

March 2018

Hypertension Control, an Annotated Bibliography

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The hypertension bibliography was developed by the U.S. Centers for Disease Control and Prevention (CDC) and RTI International with the assistance of Resolve to Save Lives and Johns Hopkins Bloomberg School of Public Health. It is designed to serve as a resource in the implementation of hypertension prevention and management programs.

1. Introduction

This bibliography is intended as a resource for the design and implementation of hypertension programs, and is useful for hypertension treatment protocol development and adaptation. The aim is to provide a brief overview of the scientific basis of key aspects of hypertension control for a comprehensive approach to hypertension management. This list is not representative of all aspects of hypertension management and is largely drawn from the scientific literature published in English.

The bibliography is organized in the following manner: first, a review of the burden of to underscore its importance as a non-communicable disease; second, a review of the evidence for protocol-based treatment; third, a review of the evidence on task sharing; fourth, a summary of the literature on medical supplies and patient-centered services; and lastly, a synopsis on information systems.

2. The Burden of Hypertension

The burden of hypertension is significant. The prevalence and the health consequences of uncontrolled hypertension make it among the world's most deadly diseases.

Bromfield S, Muntner P. High blood pressure: the leading global burden of disease risk factor and the need for worldwide prevention programs. *Current hypertension reports*. 2013 Jun 1;15(3):134-6.

In 2010, high blood pressure was ranked as the leading single risk factor for global burden of disease. High blood pressure was one of the five leading risk factors for global burden in all regions except Oceania, Eastern sub-Saharan Africa, and Western and sub-Saharan Africa.

Lewington S, Lacey B, Clarke R, Guo Y, Kong XL, Yang L, et al. The Burden of Hypertension and Associated Risk for Cardiovascular Mortality in China. *JAMA Intern Med*. 2016;176(4):524-32.

This prospective cohort study of 500,223 adults in China showed that 32.5% of participants had hypertension. Among participants with hypertension and prior cardiovascular disease, only 13.0% had their hypertension controlled. Uncontrolled hypertension was associated with a 4.1 relative risk for cardiovascular disease mortality for adults age 35 to 59. Uncontrolled hypertension accounted for around one-third of deaths due to cardiovascular disease at 35 to 79 years of age in China in 2010.

Prince MJ, Ebrahim S, Acosta D, Ferri CP, Guerra M, Huang Y, et al. Hypertension prevalence, awareness, treatment and control among older people in Latin America, India and China: a 10/66 cross-sectional population-based survey. *J Hypertens*. 2012;30(1):177-87.

In cross-sectional surveys of 17,014 people aged 65 years and over in urban and rural sites in Latin America, India, and China, the prevalence of hypertension ranged between 52.6% (Peru) and 79.8% (Puerto Rico) in urban sites, and between 42.6% (Peru) and 56.9% (China) in rural sites. Hypertension control was lowest in rural China (2%), urban India (12%), and rural India (9%).

Lu J, Lu Y, Wang X, Li X, Linderman GC, Wu C, Cheng X, Mu L, Zhang H, Liu J, Su M. Prevalence, awareness, treatment, and control of hypertension in China: data from 1.7 million adults in a population-based screening study (China PEACE Million Persons Project). The Lancet. 2017 Dec 9;390(10112):2549-58.

In a sample of 1,738,886 participants in China, 44.7% had hypertension. Of those with hypertension, only 44.7% were aware of their diagnosis, 30.1% were taking prescribed antihypertensive medications, and 7.2% had achieved control.

Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control. Circulation. 2016 Aug 9;134(6):441-50.

This meta-analysis of 135 population-based studies spanning 90 countries reported that 31.1% of the world's adults had hypertension; 28.5% in high-income countries and 31.5% in low- and middle-income countries. In 2010, an estimated 349 million people in high-income countries and 1.04 billion people in low- and middle-income countries had hypertension.

3. Hypertension Treatment Protocols

The chosen hypertension treatment protocol should be simple yet detailed, and include: specific medication dosage and a schedule for titration or addition of medications if blood pressure is not controlled to establish standard treatment of patients.

3.1 An Overview of the Public Health Approach to Hypertension Treatment

Frieden TR, Bloomberg MR. Saving an additional 100 million lives. The Lancet. 2017 Sep 12.

Insights from the MPOWER technical package that successfully aimed at controlling tobacco can be applied to the worldwide effort to improve hypertension control.

Ten years ago, Thomas Frieden and Michael Bloomberg suggested a way to prevent 100 million deaths from tobacco that led to the development and well-known success of the MPOWER technical package. Recently, they launched a new cardiovascular initiative called RESOLVE aiming to prevent an additional 100 million deaths globally. The RESOLVE initiative focuses on three specific interventions: artificial trans-fat elimination, dietary sodium reduction, and effective treatment of hypertension. Five essential components have been identified for the scalable treatment of hypertension: protocols, task sharing, medical supplies, patient-centered services, and information systems. RESOLVE builds on the recently released World Health Organization Global Hearts Initiative and is housed at Vital

Strategies, a global health non-profit organization. The approach will provide support global and national efforts to scale up focused and effective interventions targeting cardiovascular disease.

Ford N, Ball A, Baggaley R, Vitoria M, Low-Beer D, Penazzato M, Vojnov L, Bertagnolio S, Habiyambere V, Doherty M, Hirnschall G. The WHO public health approach to HIV treatment and care: looking back and looking ahead. *The Lancet Infectious Diseases*. 2017 Oct 20.

In the effort to improve hypertension control globally, lessons can be learned from recent public health approaches to end the AIDS epidemic.

In 2006, the World Health Organization aimed to develop a public health approach for delivering antiretroviral therapies in order to end the AIDS epidemic. The resulting approach has been adopted widely and provided the basis for scaling up treatment to over 19.5 million people. In the effort to end AIDS as a public health threat by 2030, there are opportunities to better tailor the public health approach to address certain challenges. Some of these challenges have included the need for expanded testing to identify people with HIV, further simplified treatment and laboratory monitoring, adapting the approach to areas with concentrated epidemics, and linking testing, treatment, and care to prevention. Evaluating the implementation of these principles can lead to key insights on how to scale-up a public health approach focused on hypertension.

3.2 The Importance of Protocols

Frieden TR, King SM, Wright JS. Protocol-based treatment of hypertension: a critical step on the pathway to progress. *JAMA*. 2014;311(1):21-2.

Adopting a standard protocol-based treatment of hypertension is a critical step in helping clinicians, teams, and patients achieve and maintain healthy blood pressures, thereby preventing myocardial infarction and stroke. Which protocol is selected is less important than the decision to select, adopt, implement, and evaluate implementation of any evidence-based protocol.

There are many major benefits of adoption and use of standardized, evidence-based protocols. Protocols reduce clinical variability that is outside the bounds of evidence-based practice. A protocol can better enlist and enable all members of the health care team to reinforce the importance of blood pressure control and the value of adherence to healthy habits, medications, and self-monitoring, and to participate in medication titration and adjustment by following standard protocol-consistent order sets. Such clarity allows qualified staff to advance patients safely and efficiently along the treatment pathway, ensures that the supervising clinician is consulted if clinical exceptions occur, and identifies patients likely to benefit from consultation for resistant hypertension. Algorithms can be incorporated into electronic health records through clinical decision support tools, registry functions, and measurement to facilitate quality improvement. A protocol can result in a more efficient and cost-effective selection of medications and treatment approaches. Standardized treatment facilitates evaluation of both the quality of care and the impact of care. Adopting a standardized treatment approach sends a strong signal to clinical staff that

hypertension control is a priority. Countries should strongly consider adopting a standard protocol for blood pressure treatment.

Handler J. Commentary in support of a highly effective hypertension treatment algorithm. JCH. 2013;15(12): 874-7.

Including a hypertension treatment algorithm in a standard protocol is a vital step in controlling rates of hypertension.

A simple hypertension treatment algorithm has contributed to blood pressure control rates of greater than 85% in the United States and is a critical step in managing population-level hypertension. The treatment algorithm in the United States is built on the fixed-dose combination drug lisinopril/hydrochlorothiazide, which is maximized in three steps before adding amlodipine.

Campbell NR, Sheldon T. The Canadian effort to prevent and control hypertension: can other countries adopt Canadian strategies?. Current opinion in cardiology. 2010 Jul 1;25(4):366-72.

The study describes important aspects of Canadian hypertension management programs and implementation in order to aid other countries in successfully increasing hypertension control rates.

In 1990s, Canada had a hypertension treatment and control rate of 13%. In 1999, Canada developed a strategy to control hypertension and formed a coalition of national organizations and volunteers to develop multiple hypertension programs. The effort was based on management recommendations, a hypertension knowledge translation program, and an outcomes assessment program. This resulted in large increases in hypertension awareness and treatment as well as lower rates of cardiovascular disease. Recent initiatives to continue to improve hypertension control include an education and a dietary salt reduction program. In 2007-2009, the treatment and control rate had increased to 66% in Canada.

Jaffe MG, Lee GA, Young JD, Sidney S, Go AS. Improved blood pressure control associated with a large-scale hypertension program. Jama. 2013;310(7):699-705.

While hypertension management for large populations is challenging, the Kaiser Permanente Northern California hypertension program shows that standardized guidelines can significantly improve blood pressure control at a population level.

This study evaluates the effect of a large-scale hypertension program, the Kaiser Permanente Northern California hypertension program, at controlling blood pressure. The program involves five key components: a health system-wide hypertension registry, measurement of hypertension control rates, the development of evidence-based practice guidelines, follow-up measurement with medical assistants, and the promotion of single-pill combination therapy. Implementation of this large-scale program was associated with a significantly better blood pressure control than state and national control rates.

3.3 Evidence for Developing Protocols

Turnbull F, Neal B, Ninomiya T, Algert C, Arima H, Barzi F, et al. Effects of different regimens to lower blood pressure on major cardiovascular events in older and younger adults: meta-analysis of randomised trials. BMJ (Clin Res Ed). 2008;336(7653):1121-3.

There is no compelling evidence that various drug classes protect older and younger adults against major cardiovascular events differently.

This meta-analysis aimed to quantify the relative risk reductions achieved with different regimens to lower blood pressure in younger and older adults. The primary outcome was total major cardiovascular events, including stroke, coronary heart disease, and heart failure. Younger adults were defined as less than 65 years old and older adults were defined as 65 years or older at the time of entry into the study. The seven comparisons of treatment were angiotensin-converting enzyme (ACE) inhibitor versus placebo, calcium antagonist versus placebo, more-intensive versus less-intensive regimens to lower blood pressure, angiotensin-receptor blocker versus control regimen, ACE inhibitor versus diuretics/ β blockers, calcium antagonist versus diuretics/ β -blockers, and ACE inhibitor versus calcium antagonists. Thirty-one trials with 190,606 participants were included. No clear difference was found between age groups in the effects of different regimens or medications in lowering blood pressure or decreasing major cardiovascular events.

Oliveria SA, Lapuerta P, McCarthy BD, L'Italien GJ, Berlowitz DR, Asch SM. Physician-related barriers to the effective management of uncontrolled hypertension. Archives of internal medicine. 2002;162(4):413-20.

An important reason physicians are not treating hypertension more aggressively is that they are willing to accept higher levels of blood pressure. Education and guidelines could help physicians better manage elevated blood pressure.

This study aimed to assess barriers to primary care physician's willingness to increase the intensity of hypertension treatment for patients. Physicians in the United States were asked to complete a survey and submit a copy of office notes after treating a patient with uncontrolled hypertension. Despite documented hypertension for at least 6 months before the patient's visit, pharmacologic therapy was initiated or changed at only 38% of visits. Even though in 93% of these visits the systolic BP values were 140 mm Hg or higher—which is above the cut-off recommended by Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure guidelines—the most frequently cited reason for not initiating or changing therapy was related to the physician being satisfied with the current blood pressure level.

Turnbull F, Neal B, Algert C, Chalmers J, Chapman N, Cutler J, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med. 2005;165(12):1410-9.

There is broadly no difference in the short-to-medium-term effects on major cardiovascular events of blood pressure lowering regimens between patients with and without diabetes.

This meta-analysis aimed to compare the effects on cardiovascular events and death of different blood pressure–lowering regimens in individuals with and without diabetes. The six primary outcomes were nonfatal stroke or death from cerebrovascular disease, nonfatal myocardial infarction or death from coronary heart disease, heart failure causing death or requiring hospitalization, total major cardiovascular events, total cardiovascular deaths, and total mortality. Twenty-seven randomized trials that included 33,395 individuals with diabetes and 125,314 without diabetes were included. Regimens based on ACE inhibitors, calcium antagonists, angiotensin-receptor blockers, and diuretics/ β -blockers reduced major cardiovascular events to a comparable extent in individuals with and without diabetes.

Law MR, Wald NJ, Morris JK, Jordan RE. Value of low dose combination treatment with blood pressure lowering drugs: analysis of 354 randomised trials. *BMJ (Clin Res Ed)*. 2003;326(7404):1427

For blood pressure medication, using a combination of low-dose drug treatments instead of one drug increases efficacy and reduces adverse events.

This meta-analysis aimed to determine the average reduction in blood pressure, prevalence of adverse effects, and reduction in risk of stroke and ischaemic heart disease events produced by the five main categories of blood pressure–lowering drugs according to dose, singly and in combination. Three-hundred fifty-four randomized double-blind placebo controlled trials including 40,000 treated patients and 16,000 patients given a placebo were included. Five categories of drugs—thiazides, β -blockers, ACE inhibitors, angiotensin II receptor antagonists, and calcium channel blockers in fixed dose—were eligible. All drugs resulted in similar decreases in blood pressure. The blood pressure–lowering effects of different categories of drugs were additive. Three drugs at half standard dose were estimated to lower systolic blood pressure by 20 mm Hg systolic and diastolic by 11 mm Hg and reduce the risk of stroke by 63% and ischaemic heart disease events by 46%, more so than one drug taken singly.

Muntner P, Whelton PK. Using predicted cardiovascular disease risk in conjunction with blood pressure to guide antihypertensive medication treatment. *J Am Coll Cardiol*. 2017;69(19):2446-56.

Those with high normal blood pressures (130-139/80-89 mmHg) and cardiovascular disease risk $\geq 10\%$ may benefit from treatment as well as those with hypertension.

Using cardiovascular disease risk instead of or in addition to blood pressure to guide antihypertensive treatment is an active area of research. This review provides an overview of studies that could inform this treatment paradigm. Meta-analyses of randomized trials demonstrate clear cardiovascular disease risk reduction benefits with treatment of systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, but these trials have generally excluded low-risk individuals. Additionally, there are data supporting antihypertensive treatment for individuals with lower blood pressure levels, especially among adults with cardiovascular disease or a high global cardiovascular disease risk.

Knowing this, one approach might be to treat all adults with systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg, as well as those with systolic blood pressure of 130 to 139 mm Hg or diastolic blood pressure of 80 to 89 mm Hg and a 10-year cardiovascular disease risk $\geq 10\%$.

Ettehad D, Emdin CA, Kiran A, Anderson SG, Callender T, Emberson J, Chalmers J, Rodgers A, Rahimi K. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet. 2016;387(10022):957-67.

Blood pressure lowering significantly reduces cardiovascular risk independent of baseline systolic and diastolic levels and comorbidities, apart from diabetes, chronic kidney diseases, and other cardiovascular diseases.

The benefits of blood pressure treatment vary depending on baseline blood pressure, the presence of comorbidities, and drug class. This systematic review and meta-analysis aimed to clarify how effective hypertension medication is at preventing cardiovascular disease and death over varying factors. One-hundred and twenty-three studies were included. Every 10 mm Hg reduction in systolic blood pressure significantly reduced the risk of major cardiovascular disease events, coronary heart disease, stroke, and heart failure though the effect on renal failure was not significant. Similar proportional risk reductions were found in trials with higher mean baseline blood pressure compared with trials with lower mean baseline blood pressure. Except for diabetes and chronic kidney disease, there was no clear evidence that proportional risk reductions in major cardiovascular disease differed by comorbidities.

Huang S, Chen Y, Zhou J, Wang J. Use of family member-based supervision in the management of patients with hypertension in rural China. Patient Prefer. Adherence. 2014;8:1035-42.

Family member-based supportive therapy for patients with hypertension is an affordable and feasible way to increase medication adherence and improve blood pressure control.

Poor medication adherence is a critical problem in the management of hypertension. This study applied a mixed-methods approach using a qualitative and quantitative study design to assess the effectiveness of a family member-based supportive therapy at improving hypertension management in a rural area of China. Over the course of the 6-month trial, uncontrolled blood pressure decreased from 87.2% to 45.7% in those who partook in the intervention. In addition, 75% of patients expressed a wish for external reminders, and 93.5% responded that they would accept the family member-based supervision showing this intervention is feasible for patients with hypertension.

Law M, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. BMJ. 2009;338:b1665.

All the classes of blood pressure lowering drugs included had similar protective effects against coronary heart disease events and stroke. Treating elevated blood pressure is important regardless of baseline level.

This meta-analysis aimed to determine the efficacy of different classes of hypertension drugs in preventing coronary heart disease and stroke; 108 trials studying difference in blood pressure between study groups and placebo were included. Participants were divided into three mutually exclusive categories: participants with no history of vascular disease, a history of coronary heart disease, or a history of stroke. In the blood pressure difference trials β blockers had a short-term special effect after a myocardial infarction over and above that due to blood pressure reduction in preventing recurrent cardiovascular events in people with a history of coronary heart disease. Calcium channel blockers had a minor additional effect in preventing stroke. All the classes of blood pressure lowering drugs otherwise had similar protective effects regardless of pretreatment blood pressure and presence or absence of existing cardiovascular disease.

3.4 Example Guidelines

Galie N, Hoeper MM, Humbert M, Torbicki A, Vachiery JL, Barbera JA, et al. Guidelines for the diagnosis and treatment of pulmonary hypertension: the Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS), endorsed by the International Society of Heart and Lung Transplantation (ISHLT). *Eur. Heart J.* 2009; 30(20): 2493-537.

Krause T, Lovibond K, Caulfield M, McCormack T, Williams B. Management of hypertension: summary of NICE guidance. *BMJ (Clin Res Ed).* 2011; 343:d4891.

Williams B, Poulter NR, Brown MJ, Davis M, McInnes GT, Potter JF, et al. British Hypertension Society guidelines for hypertension management 2004 (BHS-IV): summary. *BMJ (Clin Res Ed).* 2004; 328(7440): 634-40.

Whitworth JA. 2003 World Health Organization (WHO)/International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens.* 2003; 21(11): 1983-92.

James PA, Oparil S, Carter BL, Cushman WC, Dennison-Himmelfarb C, Handler J, et al. 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). *JAMA.* 2014; 311(5): 507-20.

Kovell LC, Ahmed HM, Misra S, Whelton SP, Prokopowicz GP, Blumenthal RS, McEvoy JW. US hypertension management guidelines: a review of the recent past and recommendations for the future. *Journal of the American Heart Association.* 2015 Dec 22; 4(12): e002315.

Weber MA, Schiffrin EL, White WB, Mann S, Lindholm LH, Kenerson JG, Flack JM, Carter BL, Materson BJ, Ram CV, Cohen DL. Clinical practice guidelines for the management

of hypertension in the community. *The journal of clinical hypertension*. 2014 Jan 1;16(1):14-26.

4. Task Sharing

Legal and operational procedures should be in place to enable community-based care and task sharing so that health care workers who are accessible to patients can provide and, following a physician's instructions and protocols, adjust and intensify medication regimens.

Ogedegbe G, Gyamfi J, Plange-Rhule J, Surkis A, Rosenthal DM, Airhihenbuwa C, et al. Task shifting interventions for cardiovascular risk reduction in low-income and middle-income countries: a systematic review of randomised controlled trials. *BMJ Open*. 2014;4(10):e005983.

Though sparse, randomized controlled trials that investigate task-shifting strategies, such as provision of medication prescriptions by nurses and telephone follow-ups post-hospital discharge, for hypertension reduction in low- and middle-income countries have been shown to significantly decrease patient mean blood pressure.

This is a systematic review of published randomized controlled trials that evaluate the use of task-shifting for the management of cardiovascular diseases in low- and middle-income countries. Studies that used task shifting—defined as non-physician health care workers (NPHWs) involved in the prescribing of medications, treatment, or medical testing—were included. Cardiovascular risk factors and diseases included hypertension, diabetes, hyperlipidaemia, stroke, coronary artery disease, or heart failure. Only three trials met the predefined criteria, two involving hypertension reduction. Both hypertension studies reported a significant mean blood pressure reduction (2/1 mm Hg and 30/15 mm Hg).

Clark CE, Smith LF, Taylor RS, Campbell JL. Nurse led interventions to improve control of blood pressure in people with hypertension: systematic review and meta-analysis. *BMJ*. 2010;341:c3995

Nurse-led interventions that involve a treatment algorithm for hypertension management can play a significant role in controlling blood pressure.

This systematic review and meta-analysis reviewed the effectiveness of nurse-led interventions for adult hypertension in primary care settings. Randomized controlled trials were included. Because most patients require a combination of antihypertensive drugs to reach target blood pressure, interventions that included a treatment algorithm for clinicians to follow were of interest. Interventions that included a stepped treatment algorithm showed greater reductions in systolic blood pressure than usual care did. Nurse-prescribing medication, telephone monitoring, and community monitoring also showed greater reductions in blood pressure and higher achievement of blood pressure targets.

Carter BL, Bosworth HB, Green BB. The hypertension team: the role of the pharmacist, nurse, and teamwork in hypertension therapy. *The Journal of Clinical Hypertension*. 2012 Jan 1;14(1):51-65.

Team-based care involving pharmacists and/or nurses has consistently been shown to be a cost-effective strategy that effectively increases blood pressure control compared to usual care.

This study discusses how team-based care is critical in hypertension therapy. Research has shown that teams involving pharmacists or nurses in patient management consistently result in increased blood pressure control. Meta-analyses and systematic reviews have reported that team-based care can reduce systolic blood pressure by as much as 4–10 mm Hg compared to usual care. Newer strategies involving telephone or web-based management that allow pharmacists or nurses to more easily communicate with their patients are also showing promise.

Santschi V, Chiolero A, Colosimo AL, Platt RW, Taffé P, Burnier M, Burnand B, Paradis G. Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. Journal of the American Heart Association. 2014 Apr 22;3(2):e000718.

Pharmacist interventions have routinely been shown to significantly reduce systolic and diastolic blood pressure compared to usual care. Different pharmacist interventions should be assessed for their effectiveness, cost-effectiveness, and time-effectiveness.

This study updated and combined previous systematic reviews to assess the effect of pharmacist interventions on blood pressure. Thirty-nine randomized controlled trials of over 14,224 patients were included. Pharmacist interventions, mainly including patient education, feedback to physician, and medication management, showed significantly greater reduction in systolic blood pressure (7.6 mm Hg) and diastolic blood pressure (3.9 mm Hg) compared to usual care. The effect tended to be larger if the intervention was led by a pharmacist and occurred at least monthly.

Labhardt ND, Balo JR, Ndam M, Grimm JJ, Manga E. Task shifting to non-physician clinicians for integrated management of hypertension and diabetes in rural Cameroon: a programme assessment at two years. BMC Health Serv Res. 2010;10:339.

Integrating hypertension into primary health care in non-physician clinician (NPC) facilities resulted in greater staff knowledge on hypertension management and increased hypertension equipment available. While blood pressure significantly decreased in patients who returned to the NPC for care, high attrition of patients remained a challenge.

Non-communicable chronic diseases, such as hypertension and diabetes, are an increasing health burden in sub-Saharan Africa. Most of the rural population still does not have access to adequate health care. This study investigates the effectiveness of task shifting hypertension and type 2 diabetes care to NPC facilities in rural health districts of Cameroon. Of the NPC facilities included, 87% received basic equipment and training on hypertension and diabetes care. After 2 years, there was a significant decrease in blood pressure among hypertensive patients with two or more facility visits. NPCs' knowledge of hypertension

treatment and possession of hypertension equipment (sphygmomanometer, stethoscope, antihypertensive drugs, functional glucose meter, and oral anti-diabetics) also increased.

Abegunde DO, Shengelia B, Luyten A, Cameron A, Celletti F, Nishtar S, Pandurangi V, Mendis S. Can non-physician health-care workers assess and manage cardiovascular risk in primary care? Bulletin of the World Health Organization. 2007 Jun;85(6):432-40.

Non-physician health care workers can reliably and effectively assess and manage cardiovascular risks in primary health care settings where there is no expert physician.

The objective of this study was to determine the reliability of implementing the WHO Cardiovascular Risk Management Package to NPHWs in primary health care settings. The results of 649 paired applications of the protocol showed over 80% agreement between expert physicians and NPHWs. This shows that NPHWs can effectively be trained to manage hypertension in settings where there are no attending physicians. Packages like the WHO Cardiovascular Risk Management Package could be a useful tool in the scaling-up of hypertension management in primary care settings.

He J, Irazola V, Mills KT, Poggio R, Beratarrechea A, Dolan J, et al. Effect of a community health worker-led multicomponent intervention on blood pressure control in low-income patients in Argentina: a randomized clinical trial. JAMA. 2017;318(11):1016-25.

A multicomponent community health worker-led intervention showed significant reductions in systolic and diastolic blood pressure and increases in the percentage of patients with controlled hypertension. Involving community health workers could be a feasible and cost-effective way of managing hypertension in the primary health care setting.

The goal of this study was to test whether a community health worker-led intervention could improve blood pressure management in low-income patients. Eighteen centers for primary health care within the national public system in Argentina participated in this cluster randomized controlled trial. Half of the centers were randomized to a multi-component intervention for 18 months, which included: a community health worker-led home intervention involving health coaching, home blood pressure monitoring, and blood pressure audit and feedback; a physician intervention; and a text-messaging intervention. A total of 1432 adult patients with uncontrolled hypertension were included. Systolic and diastolic blood pressure decreased significantly more in the intervention group than in the control group. In addition, the proportion of patients with controlled hypertension significantly increased in the intervention group.

Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. JAMA. 2006;296(21):2563-71.

Long-term pharmacist interventions can play a key role in decreasing hypertension patient blood pressure and increasing medication adherence and persistence.

Nonadherence to hypertension medication diminishes the benefits of pharmacotherapies and can be particularly challenging in older adults. This study aimed to evaluate the effectiveness of a pharmacy care program to improve medication adherence and its associated effects on blood pressure. Patients aged 65 years or older taking at least four chronic medications were included in this study. The pharmacy care program included three elements: individualized medication education, medications dispensed using an adherence aid, and regular follow-up with clinical pharmacists every two months. After six months of intervention for all patients, medication adherence and systolic blood pressure significantly improved. Patients were then randomized to continue the intervention or return to usual care for another six months. Those who continued the intervention for the next six months maintained blood pressure and adherence rates, while those in the usual care had decreased adherence and increases in blood pressure.

Marra C, Johnston K, Santschi V, Tsuyuki RT. Cost-effectiveness of pharmacist care for managing hypertension in Canada. *Canadian Pharmacists Journal/Revue des Pharmaciens du Canada*. 2017;150(3):184-97.

Interventions involving pharmacist management of hypertension are cost-effective and predicted to save money and improve long-term health outcomes.

This study used a Markov cost-effectiveness model to determine the effect of pharmacists providing advanced scope of practice for management (prescription, education, consultation) of hypertension compared with usual care on long-term cardiovascular and renal disease health outcomes. To determine cost-effectiveness, the model included health outcomes, costs, and quality of life. The results suggest that a systolic blood pressure reduction of 18.3 mmHg results in an estimated 0.21 fewer cardiovascular events per a person, 0.3 additional life-years, 0.4 additional quality-adjusted life-years, and \$6364 Canadian dollar cost savings over a lifetime, thereby showing pharmacist interventions to provide good value for money.

Tsuyuki RT, Houle SK, Charrois T, Kolber M, Rosenthal MM, Lewanczuk RZ, Cooney D, McAlister FA. A randomized trial of the effect of pharmacist prescribing on improving blood pressure in the community: the Alberta clinical trial in optimizing hypertension (RxACTION). *Canadian Journal of Cardiology*. 2014;30(10):S125-6.

Interventions involving pharmacist-led assessments, prescriptions, education, follow-up and monitoring are shown to have a significant positive impact on patient blood pressure management.

This randomized controlled trial enrolled adult patients with above-target blood pressure from 23 communities in Alberta, Canada. The intervention group received a blood pressure and cardiovascular risk assessment, hypertension education, antihypertensive medication prescriptions, laboratory monitoring, and monthly follow-up visits all by their pharmacist for six months. The control group received written hypertension information, a card for blood pressure recording, and usual care from their pharmacist or physician. After six months, the intervention group participants had a significantly larger average decrease in blood pressure and were 2.32 times more likely to achieve blood pressure target levels compared to the control group.

Tsuyuki RT, Al Hamarneh YN, Jones CA, Hemmelgarn BR. The effectiveness of pharmacist interventions on cardiovascular risk: the multicenter randomized controlled RxEACH trial. *Journal of the American College of Cardiology*. 2016 Jun 21;67(24):2846-54.

Incorporating pharmacists in cardiovascular risk management results in greater reduction of risk for cardiovascular disease events.

This study aimed to evaluate the effectiveness of a community pharmacy-based intervention on cardiovascular risk in participants at high risk for cardiovascular disease. This randomized controlled trial was conducted in 56 community pharmacies in Alberta, Canada. The intervention group received a Medication Therapy Management review from their pharmacist and cardiovascular disease risk assessment and education. The control group received usual pharmacist care. After three months, there was a 21% difference in change in risk for cardiovascular disease events between the intervention and usual care group. The intervention group had greater improvement in risk for cardiovascular disease events, low-density lipoprotein cholesterol, systolic blood pressure, glycosylated hemoglobin, and smoking cessation.

5. Medical Supplies

Regular and uninterrupted supply of quality-assured medications and equipment for accurate measurement of blood pressure should be established.

Khatib R, McKee M, Shannon H, Chow C, Rangarajan S, Teo K, et al. Availability and affordability of cardiovascular disease medicines and their effect on use in high-income, middle-income, and low-income countries: an analysis of the PURE study data. *Lancet (London, England)*. 2016;387(10013):61-9.

Cardiovascular prevention medications are both unavailable and unaffordable for a substantial proportion of communities in upper middle-income, lower middle-income, and low-income countries. Increasing access and reducing cost will be vital to reducing the burden of cardiovascular disease.

Medicines to prevent recurrent cardiovascular disease are becoming more widely available. This study aimed to determine whether low use of these medications was due to lack of access or affordability. The authors analyzed data regarding availability and costs of aspirin, β -blockers, angiotensin-converting enzyme inhibitors, and statins in pharmacies from 596 communities in 18 countries. The authors compared results from high-income, upper middle-income, lower middle-income, and low-income countries. All four cardiovascular disease medicines were available in 95% of urban and 90% of rural communities in high-income countries, 80% of urban and 73% of rural communities in upper middle-income countries, 62% of urban and 37% of rural communities in lower middle-income countries, 25% of urban and 3% of rural communities in low-income countries (excluding India). The four cardiovascular disease medicines were potentially unaffordable for 0.14% of households in high-income countries, 25% of upper middle-income countries, 33% of lower middle-income, 60% of low-income countries (excluding India), and 59% of households in India.

Tran DN, Njuguna B, Mercer T, Manji I, Fischer L, Lieberman M, et al. Ensuring patient-centered access to cardiovascular disease medicines in low-income and middle-income countries through health-system strengthening. *Cardiol Clin*. 2017;35(1):125-34.

Significant challenges with distributing cardiovascular disease medications relate to on-the-ground problems. Countries should address availability, accountability in the supply chain, and medication adherence when improving access to and uptake of cardiovascular medications.

Up to 80% of cardiovascular deaths occur in low- and middle-income countries. Translating cardiovascular disease treatment guidelines into practice is hindered in these countries due to inadequate health care systems that are unable to provide sufficient access to lifesaving medications. This review identifies three challenges to patient-centered access to hypertension drugs: lack of availability of medicines, lack of accountability in the supply chain, and poor medication adherence. Pilot programs have shown that access to cardiovascular medication can be improved by standardizing supply chain management, improving human resource efficiency, and extending supply chain considerations, which results in improved patient adherence.

Mendis S, Fukino K, Cameron A, Laing R, Filipe A, Khatib O, Leowski J, Ewen M. The availability and affordability of selected essential medicines for chronic diseases in six low- and middle-income countries. *Bulletin World Health Organization*. 2007; 85(4): 279–288

Country-specific policies are needed to improve access to essential cardiovascular medicines. Medication affordability should be controlled through creating policies and incentives for generics, introducing market competition, regulating prices through taxes, and controlling mark-ups. Availability may be improved by increasing governance, management efficiency, and local supply options.

This study aimed to assess the availability and affordability of 32 cardiovascular disease, diabetes, chronic respiratory disease, glaucoma, and palliative cancer care medications in public and private medicine outlets in six low- and middle-income countries (Bangladesh, Brazil, Malawi, Nepal, Pakistan and Sri Lanka). In all countries $\leq 7.5\%$ of these 32 medicines were available in the public sector, except in Brazil (30%) and Sri Lanka (28%). Median price ratios varied substantially. In the private sector of some countries, the cost of innovator products was three times more than generic medicines. One month's supply of combination treatment for coronary heart disease costs 18.4 days' wages in Malawi, 6.1 days' wages in Nepal, 5.4 in Pakistan, 5.1 in Brazil, 1.6 days' wages in Bangladesh, and 1.5 days' wages in Sri Lanka.

Chen CC, Blank RH, Cheng SH. Medication supply, healthcare outcomes and healthcare expenses: longitudinal analyses of patients with type 2 diabetes and hypertension. *Health Policy*. 2014;117(3):374-81

Improving appropriate medication supplies for patients results in better health care outcomes than oversupply or undersupply and lower health care costs than oversupply.

This study aimed to examine the effect of whether the appropriateness of the quantity of drug obtained is correlated with better health care outcomes and lower health care costs. Over 7 years, adult patients newly diagnosed with type 2 diabetes or hypertension in Taiwan were followed. Patients who were undersupplied or oversupplied with medications tended to have worse health care outcomes than those with an appropriate medication supply. Oversupply of medication was also associated with higher health care costs.

6. Patient-Centered Services

Treatment services should reduce the barriers to adherence, including reduction (preferably elimination) of costs for medications and medical visits, increasing patient convenience of medical visits and medication refills (e.g., every three months for stable patients), use of once-daily treatment regimens, use of fewer tablets (e.g., through combination medications), improving access to free blood pressure monitoring (e.g., in public places, at home), and public education to increase awareness of the importance of blood pressure control .

Labhardt ND, Balo JR, Ndam M, Manga E, Stoll B. Improved retention rates with low-cost interventions in hypertension and diabetes management in a rural African environment of nurse-led care: a cluster-randomised trial. Tropical medicine & international health: TM & IH. 2011;16(10):1276-84.

Low-cost interventions, like sending reminder letters or incentivizing patient visits, can significantly improve retention of patients undergoing hypertension and diabetes management in nurse-led facilities.

Due to the current environment of task-shifting, this study aimed to identify which interventions would improve patient retention in nurse-led cardiovascular care in rural African health districts. A randomized trial was completed with three groups: a control group, a group that received the incentive of one-month free treatment every fourth month of visits, and a group that received reminder letters in case of a missed follow-up. A total of 33 centers were included. At the end of one year, retention rates in groups two and three were significantly higher at 60% and 65%, respectively, than 29% in the control group.

Margolis KL, Asche SE, Bergdall AR, Dehmer SP, Groen SE, Kadrmas HM, et al. Effect of home blood pressure telemonitoring and pharmacist management on blood pressure control: a cluster randomized clinical trial. Jama. 2013;310(1):46-56.

Home blood pressure telemonitoring and pharmacist case management is a highly effective method of controlling blood pressure in patients.

The objective of this study is to determine whether a home blood pressure telemonitoring and pharmacist case management intervention improves blood pressure control; 452 adults with uncontrolled hypertension were recruited to this cluster randomized clinical trial. Eight clinics were randomized to provide usual care, and eight clinics were randomized to provide the telemonitoring intervention to patients. Patients in the intervention group received home blood pressure telemonitors and transmitted blood pressure data to pharmacists who were then able to adjust antihypertensive therapy as needed. Blood pressure was significantly

better controlled in the intervention group during 12 months of intervention and six months of post intervention follow-up.

James K, Dolan E, O'Brien E. Making ambulatory blood pressure monitoring accessible in pharmacies. Blood pressure monitoring. 2014;19(3):134-9.

Ambulatory blood pressure measurement data from pharmacies is similar to those recorded in primary care practices. Ambulatory blood pressure measurements could be collected in pharmacies so they are more accessible to a greater number of hypertension patients.

Ambulatory blood pressure measurements are recommended for the diagnosis and management of hypertension. This study aimed to compare measurement in a pharmacy and primary care clinic setting to determine if the technique could be made more accessible to patients. Ambulatory blood pressure measurement data was compared for 46,978 patients in Ireland. The blood pressure characteristics of patients with ambulatory blood pressure measurements recorded in pharmacies was similar to those recorded in primary care practices.

Bobrow K, Farmer AJ, Springer D, Shanyinde M, Yu LM, Brennan T, et al. Mobile phone text messages to support treatment adherence in adults with high blood pressure (SMS-Text Adherence Support [StAR]): a single-blind, randomized trial. Circulation. 2016;133(6):592-600.

A text message intervention that provided hypertension patients with information resulted in the greatest decrease in blood pressure.

This study aimed to evaluate the effectiveness of mobile phone messages to deliver automated adherence support for blood pressure medication. The randomized controlled trial was conducted in South Africa with 1,372 patients randomized to one of three arms: information-only text messages, interactive text messages, or usual care. At 12 months, there was a drop in blood pressure and increase in proportion of patients with controlled blood pressure for those who received educational text messages. There was no evidence that an interactive intervention increased this effect.

Cooper LA, Roter DL, Carson KA, Bone LR, Larson SM, Miller ER, et al. A randomized trial to improve patient-centered care and hypertension control in underserved primary care patients. J Gen Intern Med. 2011;26(11):1297-304.

Interventions that enhance physicians' communication skills and encourage patients to play an active role in their care increases communication and engagement in care and may improve blood pressure control in vulnerable populations.

Vulnerable populations, such as African Americans and persons with lower socioeconomic status, are disproportionately affected by hypertension yet receive less patient-centered care. The objective of this study is to compare the effectiveness of patient-centered interventions for underserved groups. A randomized control trial with 12 months follow-up was conducted in the United States. In the intervention groups, physicians were trained on communication skills and patients were coached by a community health worker at varying intensities. Trained physician visits for the intervention groups had significantly more

positive communication change, physicians' participatory decision making, and patient involvement in care related to doctor facilitation. While improvements in patient adherence and blood pressure control did not differ significantly between intervention and control groups, non-significant reductions in blood pressure were observed in the intervention groups for patients with uncontrolled hypertension at baseline.

Sieverdes J, Gregoski M, Patel S, Williamson D, Brunner-Jackson B, Rundbaken J, et al. mHealth medication and blood pressure self-management program in Hispanic hypertensives: a proof of concept trial. Smart Homecare Technology and TeleHealth. 2013;1:1-10.

Electronic measures, such as wireless-enabled blood pressure monitors, text message reminders and encouragement, and electronic pill-boxes, increase patient adherence and allow physicians to better monitor patients' progress.

This proof of concept randomized trial aimed to investigate how mHealth (i.e., mobile health) could improve blood pressure self-management in patients with hypertension. Patients were given a cellular electronic medication tray that provided a reminder signal for patients when to take their medications. Smartphone messages were also used to remind patients to take at-home blood pressure measurements using a Bluetooth-enabled monitor and encourage patients to adhere to the program. Patients in the control group strongly believed the program helped them remember to take their medication, were more compliant with blood pressure control instructions, and had greater reductions in blood pressure.

Hareri HA, Abebe M. Assessments of Adherence to Hypertension Medications and Associated Factors among Patients Attending Tikur Anbessa Specialized Hospital Renal Unit, Addis Ababa, Ethiopia 2012. IJNS. 2013;3(1):1-6.

Adherence to hypertension medication is low. Health workers should take time to inform patients of the benefits and risks of medications and be aware of factors that put patients at a greater risk of non-adherence.

Adherence to hypertension medication is a crucial part of cardiovascular management that is often overlooked. This study aimed to assess hypertension medication adherence rates and risk factors for low adherence in Ethiopia. Two-hundred and eighty-six patients were sampled. The adherence level was generally low at 69.2%. Adherence was better in patients who had been better informed about their medication, and varied depending on marital status, work status, health care facility visited, and duration of hypertension and treatment.

7. Information Systems

Information systems should allow real-time feedback on adherence and blood pressure control of individual patients and assessment of control rates in cohorts of different treatment systems to facilitate continuous and real-time program improvement.

Letebo M, Shiferaw F. Adapting HIV patient and program monitoring tools for chronic non-communicable diseases in Ethiopia. Globalization and health. 2016;12(1):26.

Countries should develop standardized intake process, enrollment, follow-up, cohort monitoring, appointment keeping, analysis, and reporting guidelines to monitor hypertension. Studying existing national guidelines may give insights to how hypertension information should be managed.

This cross-sectional study assessed existing monitoring and evaluation tools in place for non-communicable diseases in Ethiopia. Because HIV care and treatment is a current widespread program in the country, the authors explored the tools being used for HIV and investigated how they might be applied to other diseases. Interviews with health care workers from four health centers were conducted. There was an obvious lack of information systems relating to non-communicable diseases in Ethiopia. Given the huge investment to set-up standardized guidelines like those for HIV care and treatment, other programs should adapt and use monitoring tools from existing program to improve information management for hypertension and other non-communicable diseases.

Aljunid SM, Srithamrongsawat S, Chen W, Bae SJ, Pwu RF, Ikeda S, et al. Health-care data collecting, sharing, and using in Thailand, China mainland, South Korea, Taiwan, Japan, and Malaysia. Value in Health: The Journal of the International Society for Pharmacoeconomics and Outcomes Research. 2012;15(1 Suppl):S132-8.

Given the importance of health-care data to evaluate the strength of a system, raise awareness of public health concerns, and make evidence-based decisions, countries should work to standardize and improve access to cardiovascular and hypertension data.

This article investigated the health care data situation in six countries from the Asia-Pacific region. In Thailand, mainland China, Taiwan, and Malaysia, the Ministry of Health is responsible for collecting and managing the health care data through various agencies both public and private. In South Korea and Japan, health insurance handles the collection and storage of health care data. All countries struggled with limited access to data due to privacy protection, fragmented health care systems, poor quality of routinely collected data, unclear policies and procedures to access the data, and control on the freedom on publication.

Campbell N, Ordunez P, Jaffe MG, Orias M, DiPette DJ, Patel P, Khan N, Onuma O, Lackland DT. Implementing standardized performance indicators to improve hypertension control at both the population and healthcare organization levels. The Journal of Clinical Hypertension. 2017 May 1;19(5):456-61.

Widespread adoption of standardized population and clinical hypertension performance indicators is important in efforts to control hypertension.

The ability to reliably evaluate the impact of interventions and changes in hypertension control is critical. Previously, a World Hypertension League Expert Committee made recommendations to standardize the reporting of population blood pressure surveys. This article adds to the recommendations and provides slight alterations that were discussed at a Pan American Health Organization expert meeting for "performance indicators". Core indicators for population surveys are recommended to include: mean systolic and diastolic

blood pressure and the prevalence of hypertension, awareness of hypertension, drug-treated hypertension, and drug-treated and controlled hypertension. Core indicators for clinical registries are recommended to include: the prevalence of diagnosed hypertension and the ratio of diagnosed hypertension to that expected by population surveys, and the prevalence of controlled hypertension, lack of blood pressure measurement within a year in people diagnosed with hypertension, and missed visits by people with hypertension.

Campbell NR, McAlister FA, Quan H. Hypertension Outcomes Research Task Force. Monitoring and evaluating efforts to control hypertension in Canada: why, how, and what it tells us needs to be done about current care gaps. Can J Cardiol. 2013;29(5):564-70.

Evaluation of hypertension programs is critical. Surveillance and monitoring efforts should include vulnerable populations and be large enough to have adequate power to measure small effect sizes and analyze subpopulations.

The Hypertension Outcomes Research Task Force is based in Canada and has existed since 2003. Members assist in the development and revision of surveys and conduct analyses that help guide hypertension programs. Task Force surveillance data indicates that many gaps in hypertension care remain. Blood pressure surveillance and monitoring is key to developing effective programs that increase hypertension control. The Task Force noted that many current surveys do not have adequate statistical power to assess vulnerable populations and surveys of vulnerable populations do not usually include blood pressure, resulting in the inability to measure the burden of hypertension in high risk populations.

Khader A, Farajallah L, Shahin Y, Hababeh M, Abu - Zayed I, Kochi A, Harries AD, Zachariah R, Kapur A, Venter W, Seita A. Cohort monitoring of persons with hypertension: an illustrated example from a primary healthcare clinic for Palestine refugees in Jordan. Tropical medicine & international health. 2012 Sep 1;17(9):1163-70.

Hypertension programs should incorporate a recording, monitoring, and reporting system in order to assess the program's successes and deficiencies and improve the program's effectiveness.

Recording and reporting systems borrowed from the DOTS framework for tuberculosis control can be used to record, monitor and report on other chronic diseases. This descriptive cohort study used routine program data collected through E-Health to monitor persons with hypertension in a primary healthcare clinic in Amman, Jordan serving Palestine refugees. There were 97 newly registered patients in the first quarter of 2012. There was a total of 4,130 patients with hypertension registered from when E-Health started in 2009, 76% were retained in care and 21% failed to present to a healthcare worker in the last three months. The E-Health data also indicated deficiencies in several components of clinical performance related to blood pressure measurements and fasting blood glucose tests to screen simultaneously for diabetes.

Khader A, Farajallah L, Shahin Y, Hababeh M, Abu - Zayed I, Zachariah R, Kochi A, Kapur A, Harries AD, Shaikh I, Seita A. Hypertension and treatment outcomes in Palestine refugees in United Nations Relief and Works Agency primary health care

clinics in Jordan. Tropical medicine & international health. 2014 Oct 1;19(10):1276-83.

E-Health can be used to regularly assess caseload, program outcomes, clinic performance, blood pressure control, and cumulative prevalence of disease-related complications regarding hypertension.

This retrospective cohort study occurred in six United Nations Relief and Works Agency (UNRWA) primary health care clinics in Jordan serving Palestine refugees diagnosed with hypertension. The objective was to evaluate the benefit of E-Health and determine the number, characteristics, program outcomes, and measures of disease control for those registered up to 2013. There were 18,881 patients registered with hypertension. Amongst those attending a clinic, 92% had their blood pressure measured, of whom 83% had blood pressure <140/90 mm Hg. Large numbers of Palestine refugees were registered and treated for hypertension; E-Health was successfully used to monitor hypertension management and performance.