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Challenges in using cardiovascular medications in Sub-Saharan Africa

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CHALLENGES IN USING CARDIOVASCULAR MEDICATIONS IN SUB-SAHARAN AFRICA

DERBEW FIKADU BERHE

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Challenges in using cardiovascular medications in Sub-Saharan Africa

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**Introduction
and Aims**

Background

Globally, cardiovascular disease (CVD) is the leading cause of mortality with an estimated 17.5 million, or 31% of all, deaths reported worldwide in 2012 [1]. Nearly 80% of these deaths occur in low- and middle-income countries [1, 2]. Moreover, the mortality rate in these countries is on a steady rise. Also in (sub-Saharan) Africa the prevalence is increasing rapidly [2, 3]. These diseases (CVDs) are a group of disorders affecting heart and blood vessels that includes ischemic, congenital or rheumatic heart diseases, cerebrovascular disease (stroke), peripheral arterial disease, and deep vein thrombosis. Hypertension is the most important risk factor for CVDs. More than a billion people globally have elevated blood pressure with 9.4 million attributed annual deaths [4]. Other important, often concomitant, risk factors for CVDs include (i) behavioral factors: unhealthy diet, physical inactivity, tobacco use and harmful use of alcohol, (ii) social-economic factors: urbanization, population ageing, poverty, stress, and culture, and (iii) disease-related and hereditary factors [1]. Some of these factors are unique or more pronounced to (Sub-Saharan) Africa including low societal awareness, little priority to fight CVDs, and human resource limitations. Genetic factors — e.g. high vascular contractility, extreme salt sensitivity, and low renin release - are another important challenge for managing CVD in the black population [5–7]. In addition, socio-economic changes in the continent have resulted in rapid urbanization, and the population adopting an unhealthy ‘Western’ lifestyle, characterized by too little exercise, stress and poor food habits [8].

It has been firmly established that treating hypertension improves cardiovascular outcomes [9–11]. However, achieving target blood pressure remains a challenge. This depends on several factors: the healthcare system, infrastructure and, access to medicine. Health Care Professionals (HCPs) related factors also play an important role. The knowledge HCPs of the diseases, pharmacotherapy, treatment guidelines and their attitude towards patient management determine how they implement their (clinical) pharmacology knowledge into practice. In addition, patient-related factors are also crucial determinants of how patients are treated and may

respond to therapy. For patients to benefit of treatment, they need to take their medication. For hypertension, a mostly symptomless disease, adherence to medication can be poor [12]. Adverse effects experienced by patients and general satisfaction with treatment are important factors for medication adherence [13–16]. Effective patient-HCP communication can result in better patient understanding of the benefits of medication as well as its risks and promote better adherence to medication.

Thus, CVD management in (Sub-Saharan) Africa is challenged by a number of factors including HCPs knowledge of, and attitudes towards medication used for CVDs, access to medication and patient specific challenges such as treatment satisfaction, and medication adherence [3, 17–19]. However, the majority of studies on hypertension and other CVDs from (Sub-Saharan) Africa are limited to prevalence reporting as attention for these diseases is only recently increasing [8, 20, 21]. Little to no attention has been paid to efficacy and safety of medicines used to treat hypertension and CVD. Especially in Africa, the first symptom of hypertension may still be that a patient experiences a stroke. Most cardiovascular diseases, if not identified early, are initially asymptomatic and need to be managed lifelong. Asymptomatic patients or patients with CV risk factors only, do not experience an immediate benefit from their antihypertensive treatment, but may experience adverse effects immediately. To ensure optimal care requires a holistic approach; i.e. from improving awareness of the disease among patients and HCPs, to provide appropriate antihypertensive treatment based on robust clinical evidence, pay appropriate attention to adverse drug events and ensure patients have access and stay adherent to treatment.

In (Sub-Saharan) Africa, there is lack of data on CVD medication use and safety, and their effect in terms of achieving treatment goals. The region faces a major challenge to tackle the increasing burden of CV diseases. This thesis aims to increase the knowledge base on current CV medication that is needed to develop effective programs to improve rational drug use for cardiovascular diseases medications.

Objectives and outline of thesis

The specific objectives of this thesis were to 1) describe HCPs' medication knowledge, 2) identify key features of cardiometabolic adverse drug reaction reports (ADRs) in Sub-Saharan Africa, 3) assess hypertension treatment practices and its determinants, and 4) evaluate the impact of adverse drug events (ADEs) and treatment satisfaction on antihypertensive medication adherence in Ethiopia.

In **chapter two**, we conducted a systematic review of original studies that assess medication knowledge of HCPs in Africa. This study intends to provide an overview of the level of HCPs knowledge differentiated by disease focus (inclusive CVDs), type of HCPs, and country of the study.

The World Health Organization (WHO) stimulated setting up or to strengthen pharmacovigilance centers on the continent to increase awareness of the importance of reporting ADRs reporting [22]. In **chapter three**, key features of cardiometabolic ADR reports in Sub-Saharan Africa were identified, and were compared with reports from the rest of the world. The study was designed to provide an insight in attention given to safety of medicines used for cardiometabolic diseases.

In **chapter 4**, we provide an overview of Ethiopian health care set up relevant for the field studies performed in thesis. **Chapter five and six** describe the results of observational study conducted in Ethiopia, the second populous country in Africa. In this study prescribing practices, treatment outcomes, and treatment experiences of more than 900 ambulatory patients were collected in six secondary and tertiary hospitals in the capital city and across northern part of the country. **Chapter five** focused on hypertension treatment practices and its determinants. The study aims to provide information on the level of patient achieving treatment goals, i.e. controlled hypertension. It also explored potential determinants of controlled hypertension, and for what patients' treatment was intensified if their blood pressure remained uncontrolled. **Chapter six** focused on antihypertensive medication adherence and if experiencing adverse drug events (ADEs) and how patients are satisfied with their treatment affect adherence.

In the **final chapter (seven)**, the findings of the different studies in this thesis are discussed and translated into practical implication and recommendations with final conclusion.

References

- (1) WHO. Cardiovascular diseases (CVDs) Fact sheet. 2016;
Available at: <http://www.who.int/mediacentre/factsheets/fs317/en/>.
Accessed Dec 26, 2016.
- (2) WHO. A global brief on hypertension: Silent killer, global public health crisis. 2013.
Available at:
http://apps.who.int/iris/bitstream/10665/79059/1/WHO_DCO_WHD_2013.2_eng.pdf.
Accessed July 16, 2016.
- (3) Cappuccio FP, Miller MA. Cardiovascular disease and hypertension in sub-Saharan Africa: burden, risk and interventions. *Intern Emerg Med* 2016; 11:299–305
- (4) Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *The Lancet* 2016;387:957–967.
- (5) Brewster LM, Seedat YK. Why do hypertensive patients of African ancestry respond better to calcium blockers and diuretics than to ACE inhibitors and beta-adrenergic blockers? A systematic review. *BMC Med* 2013;11:141
- (6) Dennison CR, Peer N, Steyn K, Levitt NS, Hill MN. Determinants of hypertension care and control among peri-urban Black South Africans: the HiHi study. *Ethn Dis* 2007; 17:484–91.
- (7) Opie LH, Seedat YK. Hypertension in sub-Saharan African populations. *Circulation* 2005; 112:3562–68.
- (8) Keates AK, Mocumbi AO, Ntsekhe M, Sliwa K, Stewart S. Cardiovascular disease in Africa: epidemiological profile and challenges. *Nat Rev Cardiol* 2017; 14:273–293.
- (9) Corrao G, Parodi A, Nicotra F, Zambon A, Merlino L, Cesana G, et al. Better compliance to antihypertensive medications reduces cardiovascular risk. *J Hypertens* 2011; 29:610–8.
- (10) Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. *Lancet* 2016; 387:957–67.

- (11) Ortegon M, Lim S, Chisholm D, Mendis S. Cost effectiveness of strategies to combat cardiovascular disease, diabetes, and tobacco use in sub-Saharan Africa and South-East Asia: mathematical modelling study. *BMJ* 2011;344: e607.
- (12) De Geest S, Sabate E. Adherence to long-term therapies: evidence for action. *Eur J Cardiovasc Nurs* 2003;2:323.
- (13) Leporini C, De Sarro G, Russo E. Adherence to therapy and adverse drug reactions: is there a link? *Expert Opin Drug Saf* 2014: S41–55.
- (14) Barbosa CD, Balp MM, Kulich K, Germain N, Rofail D. A literature review to explore the link between treatment satisfaction and adherence, compliance, and persistence. *Patient Prefer Adherence* 2012; 6:39–48.
- (15) Saarti S, Hajj A, Karam L, Jabbour H, Sarkis A, El Osta N, *et al.* Association between adherence, treatment satisfaction and illness perception in hypertensive patients. *J Hum Hypertens* 2016;30:341–5.
- (16) Sa'ed HZ, Al-Jabi SW, Sweileh WM, Morisky DE. Relationship of treatment satisfaction to medication adherence: findings from a cross-sectional survey among hypertensive patients in Palestine. *Health Qual Life Outcomes* 2013; 11:191.
- (17) Aagaard L, Strandell J, Melskens L, Petersen PS, Hansen EH. Global patterns of adverse drug reactions over a decade. *Drug Saf* 2011; 35:1171–82.
- (18) Ampadu HH, Hoekman J, de Bruin ML, Pal SN, Olsson S, Sartori D, *et al.* Adverse Drug Reaction Reporting in Africa and a Comparison of Individual Case Safety Report Characteristics Between Africa and the Rest of the World: Analyses of Spontaneous Reports in VigiBase®. *Drug Saf* 2016; 39:335–45.
- (19) Mocumbi AO. Lack of focus on cardiovascular disease in sub-Saharan Africa. *Cardiovasc Diagn Ther* 2012; 2:74–7.
- (20) Kayima J, Wanyenze RK, Katamba A, Leontsini E, Nuwaha F. Hypertension awareness, treatment and control in Africa: a systematic review. *BMC Cardiovasc Disord* 2011; 13:54.
- (21) van de Vijver S, Akinyi H, Oti S, Olajide A, Agyemang C, Aboderin I, *et al.* Status report on hypertension in Africa-consultative review for the 6th Session of the African Union Conference of Ministers of Health on NCD's. *Pan Afr Med J* 2013; 16:38.
- (22) Strengthening Pharmaceutical Systems (SPS) Program. Safety of Medicines in Sub-Saharan Africa. Assessment of Pharmacovigilance Systems and their Performance. Submitted to the US Agency for International Development by the Strengthening Pharmaceutical Systems (SPS) Program; 2011; Management: Arlington, VA.

