Cardiovascular disease in the Americas: optimizing primary and secondary prevention of cardiovascular disease series: cardiovascular disease in the Americas

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Summary

While, many interventions can prevent cardiovascular disease (CVD), and its resulting morbidity or mortality, these are used sub-optimally in most countries. Therefore, health systems need to develop new approaches to ensure that proven CVD therapies are delivered widely. In this review, we describe five impactful implementation strategies which include: (1) Task shifting, (2) Use of mobile-Health (mHealth) support and virtual access to care, (3) simplified diagnostic and management algorithms for the prevention of CVD, (4) improving the use of combinations of medicines (i.e., polypill), and (5) patient engagement and role of patient-nominated peer support (i.e., treatment supporters). Adapting and tailoring these strategies to the local context in different settings in various countries in the Americas and the Caribbean can reduce the morbidity and mortality of CVD substantially.

Keywords: Cardiovascular disease; Primary prevention; Secondary prevention; Implementation

Introduction

Despite impressive advances in our ability to prevent and treat cardiovascular disease (CVD),[1] the downward trends in age-standardised mortality seen in recent decades in many places, including the Americas, have started to reverse. This is happening against a background of populations growing and ageing, so that the overall burden of disease in populations is increasing markedly, at a time when many countries are facing critical shortages of money and resources, especially health workers.[2]

If health systems are to respond to these challenges, they must transform their existing approaches to prevention and treatment. The first of these two papers described trends in CVD incidence, risk factors, mortality, current policies, and strategies at the population-level across the Americas and the Caribbean.[3] While some, but still too little progress, has been made with population-based measures, such as tobacco control and sugar reduction,[4] systematic identification of those with risk factors and their management through evidence-based interventions are far from optimal even in wealthier countries (both in the Americas and globally).[5–8] In this second paper of the Series Cardiovascular Disease in the Americas, we will focus on novel implementation strategies for the up scaling of established interventions that would be most impactful in reducing the burden of CVD.

Health systems are complex, with a series of inputs as described by the World Health Organization, including service delivery and health workforce (i.e., health workers, patients, and their friends and families), access to essential medicines and, increasingly, health information systems and technology, all ideally coming together in a contextually appropriate mix within a managed and financially viable system.[9] In this review, we consider innovations related to these inputs, recognising that none is a panacea and, if mishandled, can have unintended adverse consequences. They are: (1) shifting basic tasks involved in screening, diagnosis and management of CV risk to Non-Physician Health Workers (NPHWs), (2) incorporation of innovations in technology, including mobile-Health (mHealth) support

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and virtual access to care, (3) easy to use diagnostic and management algorithms for the prevention of CVD, (4) ensuring that effective medicines, are accessible at low-cost (i.e., polypill), and (5) engaging patients and utilizing peer support (i.e., treatment supporters) to optimize adherence to medication and lifestyle modifications (Fig. 1, Table 1). These concepts will be discussed below.

Search strategy and selection criteria for this review

References for this narrative review were identified through searches of PubMed using the terms: "global" OR "worldwide" OR "North America" OR "Latin America" OR "Caribbean" AND a term for each of the 5 components highlighted below, including, "Task Shifting", "Task Sharing", "Non-physician Health Worker, "Community Health Worker", "mHealth", "Mobile Health", "Digital Health", "Virtual Care", "polypill", and "treatment supporter". Articles were also identified through searches of the authors' own files. The final reference list was generated based on originality and relevance to the broad scope of this Review.

Task shifting and sharing: a community-based approach to risk factor and lifestyle modification

The global shortage of trained health care providers has encouraged exploration, in many countries, of alternative strategies for redistributing the tasks involved in health care delivery. This redistribution involves changes to the tasks of different types of health workers, reallocation of roles and responsibilities between health workers and patients (and their carers), and greater use of machines, such as portable diagnostics, now augmented by artificial intelligence.[10] The challenge is how to bring the right mix of these resources together in the right place at the right time to meet the needs of the patient as they move through the different levels (primary, secondary, and tertiary) of the health system. This model, if well-managed, can promote continuity and coordination of care, crucial for managing chronic diseases like CVD and this can significantly reduce hospitalizations and improve outcomes, while avoiding unnecessary or wasteful procedures.[11] If poorly managed, it can make things worse.

Achieving this transformation is now urgent. Canada, a high-income country (HIC) in the Americas, is

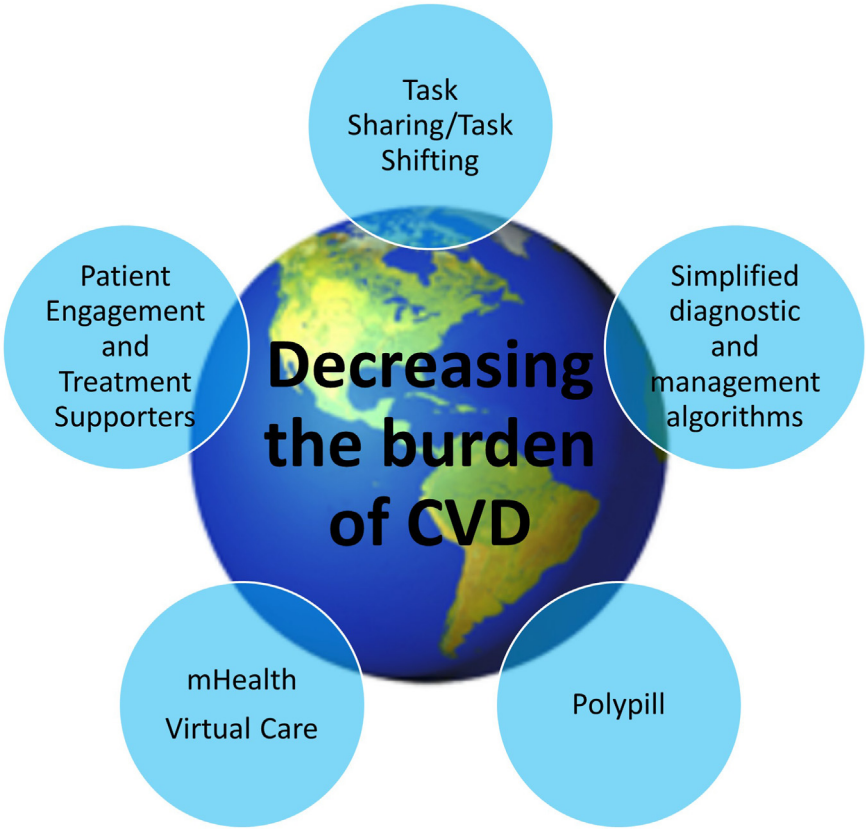

Fig. 1: Outline of 5 strategies to decrease the burden of cardiovascular disease.

Strategy	Application by Country income level	Advantages/disadvantages
Task shifting	LIC and MIC > HIC	- NPHW infrastructure more developed and accepted in LIC and MIC where shortages of health care providers are more pronounced. - Concerns in HIC of replacing trained physicians with NPHWs, rather than supplementing the existing workforce have been raised
Mobile health technologies	HIC > MIC > LIC	- Limited access and costs are potential barriers in LIC < MIC > HIC
Simplified diagnostic and management algorithms	LIC and MIC > HIC	- A larger shift in diagnostic paradigms required in HIC. Adherence to HIC guidelines require more health system infrastructure and resources
Low-cost available medicines (i.e., Polypill)	LIC and MIC > HIC	- Polypill could address cost and availability barriers that are more pronounced in LIC/MIC
Patient engagement and peer support	Universal	No disadvantages to engaging patients and family to help address the burden of CVD

LIC, Low-income country; MIC, middle-income country; HIC, high-income country; NPHW, non-physician health worker; CVD-cardiovascular disease.

Table 1: **Novel implementation strategies for the up scaling of established interventions that would be most impactful in reducing the burden of CVD.**

projected to have a shortfall of 44,000 physicians (out of a total of 120,000 physicians), including 30,000 family physicians, by 2028, and 117,600 nurses by 2030.[12] Physician shortages are also expected to grow in the United States with a deficit of about 122,000 physicians by 2032.[13] These both have consequences for middle-income countries (MIC) and Low-income country (LIC), which already face even greater shortages of health care workers (doctors, nurses, midwives, pharmacists, etc.) and which are losing those that migrate to HIC to fill these gaps. In 2016 the World Health Organization estimated that there would be a global shortfall of 18 million health workers by 2030, mostly in LIC and MIC.[14] While more recent projections are lower, at 12.9 million, they are still far beyond our ability to produce them in the time available.[2] This calls for a paradigm shift in our health care delivery if we are to adequately address the growing burden of CVD and other non-communicable diseases.

While increased training of nurses, physicians, and other health workers is required, this will take time and must be accompanied by measures to retain those who are now employed. However, such measures have proven difficult to implement due to an unwillingness to provide the financial and non-financial rewards necessary and to improve working conditions. Therefore, those managing health systems have been exploring a complementary strategy of increasing task shifting and task sharing, creating new occupational groups, such as physician assistants/associates, nursing assistants and other NPHWs, who can relieve doctors and nurses of some of their simpler and more routine tasks. These groups undertake training courses that are much shorter and more limited than those taken by members of the health professions they are assisting, and are accountable to, and have correspondingly narrower scopes of practice.

There is now good evidence that nurses can achieve as good or even better outcomes as doctors in the routine management of uncomplicated chronic diseases.[15] A different question is whether NPHWs can also achieve favourable clinical outcomes, with some evidence that they can in certain circumstances.[16] This approach has been used in many LIC and MIC for the management of some infectious diseases and to treat and prevent vitamin deficiencies and was recently re-established in the management of the Human Immunodeficiency Virus (HIV). A systematic review of task-shifting for HIV care in Africa, showed that NPHWs were cost-effective and delivered high-quality care to a larger population than traditional physician-centered models, although this was in settings facing extreme shortages of physicians.[17] Another systematic review examined the use of NPHW in management of non-communicable diseases.[18] It included 22 studies although sixteen involved other health professionals (nurses and midwives) and only 6 involved non-professional health workers. It found that this occupational group could be effective in screening for cancer, CVD, depression, and epilepsy, although in most of these cases the evidence was from a single study. There was also evidence that they were effective in prescribing within protocols for depression and epilepsy.

The HOPE 4 study was a comprehensive, collaborative model of care involving NPHWs and the provision of cost-free CV medications in patients with newly diagnosed or poorly controlled hypertension.[19] The intervention was implemented across 30 communities in Colombia and Malaysia and achieved strongly positive results with participants in the intervention group experiencing a 40% greater reduction in Framingham Risk Score 10-year risk at 12 months compared to controls. The model evaluated in the HOPE 4 study not only screened, and diagnosed patients with CV risk, but also initiated treatment for effective risk factor modification. Subsequently, a systematic review of task shifting in LMIC for the management of hypertension demonstrated a mean drop of systolic blood pressure of

3.7 mmHg when community health workers were the NPHWs, with larger effect sizes when management was by health professions, such as pharmacists (8.1 mmHg) and nurses (5.3 mmHg).[20] Most recently, a large scale, cluster randomized controlled trial, involving 163 villages and over 33,000 patients in China, demonstrated that NPHWs (community health workers) initiating antihypertensives in patients with untreated or poorly controlled blood pressure, not only reduced blood pressure in the intervention group [net between group difference in systolic blood pressure reduction was –23.1 mm Hg (95% CI –24.4 to –21.9; $p < 0.0001$)], but also showed a significant reduction in their primary composite outcome of myocardial infarction, stroke, heart failure requiring hospitalisation, and cardiovascular disease death over 36 months (1.62% vs 2.40% per year; hazard ratio [HR] 0.67, 95% CI 0.61–0.73; $p < 0.0001$).[21] NPHWs also provide valuable education and counselling on CVD risk factors, medications, and lifestyle modifications, contributing to patient empowerment and improved health outcomes.[21]

Task shifting and task-sharing have also been successfully implemented in HIC. Both blood pressure and blood sugar control in people with diabetes have been improved through task shifting to NPHWs, both nurses and other health workers.[22–25] While task shifting to NPHWs is often a necessity in rural and under-serviced areas, it can also be adapted to help address gaps in CVD primary and secondary prevention among disadvantaged populations in HIC that often lack access to care.[26–28]

While several initiatives are underway to increase task shifting to NPHWs in the management of CVD risk, The Hearts Technical Package exemplifies this at the international level.[29] Launched in 2016, the Hearts in Americas Initiative started in 4 countries and is now operating in more than 22 across the Americas and the Caribbean and sets out the structure needed for a successful program to address CVD risk in primary care. This program supports task shifting and is working to reduce CVD by scaling up a standardized set of disease management and risk reduction interventions at the primary care level.[29] Other, local programs of care for secondary prevention of CVD, are being implemented, often by pharmacists and nurse-practitioners.[30]

Physician oversight and contextualized implementation

Although they are conflated in much of the literature, as noted above, it is essential to differentiate NPHWs who are members of health professions, such as nurses, midwives, and pharmacists, from those in subsidiary occupations such as other NPHW. The former can often operate autonomously, within a defined scope of practice, as they are professionally liable to regulators for their actions. The latter must be supervised by a health professional who takes this responsibility for tasks that are delegated. This is an important distinction because the work involved in supervision may outweigh any benefits of delegation.[31] Factors to be considered include the complexity of the disease being diagnosed and treated. Non-professional occupations should never be seeing undifferentiated patients but can work effectively where there are simplified diagnostic and management algorithms.

Second, the training of the NPWH will also impact their scope of practice. For example, a physician assistant or associate in a HIC may be trained to undertake certain technical tasks, such as administration of diagnostic tests. The unfortunate experience with physician associates in the United Kingdom, where this new occupation was introduced with minimal thought, provides a cautionary example.[32] However, a community health worker or village volunteer (especially in LIC and MIC) might be limited to performing tasks relating to screening (i.e., blood pressure) or education (i.e., smoking cessation and medication adherence).

Finally, the third factor that limits the wide-spread adoption of NPHWs for the diagnosis and management of CVD risk are concerns regarding adequate training and supervision of NPHWs. Governmental and regulatory policies restricting practices of NPHWs (i.e., prescribing essential medications) are a significant barrier to the implementation of The Hearts Technical Package.[29] Societal attitudes would have to evolve and adapt to this new growing workforce within the health system. There is a need to ensure a continued pipeline of appropriately trained health care professionals, including physicians and nurses, while developing a cadre of NHPWs who can support them in delivering systematic screening, diagnosis and basic management, including education for CVD risk.[18]

Contextually appropriate implementation strategies for the management of CVD are also crucial when considering the successful integration of NPHWs into the health system. By involving local stakeholders in the development and implementation of CVD risk management strategies, more impactful results can be realized.[33] This concept is particularly relevant when considering indigenous populations. In 2018, it was estimated that approximately 58 million people from 800 indigenous groups lived in Latin America, representing around 10% of the total population.[34] These groups often suffer major disadvantage in accessing care, reflecting the impact over centuries of colonial structures and attitudes that have deprived them of political power, economic resources, and access to services such as health and education.[35] A high prevalence of diabetes was reported (12.5%; 9.6–16.1%) in a population-representative survey of indigenous Mayan communities in Guatemala (approximately 75% under 50 years).[36] Similarly, in an indigenous population of Mexico (mean age of 35.8 ± 13.0 years), a prevalence of metabolic syndrome of 53.1% was reported.[37] In

addition, high rates of smoking in the indigenous population have been associated with its use as a tool for traditional practices.[37] These disparities in the CVD risk persist in the Indigenous populations in HIC as well. In comparison to non-Indigenous individuals, the age-standardized cardiovascular disease mortality is 30% higher for First Nations men and 76% higher for First Nations women in Canada.[38]

The system of beliefs and practices, such as the notion of spiritual balance and the preference for traditional medicine instead of conventional medical care, can influence adherence to pharmacological treatment and control of risk factors. For instance, dietary recommendations may not consider the importance of traditional foods, and physical activity guidelines may not align with indigenous norms and practices.[39] Moreover, mistrust in healthcare systems and healthcare providers, can deter Indigenous people and disadvantaged groups within the general population from seeking and adhering to treatment.[40] The involvement of NPHWs who are from the local communities has potential to address some of these issues, but caution is still needed as experiences with Roma health mediators in Eastern Europe suggests.[41] Thus, implementation programs and the training of NPHWs should consider these factors, seek early engagement of appropriate stakeholders and tailor interventions to reduce the gaps in CVD risk management within these communities. Task sharing and task shifting to NPHWs could be an effective strategy to mitigate the effects of the inequitable distribution of resources to these populations.

Digital and Mobile Health M-health applications for primary and secondary prevention

The rapid evolution of technology and digital health interventions (DHI) has facilitated development of new models of prevention of cardiovascular disease. Digital health refers to the systematic application of information, technologies, and data to support health care decision making and provision to improve health outcomes.[42] Mobile health, or mHealth, is a type of digital health that involves the use of mobile devices such as smartphones and tablets, to support both health care delivery and dissemination of information.[43] Digital health is a rapidly evolving area of health care delivery which has the potential to enhance the reach and scope for CVD prevention across a variety of settings globally. It can take advantage of the remarkable growth of mobile internet in many LMICs, sometimes leapfrogging HICs that have traditionally depended on landlines. In 2018, it was estimated that the total number of internet users had surpassed 3.5 billion globally.[44] This rapidly expanding communication infrastructure offers significant opportunities to shift screening, diagnostic and management strategies for CVD away from traditional health care settings. Since 2008, over a thousand digital health applications have been documented, which can take many different forms. In a joint document by the World Bank Group, the WHO, and United States Agency for International Development digital health interventions (DHI) have been recognized as a tool to "scale up health interventions and engage civil society".[44] They provide an opportunity to address health system challenges, at an individual, community and population health level (Fig. 2).[44]

Recognizing the potential applications of digital health, the WHO has made recommendations on the use of digital interventions for health system strengthening. They classify interventions into those which target patients, those for healthcare providers, those for health system/resource management, and interventions for data services. DHI encompass a large array of applications, which will continue to expand as our technological advances do (Fig. 3).

Patient-focused DHI include mobile applications and messaging services that can deliver health information and promote health awareness. For instance, mobile applications can help users track their physical activity, dietary intake, medication adherence and other health behaviours, providing data and feedback to users and providers to promote behaviour change.[45] DHI has demonstrated benefits in areas such as smoking cessation,[46] HbA1c lowering,[47] blood pressure control,[48] and weight loss.[49] A meta-analysis reviewing 9 RCT and cohort studies using DHI for both primary and secondary CVD prevention revealed a beneficial effect of DHI on CVD risk factors and outcomes, with a nearly 40% relative risk reduction in CVD, particularly with regards to secondary CVD prevention.[50] The interventions included telemedicine, web-based strategies, email, mobile phone applications, text messaging and monitoring sensors. Some caution is, however, required. Effective engagement with the information that these devices yield can be time consuming, may be a low priority given the challenge of merely surviving,[51] especially where the presence of CVD risk factors doesn't interfere with everyday life. It is, however, also important to note that the most effective means of addressing these health problems is through population-based measures and especially those targeting the price, availability, and marketing of harmful substances such as tobacco.

There has been especially rapid uptake of wearable devices. While wearable technology has been regularly used in diagnosis, treatment and therapy in cardiology, these technologies have continued to become more accessible, enabling detection of risk factors and early intervention.[52] For instance, a Spanish study reported that a 12-lead Holter device with compression capabilities for low-bandwidth mobile technology could used to detect arrythmias in rural areas of LMICs where there are few medical personnel.[53] A single -center study in

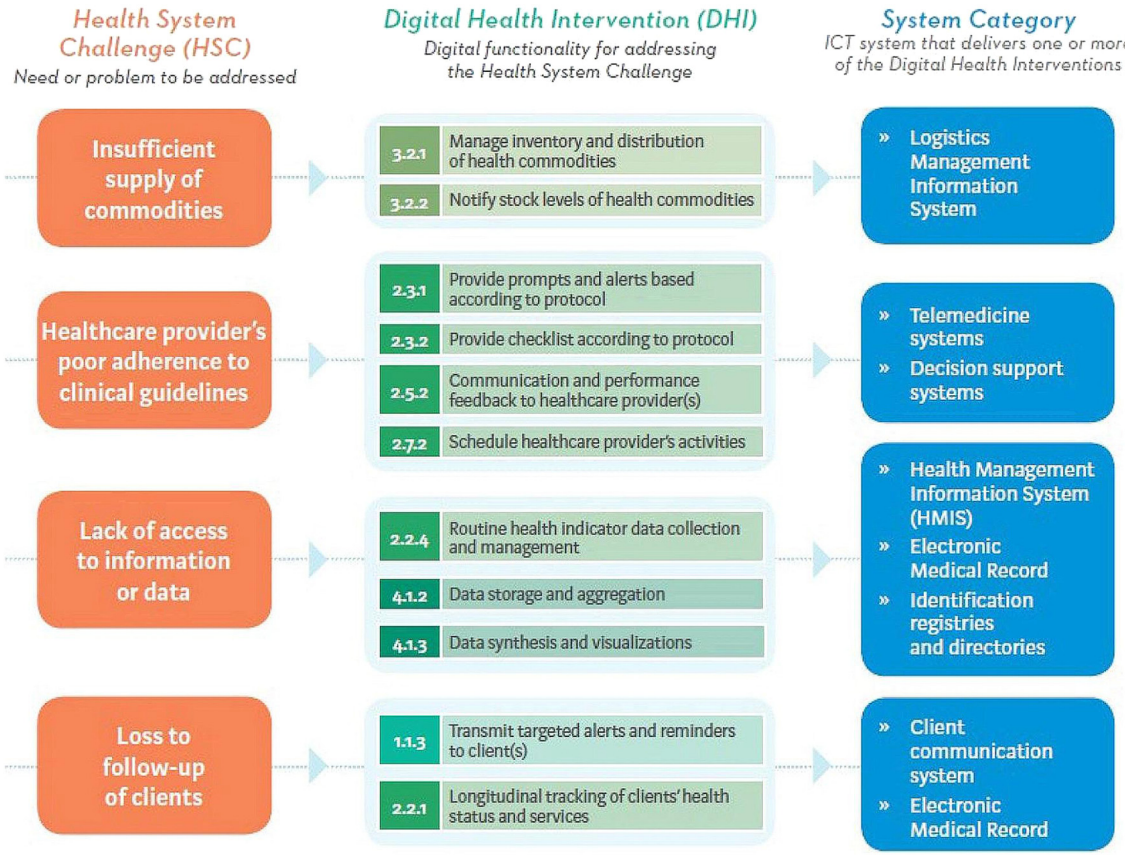

Fig. 2: Examples of how digital health interventions could address health system challenges, implemented using ICT systems. *ICT-Information and Communication Technology. (Source: WHO, Classification of digital health interventions v1.0: a shared language to describe the uses of digital technology for health. Geneva: World Health Organization; 2018).[44]

the United States found that remote monitoring for heart-failure patients in underserved communities showed significant reductions in health care utilization.[54] Virtual cardiac rehab programs have become increasingly common and can leverage digital platforms to deliver these interventions remotely, enabling individuals to participate in rehabilitation activities from their homes.[55] This facilitates adherence to establish CVD management guideline, despite geographic and financial limitations.

While the digital solutions have been mostly evaluated in high-income areas, there are instances of DHI

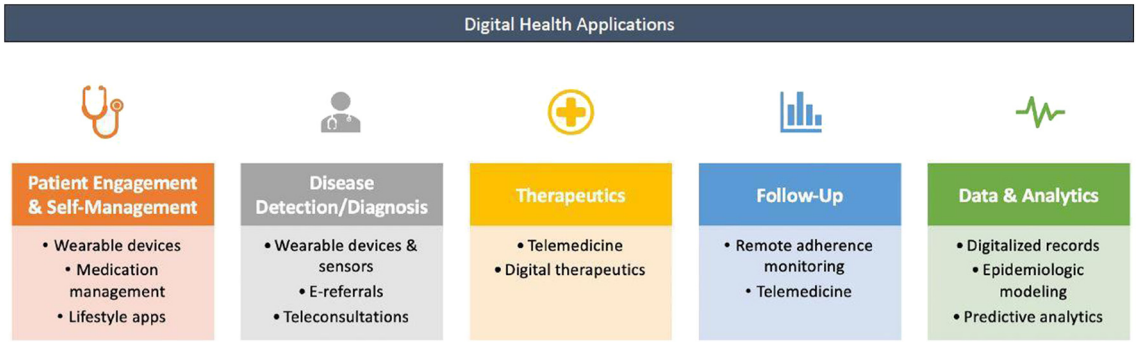

Fig. 3: Evolving applications of digital technology in health and health care.

that have shown promise in LIC and MIC settings. For example, an RCT of mHealth interventions involving mobile and web-based applications in low-income, urban settings in Argentina, Guatemala, and Peru achieved a reduction in body fat and improvement in eating behaviours.[56]

Telecardiology has also demonstrated potential use in rural areas where there is limited access to cardiologists and medical facilities. These involve teleconsultation, tele-monitoring systems and prehospital triage. In a study conducted in a remote Himalayan community in India, teleconsultations helped rapidly identify patients who required transfer to larger centres for management of CVD, in a population that does not have access to rapid specialist care.[57] Another study in India providing tele-ECG support to rural community health centers was found to reduce the time to ASA administration in patients with acute coronary syndrome.[58] Telecardiology promotes health equity, it is applicable to many settings, and leads to increased access to specialist care and early treatment initiation.

Looking to the future, digital health technologies will undoubtedly be influenced by advances in artificial intelligence (AI). Thus far, AI has demonstrated some promise in the detection and diagnosis of CVD, with its ability to analyse large quantities of patient and population data. For instance, ECG and risk factor assessment AI technologies have been found to predict 5-year atrial fibrillation risk, which has the potential to prevent AF-related morbidity and mortality.[59] Another wearable ECG-AI technology has shown promise in early identification of pulmonary hypertension, a condition which is often difficult to identify, especially in low resource settings.[60] A deep learning model has been found to assist in analysis of myocardial perfusion imaging to predict future coronary disease, while an AI-based triage system was found to improve door-to-balloon times, which has the potential to assist with facilitating prompt access to care, even in settings where specialist clinicians are not readily available.[61] However, care is required. Machine learning is notoriously vulnerable to problems arising when trained on data from one population and applied to another.[62] This is a significant issue given the scarcity of high-quality data from LMIC than can be used to train the algorithms.

Despite the potential benefits of mHealth and virtual applications in preventing and managing of CVD, several barriers and challenges may hinder their implementation. The most obvious relate to affordability and access, to both technology and internet provider access. Even in many HICs, a remarkably high proportion of people in poorer areas lack internet access.[63] There is also a generational divide and, although some older people have embraced the virtual world, many, and especially those with physical or visual impairment, will struggle. This calls for explicit measures to make technology age friendly and help with literacy of patients in the use of health-related DHI.[64] However, this is a problem that will likely diminish as today's younger cohorts age. Trust in DHI is also essential. Clinicians must trust AI sufficiently to use it but not so much that they accept it unquestionably.[65] Clinicians and the public require reassurance about the protection of data generated by these devices, especially in countries that are making extensive use of digital surveillance[66] or where they are associated with commercial entities seeking to harvest their data. DHIs do, however, have the potential to improve our reach with CVD prevention and treatment on a global scale. As DHI continue to evolve we must also consider how these can be leveraged into bridging geographic and economic barriers to ultimately reduce the burden of CVD in the Americas.

Simplified diagnostic and management algorithms

Current American Heart Association CVD diagnostic and management guidelines describe what is considered best practice in HIC.[67] However, applicability of the AHA guidelines to practice in LMIC is unclear. Further, adherence to these recommendations requires significant health care resources and infrastructures that may be limited in LIC and MIC, including in the Americas and the Caribbean. For example, cardiac computed tomography angiography is recommended in HIC in intermediate-risk patients following a negative acute coronary syndrome evaluation. However, the availability of cardiac computed tomography is limited in most communities in Latin America and many communities in Canada. Stress imaging is recommended in patients with known coronary artery disease presenting with acute, intermediate-risk chest pain. However, access to these imaging modalities may also be limited in many communities. To help address gaps in guideline recommendations and available resources, the World Health Organization has developed a "package of essential noncommunicable (PEN)" disease interventions for cardiovascular disease prevention in low-resource settings.[68] This document emphasizes CVD risk stratification and targeting high-risk individuals, with some modifications, such as the assumption of population mean cholesterol values when the measurement of individual cholesterol levels is precluded by resource limitations. However, this package of interventions remains limited by 1) the extrapolation of risk prediction tools to low-resource settings, where their validation may not have been performed[69]; and 2) the assumption that CVD prevention is most efficient when focused on high-risk groups within populations.[70,71] There is a paucity of evidence on the proportion of CV events occurring in high-versus low-risk groups in LIC and while the available evidence supports monitoring CVD risk when health care resources are available, the fundamental premise of risk stratification

as an efficient means of CVD prevention should be re-evaluated give the existing challenges and gaps in effective implementation.[72]

A survey conducted among 102 national cardiac societies of the applicability of the European Society of Cardiology's guidelines to countries of different income levels.[73] Of 875 guideline recommendations, 29%, 11% and 5% could not be implemented because of lack of the necessary resources in LIC, LMIC and UMIC, respectively.

A review described 5 categories of factors that may impede the implementation of clinical guidelines in LMIC.[74] These include: (1) organizational factors, such as physical environment and working condition (i.e., time, priorities); 2) healthcare provider characteristics, such as knowledge; (3) guideline-related factors, such as complexity and local applicability; (4) patient factors, including preferences and values; and (5) institutional factors, such as local policies and rules limiting implementation of evidence-based guideline recommendations. Simplified diagnostic and management algorithms for CV risk factors and disease might help overcome some of these barriers. However, they must take account of the often-complex pathways that patients take in their quest for treatment.[75]

Among CV risk factors, hypertension accounts for the largest population burden of CVD.[76,77] Hypertension may be particularly amenable to simplified diagnostic and treatment algorithms because blood pressure measurement is inexpensive and can be performed by NPHWs. Although Latin American and Caribbean countries perform better than the average with respect to hypertension identification and treatment, large shortcomings are still observed, with only about 60% of individuals with hypertension being diagnosed and less than one-third of patients having their blood pressure controlled.[78] Existing algorithms can be complex and require resources, such as monitoring renal function and potassium levels, that are not readily available in some communities in LMICs. There is therefore a need for safe, algorithmic, accessible, non-toxic, and effective (SAANE) approaches to identifying and treating hypertension.[79]

Tackling other CV risk factors may pose different challenges. Diabetes and hypercholesterolemia require laboratory testing to diagnose, although point-of-care testing may be an emerging approach that could reduce the need for blood collection and analysis.[80] Lifestyle-related risk factors, such as physical inactivity, harmful alcohol use and smoking have complex origins and any individualised measures, such as these, can at most, complement effective action at a population. However, approaches, such as task-shifting and m-health described previously could play some role in addressing these CV risk factors.

Studies such as HOPE-4 and the China Rural Hypertension Control Project describe similar strategies (outlined in Fig. 1) that serves as a template for simplified diagnostic and treatment processes.[19,21] The ongoing development of such strategies may be an important means of CV risk reduction in the Americas in future.

Fixed-dose combination medications-polypill

Several classes of medications are proven to be very effective at reducing risk in primary or secondary CVD prevention populations. However, use of these medications remains low both in the Americas and globally. Hypertension is the most common risk factor for CVD, but less than half of individuals with hypertension in the Americas achieve adequate control.[6] High cholesterol is the second largest risk factor for CVD, but statin use in eligible persons remains low in both primary and secondary CVD prevention.[81] In individuals with established CVD, less than a quarter receive three or more of the proven medications (statins, angiotensin converting enzyme inhibitors/angiotensin receptor blockers, beta blockers and aspirin) that prevent another vascular event. These data highlight the need for better approaches to improve the delivery of effective, low-cost medications to prevent CVD in those who are eligible to receive them. The fixed-dose combination, aka "polypill", is an innovative approach to tackling the current suboptimal medical treatment of CVD and its risk factors by incorporating key medications that lower CV risk into a single, daily-dose pill. Although several polypill formulations exist, most share the common feature of including at least 2 blood pressure lowering drugs and a statin, with or without aspirin. For patients elevated cholesterol but no hypertension, diabetes, or left ventricular dysfunction, may benefit from a polypill of generic cholesterol lowering medications.[82]

Since the introduction of the polypill concept over two decades ago, multiple clinical trials have tested the effects of different formulations on important clinical outcomes such as adherence, risk factor control, and adverse cardiovascular events. Consistent improvement in medication adherence and reductions in blood pressure and cholesterol levels have also been observed in studies comparing polypills to a control group (either usual care or placebo).[83,84] More recently, the clinical impact of polypills have been examined in both primary and secondary CVD prevention in a series of large, clinical outcome trials. Three large clinical trials have now demonstrated that fixed dose combination (FDC) therapy or polypills reduce the risk of developing a CVD event in populations without CVD (i.e., primary CVD prevention).[84–86] Meta-analysis of these studies in primary prevention of CVD has demonstrated that an FDC or polypill treatment strategy can reduce the risk of a major adverse CVD event by 38%, and a fatal CVD event by 35%.[87] In individuals with a recent myocardial infarction (i.e., secondary CVD prevention), Castellano

et al. compared the effect of a polypill with usual care for the prevention of a major CVD event. Compared to usual care, a polypill significantly reduced the risk of a major adverse cardiovascular event by 24%, driven by better adherence in the polypill group.[88]

From a health system perspective, polypills are also an affordable CVD prevention strategy. In The International Polycap Study-3 (TIPS 3), Lamy et al. examined the cost of a polypill (substituting the cheapest equivalent price of each component) in HIC and MIC and found that it was affordable in all countries at different income levels based on household capacity to pay or gross national income thresholds.[89] Interestingly, the largest benefits from a cost standpoint were observed in HIC, because of the avoidance of hospitalizations and procedures, which are more costly and more commonly performed in these countries. Polypills are also cost effective in secondary CVD prevention.[90] Overall, these data support the widespread adoption of polypills as an affordable strategy to reduce CVD burden across a wide range of health resource settings.

The primary challenge is now related to implementation of this new technology, where several important barriers have been identified. The first (and likely most relevant) barrier is the lack of interest from pharmaceutical companies to bring such a technology to scale given that polypills, as low-cost, off patent medications, yield low profits. Overcoming this likely requires concerted actions by multiple stakeholders (i.e., governments, insurance providers, pharmaceutical industry) to find models that can deliver low prices but adequate profits.[91] The recent inclusion of polypills to the WHO Essential Medicines List, which is widely used by governments to prioritize which drugs are procured and supplied to the public sector, is a key step in improving uptake. A second key barrier is the highly complex regulatory systems that exist across countries to approve medications, calling for more streamlined approaches when the safety profiles of component drugs have long been established.[91] This should be addressed when creating new multi-country medicines regulatory bodies, such as the recent initiative in Africa.[92] A third barrier is a mistaken perception from within parts of the medical community that a polypill strategy undermines other treatment strategies, such as promotion of a healthy lifestyle, and personalized approaches to medical care. In fact, polypills should be considered complementary to these current approaches; it is a ***foundational approach*** that provides a consistent degree of CVD risk factor reduction to individuals, which can be enhanced by additional modifications to lifestyle and personalized treatment strategies. Given the now established clinical efficacy of a polypill strategy in both primary and secondary CVD prevention, there is a need to formally incorporate this approach into existing clinical guidelines and CVD prevention strategies.

Treatment supporters (peer/family support)

Optimizing existing infrastructures is key to an efficient healthcare system. The inclusion of a patient's family member or friend as an integral part of their health care team is an important strategy to improve care. Family support can help promote adherence to medications and lifestyle modifications and ensure appropriate ongoing follow-up. This concept has been established as a supportive treatment strategy in diseases like HIV where the use of treatment supporters, defined as uncompensated, patient-nominated friends or family who help ensure optimal adherence to recommended therapies and clinic appointment schedules, has demonstrated efficacy.[93–96] The management of CVD risk carries many similarities to that of other chronic diseases, like HIV, suggesting that treatment supporters could be an intervention that is cost-effective and scalable for patients with CVD risk.[97–99] A 2017 cluster-randomized controlled trial conducted by Shen et al. reported significantly greater increases in adherence to blood pressure monitoring and CVD medications from baseline to 6-months follow-up in the treatment group compared to the control.[100] Treatment supporters also contribute to patient education by providing information about CVD, treatment options, and self-management strategies, thereby empowering patients to take an active role in their care. Involving treatment supporters in educational interventions for CVD patients leads to increased knowledge, self-efficacy, and engagement in self-management behaviours. The sub-analysis of the HOPE 4 trial also demonstrated the positive impact of treatment supporters with a significant improvement in medication adherence in participants with regular exposure to participant-nominated supporters.[101] However, while family support brings clear benefits, it is important to recognise that the patient and their supporter may face other barriers that they cannot overcome on their own.[51]

Patient adherence to guideline-recommended medications and lifestyle modifications remain barriers to optimal care. However, mechanisms to improve adherence utilized in other chronic conditions are likely also applicable to CVD risk management. Treatment supporters, coached by NPHWs or health-care providers, could help promote an effective self-management program for patients with or at risk of CVD, thus proving to be an effective strategy against the burden of CVD.

Limitations

The five implementation strategies described in this manuscript were selected based on the extensive research and clinical experience of the authors, augmented by narrative reviews of the literature. Unfortunately, reflecting the highly skewed distribution of health services research, there are important gaps in the evidence we can draw on that limit our ability to identify

those factors that will influence the ability to implement them successfully. Consequently, we stress that while we have identified interventions that can work, further research is needed to determine what is necessary for them to work in different contexts, taking account the varied opportunities and constraints that exist in these extremely diverse continents.

Conclusions

Today, a very large share of the burden of CVD can be prevented and treated with safe and relatively inexpensive measures. Unfortunately, this is not happening, including in many parts of the Americas and the Caribbean. Existing Health Care Systems are not adequately equipped to address this burden of disease and gaps will continue to widen between evidence and practice as human resources become scarcer. Adopting innovative and evidence-based solutions including task shifting to NPHWs and Treatment supporters, optimizing wide-scale use of mHealth and virtual technologies, simplifying our complex guideline recommendations and implementation of a polypill for CVD can significantly reduce the morbidity and mortality associated with this chronic disease.

This will, however, only happen if the innovative models of care that are being developed, some described above, are supported by effective governance systems that ensure that the necessary resources are procured, such as the purchase of Pollypills and training of NPHWs, that areas of unmet needs are identified and addressed, that risks such as corruption and absenteeism are tackled,[102] the necessary funding is secured, and the models of care are co-created with the communities who are the intended beneficiaries. In this light it is important to note that the very successful HOPE-4 project involved extensive evaluations to understand the local situations and create contextually appropriate interventions.[103,104]

Contributors

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Declaration of interests

We declare no competing interests.

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