018). Therefore,

continued focus on tests and treatment will improve the health outcomes of patients. A vertical approach might not be the best way to address the dual disease burden situation, but rather an integrated management and holistic approach to the present significant problems. A good suggestion for such an approach is to include hypertension as part of the regular HIV care and health education programmes, getting the benefit of the widespread HIV awareness. Knowledge about comorbidities is critical to the future care and treatment models of HIV. The shift in disease epidemiology makes the need for integrated implementation and management of disease inevitable.

Gender-based violence remains one of the significant public health problems and has a severe impact on women's health and wellbeing. The interventions to address hypertension in central Asia and other LMICs need to consider this factor of IPV. Stress caused by violence perpetrated by a spouse or partner could be a confounding factor in having hypertension in young women. Hypertension is costly as a chronic illness requiring medication and specialised dietary requirements. Young women in the Kyrgyzstan Republic (and globally) are not financially independent and cannot bear management and treatment costs alone. All efforts should be made to prevent the development of hypertension among women and other vulnerable groups. This study suggests that measures to eliminate abuse will also aid in the decrease of hypertension among young women who have experienced intimate partner violence. Due to the discovery that IPV is a significant determinant of hypertension among women, it has become more convenient to change the local policies and programmes to promote women's care and security. The findings of the multilevel analysis highlight the importance of implementing public health preventive measures at the high-risk person level and the high-risk neighbourhood level. Interventions that target an individual's social and physical settings and health care systems are required to eliminate or reduce hypertension risk. These interventions must be multidimensional, i.e., they must take place at multiple levels simultaneously or in close succession (Paskett *et al.*, 2016). Behaviour changes, such as healthier food intake through legislative changes, like raising taxes on unhealthy foods or drinks; changes in the delivery of health care services; and environmental changes by making healthy food more accessible, are all possible outcomes of multilevel interventions (Paskett *et al.*, 2016). Community-based programmes, which connect communities and health systems and involve a variety of treatments like education and outreach, self-management, and home-based care, have emerged as a viable way to close access gaps and reduce geographic variations, which also play a significant role in the prevalence of hypertension (Brownstein *et al.*, 2007; Perry *et al.*, 2014). According to previous studies, community-based hypertension screening and case management strategies can save money, while improving outcomes (Jeet *et al.*, 2017; Kim *et al.*, 2016).

The study identified a positive association between indoor air pollution and hypertension in urban and rural areas. Indoor air pollution and cooking fuels can be controlled by introducing clean fuel/electricity such as LPG, a fuel recognised to reduce HAP levels. Governments should adopt renewable energy incentives to reduce dependence on solid fuels (McLean *et al.*, 2019) and create awareness on the risks of using solid fuels among high-risk groups, especially women who, culturally, engage in cooking. The findings will inform future intervention studies and policy changes by generating knowledge to effectively control HBP in LMICs. Given the importance of blood pressure control in reducing CVD risk, there is an urgent need for strategies to promote HBP diagnosis at local health facilities and the community level and prompt treatment initiation and follow-up of cases. In addition, salt reduction in food requires commitment at both provincial and national levels.

This study has produced substantial and recent evidence on the effect of urbanicity on the development of hypertension in resource-limited situations among inhabitants in urban regions versus those in rural areas. It is, therefore, pertinent to examine the impact of urbanisation as it relates to the threats that arise from hypertension. As a result, hypertension management and control are crucial in nations like South Africa and other LMICs experiencing significant poverty and socio-economic disparity. Government and policymakers should roll out community-specific hypertension prevention measures targeting rural and urban residents using data on the prevalence and variables associated with hypertension.

Our findings revealed that health expenditure was increasing substantially relative to GDP growth in almost all income levels. This increase in spending has become a significant concern for governments and policymakers. Therefore, the health sector should advocate for integrated multi-sector city planning that prioritises health sustainability, particularly in rapidly changing LMICs. Like the High-Income Countries (HICs), LMICs must also gain and utilise knowledge to grow their economies. LMICs should increase the gross economic expenditure on R&D to familiarise themselves with the cutting edge technology used to treat burgeoning outbreaks of hypertension disease (Sokolov-Mladenović *et al.*, 2016). It is important to involve patients in clinical decision-making and access multi-disciplinary care (Burgoyne, 2021). Socio-economic factors are an essential benchmark of health system performance for managing hypertension in LMICs against which future progress can be compared, implying that lessons could be learned from approaches adopted by those health systems. An assessment of a healthcare's ability to deliver comprehensive yet inexpensive treatment to widespread diseases like hypertension can be regarded as a measure of such a country's ability to fulfil its national and international healthcare targets, such as moving towards universal health coverage. Specifically, as LMICs undergo the epidemiological transition from infectious to chronic diseases, such health system performance measures could help track countries' progress in shifting health services to chronic

condition care. (Geldsetzer *et al.*, 2019). It is important to standardise healthcare costs across countries for ease of reference and comparisons to better monitor and facilitate fund allocation decision-making.

6.3. IMPLICATIONS FOR FUTURE RESEARCH

Quantitative bibliometric results conclude nothing about the quality of research conducted worldwide. This means that additional research is required to contextualise our findings and provide in-depth insights regarding what types of theoretical and methodological approaches are used to research and national research priorities. In addition, this research will also enrich the current understanding of the historical and structural determinants of global bibliometric trends and inequity. Future studies should also be conducted outlining the types of hypertension research completed until now, and they should identify research gaps to guide future investments in hypertension research in Africa. Further studies on hypertension research output in Africa should assess quality, research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, and country-level social factors beyond population size and country income that may predict higher research impact, higher research impact, and country-level social factors beyond population size and country income that may predict higher research output.

Future studies should investigate causality from IPV and hypertension and explore if there exists an affirmative status of causality later in life. In addition, qualitative research on IPV victims' coping methods for managing hypertension will guide direct medical and social programmes to help these women. Considering resource difficulties in low- and middle-income settings, self-management and community health empowerment models are great approaches and considerably cost-effective. More research on the health determinants of diseases will

result in the development of a complementary vision which will help to detect gaps, allow troubleshooting, and find efficient solutions to several healthcare problems.

Further research is needed to construct novel risk scores for hypertension that include both individual and contextual factors to identify people at higher risk for having hypertension and examine opportunities for the improved use of preventive interventions that ensure the delivery of proactive and personalised treatment of the victims. The current methods do not account for the underlying contextual factors contributing to hypertension. There are significant health and economic benefits of performing early diagnosis, proper care, and effective hypertension control. Treating complications necessitates expensive measures that deplete the budgets of both individuals and governments. Similarly, additional decomposition studies may provide more information about crucial factors that could explain the differences in the risk of hypertension among high-risk individuals and those living in high-risk locations. Further research is also needed to identify innovative ways of integrating hypertension prevention and care strategies in different populations in LMICs and the cost-effective ways of implementing policies to address the high prevalence.

Studies revealed a positive correlation between hypertension and air pollution inside the households, particularly those located in rural areas with uneducated residents, especially women. Further studies should confirm the findings of this study as a prospective cohort study. Indoor cooking and biomass fuel use are important risk factors. Therefore, issues of energy and indoor air pollution should be considered in policies and interventions to reduce the burden of hypertension in countries where the domestic use of biomass fuels is frequently used.

Finally, a simulation study is believed to be more informative to policymakers instead of an assessment based on historical trends. Using simple economic models, improvement scenarios

on hypertension can be measured. This study has provided insights on novel risk factors for hypertension using a different analytical approach to better understand the condition in LMICs. We have identified that hypertension has a link with HAP, GBV, place of residence and socioeconomic determinants. It is, therefore, pertinent to measure the burden of hypertension by eliminating risk factors such as HAP and GBV and improving the health of individuals living in LMICs. Policymakers will have a better idea of what to expect in terms of improved wellbeing and achievements of set targets.

6.4. STUDY LIMITATIONS AND METHODOLOGICAL CONSIDERATION

The author of the research admits that not every journal publication is indexed in web of science databases such as PubMed. Due to this, several relevant articles concerning this research from various countries may be missed. However, a comprehensive search strategy incorporating the names (and alternative names where appropriate) of all countries in the WHO African region, limitations by the relevant fields, and without language or study design restrictions were employed. The study did not assess the quality of hypertension research. Although all included studies were indexed in PubMed, it is unclear if any of these studies are high quality and are more likely to have a high research impact. The study focused on the absolute number of publications, i.e., the quantity of the articles under observation, indexed per country as a measure of productivity.

Historically, earlier articles were likely to accrue more citations than recent ones. The number of sources was divided by the number of years to determine a citation rate/mean citation per year. The author acknowledges that the study's findings are influenced by choice of the research question and our exclusion and inclusion criteria. Also, the citation ranking can vary depending on the date of retrieval.

Although topic modelling has previously been used to analyse medication safety research trends (Zou, 2018), we believe this is the first study to apply unsupervised machine learning to assess hypertension research subjects and patterns over the past century. The procedure of data analysis was relatively objective. However, most of the papers included in the database were written in English, which means that relevant studies published in other languages may have been overlooked. The study examined articles, reviews, and editorials published in academic journals indexed in PubMed as part of the study design. Therefore, this research does not claim to represent all the work done on the topic under review, such as the work that may have been published in other formats (e.g., books, reports, and national journals). This research only provides approximate terms of country contributions to global scientific production because we could not manually search all the retrieved papers to ensure their relevance. Even though we believe our findings reflect broad trends in the hypertension research environment. It is important to note that common lexicons for sentiment analysis have many limitations when applied to health literature. For example, in the used lexicon, "negative" terms are likely not negative in the scientific literature. They might represent that no disease symptoms were found in the subject; hence reported negative (ex: symptoms, inhibition etc.) and the same with "positive" labels (ex: survival, advanced, progressive) are more likely to have negative sentiment in hypertension-based literature. For example, they might represent that the disease symptoms were found in the subject; hence likely to be reported positive.

The data used was cross-sectional; therefore, no causal relationship can be inferred between the risk factors and hypertension. The study could not measure the associations between hypertension and several important determinants like dietary habits, physical activity, diabetes, salt intake, smoking and family history of hypertension due to the absence of the data in the survey. The results may not be generalised for Namibia and other LMICs due to the small sample size and are probably underpowered to detect differences compared to India's larger sample size. data regarding the epidemiology of hypertension over time among PLHIVs in Africa is limited, representing the heterogeneous population. This study uses secondary data, and therefore, other confounding factors such as stress levels could not be accounted for from the data. Secondly, the time and period of abuse could not be determined. Hence, it is difficult to conclude that participants were hypertensive before the abuse. Other comorbidities such as obesity that increase the chance of having hypertension were controlled. The study cannot determine if the hypertension status of these young women was pregnancy-related, as is the case of pre-or postpartum hypertension.

DHS data don't include information on established indicators used to measure wealth, such as household expenditures or incomes. Asset-based wealth index could only be used as a proxy indicator of household economic status, whereas the comparison between individual income and expenditures, if possible, could provide a genuine financial status regarding each household (Filmer & Pritchett, 2001; Montgomery *et al.*, 2000). Since we could not estimate the time spent by the participants and their exposure to the environmental factors, the study could not conclude whether the associations of neighbourhood characteristics with current hypertension were due to cumulative effects or not.

The data used at the national level to evaluate the association between hypertension and indoor air pollution was obtained under minimal resource settings. More than 70% of the respondents were women, which may explain why the association between HAP and hypertension was significant among women but not men. In addition, the study could not account for certain factors that might affect actual indoor air pollution and blood pressure measurement, including information on cooking time, the type of building and ventilation, which was shown to be linked to the prevalence of hypertension. The DHS data do not include information on cooking fuels other than just solid fuel in the household. Some households reported using more than one fuel, which would lead to misclassification in the exposure definition and bias in the estimated associations (Piedrahita et al., 2016). The study did not include information on ambient air pollution, which may also be associated with high blood pressure. There was little or no information on the use of blood pressure medication. Lastly, several studies have used self-reported primary cooking fuel as a practical proxy for HAP; this is an inherently limiting indicator (W.H.O, 2016). For cooking, heating, and lighting, one-third of the world's population uses organic materials such as wood, dung, or charcoal (biomass fuel). This energy use is linked to high levels of indoor air pollution and increased respiratory infections such as pneumonia, tuberculosis, chronic obstructive pulmonary disease, low birth weight, cataracts, cardiovascular events, and all-cause mortality in both adults and children (Fullerton et al.). The mechanics underlying these connections are not entirely known. Much health-related exposure to air pollution from cooking fuel happens outside homes, not inside (Smith & Pillarisetti, 2018). This is because solid cooking fuel is toxic enough to impact ambient (outside) air pollution levels significantly and, as a result, can induce illness far away from the source (Smith & Pillarisetti, 2018). Carbon monoxide, formaldehyde, and other hazardous chemicals released by natural gas and propane burners are highly toxic to humans and animals. Fumes exiting the chimneys of wood stoves and fireplaces produce heavy wood smoke, contributing to indoor and outdoor air pollution (W.H.O, 2014).

The ecological study included a large data set across 53 countries. There are some limitations to be considered when interpreting the findings of this study. Even though the data collection strategy was standardised, the reporting system in each country might differ. Secondly, data for some countries might be missing, or some countries have no data; hence the findings should

be generalised with caution. An ecological study does not characterise potential cofounders, making it challenging to draw definitive conclusions and hence cannot determine causality (Beaglehole & Bonita, 2008).

6.5. Study strengths

Regardless of these limitations mentioned above, this study provides additional insights into research priority areas and several other characteristics in hypertension research. The review thoroughly examined hypertension articles from various medical specialities publications. An empirical analysis that used latent Dirichlet allocation modelling to identify key research themes was employed to examine themes' dynamics and intellectual structure. The findings gave a complete overview of hypertension-related research subjects highlighting how hypertension has evolved. The results of this study could help us better understand hypertension research trends and propose areas for further research.

The data used are from a large, population-based survey with high response rates covering 12 LMICs. DHS is a nationally representative survey that allows researchers to conduct further research requiring problems based on the data across several countries. The DHS data were collected using the same approach in all participating countries, allowing comparisons across countries. For example, in study IV, the risk of prevalent hypertension among PLHIV and HIV-negative individuals in 5 LMICs allowed comparison. The findings from the study provide additional information that may reshape the health care systems in resource-limited settings and globally at a larger scale. Secondly, A meta-analysis and decomposition analysis was employed to decompose the difference in outcome variables between 2 groups into two components explained in the methodology section. The study determined the critical factors responsible for the inequality.

The study focused on GBV and consequent hypertension among women in the Kyrgyz Republic. The DHS also adheres to stringent ethical rules in collecting domestic violence data. Hypertension and IPV are both known to have detrimental consequences for women, and this study showed a positive relationship between the two risk factors.

The study investigated the influence of urbanicity on the risk of having hypertension in LMICs. A meta-analytical approach and a propensity matching technique were employed to understand the HBP patterns in rural-urban areas and to compare the baseline characteristics of the respondents for all the variables before and after propensity matching to eliminate bias. The propensity score was used to account for the differences in baseline characteristics between respondents living in urban areas and respondents living in rural areas—the propensity score approach controlled all observed confounding factors that might influence the result.

The ecological study provides a quick and effortless way of determining associations between factors of interest and outcome and adds to the literature demonstrating the importance of socioeconomic determinants and hypertension in LMICs. It highlights the need for further research to understand how socioeconomic determinants interact in such populations at individual levels. However, the findings suggest that countries with a pronounced burden of hypertension also have increased poverty, high unemployment rates, and invest less in health care, affecting the economy and health systems.

6.6. CONCLUSIONS

The research examined the novel risk factors of hypertension in LMICs by building convincing evidence to seek solutions to reverse this burgeoning epidemic. The study was carried out in four phases. Evidence harvesting and mapping were done in the first phase by examining hypertension research productivities in Africa and other LMICs. Countries with high volumes of hypertension-related publications have a low prevalence of hypertension. In contrast, countries with low volumes of hypertension-related publications to global hypertension research output as indexed in PubMed — albeit less than 5% — have increased approximately three-fold. The

number of these publications has been growing exponentially over the 20-year period. A topic modelling approach was used to examine 100 years of hypertension research. Over 500,000 uncovered topics were taken and grouped into four categories (i.e., preclinical, epidemiology, complications, and treatment-related studies). This phase provides insights into the historical development, trends, and patterns of hypertension research. The major referenced topics in hypertension research were coronary heart disease, blood pressure, and hypertension. These findings could help identify priority areas and guide future research.

At the individual level, we examined the contribution of HIV and GBV on the risk of having hypertension. The results revealed that variations exist among HIV-positive and negative individuals. Hypertension is prevalent among the PLHIVs in India, while hypertension is prevalent among HIV negative participants in Namibia. PLHIVs are successfully linked to clinical care and treated with Antiretroviral Therapy (ART), and attention must turn to maintain their restored health to realize the benefit. The existing and expanding healthcare infrastructure presents an opportunity to incorporate additional preventive interventions for other diseases, most importantly hypertension, even though some researchers argue that integrating non-HIV medical services with HIV clinical care could reduce patient care and support. The benefits of an integrated approach could be profound, and support for this approach has been fast-growing (Hyle et al., 2019). Decision-makers in public health and medicine must recognize the potential human and health costs associated with the high prevalence of hypertension among PLHIVs. The study found that GBV is a significant problem in the Kyrgyzstan republic, and other LMICs, contributing to hypertension risk. There is a need for more awareness of the impact and repercussions of GBV on the lives of individuals who experience any form of abuse, particularly among rural residents, those with secondary and higher education, and unemployed

individuals. This study recommends a multi-sectorial approach to addressing interpersonal violence against women, girls, and children.

At the contextual composition level, the multilevel analysis revealed that the individual compositional and contextual measures of socioeconomic status were independently associated with the risk of having hypertension. With this finding, there is a need to implement multilevel hypertension prevention strategies at different contextual levels. Therefore, prevention strategies should be implemented not only at the individual level; socioeconomic status and contextual levels should be considered.

The study examined the association between indoor air pollution and hypertension in the community and found positive associations, particularly in low-income households, women with no education, and those living in rural areas. The findings suggest that the risk of hypertension may be reduced by eliminating or reducing indoor air pollution, particularly among Albania's most vulnerable groups and other similar countries from resource-limited settings. One of the most significant contributions to residential air pollution is using bad fuels for cooking and heating. Therefore, to minimize house air pollution, it is imperative to create awareness about HAP and its health effects to reduce the risk of CVDs in the population at large. Major interventional strategies need to be implemented at various levels to reduce HAP, and its effects on health. Research and consolidation of nationwide data by all countries will help generate regional data regarding HAP in different regions to inform policy and decision making through behavioural interventions and cost-effective methods to improve household air quality during cooking and heating.

The study examined the HBP patterns in rural and urban areas. The findings revealed three different patterns of associations, namely pro-urban, pro-rural and no-difference. In eight countries (Bangladesh, Benin, Ghana, India, Lesotho, Namibia, Nepal, and South Africa),

respondents living in urban areas were more likely to be hypertension than those living in rural areas. The second pattern showed a pro-rural association in three countries (Albania, Kyrgyz Republic, and Tajikistan). Pro-rural and pro-urban associations were similar in Haiti. Poverty, illiteracy, and unemployment were factors that explained the patterns.

The study used the propensity score matching technique to examine the influence of urbanicity on hypertension risk in South Africa. The study reveals that hypertension is a significant problem in urban regions of South Africa. An increase in age, higher education level, and higher socioeconomic status were positively associated with being hypertensive. Public health efforts are urgently necessary for effective prevention and control of this progressive disease for a diverse group of people from different geographic areas on a priority basis to reduce its health and economic burden. The health system of South Africa needs to develop strategies to increase the required screening and diagnosis of hypertension in both rural and urban areas. Finally, the study found countries with high GDPs that invest in health and improve the

multidimensional poverty index have a lower prevalence of hypertension. Therefore, we recommend that health financing reform across all LMICs as part of progress toward universal health coverage mean more than mobilizing additional funding and managing the transition from donor support.

Hypertension is a global concern as it causes premature death and imposes colossal health and economic burden on a nation. Researchers and policymakers should focus on the emerging risk factors of hypertension. Evidence has established that their contribution to the high burden across different countries is significant.

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