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Standardized treatment to improve hypertension control in primary health care: The HEARTS in the Americas Initiative

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Abstract

Hypertension is the leading risk factor for cardiovascular disease (CVD) worldwide. Despite the availability of effective antihypertensive medications, the control of hypertension at a global level is dismal, and consequently, the CVD burden continues to increase. In response, countries in Latin America and the Caribbean are implementing

the HEARTS in the Americas, a community-based program that focuses on increasing hypertension control and CVD secondary prevention through risk factor mitigation. One key pillar is the implementation of a standardized hypertension treatment protocol supported by a small, high-quality formulary. This manuscript describes the methodology used by the HEARTS in the Americas program to implement a population-based standardized hypertension treatment protocol. It is rooted in a seamless transition from existing treatment practices to best practice using pharmacologic protocols built around a core set of ideal antihypertensive medications. In alignment with recent major hypertension guidelines, the HEARTS in the Americas protocols call for the rapid control of blood pressure, through the use of two antihypertensive medications, preferably in the form of a single pill, fixed-dose combination, in the initial treatment of hypertension. To date, the HEARTS in the Americas program has seen the improvement in antihypertensive medication formularies and the establishment of pharmacologic treatment protocols tailored to individual participating countries. This has translated to significant increases in hypertension control rates post-program implementation in these jurisdictions. Thus, the HEARTS in the Americas program could serve as a model, for not only the Americas Region but globally, and ultimately decrease the burden of CVD.

1 | INTRODUCTION

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality globally, affecting more than one billion people and accounting for one in three deaths.[1] This equates to approximately 18 million deaths annually, the majority of which could be prevented through risk factor mitigation.[2]

In the World Health Organization (WHO) Region of the Americas, CVD is rampant. For instance, in 2017, there were 14 million new cases of CVD, bringing the total number of persons in that context living with CVD to 79.9 million. Unfortunately, in the same year there were some 2 million deaths attributable to CVD.[3] The reason for these staggering statistics is centered around the high prevalence of unaddressed CVD risk factors such obesity, elevated blood pressure, physical inactivity, tobacco use, harmful use of alcohol, elevated blood glucose, and poor diet, including excess salt intake which are all common in this setting.[4,5] Without significant and sustained interventions to control CVD risk factors, we are certain to see a continuation or worsening in the disease trajectory of high levels of death and disability associated with CVDs in future years.[6,7]

Hypertension is the leading risk factor for CVD. Fortunately, hypertension can be prevented and controlled.[8] Across the Americas, hypertension prevalence is consistently high and levels of awareness, treatment, and control are low.[9] Many of the countries in this region, with their limited resources and vulnerable economies, have not yet implemented effective and comprehensive public policies or built up their primary healthcare system to allow them to tackle the rising CVD burden.

In response to the growing burden of CVD across the Americas, a comprehensive CVD risk reduction program, HEARTS in the Americas, was launched at the end of 2016. HEARTS is an acronym for Healthy-lifestyle counseling, Evidence-based treatment protocols, Access to essential medicines and technology, Risk-based CVD management, Team-based care, and Systems for monitoring.

This paper focuses on content found in the Evidence-based protocols (E) module; however, other critical aspects to improving the control rate of hypertension are highlighted in the other five modules. Such aspects include enhancing team-based care by task shifting including utilizing medical assistants and nonphysician clinicians such as nurse practitioners and pharmacists and delivering care in community settings.

2 | HEARTS IN THE AMERICA—A MODEL OF CARE FOR CARDIOVASCULAR RISK MANAGEMENT

HEARTS is positioned to become the model of care for cardiovascular risk management in the Americas by 2025, with a special emphasis on the detection, treatment, and control of hypertension, as well as secondary CVD prevention in primary health care.[10] This comprehensive program, led by Ministries of Health, with the participation of key stakeholders and technical support from the Pan American Health Organization (PAHO), is built on several strategic pillars and functions. HEARTS aims to address and correct deficiencies in the existing hypertension management model in the Americas. The program is also a component of the larger, Global Hearts Initiative, which was developed by the WHO in partnership with the US Centers for Disease Control and Prevention, Resolve to Save Lives, the World Hypertension League, and the World Heart Federation among other

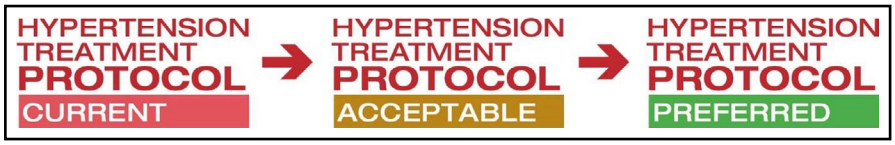

FIGURE 1 Diagram for transitioning in a stepwise process with a standardized antihypertensive formulary and pharmacologic treatment protocol from a current protocol scenario (feasible immediately), to an acceptable protocol scenario (feasible in 6-12 mo), to a preferred protocol scenario (feasible in 18-24 mo)

partners to strengthen existing healthcare systems and to improve cardiovascular outcomes globally.

The initiative seeks to smoothly and progressively integrate HEARTS into existing health-delivery services to promote the adoption of global best practices in the prevention and control of CVD and to improve the performance of the services through better control of high blood pressure and the promotion of secondary prevention, with emphasis on primary health care.

Country participation is voluntary, but participating countries must demonstrate a political commitment to the initiative and a broader NCD and CVD agenda. The most compelling reason for individual country participation is the national recognition of the increasing disease burden of CVD, led by hypertension, and its human and economic costs. This recognition is coupled to the present poor control of hypertension with the desired outcome of a rapid and marked increase in the rate of hypertension control at a population level. After completing the proof of concept in Barbados and the participation of Colombia, Chile, and Cuba (the four founding countries) in mid-2017 and demonstrating that the model of HEARTS produces success, the program continues its regional and in-country expansion to its present composition of 12 countries with further country participation in the near future. While this number could be viewed as small, the program has been implemented in some of the largest countries geographically and by population in the region, including Mexico, Argentina, Colombia, and Peru. In addition, the countries participating make up an extremely diverse group in terms of demographics, size, location, and culture.

3 | THE HEARTS TREATMENT PROTOCOL AND MEDICATION STRATEGY

One prominent strategic pillar of HEARTS is the *Treatment Protocols and Medication Strategy* (Figure 1). To strengthen this pillar, a technical meeting was held in Panama in November 2019, which brought together over 40 technical experts including cardiologists, nephrologists, pharmacists, primary care professionals, and the Ministry of Health personnel from 12 HEARTS countries, and international consultants. Building upon the progress and lessons learned from the first HEARTS implementation countries and following the guiding principles of the WHO HEARTS technical package, a key objective of this meeting was to build a regional strategy toward standardized treatment to accelerate the control of hypertension in the primary healthcare setting.[11] This strategy combines the use of:

1. A small and simplified pharmacologic antihypertensive formulary to improve the access, quality, affordability, and availability of medications
2. The use of standardized treatment protocols (also known as treatment "algorithms").[12]

In this pillar, the term "protocol" is used in a broad context and similar to that of an "algorithm." This differs from how the term protocol is used in the context of a "clinical trial." At the core of the formulary and protocols is an emphasis on the initial use of two antihypertensive medications in the individual with hypertension, preferably in a fixed-dose combination (FDC). FDCs reduce patient pill burden and have been shown to increase treatment adherence, one of the key challenges in hypertension control. This meeting had two powerful incentives: the inclusion of FDC antihypertensive medicines in the recently approved 2019 WHO Model List of Essential Medicines and the speedy inclusion of such medications in the PAHO Strategic Fund list.[13,14]

A more specific goal of the 2019 Panama HEARTS in the Americas technical meeting was to document current antihypertensive medication formularies available in the HEARTS countries. It is important to note that the blood pressure threshold to initiate pharmacologic treatment and the blood pressure target to reach are decisions made by each individual country. However, the Evidence-based protocols, E, module does give guidance to both the treatment initiation threshold and target blood pressure. Interestingly, all present countries initiate pharmacologic treatment at a threshold of > or equal to 140/90 mmHg with a target blood pressure of < 140/ 90 mmHg. Current, acceptable, and preferred treatment protocols for all HEARTS countries were reviewed or developed at the technical meeting. In this manuscript, the steps taken in the formulation of a framework for the development and introduction of formularies and protocols for the management of hypertension are described. This process provides a blueprint that can be used in any world region, country, or substantial jurisdiction to design a standardized approach to improving population hypertension control but can be tailored to that specific clinical environment, such as enhanced use of nurses and pharmacists to deliver care.

4 | DEVELOPING A SMALL AND SIMPLE ANTIHYPERTENSIVE FORMULARY

Most if not all recent hypertension pharmacologic treatment guidelines recommend the use of three classes of antihypertensive

medications for the initial treatment of hypertension.[15-17] Thus, a small and simple formulary would consist of these three classes, including the two subclasses of RAAS inhibitors (ACEI and ARB), for a total of four groups of medications.

The initial step in planning and the ultimate implementation of the formulary is to select a primary (and if appropriate, secondary) antihypertensive agent based on the presence of ideal characteristics (Table 1) from each of these four groups of medications. Because this formulary is designed for the primary treatment of hypertension, those with concomitant diseases, for example, heart failure could require additional medications, some of which may also lower blood pressure, such as beta-blockers.

Next, each agent selected within each medication group, primary and secondary, should be compared to these ideal characteristics. As an example, within the thiazide and thiazide-like diuretic group the primary agent selected could be chlorthalidone and the secondary agent could be hydrochlorothiazide. Similar selections could be made for the other three groups. Interestingly, there is almost universal agreement that within the calcium channel blocker class the primary and sole agent is amlodipine, and therefore, a secondary agent is not necessary. Given this supposition, a formulary for the initial treatment of hypertension could consist of as little as seven agents. It should be noted that when considering an FDC antihypertensive medication of two or more agents, each agent within the combination should be compared to this ideal characteristic list.

TABLE 1 Ideal characteristics of an individual antihypertensive pharmacologic medication (adapted from Patel, Ordunez, DiPette et al, 2016)[18]

Favorable characteristics
High efficacy
Additive/synergistic blood pressure reduction when used in combination
Supported by clinical trials
Tolerable—with limited side effect profile and requiring minimal laboratory monitoring
Affordable
Available
Appropriate for regional considerations
Once daily dosing
Scored tablet to allow split tablet dosing and easy titration

5 | STANDARDIZED AND STRAIGHTFORWARD TREATMENT PROTOCOLS

A major obstacle to hypertension control is the absence of a comprehensive, standardized, population/public healthcare-based approach for the detection and treatment of hypertension within existing primary healthcare services. Other obstacles include limited access to safe and effective medications and lack of systems to effectively deliver prevention, screening, and treatment.[19] It is becoming increasingly clear from the early results of the HEARTS in the Americas Initiative, and its precursor the Standardized Hypertension Treatment and Prevention Project, that one effective strategy which leads to a rapid improvement in hypertension control rates is to implement a population-based, standardized antihypertensive pharmacologic treatment protocol.[18]

Similar to the determination of the ideal characteristics of a formulary medication, the first step in planning, creating, and implementing a standardized, simple protocol is to determine its ideal characteristics (Table 2). An ideal protocol should align with well-designed, evidence-based clinical guidelines that form the foundation for effective and safe clinical practice. It should address and be targeted to the vast majority of individuals with hypertension that can be managed and treated at the primary care level as opposed to complex individuals, for example, presence of co-morbid conditions, chronic renal failure, and secondary hypertension. Likewise, a protocol defines a specific, stepwise treatment of hypertension and thus differs significantly from a guideline.

In addition, the protocol should also note clinical contraindications and precautions. For example, if an ACEI or ARB is used in the protocol, it would be contraindicated for women who are or could become pregnant. The following flowchart (Flowchart 1) depicts the transition in a stepwise process from a current protocol scenario to a more acceptable scenario to a preferred scenario. Table 3 provides an example of the stepwise transition process and estimated timeline toward the implementation of each protocol scenario.

Following the identification of the ideal characteristics of the protocol, the next step is to identify the individual antihypertensive medication groups and the individual agents within each group to be used, and then, the protocol needs to be delineated. An approach to the planning and implementation of the protocol that has been met with significant initial success in HEARTS in the Americas countries, as introduced above, has been to identify a "present" or current protocol that can be put in place immediately. This step utilizes the present antihypertensive classes/groups and the individual medications within each class/group that are already readily available locally and/or nationally. The next step is to plan and develop an "acceptable" protocol, which always is an improved version of the current protocol or at least one step ahead toward the preferred protocol. An acceptable protocol is one in which many of the classes and individual medications that make up the protocol meet some or many of the ideal characteristics listed above. Importantly, the present protocol may be the same as the acceptable protocol may differ.

If the acceptable protocol differs from the current one, then the acceptable one is an improvement on the current one and can be implemented in a short period of time such as months to a year. The next step is to plan and implement a preferred protocol. A preferred protocol is one in which the classes/groups and individual medications within each step meet almost or all the ideal characteristics listed above. It can also be defined as "aspirational" or "ideal" in that to obtain the classes/groups, and agents may require a longer time. For instance, it would require significant changes in a national

essential medication list, budgetary considerations, and medication supply-chain logistics to assure availability and sustainability. This process may take a year or more. Example protocol scenarios and medications are presented in Tables 4-6. Table 7 defines the characteristics of each protocol used in the examples (current, acceptable, and preferred).

Through the experience of the HEARTS in the Americas, we have found that implementation, scale-up, and institutionalization of a national, regional, or state/province hypertension treatment protocol can be difficult. A few elements that make it particularly challenging includes its primary care focus; the resistance from primary care providers generated by a concern about the rapidity of dose escalation, resistance from specialists who feel their domain of influence may be challenged; reluctance to use two medications including in a FDC as initial treatment; tension between primary health care and specialists; the need for many provinces/states in a country or countries in a region to adopt new medication policies and procurement mechanisms; and legal, programmatic, and financial barriers. An additional yet more specific barrier is the reticence to allow nonphysicians to titrate medications even under supervision. A standardized protocol could help overcome this barrier. These barriers, as well as others, need to be defined and addressed at the initiation of the planning and implementation process. Most if not all of these can be effectively countered with evidence-based education.

6 | INCORPORATION OF TWO MEDICATION TREATMENT PREFERABLY IN A FIXED-DOSE COMBINATION IN THE INITIAL TREATMENT OF HYPERTENSION INTO THE PROTOCOL AND NATIONAL FORMULARIES

A strong consideration in a population health system–based treatment approach to hypertension is to utilize two antihypertensive pharmacologic agents together, ideally as a FDC in the initial treatment of hypertension. This is emerging as a best practice for a safe, effective, shorter, and convenient strategy to rapidly increase the control rate of hypertension in both high- and low-middle income countries.[19-21] HEARTS in the Americas promotes the inclusion of the four single pill, FDC antihypertensive medications (lisinopril + amlodipine; lisinopril + hydrochlorothiazide; telmisartan + amlodipine; and telmisartan + hydrochlorothiazide) which are now in the *2019 WHO Model List of Essential Medicines* and in the *PAHO Strategic Fund Medication List* to ensure affordable, sustainable, safe, efficient, and effective patient access to current and future hypertensive medications.[10]

This initiative also supports HEARTS countries in adopting new treatment protocols. A single pill, FDC, has substantial advantages for patients and healthcare programs including most (70%-80% of individuals) will need two agents eventually; two agents selected from complementary classes yields greater blood pressure (BP) reduction efficacy, which allows the usage of lower doses of each agent and a reduction in side effects of either agent; reduces clinical/therapeutic inertia; improves adherence; allows simpler dose schedules; decreases pill burden; lowers the BP equally among diverse demographic groups (sex, age, race, and ethnicity); simplifies logistics leading to fewer medication stock-outs; provides greater ease of task sharing, training, and supervision; and efficient for supply chain management and procurement at scale.[18,20,22-24]

Moreover, as mentioned above, the combination of two or more antihypertensive medications from complementary classes/groups in a single pill acts with an additive or synergistic BP reduction mechanism. This enables improved clinical results for controlling BP levels, thereby reducing overall healthcare and societal costs for patients and governments—while allowing more people to be treated.[24]

Similar to selecting individual agents, selecting two agents in two individual pills or preferably in a single pill FDC follows the same steps: (1) Select the two classes proposed as acceptable and preferred; (2) select the acceptable and preferred individual agents within each of the two classes; and (3) select which preferred or acceptable combinations and agents are available and affordable.[20] One particular advantage of initially using two agents in the treatment protocol is that it dramatically simplifies the total titration

TABLE 2 Characteristics of an ideal protocol

Characteristics of an ideal protocol
Defines a specific treatment pathway
Must be primary care-based
Uses fewest treatment titration steps possible
Linear with no branch points
Directive
Can be applied to manage the vast majority of cases of hypertension
Defines specific pharmacologic medication classes
Defines specific pharmacologic medication dosages
Uses the half-maximal blood pressure reduction dose of the medication (or medications if an initial FDC is used) in the initial treatment step

TABLE 3 Sample stepwise process to transition a protocol from a current protocol scenario to an acceptable protocol scenario, to a preferred protocol scenario

Step 1
A formulary and current protocol, which can be immediately put in place given current and available antihypertensive pharmacologic classes and medications
Step 2
A formulary and acceptable protocol, which includes classes and medications with some/more "ideal characteristics" than currently available and can be implemented, while not immediately, within 6 to 12 mo (note: this protocol may be the same as the current/present protocol)
Step 3
A formulary and preferred protocol, which includes classes and medications with all of the ideal characteristics, however, implementation would require a longer time such as 1 to 2 yr

steps to as little as four dose titration steps as opposed to six dose titration steps found in single initial agent treatment protocols. As an example, the following combinations of medications in order of preference could be as follows: (1) angiotensin receptor blocker-calcium channel blocker; (2) angiotensin-converting enzyme inhibitor-calcium channel blocker; (3) angiotensin receptor blocker-thiazide or thiazide-like diuretic; and (4) angiotensin-converting enzyme inhibitor-thiazide or thiazide-like diuretic. It is important to note that the combination of an angiotensin-converting enzyme inhibitor and angiotensin receptor blocker is contraindicated due to a high risk of adverse effects. After selecting classes to be combined, then the selection of the individual agents within each class can be made following the ideal characteristics of individual agents.

At the healthcare system level, factors, such as a lack of clinic and provider access, poor availability of quality, affordable and reliable medications, the inability to sustain recognition and treatment programs once initiated, and budgetary constraints, all prevent the widespread use of antihypertensive medications, which contributes to poor treatment and control rates.[23] The prescribing practice is driven by many considerations including accessibility, ease of use, cost, and tolerance of therapy. Unfortunately, despite the simplicity of the concept behind FDC therapy and evidence of enhanced efficacy and patient adherence, its success will ultimately rest on cost. Pooled procurement initiatives can be an effective mechanism for improving access to high-cost medications and new medications. The addition of the four FDCs mentioned above to the PAHO Strategic Fund is an important first step in helping HEARTS countries have access to FDCs as critical health products that should be widely available and affordable throughout health systems. Increased efforts to include FDCs on national formularies and to positively address clinical inertia by making them more available and affordable are likely to reap the noteworthy clinical benefit.

7 | HEARTS IN THE AMERICAS INITIATIVE—RESULTS/PROGRESS TO DATE

As a result of the launch of the first strategic pillar, a much greater understanding of the current policy and pharmacological landscape of the HEARTS countries was formed, as well a more concrete roadmap/process of how countries can transition to preferred treatment scenarios and maximize procurement processes by the end of 2021. For instance, at the inception of HEARTS in the Americas in 2016, there were over 50 medications and more than 100 preparations being used for the treatment of hypertension in the primary care setting. Following the strategy to develop smaller and simpler formularies, HEARTS is moving toward a formulary that consists of 7-8 core, high-quality medications with 19-20 preparations for use in primary care.

Moreover, as evidenced by their self-reported actual protocol scenarios (below), among the 12 countries participating in the HEARTS in the Americas Initiative, there is great diversity in implementation stages and medications being used. Indeed, each HEARTS country has the freedom to decide its protocol. Still, most HEARTS countries are anticipating transitioning to a protocol using either two separate medications or in a single pill, FDC, as the first step in their treatment protocols by the end of 2021. Further, select Latin American and Caribbean countries are among the first in the world to include FDC antihypertensive medications in their protocols, for example, Cuba, Colombia, Ecuador, and Trinidad and Tobago. Tables 8 and 9 list the current and preferred protocols from the HEARTS countries.

Through this process, we learned that as new acceptable and better yet, preferred protocols were developed, and implemented, significant synergistic changes in national medication formularies followed. It was also acknowledged that while a single national or even regional formulary and protocol would be optimal, local context of that dictates the development of distinctly different formularies and protocols in local areas such as provinces or states within a country. With the implementation of this strategy, the feasibility and advantages of using a pooled procurement mechanism, such as the PAHO Strategic Fund or similar, to secure a standard set of high-quality, competitively priced antihypertensive medications and, in particular, in a FDC, for all countries in the Region would be exponentially increased.

The HEARTS in the Americas Initiative is active in 12 countries and 371 health centers throughout Latin America and the Caribbean covering approximately 6 million adults in program catchment areas. Results emerging from the initiative demonstrate significant increases in hypertension control rates in the first cohort of participating countries. For instance, following less than one year of the full implementation of the program (from 2016 to 2017) in a community health center in the city of Matanzas, Cuba, the proportion of the hypertensive population registered as having hypertension increased from 52.9% to 88.2%, the proportion of those drug-treated who were controlled increased from 59.3% to 68.54%, and the estimated population rate of control went from 29.1% to 57.9%. In addition, there was an impressive increase in the prescription of antihypertensive

TABLE 4 Example of current protocol: A protocol that can be immediately put in place given the current availability of medications (all medications are in separate pills and once daily)

Step 1 (once the diagnosis of hypertension has been made)
Losartan 50 mg and amlodipine 5 mg
Step 2 (titration, if warranted)
Losartan 100 mg and amlodipine 10 mg
Step 3 (titration, if warranted)
Losartan 100 mg and amlodipine 10 mg and hydrochlorothiazide 25 mg
Step 4 (titration, if warranted)
Losartan 100 mg and amlodipine 10 mg and hydrochlorothiazide 50 mg
Step 5 (if blood pressure not at control level)
Start a fourth medication or refer to specialist

TABLE 5 Example of acceptable protocol: A protocol that includes more medications with ideal characteristics than are currently available and can be implemented within 6 to 12 mo (this protocol may be the same as the current protocol). All medications are in separate pills and once daily

Step 1 (once the diagnosis of hypertension has been made)
Valsartan 160 mg and amlodipine 5 mg
Step 2 (titration, if warranted)
Valsartan 320 mg and amlodipine 10 mg
Step 3 (titration, if warranted)
Valsartan 320 mg and amlodipine 10 mg and hydrochlorothiazide 25 mg
Step 4 (titration, if warranted)
Valsartan 320 mg and amlodipine 10 mg and hydrochlorothiazide 50 mg
Step 5 (if blood pressure not at control level)
Start a fourth medication or refer to specialist

TABLE 6 Example of preferred protocol: All medications meet most if not all of the ideal medication characteristics; however, implementation would require a greater period of time (a year or more) based on needed changes in the national formulary, new procurement and budgetary processes, and health system education

Step 1 (once the diagnosis of hypertension has been made)
Telmisartan 40 mg and amlodipine 5 mg *(in a FDC preparation and once daily)*
Step 2 (titration, if warranted)
Telmisartan 80 mg and amlodipine 10 mg
Step 3 (titration, if warranted)
Telmisartan 80 mg and amlodipine 10 mg and chlorthalidone 12.5 mg
Step 4 (titration, if warranted)
Telmisartan 80 mg and amlodipine 10 mg and chlorthalidone 25 mg
Step 5 (if blood pressure not at control level)
Start a fourth medication or refer to specialist

medications recommended in the protocol from 78.2% to 93.7%. This increase validates the feasibility and acceptability of the protocol and was the main driver of the improvement in control rates. Based on these positive results, new efforts to disseminate and scale-up aspects of the program to the full Cuban population have started.[25] Moreover, the Health Outcomes Prevention and Evaluation 4 (HOPE-4) study in Colombia used a comprehensive model of care that included using a FDC of two antihypertensive agents (ARB and a CCB) in the treatment of hypertensive individuals and achieved a hypertension control rate that increased from 11.5% to 68% within one year of follow-up.[26] Indeed, these results are promising, given that Kaiser Permanente in California, the global model of an excellent hypertension program, needed over 13 years to improve the hypertension control rate from 44% to almost 90%.[12]

TABLE 7 Characteristics that define each example protocol: current, acceptable, preferred

Current Protocol
Highly dependable medications that are currently available in the country or jurisdiction and are already included in the current national medication formularies.
Often not an acceptable or preferred protocol because it uses one or more short-acting, antihypertensive agents, which are important impediments for treatment adherence.
Acceptable Protocol
A clear improvement on the current protocol. Still based on the medications available in the country or jurisdiction, but with a substantive change in the pharmacologic strategy (longer-acting, a synergy between two or more medications, rapid and easy dose titration) which leads to better adherence, lower clinical inertia, and better hypertension control
Improves upon the current protocol in that it uses a longer-acting angiotensin receptor blocker, for example, valsartan. Not preferred because it uses the shorter-acting thiazide diuretic, hydrochlorothiazide.
Preferred Protocol
It represents the best standard of practice. Compatible with the definition of the ideal protocol. Leads to better adherence, lower clinical inertia, and rapid, better hypertension control.
Improves upon the acceptable protocol in that it uses the two agents in the initial treatment step, the angiotensin receptor blocker, telmisartan, and the calcium channel blocker, amlodipine in a fixed-dose (single pill) combination and uses the long-acting thiazide-like diuretic, chlorthalidone.

8 | CONCLUSIONS

In conclusion, there are significant opportunities for improving hypertension control globally, including the diligent implementation of a standardized and comprehensive approach to hypertension treatment and control, such as Global HEARTS. A central and critical approach is designing and implementing a standardized treatment protocol pillar and securing the availability and affordability of high-quality antihypertensive medications, thus leaving no one behind. The HEARTS in the Americas Initiative is an example of a standardized and innovative approach to hypertension control that is being replicated in other world regions. Training and program development practices and lessons learned by HEARTS in the Americas will continue to serve as a model for other regions worldwide to catalyze the actions needed to improve hypertension control and ultimately reduce the disease burden of CVD.

AUTHOR CONTRIBUTIONS

Donald J. DiPette was the lead author and responsible for content, drafting, writing, and coordinating the manuscript. Kenneth Goughnour, Eric Zuniga, Jamario Skeete, Emily Ridley, and Pedro Ordunez played key roles in content, writing, and editing the manuscript. Sonia Angell, Jeffrey Brettler, Norm RC Cambell, Antonio Coca, Kenneth Connell, Rohit Doon, Marc Jaffe, Patricio Lopez-Jaramillo, Andrew Moran, Marcelo Orias, Daniel J Pineiro, Andres

TABLE 8 Current protocols as reported during the Panama Technical Meeting

Current	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Barbados	CHLOR 25 OD	CHLOR 25 OD + LIS 10 (or LOS 50) OD	CHLOR 25 OD + AML 5 OD + optimize LIS (or LOS 100) OD			
Chile	LOS 50 OD + AML 5 OD or ENL 5 BID + AML 5 OD	LOS 50 BID + AML 10 OD or ENL 10 BID + AML 10 OD	LOS 50 BID + AML 10 OD + HCTZ 25 OD or ENL 20 BID + AML 10 OD + HCTZ 25 OD	LOS 50 BID + AML 10 OD + HCTZ 50 OD or ENL 20 BID + AML 10 OD + HCTZ 50 OD		
Colombia (Cali)	HCTZ 12.5 OD or LOS/HCTZ 50/12.5 ½ tablet OD	LOS/HCTZ 50/12.5 OD	LOS/HCTZ 100/25 OD	LOS/HCTZ 100/25 OD + AML 2.5 OD	LOS/HCTZ 100/25 OD + AML 5 OD	LOS/HCTZ 100/25 OD + AML 10 OD *If resistant: Add SPIR or MP
Cuba	ENL 10 BID + HCTZ 12.5 OD	ENL 20 BID + HCTZ 25 OD	ENL 20 BID + HCTZ 25 OD + AML 5 OD	ENL 20 BID + HCTZ 25 OD + AML 10 OD		
Argentina	AML 5 OD	AML 5 OD + LOS 50 OD	AML 5 OD + LOS 100 OD	AML 10 OD + LOS 100 OD	AML 10 OD + LOS 100 OD + HCTZ 25 OD	
Ecuador	LOS 50 BID + CHLOR 12.5 OD	LOS 50 BID + CHLOR 25 OD	LOS 50 BID + CHLOR 25 OD + AML 5 OD	LOS 50 BID + CHLOR 25 OD + AML 10 OD		
Panama	ACEI (PER or LIS) (or ARB (IRB or CAND) if ACEI contraindicated) or CCB (AML)	ACEI (PER or LIS) + CCB (AML) or ACEI (PER or LIS) + DIU (CHLOR or INDAP)	ACEI (PER or LIS) + CCB (AML) + DIU (CHLOR or INDAP)	ACEI (PER or LIS) + CCB (AML) + DIU (CHLOR or INDAP) + other DIU or alpha blocker or beta blocker		
Trinidad and Tobago	IRB 150 (or CAND 16) OD + AML 5 OD	IRB 300 (or CAND 32) OD + AML 10 OD	IRB 300 (or CAND 32) OD + AML 10 OD + CHLOR 12.5 OD	IRB 300 (or CAND 32) OD + AML 10 OD + CHLOR 25 OD		
Dominican Republic	ENL 10 BID + HCTZ 12.5 OD or LOS 50 OD + HCT 12.5	ENL 10 BID + HCTZ 12.5 OD + AML 2.5 OD or LOS 50 OD + HCTZ 12.5 OD + AML 2.5 OD	ENL 20 BID + HCTZ 12.5 OD + AML 2.5 OD or LOS 100 OD + HCTZ 12.5 OD + AML 2.5 OD	ENL 20 BID + HCTZ 12.5 OD + AML 5 OD or LOS 100 OD + HCTZ 12.5 OD + AML 5 OD	ENL 20 BID + HCTZ 25 OD + AML 10 OD or LOS 100 OD + HCTZ 25 OD + AML 10 OD	
Mexico (Chiapas)	TEL 40 OD + NIF 30 OD	TEL 80 OD + NIF 60 OD	TEL 80 OD + NIF 60 OD + HCTZ 12.5 OD	TEL 80 OD + NIF 60 OD + HCTZ 25 OD		
Mexico (Sonora)	TEL 40 OD + AML 5 OD	TEL 80 OD + AML 10 OD	TEL 80 OD + AML 10 OD + HCTZ 12.5 OD	TEL 80 OD + AML 10 OD + HCTZ 25 OD		
Peru	HCTZ 12.5 OD + LOS 50 BID (or ENL 10 BID)	HCTZ 12.5 OD + LOS 50 BID (or ENL 10 BID) + AML 5 OD				
Saint Lucia	AML 5 OD	AML 5 OD + LOS 50 OD	AML 5 OD + LOS 100 OD	AML 10 OD + LOS 100 OD	AML 10 OD + LOS 100 OD + CHLOR 12.5 OD	AML 10 OD + LOS 100 OD + CHLOR 25 OD
British Virgin Islands	AML 5 OD	AML 5 OD + LIS 10 OD	AML 5 OD + LIS 20 OD	AML 10 OD + LIS 20 OD	AML 10 OD + LIS 20 OD + INDAP 1.5 OD	

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; AML, amlodipine; ARB, angiotensin II receptor blockers; CAND, candesartan; CCB, calcium channel blockers; CHLOR, chlorthalidone; DIU, diuretic; ENL, enalapril, HCTZ, hydrochlorothiazide; INDAP, indapamide; IRB, irbesartan; LIS, lisinopril; LOS, losartan; MP, metoprolol; NIF, nifedipine; OD, once daily; PER, perindopril; SPIR, spironolactone; TEL, telmisartan.

TABLE 9 Preferred protocols as reported during the Panama Technical Meeting

Preferred	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Barbados	AML 5 OD + TEL 40 OD (or VAL 160)	AML 10 OD + TEL 80 OD (or VAL 320)	AML 10 OD + TEL 80 OD (or VAL 320) + CHLOR 25 OD			
Chile	TEL/AML 40/5 OD	TEL/AML 80/10 OD	TEL/AML 80/10 OD + HCTZ 12.5 OD	TEL/AML 80/10 OD + HCTZ 25 OD		
Colombia	TEL/AML 40/5 OD	TEL/AML 80/10 OD	TEL/AML 80/10 OD + HCT 25 OD	TEL/AML 80/10 OD + HCT 50 OD		
Cuba	LIS/HCTZ 20/25 ½ pill OD	LIS/HCTZ 20/25 OD	LIS/HCTZ 20/25 OD + AML 5 OD	LIS/HCTZ 20/25 OD + AML 10 OD		
Argentina	TEL/AML 40/5 ½ pill OD	TEL/AML 40/5 OD	TEL/AML 40/5 2 pills OD	TEL/AML 40/5 2 pills OD + CHLOR 25 OD		
Ecuador	TEL/AML 40/5 OD	TEL/AML 80/10 OD	TEL/AML 80/10 OD + CHLOR 12.5 OD			
Panama	*1 med*: ACEI (PER or LIS) (or ARB (IRB or CAND) if ACEI contraindicated) or CCB (AML) or DIU (CHLOR or INDAP) or If BP > 160/100: FDC (2 meds at low dose)	*1 med at full dose*: ACEI (PER or LIS) or ARB (IRB or CAND) or CCB (AML) or DIU (CHLOR or INDAP) or FDC (2 meds at low dose)	FDC (2 meds at full dose) or FDC (3 meds at low to medium doses)	FDC (3 meds at full dose)		
Trinidad and Tobago	TEL 40 OD + AML 5 OD	TEL 80 OD + AML 10 OD	TEL 80 OD + AML 10 OD + CHLOR 12.5 OD	TEL 80 OD + AML 10 OD + CHLOR 25 OD		
Dominican Republic	LIS/HCTZ 20/12.5 OD or TEL/AML 40/5 OD	LIS/HCTZ 40/25 OD or TEL/AML 80/10 OD	LIS/HCTZ 40/25 OD + AML 5 OD or TEL/AML 80/10 OD + HCTZ 12.5 OD	LIS/HCTZ 40/25 OD + AML 10 OD or TEL/AML 80/10 OD + HCTZ 25 OD		
Mexico	PER/AML 5 /5 FDC or IRB/AML 150 /5 FDC	PER/AML 10 /10 FDC or IRB/AML 300/10 FDC	PER/AML/INDAP 10/10/2.5 FDC or OLM/AML/ HCTZ 40/10/12.5 FDC	PER/AML/INDAP 10/10/2.5 FDC + SPIR 25 OD or OLM/AML/ HCTZ 40/10/12.5 FDC + BIS 2.5 OD	PER/AML/INDAP 10/10/2.5 FDC + SPIR 50 OD or OLM/AML/ HCTZ 40/10/12.5 FDC + BIS 5 OD	
Peru	LIS 10 OD (or CAND 16)	LIS 10 OD + HCTZ 12.5 OD	LIS 10 OD + HCTZ 12,5 OD + AML 5 OD			

(Continues)

TABLE 9 (Continued)

Preferred	Step 1	Step 2	Step 3	Step 4	Step 5	Step 6
Saint Lucia	TEL/AML 40/5 OD	TEL/AML 80/10 OD	TEL/AML 80/10 OD + CHLOR 12.5 OD	TEL/AML 80/10 OD + CHLOR 25 OD		
British Virgin Islands	TEL/AML 40/5 OD	TEL/AML 80/5 OD	TEL/AML 80/10 OD	TEL/AML 80/10 OD + CHLOR 25 OD		

Abbreviations: ACEI, angiotensin-converting enzyme inhibitors; AML, amlodipine; ARB, angiotensin II receptor blockers; BIS, bisoprolol; CAND, candesartan; CHLOR, chlorthalidone; DIU, diuretic; FDC, fixed-dose combination; HCTZ, hydrochlorothiazide; INDAP, indapamide; IRB, irbesartan; LIS, lisinopril; meds, medications; OD, once daily; OLM, olmesartan; PER, perindopril; SPIR, spironolactone; TELM, telmisartan; VAL, valsartan.

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DISCLAIMER

PO is a staff member of the Pan American Health Organization. The authors alone are responsible for the views expressed in this publication, and they do not necessarily represent those of the Pan American Health Organization.

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