Candidate Interventions for **Integrating Hypertension** and Cardiovascular-Kidney-Metabolic Care in Primary Health Settings: HEARTS 2.0 Phase 1

#### **ORIGINAL RESEARCH**

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#### ABSTRACT

**Background:** HEARTS in the Americas is the regional adaptation of the WHO Global HEARTS Initiative, aimed at helping countries enhance hypertension and cardiovascular disease (CVD) risk management in primary care settings. Its core implementation tool, the HEARTS Clinical Pathway, has been adopted by 28 countries. To improve the care of hypertension, diabetes, and chronic kidney disease (CKD), HEARTS 2.0 was developed as a three-phase process to integrate evidence-based interventions into a unified care pathway, ensuring consistency across fragmented guidelines. This paper focuses on Phase 1, highlighting targeted interventions to improve and update the HEARTS Clinical Pathway.

**Methods:** First, the coordinating group defined the project's scope, objectives, principles, methodological framework, and tools. Second, international experts from different disciplines proposed interventions to enhance the HEARTS Clinical Pathway. Third, the coordinating group harmonized these proposals into unique interventions. Fourth, experts appraised the appropriateness of the proposed interventions on a 1-to-9 scale using the adapted RAND/UCLA Appropriateness Method. Finally, interventions with a median score above 6 were deemed appropriate and selected as candidates to enhance the HEARTS Clinical Pathway.

**Results:** Building on the existing HEARTS Clinical Pathway, 45 unique interventions were selected, including community-based screening, early detection and management of risk factors, lower blood pressure thresholds for diagnosing hypertension in high-CVD-risk patients, reinforcement of single-pill combination therapy, inclusion of sodium-glucose cotransporter-2 inhibitors for patients with diabetes, CKD, or heart failure, expanded roles for non-physician health workers in team-based care, and strengthened clinical documentation, monitoring, and evaluation.

**Conclusion:** HEARTS 2.0 Phase 1 identifies key interventions to integrate and improve hypertension and cardiovascular-kidney-metabolic care within primary care, enabling their seamless incorporation into a unified and effective clinical pathway. This process will inform an update to the HEARTS Clinical Pathway, optimizing resources, reducing care fragmentation, improving care delivery, and advancing health equity, thereby supporting global efforts to combat the leading causes of death and disability.

# **INTRODUCTION**

The World Health Organization's (WHO) Global HEARTS Initiative (1) supports health ministries in developing cardiovascular disease (CVD) prevention strategies, focusing on hypertension management. HEARTS in the Americas, the regional adaptation coordinated by the Pan American Health Organization (PAHO), currently reaches 37 million adults, with 5.7 million receiving hypertension treatment, across over 7,200 primary healthcare (PHC) centers in 33 countries. The program aims to transform health services and clinical practice to enhance hypertension control and integrated CVD risk management in PHC (2). High systolic blood pressure (SBP) is the main risk factor for ischemic heart disease (IHD) and stroke (3), and countries with the highest levels of population hypertension control tend to have low IHD and stroke mortality rates (4).

The HEARTS Clinical Pathway, the central tool for HEARTS in the Americas (5), aligns with the 2021 WHO pharmacologic hypertension guidelines (6) and is shaped by HEARTS control drivers (7). It features a standardized treatment protocol, initiating at blood pressure (BP)  $\geq$ 140/90 mmHg, with monthly intensifications until BP is controlled (8), prioritizing long-acting agents and single-pill antihypertensive combinations (SPC) (9). CVD risk is assessed using WHO risk charts, with high risk defined by IHD, stroke, diabetes mellitus, CKD, or a 10-year CVD risk  $\geq$ 10%. Immediate treatment is recommended for high-risk patients with SBP  $\geq$ 130 mmHg, with rapid titration to reach a SBP <130 mmHg. High-intensity statins and low-dose aspirin are advised for patients with established CVD, while moderate-intensity statins without aspirin are recommended for those patients at high risk but without established CVD (10).

The HEARTS Clinical Pathway, currently implemented in 28 countries across Latin America and the Caribbean region, has been essential in standardizing management in implementing countries (11). This tool also commits health authorities to ensure access to high-quality, affordable essential medicines, clinically validated automated blood pressure measurement devices (BPMD), and other critical resources (12). Designed for broad implementation at the PHC level, it promotes a team-based care model that involves patients and non-physician health workers (NPHW).

The rising prevalence of obesity, hypertension, and diabetes, coupled with the emergence of the Cardiovascular-Kidney-Metabolic Syndrome (CKM)—a serious health disorder attributable to connections among obesity, diabetes, CVD, and CKD—underscores the urgent need to adopt innovative clinical practices (13, 14). Additionally, HEARTS countries have called for more comprehensive management tools for noncommunicable diseases (NCDs), while PAHO's Better Care for NCDs advocates for an integrated approach to strengthening PHC capacity (15). These factors highlight the pressing need to update the current HEARTS Clinical Pathway.

To advance the HEARTS Clinical Pathway for cardio-renal-metabolic management, we developed HEARTS 2.0—a three-phase process to integrate and align evidence-based interventions into a unified care pathway. Phase 1 identifies synergistic interventions for hypertension, CVD prevention, diabetes mellitus, and CKD that can be integrated into the pathway. Phase 2 will assess countries' readiness for implementation, while Phase 3 will select interventions to update the pathway and develop strategies for broader adoption. This stepwise approach ensures participation from countries and stakeholders, reinforcing the inclusive and evidence-based framework of HEARTS in the Americas.

This paper describes the design, conduct, and outcomes of Phase 1 of HEARTS 2.0, presenting a detailed list of candidate interventions for integration into the updated HEARTS Clinical Pathway. The aim is to create a more cohesive and integrated pathway that enhances multimorbidity management, reduces care fragmentation, and fosters coordinated action within primary healthcare systems.

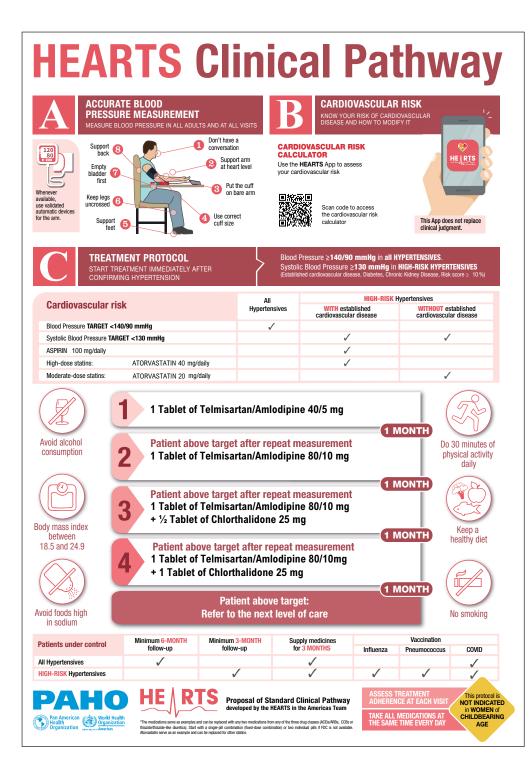
### **METHODS**

HEARTS 2.0 Phase 1 followed a systematic and multi-step process. First, the coordinating group defined the project's scope, objectives, and overarching principles, and created data collection tools. Second, a group of multidisciplinary international subject-matter experts, familiar with both the Global HEARTS initiative and HEARTS in the Americas was invited to propose interventions to enhance the current HEARTS Clinical Pathway. Third, the coordinating group reviewed and consolidated the improvement proposals, leading to the identification of unique interventions. Fourth, experts appraised the appropriateness of the proposed interventions for relevance and suitability. Fifth, the highest-scoring interventions were deemed appropriate and selected as candidates to enhance the HEARTS Clinical Pathway.

The project adhered to three overarching principles: first, all interventions should build upon the existing HEARTS Clinical Pathway (Figure 1); second, new interventions (whether modifications or additions) would only be considered if supported by robust scientific evidence, prioritizing those endorsed by leading clinical practice guidelines or widely recognized as beneficial through international consensus; and third, each intervention had to be feasible and safe for large-scale implementation in diverse PHC settings.

Seventy-one international experts were invited reflecting diverse representation across geographical regions, income levels, demographics, professional backgrounds, and research experience, including key representatives from global and regional organizations developing relevant clinical guidelines. Experts were asked to propose up to three impactful interventions in areas covered by the HEARTS Clinical Pathway, such as diagnosis, risk assessment, treatment, continuity of care, delivery systems, immunization, and follow-up. For each proposal, experts were instructed to propose only interventions supported by robust evidence, particularly those endorsed by leading guidelines or international consensus. They also provided references for supporting evidence and a justification for each intervention.

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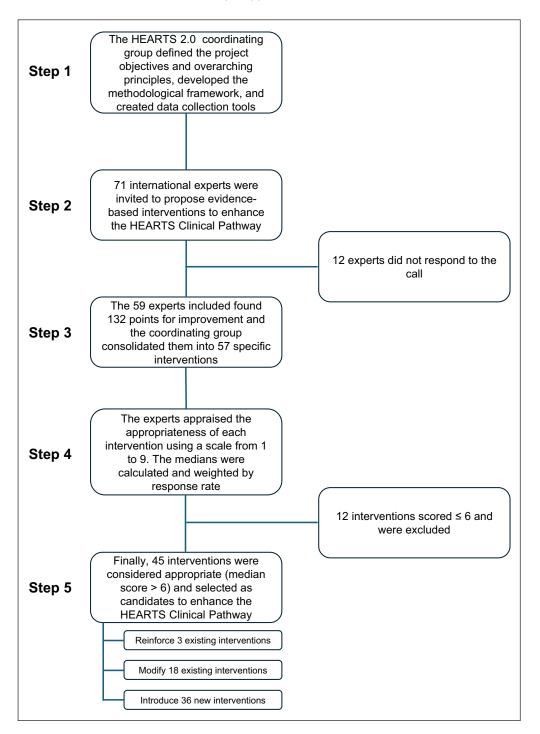
**Figure 1** The HEARTS Clinical Pathway.

The coordinating group reviewed and consolidated the proposed interventions, which were then presented to the experts, along with their intervention areas, recommended actions (remove, reinforce, modify, or include), and supporting evidence (see "Appropriateness Exercise Instrument" in the supplementary materials). Experts rated each intervention for appropriateness using the RAND/UCLA Appropriateness Method (16). This method consists in a systematic approach to evaluate the suitability of specific interventions, tests, or procedures for clinical scenarios or populations. These assessments combine expert judgment, clinical guidelines, and scientific evidence to ensure that interventions align with best practices and are contextually relevant. Experts rate the appropriateness of interventions using a scale of 1 to 9, and appropriateness is defined based on the expected health benefit outweighing the expected negative consequences. Each intervention is categorized as appropriate if the median of the ratings falls in the top third, uncertain if the median falls in the middle third, and inappropriate if the median of the responses falls in the bottom third. Since experts were free to respond according to their expertise, and to avoid bias, the medians were weighed by the response rate.

Finally, the assessment results were shared with all experts for additional comments or objections. Interventions with a median score above 6 were deemed appropriate and selected as candidates to enhance the HEARTS Clinical Pathway.

# RESULTS

Figure 2 summarizes the process for evaluating the appropriateness of candidate interventions to be incorporated into the HEARTS Clinical Pathway. Of the 71 experts invited, 59 responded to the call (see Table "Characteristics of experts" in supplementary materials), contributing 132 proposals for improvement. These proposals were consolidated into 57 specific interventions, highlighting the acceptability of the current HEARTS Clinical Pathway—no interventions were recommended for removal—and multiple opportunities for enhancement.



The assessment resulted in three key actions for improvement: a) reinforcing three existing interventions of significant value that could benefit from greater emphasis; b) modifying 18 existing components to align with current best practices; and c) introducing 36 new specific interventions to address emerging challenges and incorporate recent advancements into the pathway (Table 1).

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**Figure 2** Flowchart summarizing the process for evaluating the appropriateness of candidate interventions to be included in the HEARTS Clinical Pathway.

ACTION RECOM- MENDED	DIAGNOSIS	RISK ASSESSMENT	NON-PHARMA- COLOGIC TREATMENT	PHARMA- COLOGIC TREATMENT	CONTINUITY OF CARE	DELIVERY SYSTEM	SYSTEM FOR MONI- TORING	IMMU- NIZATION	TOTAL
Include	3	8	7	6	7	3	2	0	36
Modify	3	4	0	6	2	0	0	3	18
Reinforce	2	0	0	1	0	0	0	0	3
Remove	0	0	0	0	0	0	0	0	0
With high median score	4/8	9/12	6/7	13/13	6/9	3/3	2/2	2/3	45/57

A total of 78.9% (45 out of 57) of the proposed interventions received high appropriateness scores and a strong expert consensus on the value of these changes. These high-rated interventions, summarized in Table 2, encompass all areas of the HEARTS Clinical Pathway, signaling a comprehensive strategy to enhance cardiovascular care. The results of this appraisal can be summarized as follows:

Table 1Number ofimprovement interventionsagreed by action and area.

INTERVENTION AREAS	ACTION TO BE TAKEN	IMPROVEMENT PROPOSALS AGREED			
Diagnosis	Reinforce	<b>1.</b> Exclusive use of clinically validated BPMD.			
		2. Improving the clinical environment for accurate BP measurement.			
	Include	<b>3.</b> Expanding community outreach for hypertension screening.			
		4. Set BP diagnostic thresholds for hypertension at ≥140/90 mmHg in the general population and SBP ≥130 mmHg for patients at high cardiovascular risk.			
Risk assessment	Modify	<b>5.</b> Set CKD definition: eGFR < 60 ml/min and/or uACR index $\ge$ 30 mg/g.			
		6. Set BP goals in elderly patients to SBP <130 mmHg.			
		7. Define a CVD risk approach for young adults (18–40 years).			
	Include	8. CKD screening for high-risk individuals using uACR and eGFR.			
		9. Assessment of HTN-mediated organ damage with ECG in high CVD risk patients.			
		<b>10.</b> Screening for dyslipidemia and diabetes in patients with HTN and obesity.			
		<ol> <li>Opportunistic screening for atrial fibrillation in high CVD risk patients of any age and those aged ≥ 65 years.</li> </ol>			
		<b>12.</b> Closely monitor individuals with a history of hypertension during pregnancy.			
		<b>13.</b> Add a warning: Avoid treatment with short-acting and parenteral agents in individuals with severe asymptomatic uncontrolled hypertension.			
Non-Pharmacologic	Include	<b>14.</b> Promote low-sodium /potassium-enriched salt.			
Treatment		<b>15.</b> Prescribe isometric exercise.			
		<b>16.</b> Warning against smoking Cannabis.			
		<b>17.</b> Warning against Electronic Cigarette use/Vaping.			
		<b>18.</b> Avoid sedentary lifestyle.			
		<b>19.</b> Prescribe exercise.			
Pharmacologic	Reinforce	<b>20.</b> SPC antihypertensive medicines.			
Treatment	Modify	<b>21.</b> Add the third drug, at half maximum dose, in the second step of the treatment protocol instead of increasing the first two drugs to maximum doses.			
		<b>22.</b> Maximum statin doses in secondary prevention (Atorvastatin 80 mg or Rosuvastatin 40 mg).			
		<b>23.</b> High statin doses in primary prevention (Atorvastatin 40 mg or Rosuvastatin 20 mg).			
		<b>24.</b> Use of Polypills (antihypertensives plus statins with or without aspirin) for primary and secondary prevention of CVD.			
		<b>25.</b> Intensify antihypertensive medication at intervals of 2 weeks instead of 4 weeks.			

INTERVENTION AREAS	ACTION TO BE TAKEN	IMPROVEMENT PROPOSALS AGREED				
		<b>26.</b> Warning on assessing childbearing potential before treatment initiation.				
	Include	<b>27.</b> Triple SPC for those patients who do not reach BP control using double SPC.				
		<b>28.</b> Spironolactone in patients with 3 drugs at maximum doses and lack of HTN control.				
		<b>29.</b> Treatment for tobacco cessation (bupropion, varenicline, nicotine substitutes).				
		<b>30.</b> Prescribe SGLT2i in patients with CKD.				
		<b>31.</b> Prescribe SGLT2i in patients with heart failure.				
		<b>32.</b> Prescribe SGLT2i in patients with diabetes and established CVD.				
Continuity of Care	Modify	<b>33.</b> Intensive BP (SBP < 130 mmHg) goals restricted to patients <80 years.				
	Include	<b>34.</b> Home BP treatment monitoring.				
		<b>35.</b> Telemedicine/mHealth apps to monitor recommendation adherence and to reduce loss to follow-up.				
		<b>36.</b> Lipid targets in high CVD risk patients.				
		<b>37.</b> An established target time to achieve BP control.				
		<b>38.</b> Warning to avoid statin discontinuation once the control target has been reached.				
Delivery System	Include	<b>39.</b> Medication intensification by non-physician healthcare workers following a protocol.				
		<b>40.</b> HTN screening and CVD risk stratification by non-physician healthcare workers.				
		<b>41.</b> Healthy lifestyle counseling and support for medication adherence by non-physician healthcare workers.				
Immunization	Modify	<b>42.</b> Influenza vaccination to all patients with HTN regardless of CVD risk level.				
		<b>43.</b> Pneumococcus vaccination should exclude patients in primary prevention <65 years.				
System for Monitoring	Include	<b>44.</b> Importance of registering clinical variables.				
		<b>45.</b> Relevance of having a strategy of performance evaluation with feedback.				

Many proposed interventions focused on early detection and intensive management of risk factors like hypertension, dyslipidemia, diabetes, CKD and atrial fibrillation (AF), underlining a preventative approach to cardiovascular health.

The interventions emphasized integrating lifestyle modifications such as a healthy diet, reduced-sodium/potassium-enriched salt consumption, and increased physical activity, while also highlighting the risks of cannabis and electronic cigarette use and reinforcing the general recommendation against tobacco use, to promote a holistic approach to patient management.

The experts stressed the expanded use of SPCs to simplify medication regimens and improve treatment adherence. They also recommended adjusting statin doses for CVD primary and secondary prevention, with maximum doses specifically suggested for those with existing CVD. Furthermore, the experts highlighted the potential benefits of sodium-glucose cotransporter-2 inhibitors (SGLT2i) for patients with diabetes, CKD, or heart failure.

Expanding the role of NPHWs was seen as crucial to improve access to care, provide patient education and support, and potentially handle tasks like medication titration under supervision, suggesting a more team-based approach to care delivery.

The experts emphasized the importance of targeted vaccination strategies to improve patient outcomes. They supported universal COVID-19 vaccination and recommended expanding influenza vaccination to include all individuals with hypertension. For pneumococcal vaccination, the experts advised prioritizing individuals aged 65 and older, focusing on those at higher risk.

Finally, the experts underscored the importance of a robust monitoring and evaluation system. They advocated systematic documentation of clinical variables, such as BP values and CVD risk levels, and recommended incorporating a performance evaluation strategy with feedback into the HEARTS Clinical Pathway.

Table 2 Candidate Interventions for the HEARTS Clinical Pathway Upgrade. BP: blood pressure; BPMD: blood pressure measuring devices; HTN: hypertension; CVD: cardiovascular disease; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; AlbU: urine albumin; CrU: urine creatine; uACR: urine albumin-creatinine ratio; ECG: electrocardiogram; AF: atrial fibrillation; SPC: single pill combination; SGLT2i: sodiumglucose co-tranporter-2 inhibitors.

The detailed breakdown of all 57 interventions, including supporting evidence and expert ratings, is available in the supplementary materials ("Results of the Appropriateness Exercise" and "Agreed Interventions and Their Supports" tables).

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### DISCUSSION

HEARTS 2.0 was designed to integrate cardiovascular-kidney-metabolic care into primary care and foster synergy across multiple evidence-based interventions. Building on a robust clinical pathway already adopted by most countries in the Americas (4, 5, 11, 17), this framework aims to address the complex needs of patients with multiple risk factors and conditions by prioritizing clinically proven solutions while emphasizing public health and health system strategies. Hypertension management remains the cornerstone of the HEARTS Clinical Pathway, anchoring other critical preventive interventions, while the PHC setting provides the foundation for delivering coordinated, people-centered care (4, 18). As far as we know, this is the first initiative of its kind and scope globally.

Strengthening interventions for accurate BP measurement aligns with global efforts to standardize BP measurement in clinical settings (19). This underscores the need for stricter regulations mandating the validation of automatic BPMDs (20) because non-validated devices increase the risk of inaccurate readings, misdiagnosis, and mistreatment of hypertension (21). Misconceptions around market approval requirements have led to the proliferation of non-validated BPMDs, with fewer than 20% of automated upper-arm and wrist devices meeting internationally accepted validation standards (22). HEARTS in the Americas promotes BP measurement accuracy including a regulatory framework mandating clinically validated BPMDs in PHC (23).

The current HEARTS Clinical Pathway already promotes a differentiated approach for people with diabetes or CKD, recommending more intensive hypertension management to achieve a target SBP of <130 mmHg (24), along with the use of statins or aspirin (10). However, it does not include guidance on how to identify these patients. For that reason, a key improvement focuses on opportunistic screening for CKD in high-risk individuals, using urine albumin-creatinine ratio (uACR) and estimated glomerular filtration rate (eGFR) thresholds (25). Hypertension remains prevalent and poorly controlled (26), while type 2 diabetes mellitus continues to rise without sufficient expansion in treatment (27, 28). Together, these conditions drive over 75% of CKD risk, worsening both hypertension and diabetes and elevating CVD risk and premature death (14). Indeed, nearly 90% of those with CKM Syndrome die from CVD before reaching end-stage kidney disease (14). Intensifying BP control to SBP <130 mmHg in high-CVD risk patients, including those with diabetes or CKD, is recommended by 2021 WHO hypertension guideline (6) and is one of the most effective interventions to reduce CVD mortality (29) and slow CKD progression (30).

Hypertension, obesity, and aging are risk factors for AF (31, 32). Opportunistic AF screening for high-CVD-risk patients could enhance the HEARTS Clinical Pathway, in line with evidence (33) and clinical guidelines (34). AF affects 10% of people aged 65 and older, with its global burden doubling since 1990 (35). AF increases stroke risk fivefold, often leading to disabling or fatal strokes. Early detection and anticoagulation can reduce stroke risk by 70%; yet 30% of individuals remain undiagnosed (34). Integrating simple, cost-effective AF case-finding into the HEARTS pathway could improve detection and access to anticoagulants, enhancing clinical outcomes (36).

Replacing regular salt with reduced-sodium/potassium-enriched salt significantly lowers BP, reduces CVD incidence, and decreases all-cause mortality (37). Adding this cost-effective intervention to the HEARTS Clinical Pathway could reduce BP and CVD risk for millions of adults in the HEARTS in the Americas program (38). Despite poor implementation, it has strong global support as an impactful measure (39–41).

Experts agreed on strengthening physical activity recommendations by advising patients on sedentary behavior and prescribing increased physical activity, supported by evidence (42, 43) and clinical guidelines (44, 45). They also recommended adding warnings about e-cigarettes/ vaping, and cannabis use due to their growing use and link to CVD (46, 47). These non-

pharmacologic strategies reinforce the HEARTS' role in empowering communities and engaging patients in their care.

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The experts strongly supported expanding SPC use to address treatment inertia, medication adherence, persistence, and effectiveness of hypertension programs, including introducing triple SPC for patients who do not achieve BP control with double SPC (48). SPCs are recommended by all major guidelines, (6, 49–51) and were included in the WHO essential medicines list (52), but adoption is hindered by procurement cost, physician reluctance, and restricted access (53). Barriers include outdated national essential medicines lists, limited market availability, fragmented procurement processes, and exclusion from insurance programs or public sector provision, leading to high out-of-pocket costs. Leveraging pooled procurement mechanisms, like the PAHO Strategic Fund, and updating national essential medicines lists could improve accessibility and affordability (54).

The availability of SGLT2i has shifted the focus of diabetes care beyond glucose control to include reducing CVD risk and preventing CKD progression (25, 55). Together with the HEARTS Clinical Pathway's recommendations for more stringent hypertension targets in patients with diabetes and CKD (5) and higher statin doses (56), these interventions form a comprehensive approach for patients with multiple conditions including the CKM syndrome. This strategy is primed for rapid expansion, as the WHO has included SGLT2i in its essential medicines list (52) and PAHO has added them to the Strategic Fund's procurement list (57).

A key improvement intervention was adopting a structured, time-sensitive approach to hypertension control. This includes shorter medication titration intervals, earlier treatment intensification, and time-bound BP targets to reduce CVD risk (58). Acknowledging that delays in BP control increase adverse outcomes, the pathway promotes timely interventions and follow-up visits within three months for high CVD-risk patients and six months for others, fostering sustained BP control, further improving CVD outcomes.

The experts supported HBPM and telemedicine/mHealth as key improvements. While HBPM is recommended by major clinical guidelines (49–51), its implementation is limited by access to clinically validated BPMDs. Telemedicine offers a potential solution for improving access to care, continuity, and follow-up, especially in underserved areas, crucial for maintaining BP control and preventing complications (59).

The experts supported reinforcing NPHW's role in hypertension screening, patient education, and treatment intensification using the HEARTS Clinical Pathway. A recent trial showed that NPHW-led intervention improved hypertension control and reduced CVD and mortality (60). However, regulatory and cultural barriers in many HEARTS-implementing countries hinder broader implementation (5, 61, 62).

The current HEARTS Clinical Pathway recommends influenza vaccination for high CVDrisk patients. However, the experts suggested this recommendation to all individuals with hypertension, regardless of their CVD risk, based on evidence that infectious diseases can act as triggers for cardiovascular events, while immunization reduces their occurrence. Influenza vaccination is highly cost-effective, supporting its widespread adoption (63).

#### STRENGTHS AND LIMITATIONS

HEARTS 2.0 Phase 1 is not designed to create clinical guidelines or position statements. Instead, it follows a systematic and rigorous appropriateness assessment process. Led by a group of multidisciplinary international experts, it aims to integrate synergistic, evidence-based interventions from existing guidelines to streamline the HEARTS Clinical Pathway and address related conditions in PHC settings. It reduces costly evaluations by harmonizing interventions already endorsed by various authorities. Indeed, key interventions identified by the experts are already part of major clinical guidelines and position statements. However, a limitation is that interventions were not assessed in terms of health budget impact or cost-effectiveness; as country-level cost and cost-effectiveness assessments were beyond the scope of the HEARTS 2.0 process. Recognizing that evidence from clinical trials may not always apply to real-world practice, further research is needed for broad implementation.

Although HEARTS promotes teamwork, and three interventions on this topic were considered appropriate, a limitation of the expert group is that almost 90% of its members are medical doctors. However, this distribution reflects the broader overrepresentation of physicians in the research field as well as in the development of clinical practice guidelines.

Finally, all experts approved the methodology and results and submitted conflict-of-interest declarations. Expert anonymity was maintained to prevent cross influence, and results were shared for feedback. Any experts involved in Phase 1 who declared any conflict of interest during this process will be excluded from HEARTS 2.0 Phase 3, which will focus on selecting interventions to update the clinical pathway and developing strategies for broader adoption.

#### **KEY FINDINGS AND NEXT STEPS**

The experts acknowledged the high technical quality of the current HEARTS Clinical Pathway while identified several areas for improvement. Proposed innovations included communitybased screening, early detection and management of risk factors, guideline-aligned BP thresholds for diagnosing hypertension in high-CVD risk patients, reinforcement of the SPC recommendation, the inclusion of new treatments for diabetes and CKD, enhanced clinical monitoring of hypertension, expanded roles of NPHWs in team-based care, and strengthening clinical documentation, monitoring and evaluation.

In HEARTS 2.0 Phase 1, experts identified candidate interventions to improve the HEARTS Clinical Pathway. As implementation approaches, the dialogue will expand to include policymakers, healthcare workers, patients, and other stakeholders in HEARTS-implementing countries. The second phase of HEARTS 2.0 will map countries' preparedness and readiness to implement these interventions, guiding future decision-making. In the third phase, a panel will prioritize interventions for inclusion in the updated clinical pathway. Some interventions may require further evaluation, while those with strong evidence but low feasibility for implementation will be advanced through advocacy and policy efforts.

### CONCLUSION

The improvement interventions identified in HEARTS 2.0 Phase 1, grounded in evidence-based principles and multidisciplinary collaboration, have the potential to transform CVD management in PHC settings. This initiative is crucial given the persistent prevalence of hypertension, the rise in type 2 diabetes, and their link to CKD. The development of an updated HEARTS Clinical Pathway will be key to optimizing resources, reducing care fragmentation, improving care delivery, and enhancing equity. Ultimately, this will push the boundaries of PHC to more effectively address the leading causes of death and disability worldwide.

## **ADDITIONAL FILE**

The additional file for this article can be found as follows:

• **Supplementary materials.** HEARTS 2.0 Phase 1. This file contains information on the composition of the group of experts who participated in the consultation, as well as the instrument used to select the candidate interventions to integrate the new clinical pathway and their support in evidence. DOI: <a href="https://doi.org/10.5334/gh.1428.s1">https://doi.org/10.5334/gh.1428.s1</a>

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### **COMPETING INTERESTS**

AR and PO are staff members of the Pan American Health Organization. The authors alone are responsible for the views expressed in this publication, and they do not necessarily represent the decisions or policies of the Pan American Health Organization.

GS, ARod, AES, MDH, and AS work for The George Institute for Global Health, which has a patent and has received investments to commercialize fixed-dose combination therapies for cardiovascular disease prevention through its social enterprise company, George Medicines. AES also declares receiving consulting fees from Servier, Abbott, Medtronic, and Sky Labs, and honoraria for lectures from Servier, Abbott, Medtronic, AstraZeneca, Aktiia, Sanofi, Novartis, and Omron. MDH has received travel support from the World Heart Federation and consulting fees from PwC Switzerland. MDH has pending patents for heart failure polypills. AF declares receiving honoraria for lectures from Boehringer-Ingelheim, Ely Lilly, Bayer, Jafron Biomedical, and Nipro Medical. GP declares receiving honoraria for lectures from Omron, Merck, Viatris and Somnomedics. MO declares receiving honoraria for lectures from GlaxoSmithKline and AstraZeneca. PL declares receiving consulting fees from Pfizer and Boehringer-Ingelheim, and honoraria for lectures from Boehringer-Ingelheim, Ferrer, Servier, Pfizer, and Novartis. DP declares receiving honoraria for lectures from Servier and holds the copyright for a decision support software to manage hypertension and diabetes. GR declares holding stocks in Catalisia SA. EZ declares receiving honoraria for lectures from Novo Nordisk, Pfizer, PTC Therapeutics, AstraZeneca, Medicamenta, and Janssen. AC declares receiving honoraria for lectures from Adium, Berlin-Chemie, Ferrer, Menarini, and Sanofi. JRF declares receiving honoraria for lectures from Novo Nordisk, AstraZeneca, Eli Lilly, Boehringer-Ingelheim, and Bayer. ST declares receiving honoraria for lectures from Boehringer- Ingelheim, Novo Nordisk, CHEP Plus, and KMH.

The remaining authors declare no conflicts of interest related to the content of this manuscript.

## **AUTHOR CONTRIBUTIONS**

AR, CR, DD, JB and PO formed the coordinating group, defining the project's scope, objectives, overarching principles, and developing the methodological framework and tools. All authors approved the study methodology, proposed improvement interventions, and appraised their appropriateness to enhance the HEARTS Clinical Pathway. AR and PO prepared the initial draft, with significant contributions from CR, DD, JB, PVdS, GS, NCh, PP, AES, AM, PW, VI, NC, AS, MH, and JS. All authors critically reviewed the manuscript, provided substantial intellectual input, and contributed to its refinement. PKW and PO served as senior authors. All authors had full access to the study data, assumed responsibility for the work's integrity, and the corresponding author accepted final responsibility for submitting the manuscript for publication.

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#### REFERENCES

- Khan T, Moran AE, Perel P, Whelton PK, Brainin M, Feigin V, et al. The HEARTS partner forumsupporting implementation of HEARTS to treat and control hypertension. *Front Public Health*. 2023;24(11):1146441. DOI: <u>https://doi.org/10.3389/fpubh.2023.1146441</u>
- 2. Ordunez P, Campbell NRC, DiPette DJ, Jaffe MG, Rosende A, Martinez R, et al. HEARTS in the Americas: Targeting health system change to improve population hypertension control. *Curr Hypertens Rep.* 2024;26(4):141–156. DOI: https://doi.org/10.1007/s11906-023-01286-w
- 3. **Moran AE, Gupta R, Global Hearts Initiative Collaborators.** Implementation of Global Hearts Hypertension Control Programs in 32 low- and middle-income countries: JACC International. *J Am Coll Cardiol.* 2023;82(19):1868–1884. DOI: https://doi.org/10.1016/j.jacc.2023.08.043

Rosende et al.

- 4. Martinez R, Soliz P, Campbell NRC, Lackland DT, Whelton PK, Ordunez P. Association between population hypertension control and ischemic heart disease and stroke mortality in 36 countries of the Americas, 1990–2019: An ecological study. *Rev Panam Salud Publica*. 2022;46:e143. DOI: <u>https://doi.org/10.26633/RPSP.2022.143</u>
- 5. Rosende A, DiPette D, Brettler J, Rodríguez G, Zuniga E, Connell K, et al. HEARTS in the Americas appraisal checklist and clinical pathway for comprehensive hypertension management in primary care. *Rev Panam Salud Publica*. 2022;2(46):e125. DOI: https://doi.org/10.26633/RPSP.2022.125
- 6. **Campbell NRC, Paccot Burnens M, Whelton PK, Angell SY, Jaffe MG, Cohn J,** et al. 2021 World Health Organization guideline on pharmacological treatment of hypertension: Policy implications for the region of the Americas. *Lancet Reg Health Am.* 2022;9. DOI: https://doi.org/10.1016/j. lana.2022.100219
- Brettler JW, Arcila GPG, Aumala T, Best A, Campbell NR, Cyr S, et al. Drivers and scorecards to improve hypertension control in primary care practice: Recommendations from the HEARTS in the Americas Innovation Group. Lancet Reg Health Am. 2022 May;9. DOI: <u>https://doi.org/10.1016/j.</u> lana.2022.100223
- 8. **DiPette DJ, Goughnour K, Zuniga E, Skeete J, Ridley E, Angell S,** et al. Standardized treatment to improve hypertension control in primary health care: the HEARTS in the Americas initiative. *J Clin Hypertens*. 2020;22(12):2285–2295. DOI: https://doi.org/10.1111/jch.14072
- 9. DiPette DJ, Skeete J, Ridley E, Campbell NRC, Lopez-Jaramillo P, Kishore SP, et al. Fixed-dose combination pharmacologic therapy to improve hypertension control worldwide: Clinical perspective and policy implications. *J Clin Hypertens (Greenwich)*. 2019;21(1):4–15. DOI: https://doi.org/10.1111/jch.13426
- 10. Ordunez P, Tajer C, Gaziano T, Rodriguez YA, Rosende A, Jaffe MG. The HEARTS app: A clinical tool for cardiovascular risk and hypertension management in primary health care. *Rev Panam Salud Publica*. 2022;28(46):e12. DOI: https://doi.org/10.26633/RPSP.2022.12
- 11. **Rosende A, DiPette DJ, Martinez R, Brettler JW, Rodriguez G, Zuniga E,** et al. HEARTS in the Americas clinical pathway. Strengthening the decision support system to improve hypertension and cardiovascular disease risk management in primary care settings. *Front Cardiovasc Med*. 2023;10:1102482. DOI: https://doi.org/10.3389/fcvm.2023.1102482
- 12. **Ordunez P, Lombardi C, Picone DS, Brady TM, Campbell NRC, Moran AE,** et al. HEARTS in the Americas: A global example of using clinically validated automated blood pressure devices in cardiovascular disease prevention and management in primary health care settings. *J Hum Hypertens*. 2023;37(2):126–129. DOI: https://doi.org/10.1038/s41371-022-00659-z
- 13. **Rangaswami J, Bhalla V, Blair JEA, Chang TI, Costa S, Lentine KL,** et al. on behalf of the American Heart Association Council on the Kidney in Cardiovascular Disease and Council on Clinical Cardiology. Cardiorenal syndrome: Classification, pathophysiology, diagnosis, and treatment strategies: A scientific statement from the American Heart Association. *Circulation*. 2019;139:e840–e878. DOI: https://doi.org/10.1161/CIR.00000000000664
- Ndumele CE, Neeland IJ, Tuttle KR, Chow SL, Mathew RO, Khan SS, et al. American Heart Association. A synopsis of the evidence for the science and clinical management of cardiovascularkidney-metabolic (CKM) syndrome: A scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636–1664. DOI: https://doi.org/10.1161/CIR.000000000001186
- 15. **PAHO.** Better Care for NCDs: Accelerating Actions in Primary Health Care. [Internet]. Available at: https://www.paho.org/en/documents/better-care-ncds-accelerating-actions-primary-health-care. (Access: 12 – Nov – 2024).
- 16. Brook RH, Chassin MR, Fink A, Solomon DH, Kosecoff J, Park RE. A method for the detailed assessment of the appropriateness of medical technologies. *Int J Technol Assess Health Care*. 1986;2(1):53–63. DOI: https://doi.org/10.1017/S0266462300002774
- 17. Satheesh G, Dhurjati R, Huffman MD, Rosende A, Rodgers A, Prabhakaran D, et. Al. Standardized treatment protocols for hypertension: Global availability, characteristics, and alignment with the hypertension guideline recommendations. *J Hypertens*. 2024;42(5):902–908. DOI: https://doi.org/10.1097/HJH.00000000003636
- Ordunez P, Campbell NRC, Giraldo Arcila GP, Angell SY, Lombardi C, Brettler JW, et al. HEARTS in the Americas: Innovations for improving hypertension and cardiovascular disease risk management in primary care. *Rev Panam Salud Publica*. 2022;46:e96. PMID: 35855441; PMCID: PMC9288223. DOI: https://doi.org/10.26633/RPSP.2022.96
- Cheung AK, Whelton PK, Muntner P, Schutte AE, Moran AE, Williams B, et al. International consensus on standardized clinic blood pressure measurement – a call to action. *Am J Med*. 2023;136(5):438–445.e1. DOI: https://doi.org/10.1016/j.amjmed.2022.12.015
- Sharman JE, Ordunez P, Brady T, Parati G, Stergiou G, Whelton PK, et al. The urgency to regulate validation of automated blood pressure measuring devices: a policy statement and call to action from the world hypertension league. J Hum Hypertens. 2023;37(2):155–159. DOI: <u>https://doi.org/10.1038/s41371-022-00747-0</u>

- Whelton PK, Picone DS, Padwal R, Campbell NRC, Drawz P, Rakotz MK, et al. Global proliferation and clinical consequences of non-validated automated BP devices. J Hum Hypertens. 2023;37(2):115–119. DOI: <u>https://doi.org/10.1038/s41371-022-00667-z</u>
- 22. Picone DS, Campbell NRC, Schutte AE, Olsen MH, Ordunez P, Whelton PK, et al. Validation status of blood pressure measuring devices sold globally. *JAMA*. 2022;327(7):680–681. DOI: <u>https://doi.org/10.1001/jama.2021.24464</u>
- Lombardi C, Picone DS, Sharman JE, Campbell NRC, Farias R, Guerre S, et al. Country experiences on the path to exclusive use of validated automated blood pressure measuring devices within the HEARTS in the Americas Initiative. *J Hum Hypertens*. 2023;37(2):120–125. Epub 2022 Jul 11. PMID: 35817799; PMCID: PMC9957722. DOI: https://doi.org/10.1038/s41371-022-00706-9
- 24. Whelton PK, O'Connell S, Mills KT, He J. Optimal antihypertensive systolic blood pressure: A systematic review and meta-analysis. *Hypertension*. 2024;81(11):2329–2339. DOI: https://doi.org/10.1161/HYPERTENSIONAHA.124.23597
- Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. *Kidney Int*. 2024;105(4S):S117–S314. DOI: https://doi.org/10.1016/j.kint.2023.10.018
- 26. World Health Organization (September 19, 2023). Global report on hypertension: the race against a silent killer. [Internet]. Available at: https://www.who.int/publications/i/item/9789240081062
- GBD 2021 Diabetes Collaborators. Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: A systematic analysis for the Global Burden of Disease Study 2021. Lancet. 2023;402(10397):203–234. DOI: https://doi.org/10.1016/S0140-6736(23)01301-6. Epub 2023 Jun 22. Erratum in: Lancet. 2023 Sep 30;402(10408):1132. DOI: https://doi.org/10.1016/S0140-6736(23)02044-5
- NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in diabetes prevalence and treatment from 1990 to 2022: A pooled analysis of 1101 population-representative studies with 82 million participants. *Lancet*. 2024;S0140-6736(24)02317-1. DOI: <u>https://doi.org/10.1016/S0140-6736(24)02317-1</u>
- 29. Liu J, Li Y, Ge J, Yan X, Zhang H, Zheng X, et al. ESPRIT Collaborative Group. Lowering systolic blood pressure to less than 120 mm Hg versus less than 140 mm Hg in patients with high cardiovascular risk with and without diabetes or previous stroke: an open-label, blinded-outcome, randomised trial. *Lancet.* 2024;404(10449):245–255. DOI: https://doi.org/10.1016/S0140-6736(24)01028-6
- 30. **Cheung AK, Chang TI, Cushman WC, Furth SL, Hou FF, Ix JH,** et al. Executive summary of the KDIGO 2021 Clinical Practice Guideline for the Management of Blood Pressure in Chronic Kidney Disease. *Kidney Int.* 2021;99(3):559–569. DOI: https://doi.org/10.1016/j.kint.2020.10.026
- 31. Jin Y, Wang K, Xiao B, Wang M, Gao X, Zhang J, et al. Global burden of atrial fibrillation/flutter due to high systolic blood pressure from 1990 to 2019: Estimates from the global burden of disease study 2019. *J Clin Hypertens (Greenwich)*. 2022;24(11):1461–1472. DOI: https://doi.org/10.1111/jch.14584
- 32. Dong XJ, Wang BB, Hou FF, Jiao Y, Li HW, Lv SP, et al. Global burden of atrial fibrillation/atrial flutter and its attributable risk factors from 1990 to 2019. *Europace*. 2023;25(3):793–803. DOI: <u>https://doi.org/10.1093/europace/euac237</u>
- Welton NJ, McAleenan A, Thom HH, Davies P, Hollingworth W, Higgins JP, et al. Screening strategies for atrial fibrillation: A systematic review and cost-effectiveness analysis. *Health Technol* Assess. 2017;21(29):1–236. DOI: https://doi.org/10.3310/hta21290
- 34. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2024;83(1):109–279. DOI: https://doi.org/10.1016/j. jacc.2023.08.017
- Freedman B, Hindricks G, Banerjee A, Baranchuk A, Ching CK, Du X, et al. World Heart Federation Roadmap on Atrial Fibrillation – A 2020 Update. *Glob Heart*. 2021;16(1):41. DOI: <u>https://doi.org/10.5334/gh.1023</u>
- Niiranen T, Schnabel R, Schutte AE, Biton Y, Boriani G, Buckley C, et al. Hypertension and atrial fibrillation: A frontier Review from the AF-SCREEN International Collaboration. *Circulation*. 2025;151(12): 863–877. DOI: https://doi.org/10.1161/CIRCULATIONAHA.124.071047
- Neal B, Wu Y, Feng X, Zhang R, Zhang Y, Shi J, et al. Effect of salt substitution on cardiovascular events and death. N Engl J Med. 2021;385(12):1067–1077. DOI: <u>https://doi.org/10.1056/</u> NEJMoa2105675
- 38. Aminde LN, Nugraheni WP, Mubasyiroh R, Rachmawati T, Dwirahmadi F, Martini S, et al. Costeffectiveness analysis of low-sodium potassium-rich salt substitutes in Indonesia: An equity modelling study. Lancet Reg Health Southeast Asia. 2024;26:100432. DOI: <u>https://doi.org/10.1016/j.</u> lansea.2024.100432
- Marklund M, Singh G, Greer R, Cudhea F, Matsushita K, Micha R, et al. Estimated population wide benefits and risks in China of lowering sodium through potassium enriched salt substitution: Modelling study. *BMJ*. 2020;369:m824. DOI: <u>https://doi.org/10.1136/bmj.m824</u>

15

- Bernabe-Ortiz A, Sal Y, Rosas VG, Ponce-Lucero V, Cárdenas MK, Carrillo-Larco RM, Diez-Canseco F, et al. Effect of salt substitution on community-wide blood pressure and hypertension incidence. Nat Med. 2020;26(3):374–378. DOI: https://doi.org/10.1038/s41591-020-0754-2
- Yuan Y, Jin A, Neal B, Feng X, Qiao Q, Wang H, et al. Salt substitution and salt-supply restriction for lowering blood pressure in elderly care facilities: A cluster-randomized trial. *Nat Med*. 2023;29(4):973–981. DOI: https://doi.org/10.1038/s41591-023-02286-8
- Arsenijevic J, Groot W. Physical activity on prescription schemes (PARS): Do programme characteristics influence effectiveness? Results of a systematic review and meta-analyses. *BMJ Open*. 2017;7(2):e012156. DOI: <u>https://doi.org/10.1136/bmjopen-2016-012156</u>
- 43. Patterson R, McNamara E, Tainio M, de Sá TH, Smith AD, Sharp SJ, et al. Sedentary behaviour and risk of all-cause, cardiovascular and cancer mortality, and incident type 2 diabetes: A systematic review and dose response meta-analysis. *Eur J Epidemiol*. 2018;33(9):811–829. DOI: <u>https://doi.org/10.1007/s10654-018-0380-1</u>
- 44. 2016 European Guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). *Eur Heart J.* 2016;37(29):2315–2381. DOI: https://doi.org/10.1093/eurheartj/ ehw106
- 45. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596–e646. DOI: https://doi.org/10.1161/CIR.00000000000678
- 46. Skotsimara G, Antonopoulos AS, Oikonomou E, Siasos G, Ioakeimidis N, Tsalamandris S, et al. Crdiovascular effects of electronic cigarettes: A systematic review and meta-analysis. *Eur J Prev Cardiol*. 2019;26(11):1219–1228. DOI: https://doi.org/10.1177/2047487319832975
- Jeffers AM, Glantz S, Byers AL, Keyhani S. Association of cannabis use with cardiovascular outcomes among US adults. J Am Heart Assoc. 2024;13(5):e030178. Epub 2024 Feb 28. PMID: 38415581; PMCID: PMC10944074. DOI: https://doi.org/10.1161/JAHA.123.030178
- 48. Rodgers A, Salam A, Schutte AE, Cushman WC, de Silva HA, Di Tanna GL, et al. Efficacy and safety of a novel low-dose triple single-pill combination compared with placebo for initial treatment of hypertension. J Am Coll Cardiol. 2024;84(24):2393–2403. DOI: <u>https://doi.org/10.1016/j.jacc.2024.08.025</u>
- 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension*. 2018;71(6):e13–e115. DOI: <u>https://doi.org/10.1161/HYP.0000000000000065</u>. Epub 2017 Nov 13. Erratum in: Hypertension. 2018 Jun;71(6):e140–e144. DOI: <u>https://doi.org/10.1161/ HYP.00000000000076</u>
- 50. 2024 European Society of Hypertension clinical practice guidelines for the management of arterial hypertension. *Eur J Intern Med*. 2024;126:1–15. DOI: https://doi.org/10.1016/j.ejim.2024.05.033
- 51. 2024 ESC Guidelines for the management of elevated blood pressure and hypertension. *Eur Heart J.* 2024;45(38):3912–4018. DOI: https://doi.org/10.1093/eurheartj/ehae178
- 52. WHO Model List of Essential Medicines 23rd list, 2023. WHO/MHP/HPS/EML/2023.02. [Internet]. Available at: https://www.who.int/publications/i/item/WHO-MHP-HPS-EML-2023.02
- 53. **O'Hagan E, McIntyre D, Nguyen T, Tan KM, Hanlon P, Siddiqui M**, et al. A cross-sectional survey of fixed-dose combination antihypertensive medicine prescribing in twenty-four countries, including qualitative insights. *Glob Heart*. 2024;19(1):73. DOI: https://doi.org/10.5334/gh.1353
- 54. Souza KM, Giron N, Vallini J, Hallar K, Ordunez P, Rosende A, et al. Barriers to access to antihypertensive medicines: insights from the HEARTS initiative in Latin American and Caribbean region. J Pharm Policy Pract. 2024;17(1):2379045. DOI: <u>https://doi.org/10.1080/20523211.2024.2379</u> 045
- 55. **McGuire DK, Shih WJ, Cosentino F, Charbonnel B, Cherney DZI, Dagogo-Jack S,** et al. Association of SGLT2 inhibitors with cardiovascular and kidney outcomes in patients with type 2 diabetes: A metaanalysis. *JAMA Cardiol.* 2021;6(2):148–158. DOI: https://doi.org/10.1001/jamacardio.2020.4511
- AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: Executive Summary: A Report of the American College of Cardiology/ American Heart Association Task Force on Clinical Practice Guidelines. J Am Coll Cardiol. 2019;73(24):3168–3209. DOI: <u>https://doi.org/10.1016/j.jacc.2018.11.002</u>. Erratum in: J Am Coll Cardiol. 2019;73(24):3234–3237.
- 57. **PAHO Strategic Fund Product List.** Aug. 2023. Available at: <u>https://www.paho.org/sites/default/files/</u> strategic-fund-product-list-230821\_0.pdf
- Lasserson DS, Buclin T, Glasziou P. How quickly should we titrate antihypertensive medication? Systematic review modelling blood pressure response from trial data. *Heart*. 2011;97(21):1771–1775. DOI: https://doi.org/10.1136/hrt.2010.221473

- 59. Boima V, Doku A, Agyekum F, Tuglo LS, Agyemang C. Effectiveness of digital health interventions on blood pressure control, lifestyle behaviours and adherence to medication in patients with hypertension in low-income and middle-income countries: A systematic review and meta-analysis of randomised controlled trials. *EClinicalMedicine*. 2024;69:102432. DOI: <u>https://doi.org/10.1016/j. eclinm.2024.102432</u>
- He J, Ouyang N, Guo X, Sun G, Li Z, Mu J, et al. Effectiveness of a non-physician community healthcare provider-led intensive blood pressure intervention versus usual care on cardiovascular disease (CRHCP): An open-label, blinded-endpoint, cluster-randomised trial. *Lancet*. 2023;401(10380):928– 938. DOI: https://doi.org/10.1016/S0140-6736(22)02603-4
- 61. **Giraldo GP, Joseph KT, Angell SY, Campbell NRC, Connell K, DiPette DJ,** et al. Mapping stages, barriers and facilitators to the implementation of HEARTS in the Americas initiative in 12 countries: A qualitative study. *J Clin Hypertens (Greenwich)*. 2021;23(4):755–765. DOI: <u>https://doi.org/10.1111/jch.14157</u>
- 62. Schwalm JD, McCready T, Lopez-Jaramillo P, Yusoff K, Attaran A, Lamelas P, et al. A communitybased comprehensive intervention to reduce cardiovascular risk in hypertension (HOPE 4): A cluster-randomised controlled trial. *Lancet*. 2019;394(10205):1231–1242. DOI: https://doi. org/10.1016/S0140-6736(19)31949-X
- 63. **García-Zamora S, Pulido L.** Vaccines in cardiology, an underutilized strategy to reduce the residual cardiovascular risk. *Arch Peru Cardiol Cir Cardiovasc.* 2024;5(1):29–39. DOI: https://doi.org/10.47487/apcyccv.v5i1.349

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