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MEASURES TO IMPROVE PRECLINICAL RESEARCH CONDUCTED TO IMPROVE THE PREVENTION AND TREATMENT OF CARDIOVASCULAR DISEASES

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Abstract. Globally, cardiovascular disease (CVD) continues to be the primary cause of morbidity and mortality. The worldwide burden of CVD is still high despite tremendous advancements in diagnosis and treatment, highlighting the critical need for more thorough and efficient preventative measures. The purpose of this narrative summary is to assess the existing cornerstones of cardiovascular prevention critically, point out areas where current methods fall short, and suggest possible future paths. The majority of deaths worldwide are caused by cardiovascular disease (CVD), which primarily affects low- and middle-income countries (LMIC). Globally, primary and secondary prevention of CVD is not at its best, but in LMICs, the gaps between evidence and practice are considerably more noticeable. Optimal primary and secondary prevention cannot be implemented due to obstacles at the patient, healthcare practitioner, and health system levels. To develop successful methods to close the observed evidence-practice gaps, it is essential to identify the specific obstacles that occur in settings with limited resources. Additionally, the greatest improvements in mortality reduction will come from focusing on the modifiable factors—such as tobacco use, hypertension, and secondary prevention for CVD—that contribute most significantly to the worldwide burden of CVD. We examine a few innovative, resource-efficient approaches to lower premature mortality from CVD, such as: (1) efficient tobacco control measures; (2) the use of simplified screening and management algorithms for individuals with or at risk of CVD; (3) expanding the availability and affordability of simplified and cost-effective treatment regimens, such as combination CVD preventive drug therapy; and (4) streamlining health care delivery through task-sharing (non-physician health workers) and improving self-management (treatment supporters). Significant decreases in CVD and associated mortality will result from the development and implementation of care systems that overcome the aforementioned obstacles.

Keywords. Health system, stroke, ischemic heart disease, cardiovascular disease, care systems, preventive drug therapy.

Introduction. With about 18.6 million fatalities per year, or nearly one-third of all deaths globally, cardiovascular disease (CVD) is the major cause of death and disability. It affects people from a wide range of demographic and socioeconomic backgrounds. CVD-related morbidity and mortality are rising disproportionately in low- and middle-income nations. Ischemic heart disease and stroke are the main causes of atherosclerotic cardiovascular disease (ASCVD), which accounts for the majority of the CVD burden. Other serious illnesses including atrial fibrillation and cardiac failure are also worrisome. Beyond the clinical results, CVD is a significant contributor to both direct and indirect medical expenses. Disability-adjusted life years (DALYs) and years of life lost

as a result of cardiovascular disease (CVD) have been gradually increasing globally, particularly as a result of ischemic heart disease, stroke, and hypertensive heart disease.The fact that CVD is still a worldwide health issue emphasizes how inadequate or poorly executed current interventions are. Even with the significant advancements and growing use of preventive cardiology in contemporary cardiovascular medicine, there are still significant gaps in the application of evidence-based therapy. Global inequality and healthcare system constraints continue to be significant obstacles, and more individualized treatments must to be put into place [1-5]. According to the 2013 Global Burden of Disease study, global fatalities from cardiovascular disease (CVD) increased by 41% between 1990 and 2013, despite a 39% decline in age-specific mortality rates. High income countries (HIC) had the lowest incidence of major and fatal CVD events. Ischemic heart disease has risen from fourth place in 1990 (41% increase) to become the leading cause of death worldwide, while stroke has risen from fifth to third place (50% increase). Low and middle income countries (LMIC), where 85% of the world's population currently resides, are expected to account for roughly three quarters of global mortality and 80% of the CVD burden (measured by disability life years lost) by 2020. Population increase and aging have had a major role in these changes. The incidence and mortality of CVD have significantly decreased in HIC, with death declines averaging 50% since the 1970s and reaching 75% in nations like Finland, the United States, and the United Kingdom [6-12]. Healthier diets, lower smoking rates, better management of risk factors like hypertension, better management of acute CVD events, and increased use of secondary prevention are some of the factors that contribute differently to each country, partly due to variations in the initial pattern of risk factors and strategies used. Even with these remarkable improvements in HIC, cardiovascular disease-related morbidity and death are still relatively high, especially in developing nations and among marginalized groups. A non-communicable disease (NCD) action plan followed the United Nations' political declaration in September 2011 to set a global objective of a 25% reduction in premature (less than 70 years) mortality from CVD, cancer, diabetes, and chronic respiratory disease by 2025. Eight indicators have been identified by this action plan to track progress toward the overall "25 × 25" goal: (1) lowering elevated blood pressure; (2) lowering tobacco use; (3) increasing physical inactivity; (4) lowering sodium intake; (5) lowering the harmful use of alcohol; (6) stopping the rise in diabetes and obesity; (7) improving access to drug therapy and counseling to prevent CVD; and (8) expanding access to basic technologies and essential medications to manage NCDs. However, unless the numerous obstacles to effective and evidence-based CVD care are removed, none of these goals will probably be achieved. Since ischemic heart disease and stroke are the two main causes of the worldwide burden of CVD, this review focuses on these disorders as well as associated risk factors [13-19]. This study examines the evidence-practice gaps in the prevention and treatment of cardiovascular disease (CVD), the obstacles to bridging these gaps, and the goals for resource-efficient therapies. Lastly, we examine a few innovative, resource-efficient population, individual, and health system ways to get over the obstacles that have been identified. When combined, these tactics increase the uptake of precision medicine and make it possible to include new pharmacological medicines. To address the difficulties of people who are at risk or who already have CVD, care pathways and multidisciplinary methods throughout the continuum of CV prevention are crucial. In the near future, improving this strategy could change how CVD is perceived and treated. Thus, the purpose of this narrative summary is to look at the fundamental elements of CV prevention, identify the main gaps that still exist in current practice, and talk about promising directions that could direct future research goals and clinical application [20-26].

The main purpose of the presented manuscript is to provide a brief analysis of measures to improve preclinical research on improving the prevention and treatment of cardiovascular diseases based on the results of authoritative scientific works.

Gaps between evidence and practice in CVD care and prevention. Data from the Prospective Urban Rural Epidemiology (PURE) study, a longitudinal cohort study being carried out in 630 urban and rural communities from 17 high-, middle-, and low-income countries with expansion underway to include 800 communities in 25 countries, show the extent of evidence-practice gaps in the prevention and management of CVD. In order to get a representative sample of adults between the ages of 35 and 70, impartial and methodical community screening was conducted. To record baseline demographics, medication use, and clinical events, standardized questionnaires, physical measurements (such as blood pressure), and laboratory tests were carried out. PURE data show that hypertension is not adequately managed globally, but particularly in LMIC. First, almost 50% of PURE participants do not know they had hypertension. Second, only a small percentage of people (less than 20%) attain acceptable blood pressure control, which is defined as a systolic blood pressure (SBP) of less than 140 mmHg and a diastolic blood pressure of less than 90 mmHg, even though the majority of people who are aware of their diagnosis of hypertension receive therapy [4-12]. Third, although it is generally accepted that at least two antihypertensive drugs are required to regulate blood pressure, the majority of participants (77%) who receive blood pressure lowering treatment only take one prescription. All of the PURE study's countries have gaps in hypertension knowledge, treatment, and control, although the gaps are greater in LMIC. These findings highlight the necessity of more extensive and comprehensive blood pressure screening in addition to more successful blood pressure management. The therapy of lipids exhibits similar evidence-practice gaps, with poor statin use8. With 19% of people with documented CVD still smoking, only 35% engaging in high levels of physical activity, and only 39% maintaining a healthy diet, many of them are still exposed to significant risk factors. The biggest issue is once again found in low-income countries (LIC). Comprehensive programs to address the structural causes of CVD, case discovery, and, where proven effective, risk factor screening for CVD prevention and treatment are required due to the persistent evidence-practice gaps in the management of CVD risk across numerous risk factors [16-23].

Improvements in the diagnosis of CV. Genomics and precision medicine.Personalized treatment strategies have been made possible by the use of genetics into CV therapy. Precision medicine, sometimes referred to as "personalized medicine," is a cutting-edge strategy for customizing illness prevention and treatment that considers variations in individuals' genes, environments, and lifestyles in order to target the appropriate treatments to the right patients at the right time. By customizing medicines to each patient's unique genetic and molecular profile, precision medicine has completely transformed the management of cardiovascular disease. Genomic sequencing, polygenic risk scores, and personalized medicine techniques have improved CVD early detection, prevention, and focused treatments. Certain gene variants linked to hereditary cardiovascular diseases as hypertrophic cardiomyopathy, long QT syndrome, and familial hypercholesterolemia have been found through genomic research. Proactive management by lifestyle changes, medication interventions, and risk-reduction techniques is made possible by early detection of certain genetic predispositions. By evaluating genetic differences that affect drug metabolism and efficacy, pharmacogenomics has also proved essential in optimizing CV medication therapy [3-13]. Treatment choices for patients having percutaneous coronary intervention (PCI) are influenced, for example, by changes in the CYP2C19 gene that impact the response to antiplatelet therapy with clopidogrel. In a similar vein, personalized dosing to reduce

the risk of bleeding problems is guided by genetic markers for warfarin metabolism. New opportunities for potentially curative therapies of genetic CV illnesses have been made possible by the development of gene-editing tools like CRISPR-Cas9. The potential to fix harmful mutations linked to diseases like Marfan syndrome and familial hypercholesterolemia at the molecular level is being investigated. By offering a thorough grasp of disease mechanisms, the integration of multi-omics techniques, such as transcriptomics, proteomics, and metabolomics, enhances precision medicine tactics. More precise risk assessment, early interventions, and the creation of innovative targeted treatments based on a person's genetic and molecular profile are all made possible by these developments [21-29].

Emerging risks and implementation failures are critical gaps. There are other, sometimes overlooked CV risk markers that are linked to the onset of CVD in addition to the conventional, well-established risk variables. The risk of CVD is increased by obesity, poor eating habits, physical inactivity, and sleep problems, all of which should be carefully considered when estimating risk. Nevertheless, these traits continue to be alarmingly common in the broader population and are still widely underappreciated despite strong evidence. Overweight and Obesity: A study examining global trends in underweight and obesity from 1990 to 2022 revealed that while underweight and thinness are still common in parts of Africa and South Asia, the combined burden of these conditions has increased in most countries due to an increase in obesity. Promoting strategies to provide access to healthy foods and avoid obesity is essential because severe undernutrition still exists in some areas [1-11]. A Mediterranean or similar diet is advised to reduce the risk of CVD, with a focus on replacing saturated fats with unsaturated fats and lowering salt intake to assist regulate blood pressure, according to the ESC guidelines. Fish, particularly fatty, should be consumed at least once a week, processed meat intake should be minimized, and a more plant-based diet that is high in fiber and includes whole grains, fruits, vegetables, legumes, and nuts should be prioritized. Furthermore, free sugar intake—especially from sugar-sweetened beverages—should not exceed 10% of total energy intake. It is becoming more well acknowledged that emerging non-conventional factors may contribute to CVD. The need for more study and incorporation into preventative measures is highlighted by the fact that many of these factors still lack solid evidence and are frequently overlooked in regular risk assessment. The necessity for integrated population-level strategies in addition to individual-level interventions is reinforced by the fact that these developing variables typically interact with conventional risk factors, resulting in a compounded and frequently multiplied increase in CV risk [17-27].

Innovative Approaches and Prospects. Significant gaps still exist in the application of guidelines, risk communication, and fair access to care, despite notable advancements in CV prevention. A comprehensive strategy that incorporates patient-centered tactics, collaborative decision-making, and interventions customized to individual traits including sex, age, race, mental health, and socioeconomic background is needed to address these issues. Future research and practice must prioritize enhancing risk communication, promoting shared decision-making, optimizing screening techniques, and identifying successful mental health therapies within CV care. To improve early detection, tailor treatment, and increase long-term adherence, novel strategies are being investigated, such as genetic testing, sophisticated risk stratification techniques, digital health technology, and developing pharmaceutical and behavioral therapies. In order to maximize engagement and achieve significant reductions in disease burden, interventions must be tailored to individual circumstances [11-17]. A static approach is unlikely to fulfill the multiple demands of persons at increased CV risk. shows the key new tactics to improve CV prevention in the future. The effectiveness of these strategies depends critically on developing a structured shared decision-

making process and boosting CV health literacy. CV prevention is changing as a result of the digital revolution, which presents previously unheard-of chances for patient-centered care, risk assessment, and early identification. Continuous remote monitoring of vital signs, physical activity, sleep patterns, and other behaviors is made possible by wearable technology, mobile health apps, and telemedicine platforms. This real-time data can help with prompt and customized therapies. Wearable technology, for instance, can continually track blood pressure, heart rate, or physical activity and immediately notify medical professionals if anomalous patterns are found, allowing for fast assessment and treatment. Otherwise, early detection of subclinical disease, such as asymptomatic atherosclerosis and vascular dysfunction, is made possible by digital instruments, which is essential for starting preventative treatments [22-29].

Discussion. Cardiovascular diseases (CVDs) continue to be the world's largest cause of death, requiring ongoing improvements in clinical practice and research. Our knowledge and treatment of CVDs have been profoundly altered by research developments. Cardiovascular (CV) care is changing as a result of recent developments in wearable technology, regenerative medicine, genomics, and artificial intelligence (AI). With a focus on precision medicine, early diagnosis, and individualized therapeutics, this study examines significant advancements that close the gap between research and clinical implementation. We also go over implementation issues and potential future paths for improving CV results. The growing significance of non-traditional and emergent risk factors is examined, along with difficulties and obstacles in medication management and lifestyle adherence. Future directions include integrating public health policies for population-level interventions, utilizing precision medicine to improve risk stratification, and optimizing the value of digital health to enhance patient involvement and adherence. In order to optimize cardiovascular prevention and ultimately lessen the worldwide burden of CVD, a multi-level strategy that combines therapeutic techniques with individualized solutions and environmental policies is needed [3-11]. However, there are obstacles to incorporating these innovations into clinical practice, such as the requirement for physician training, financial constraints, regulatory obstacles, and data privacy issues. To achieve equitable and scalable implementation, addressing these challenges will involve cooperation between researchers, clinicians, legislators, and business executives. The most promising research-driven developments in cardiovascular medicine are examined in this overview, along with how they will be implemented in clinical settings. We hope to demonstrate how the most recent advancements in genomics, digital health, regenerative medicine, and minimally invasive interventions can improve patient outcomes and ultimately create a future in which cardiovascular care is more accurate, preventive, and customized than it has ever been. The generalizability of results to real-world situations is limited by the fact that many clinical studies concentrate on specific patient populations [14-21]. Real-world data is becoming more and more necessary to evaluate the long-term safety, effectiveness, and cost-efficiency of innovative CV treatments. Increasing post-marketing surveillance programs, registries, and real-world evidence studies will shed light on how well new medicines work in a variety of demographics. Real-world data can be made more useful for healthcare decision-making by AI-driven analytics. There are still gaps in the practical application of clinical guidelines, despite notable advancements in CV prevention. Promising opportunities for early identification, customized treatments, and improved adherence are presented by the integration of conventional and emergent risk factors with cutting-edge approaches, such as digital health, precision medicine, novel pharmacotherapies, and population-level interventions. Maximizing preventative outcomes requires removing obstacles at the system, clinician, and patient levels while also promoting shared decision-making and fair access to healthcare. CV prevention can advance toward a more accurate, inclusive, and globally

impactful paradigm with the potential to lower the global burden of CVD by grounding these strategies within implementation science and health equality frameworks [22-29].

Conclusions. The bulk of NCD deaths worldwide are caused by CVD, with LMICs accounting for around 80% of these deaths. The conclusions in this review are supported by a substantial amount of evidence. But there are knowledge gaps, especially with regard to LMIC. describes the knowledge gaps about resource-effective CVD prevention and treatment strategies and offers recommendations for how to close these gaps. This review has shown that there are substantial evidence-practice gaps in the management and prevention of CVD, especially in LMIC, based on the evidence currently available.

The projected goal of a 25% reduction in premature mortality from CVD by 2025 in some countries could be met or even surpassed by focusing on important modifiable factors, such as tobacco use, hypertension, and secondary prevention of CVD with resource-efficient strategies in at-risk populations within LMIC, in conjunction with population-level policies. Effective tobacco control measures, the use of streamlined screening and management algorithms for individuals with or at risk of CVD, the expansion of accessible and reasonably priced treatment regimens, such as combination CVD preventive medication therapy, and the simplification of health care delivery through task-sharing (NPHWs) and self-management optimization (treatment supporters) are some strategies.

The smooth integration of research advancements into clinical practice is critical to the future of cardiovascular care. Patients and medical professionals can receive extremely accurate diagnosis and treatment results thanks to the combination of AI with precision medicine. The paradigm of CV management is changing in favor of a more individualized, proactive, and patient-centered approach as a result of ongoing developments in precision medicine, AI-driven diagnostics, and innovative treatments. This approach can lead to major advancements in CVD management and better CV health outcomes. The future of CV treatment will be shaped in large part by ongoing research and interdisciplinary cooperation.

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