

PRIMER

A Crossroads in Cardiovascular Medicine: Progress and Barriers to Impact

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ABSTRACT: During the past 75 years, advances in cardiovascular science and technology have significantly reduced morbidity and mortality. In 2012, Drs Nabel and Braunwald reviewed this progress in *A Tale of Coronary Artery Disease and Myocardial Infarction*, highlighting the landmark innovations that contributed to the decline in cardiovascular death rates from 1950 to 2010. Since then, groundbreaking developments in pharmacologic therapies, interventional procedures, surgical techniques, and molecular medicine—including gene editing and RNA-based treatments—have emerged. However, despite these innovations, improvements in cardiovascular mortality have stalled, driven not only by epidemiologic shifts but also by persistent inequities in implementation. This article examines the past 15 years of progress in cardiovascular medicine and proposes a forward-looking roadmap focused on prevention, responsible innovation, and thoughtful health care delivery to ensure technological advancements translate into improved health outcomes for all.

Key Words: artificial intelligence ■ cardiovascular mortality ■ digital health ■ innovation ■ prevention

In 2012, to mark the 200th anniversary of the *New England Journal of Medicine*, Dr Elizabeth Nabel and Dr Eugene Braunwald published *A Tale of Coronary Artery Disease and Myocardial Infarction*,¹ a comprehensive review of major advancements in cardiovascular medicine. Their article highlighted the dramatic decline in cardiovascular mortality, attributing progress to key scientific breakthroughs from 1950 to 2009 (Figure 1), although cautioning that coronary artery disease remained a leading cause of morbidity and mortality.

Fifteen years later, we stand at a crossroads: although scientific advancements have continued at an extraordinary pace, cardiovascular mortality has stagnated. This stagnation reflects a widening disconnect between innovation and equitable implementation. This article provides a critical examination of “Where We’ve Been” in the past 15 years, “Where We Are” with a stall in mortality gains, “What’s Holding Us Back,” including the systemic, structural, and behavioral barriers that have prevented these advancements from translating into equitable improvements in cardiovascular outcomes, and last, “Where We

Must Go,” offering a roadmap to improve cardiovascular health.

WHERE WE’VE BEEN: LEGACY OF PROGRESS AND MAJOR MILESTONES

Since Nabel and Braunwald’s review, significant advances have extended the legacy of progress in cardiovascular science and technology, driven by developments in both biomedical and digital innovation (Figure 2). Over the past 15 years, our understanding of cellular and molecular mechanisms—including genetics, genomics, cell biology, and metabolism—has deepened, alongside breakthroughs in diagnostics and therapeutics, such as novel drugs, biologics, medical devices, surgical techniques, and digital health tools, including artificial intelligence (AI). These innovations have contributed to improvement in cardiovascular care and have even introduced the possibility of disease-modifying or curative therapies for select conditions. Yet real-world clinical

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Nonstandard Abbreviations and Acronyms

AI	artificial intelligence
GLP-1	glucagon-like peptide-1
PCSK9	proprotein convertase subtilisin/kexin type 9
SGLT2	sodium-glucose cotransporter 2

application has been uneven, constrained by fragmented systems, cost barriers, and other systemic limitations.

Biopharmacotherapeutics and Advanced Biotechnology Platforms

Advancements in biopharmacologic therapies, including direct oral anticoagulants, angiotensin receptor–neprilysin inhibitors, SGLT2 (sodium-glucose cotransporter 2) inhibitors, PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitors, and GLP-1 (glucagon-like peptide-1) receptor agonists, have significantly improved cardiovascular outcomes in clinical trials, providing targeted treat-

ments for hyperlipidemia, diabetes, and heart failure. Additionally, over the past decade, cardiovascular medicine has been transformed by advancements in precision medicine, gene therapy, RNA-based therapeutics, and xenotransplantation. Although some technologies have already reached clinical practice, others remain in development with the potential to reshape treatment paradigms. These biopharmacotherapeutic advances can be largely attributed to the impact of basic discoveries and surging strength of translational and team science, with investigators and clinicians across multiple disciplines coming together to push forward these breakthrough discoveries.

Innovation in Surgical and Medical Technologies

Since 2012, cardiothoracic surgery has evolved significantly, particularly in coronary artery bypass grafting. Minimally invasive, robotic, and off-pump techniques have further enhanced precision, reduced blood loss, and improved recovery times. In the United States, interventional cardiology and cardiothoracic surgery have converged through percutaneous valve interventions, increasing

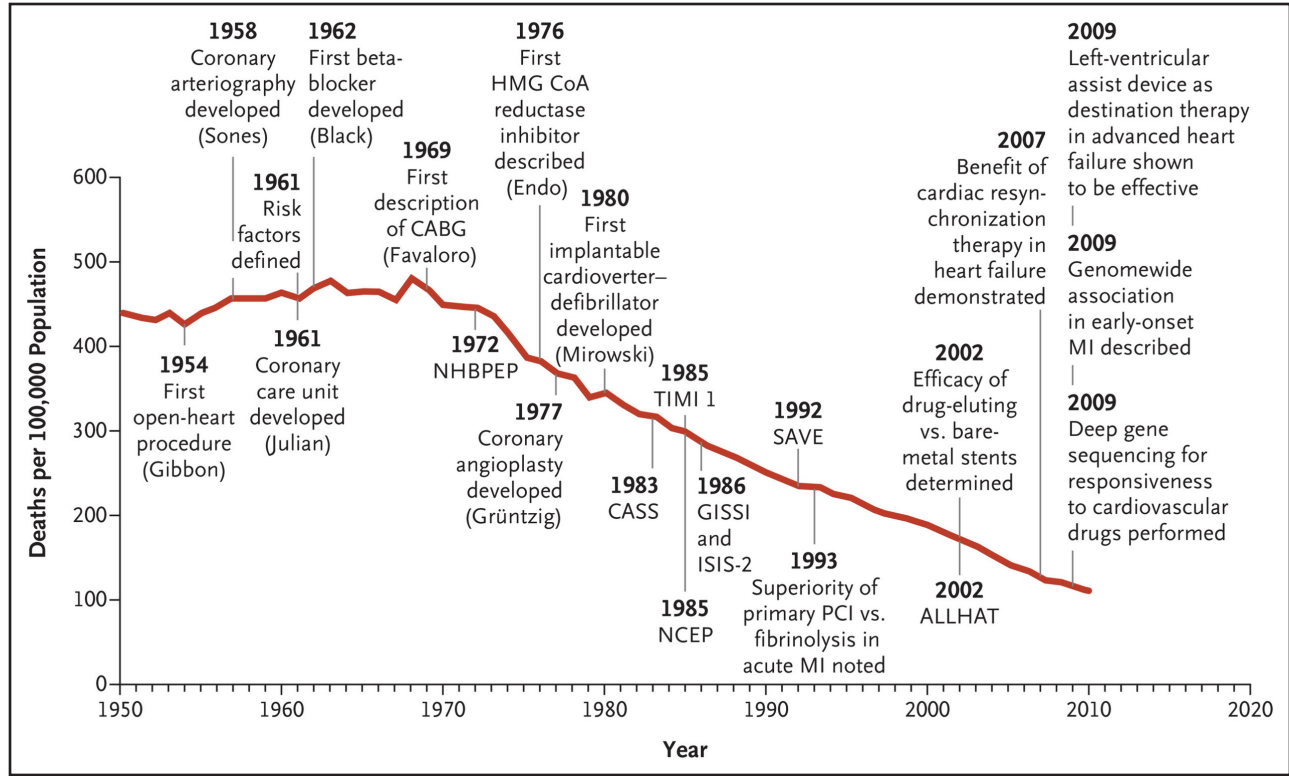


Figure 1. Decline in deaths from cardiovascular disease in relation to scientific advances. Adapted from Nabel and Braunwald, 2012,¹ this timeline illustrates the significant decline in cardiovascular mortality over the late 20th and early 21st centuries, driven by major advances in cardiovascular medicine. ALLHAT indicates Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial; CABG, coronary artery bypass surgery; CASS, Coronary Artery Surgery Study; GISSI, Italian Group for the Study of Streptokinase in Myocardial Infarction; HMG-CoA, 1-hydroxy-3-methylglutaryl coenzyme A; ISIS-2, Second International Study of Infarct Survival; MI, myocardial infarction; NCEP, National Cholesterol Education Program; NHBPEP, National High Blood Pressure Education Program; PCI, percutaneous coronary intervention; SAVE, Survival and Ventricular Enlargement; and TIMI 1, Thrombolysis in Myocardial Infarction 1. Reprinted with permission from Massachusetts Medical Society.

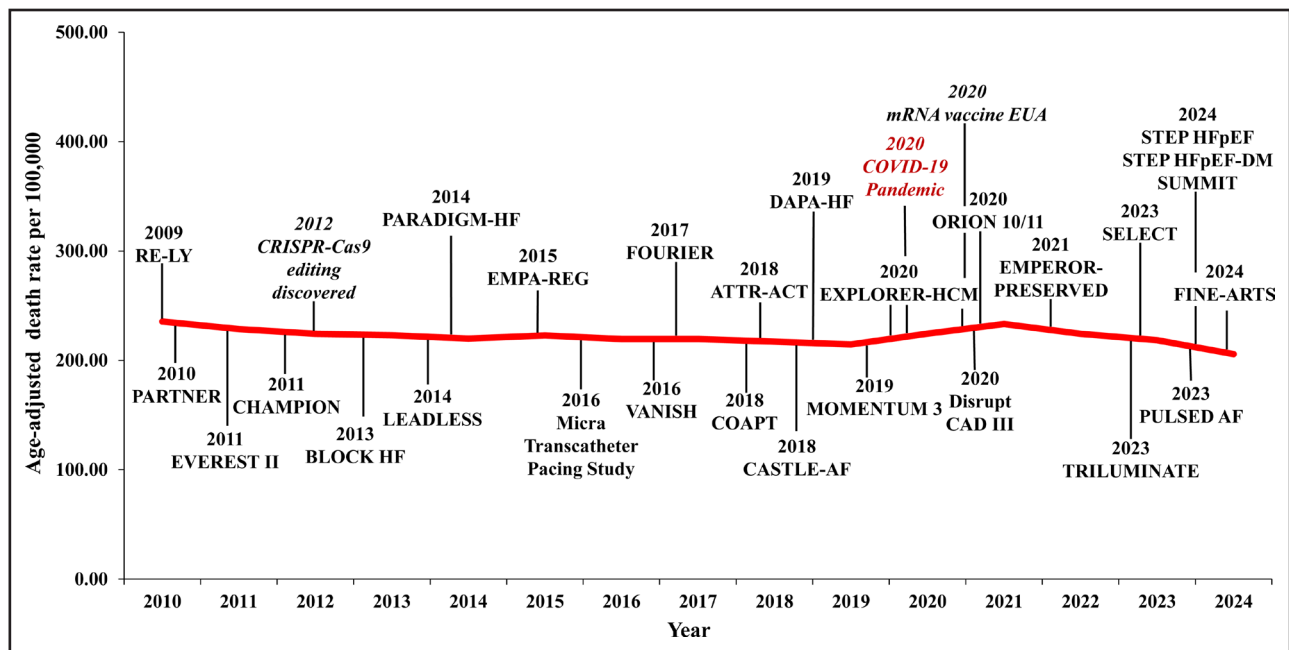


Figure 2. Landmark advances and deaths from cardiovascular disease (2010–2024).

This figure highlights key landmark advances in cardiovascular medicine, spanning therapeutic, interventional, and surgical breakthroughs. Each milestone represents a pivotal clinical trial or innovation that significantly influenced patient care and medical practice. Detailed descriptions of these advances are provided in the sections below. ATTR-ACT indicates Transthyretin Amyloidosis Cardiomyopathy Clinical Trial; BLOCK HF, Biventricular Versus Right Ventricular Pacing in Heart Failure Patients With Atrioventricular Block; CASTLE-AF, Catheter Ablation for Atrial Fibrillation With Heart Failure; CHAMPION, Cardio Micro-Electro-Mechanical System Heart Failure Sensor Allows Monitoring of Pressures to Improve Outcomes in NYHA Functional Class III Heart Failure Patients; COAPT, Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients With Functional Mitral Regurgitation; CRISPR, clustered regularly interspaced short palindromic repeats; EMPA-REG, Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes Mellitus Patients; DM, diabetes mellitus; EMPEROR-PRESERVED, Empagliflozin Outcome Trial in Patients With Chronic Heart Failure With Preserved Ejection Fraction; EUA, emergency use authorization; EVEREST II, Endovascular Valve Edge-to-Edge Repair Study; EXPLORED-HCM, Mavacamten for Treatment of Symptomatic Obstructive Hypertrophic Cardiomyopathy; FINE-ARTS, Finerenone Trial to Investigate Efficacy and Safety Superior to Placebo in Patients With Heart Failure; FOURIER, Further Cardiovascular Outcomes Research With PCSK9 Inhibition in Subjects With Elevated Risk; HFpEF, heart failure with preserved ejection fraction; MOMENTUM 3, Multicenter Study of MagLev Technology in Patients Undergoing Mechanical Circulatory Support Therapy With HeartMate 3; PARADIGM-HF, Prospective Comparison of Angiotensin Receptor–Neprilysin Inhibitor With Angiotensin-Converting–Enzyme Inhibitor to Determine Impact on Global Mortality and Morbidity in Heart Failure; PARTNER, Placement of Aortic Transcatheter Valves; PULSED-AF, Pulsed Field Ablation to Irreversibly Electroporate Tissue and Treat AF; RE-LY, Randomized Evaluation of Long-Term Anticoagulation Therapy; TRILUMINATE, Trial to Evaluate Cardiovascular Outcomes in Patients Treated With the Tricuspid Valve Repair System; SELECT, Semaglutide Effects on Cardiovascular Outcomes in People With Overweight or Obesity; STEP, Semaglutide Treatment Effect in People With Obesity; and VANISH, Ventricular Tachycardia Ablation Versus Escalation of Antiarrhythmic Drug Therapy in Ischemic Heart Disease.

access to life-saving treatments. Remote-control and telerobotic systems are improving procedural accuracy and will allow for increasingly complex procedures to be done minimally invasively, in more complex patients and in regions that previously did not have access to these therapies. Early successes include transcatheter telestenting² and telerobotic percutaneous coronary interventions,³ signaling the potential for remote cardiovascular procedures.

Similarly, advancements in mechanical circulatory support have also transformed heart failure management. In electrophysiology, early rhythm control has expanded catheter ablation use in atrial fibrillation,⁴ with pulsed field ablation, approved in 2023, offering greater precision and reduced tissue damage.⁵ Last, wearable and implantable devices are also revolutionizing cardiovascular monitoring. Physiologic conduction

system pacing, leadless pacemakers, and novel catheter ablation techniques continue to expand treatment options. These major milestones in surgical and device-based interventions have redefined cardiovascular care.

Digital Revolution and AI in Cardiovascular Medicine

The digital revolution has transformed health care, driven by advancements in AI, wearable technology, and big data. The rise of cloud computing, large language models like ChatGPT, and AI-powered imaging has accelerated biomedical research and diagnostics, particularly in cardiovascular medicine. In cardiovascular imaging, machine learning algorithms have enhanced coronary computed tomography angiography by automating plaque analysis

and improving the detection of high-risk features.⁶ AI has also been applied to ECGs to predict atrial fibrillation⁷ and left ventricular dysfunction,⁸ whereas echocardiography-based models assist in assessing cardiac structure and function.⁹ Looking ahead, we still need additional time to assess the full benefit of the digital revolution and AI in cardiovascular medicine.

WHERE WE ARE: THE STALL IN MORTALITY GAINS AND WHY

In spite of groundbreaking advancements in cardiovascular research and treatment, the benefits have not translated into improved health outcomes for all populations. Although the United States leads in medical innovation, its health care outcomes lag many industrialized nations, in the face of unsustainable and ever-rising costs. Life expectancy peaked at 78.8 years in 2014 and has since declined, even before the COVID-19 pandemic.¹⁰ Likewise, the steady decrease in cardiovascular mortality seen from the 1950s through the early 2000s has surprisingly stagnated—and even reversed (Figure 3).¹¹

This trend can be explained by the rising chronic disease burden and widening health disparities. A key driver of this stagnation is the increasing prevalence of noncommunicable diseases, including obesity, diabetes, and kidney disease (Figure 4).¹² Since the 1960s, obesity rates have more than tripled in the United States, surging from 11.6% in 1990 to >40% in 2022.¹³ Further, nearly 48%

of US adults have hypertension, yet only 59.2% are aware of their condition, and just 20% have their blood pressure controlled.¹⁴ Similarly, 14.7% of adults have diabetes, but nearly 23% remain undiagnosed, whereas 38% have prediabetes, yet only 19% have been diagnosed.¹⁵ Given the high prevalence of cardiovascular risk factors, there is an urgent need for enhanced screening, early detection, and prevention-based care. Still, only 5.3% of adults aged 35 years and older received all recommended high-priority preventive services in 2020,¹⁶ and screening rates for blood pressure, cholesterol, and blood glucose declined between 2019 and 2021, most likely because of the impacts of the COVID-19 pandemic, further widening gaps in early detection.¹⁷ The growing burden of metabolic disease has stalled progress in cardiovascular mortality. This stall has been exacerbated by disparities in health care access and social determinants of health, a chasm that is driven further by health care costs.

Efforts to implement secondary prevention also face significant obstacles. In 2016, only half of patients with atherosclerotic cardiovascular disease were prescribed statins, and just 20% received lifestyle counseling for modifiable risk factors.¹⁸ Clinicians are expected to manage risk individually, yet time constraints and poor reimbursement structures, where procedural interventions are disproportionately incentivized, make preventive interventions difficult to implement. Although value-based models offer a potential solution, their adoption remains inconsistent across the US health care system, which continues to reward insurers and pharmacy

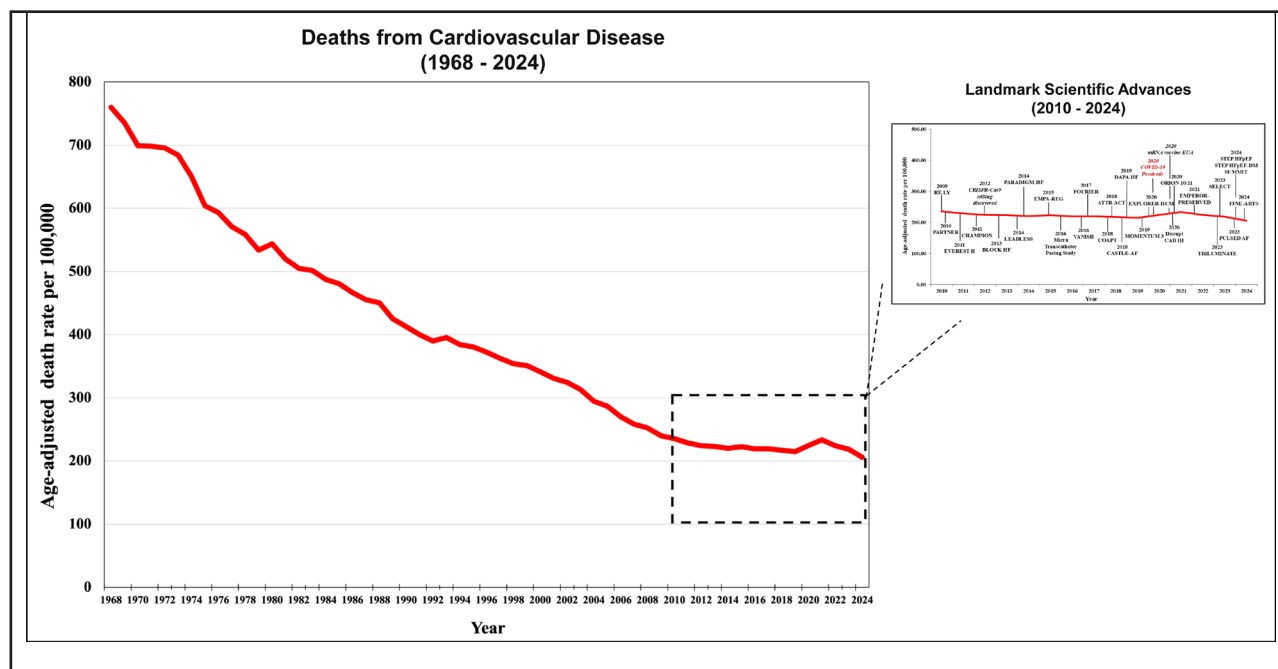


Figure 3. Deaths from cardiovascular disease (1968–2024).

This graph shows trends in cardiovascular mortality from 1968 to 2024 from the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research database.¹¹ The highlighted section emphasizes changes over the past 15 years. The inset illustrates key landmark studies, which are explored in greater detail in Figure 2.

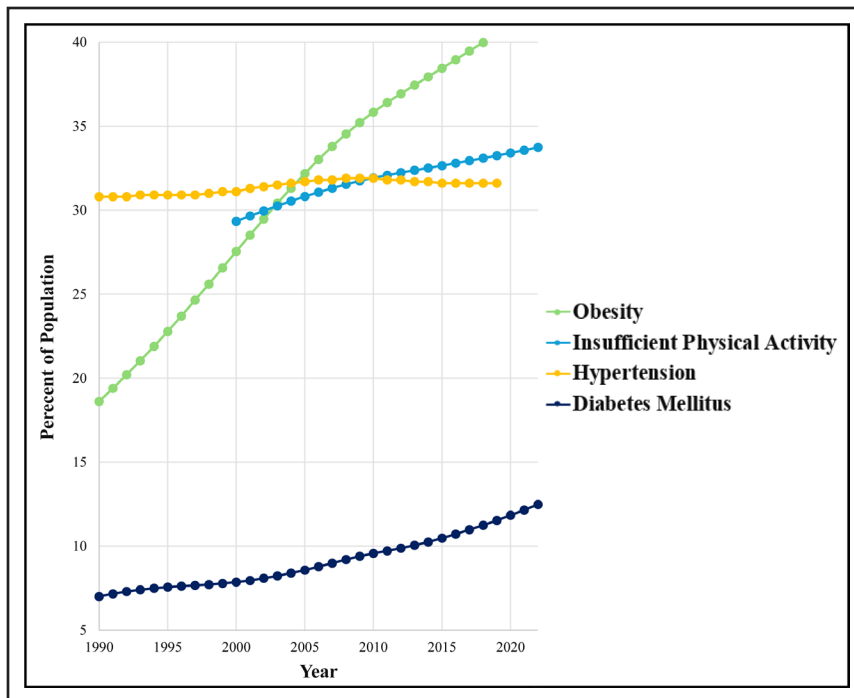


Figure 4. Rates of risk factors and noncommunicable diseases.

This figure displays age-standardized prevalence rates of noncommunicable diseases in the United States from 1990 to 2022, based on data from the World Health Organization. The data show a marked rise in obesity and diabetes during this period.

benefits managers over patients and providers. Additionally, fragmented care and inadequate infrastructure further restrict screening, early detection, and preventive treatment.¹⁹

Structural inequities, including systemic racism, economic instability, and geographic disparities, mean that a person's zip code is often a stronger predictor of cardiovascular health than their genetic profile. Minority and low-income populations continue to experience disproportionately higher rates of cardiovascular disease, limited access to preventive care, and lower use of advanced therapeutics.²⁰ Limited access to healthy foods, safe environments for physical activity, and quality health care further widen this gap.

Compounding these challenges is a health care system that remains largely reactive, prioritizing treatment over prevention in both practice and compensation models. Without a shift toward primary and primordial prevention—emphasizing early intervention, equitable access to care, and addressing social determinants of health—scientific progress alone will not be enough to reverse the troubling trends in cardiovascular mortality.

WHAT'S HOLDING US BACK: STRUCTURAL INEQUITIES, DELIVERY FAILURE, DIGITAL DIVIDES

Systemic, economic, and social obstacles prevent approved treatments from reaching those in need. It has been described²¹ that this reflects a major gap in delivery, in which scientific progress fails to reach its maximum potential because it is inaccessible to those who might

benefit most. This valley of death driven by health inequities disproportionately affects low-income, minority, and rural populations, where cardiovascular disease burden is highest. Key barriers include inadequate health infrastructure in underserved areas, high and unsustainable costs, insurance gaps, and underuse of even affordable medications like statins.²² Further, real-world uptake of breakthrough therapies is constrained by pricing, insurance coverage, and unequal prescribing patterns across populations. For example, SGLT2 inhibitors and GLP-1 receptor agonists—despite their proven cardiovascular benefits—remain underprescribed in populations at high risk for health disparities,²³ highlighting the gap between scientific promise and population-level impact. Access to surgical and device-based innovations remains geographically limited. Rural hospitals and underserved regions often lack the infrastructure, personnel, and capital investment to offer these services, reinforcing health disparities. The digital divide wedges a further gap, limiting telehealth opportunities and digital advances to patients who may not have internet or the ability to operate a computer. Fragmented health care systems reinforce acute treatment over prevention, whereas mistrust, misinformation, and cultural factors further hinder adherence to proven therapies.

Closing this health equity valley of death requires systemic reforms to improve affordability, access, and care delivery. Currently, there is insufficient primary and community care, lack of access to mobile clinics and telehealth services, and inadequate Medicare and Medicaid coverage to a significant portion of the population. AI and digital tools offer promise but must be equitably implemented. Ultimately, translating breakthroughs into

real-world health improvements demands modified reimbursement models and a shift toward prevention, accessibility, and systemic reform. We must align biomedical innovation with system-level readiness to deliver care that is not only effective but also inclusive and accessible.

WHERE WE MUST GO

Ensuring access to treatments remains a critical priority, yet an equally urgent challenge is shifting from reactive acute care to proactive prevention and early intervention. As mentioned above, enhanced screening and patient education is needed to improve health outcomes and narrow gaps in disparities. The future of cardiovascular care depends on reclaiming prevention as a central pillar of practice. Community-based prevention models offer a promising solution but depend on sustainable reimbursement and infrastructure investment for effective implementation. Taking hypertension as a case example, for every 5-mmHg reduction in systolic blood pressure, there is a 10% decrease in cardiovascular events.²⁴ In 2019, estimated annual costs associated with hypertension were \$219 billion,²⁵ and cost-effectiveness analyses have shown intensive treatment of hypertension to be cost-effective or even cost-saving.²⁶ Implementing multidisciplinary, team-based care including pharmacists is estimated to save \$900 million in Medicare costs over 5 years while reducing rates of heart attack, stroke, and deaths from cardiovascular causes.²⁷

Although digital health technologies can bridge gaps by enhancing adherence, early intervention, and personalized health coaching, their high costs remain a challenge. Scaling precision public health faces significant hurdles, including fragmented health data, access and equity gaps, financial and reimbursement constraints, regulatory uncertainties, and insufficient workforce training and infrastructure for widespread adoption.

AI has rapidly expanded into clinical decision-making, research, and patient monitoring, offering a future where real-time data from wearables and medical devices could further personalize cardiovascular care and improve outcomes. AI-driven precision health presents a transformative opportunity by analyzing genetic, lifestyle, community, and environmental data to identify disease risk patterns and enable targeted, proactive interventions for high-risk populations.²⁸ However, AI applications risk perpetuating disparities if not developed and deployed thoughtfully. Underrepresentation in training datasets of diverse populations representative of the full populace in need, unequal access to digital tools, and limited broadband connectivity pose significant challenges to equitable implementation. At present, AI, wearables, and tools for precision phenotyping

are disproportionately used by younger, healthy subjects, creating an implementation need for elderly and frail populations who may truly benefit most from these technologies. Equity-driven oversight frameworks and transparency in algorithm development are critical next steps to ensure responsible adoption. Formal AI education for health care providers is an essential tool to help mitigate risk of worsening health disparities. We have not yet seen the potential of how the power of AI may transform health care and improved outcomes in cardiovascular medicine.

In summary, ensuring that innovation serves all patients—not just those with financial and geographic access—requires a fundamental shift toward proactive, equity-driven policies. Systemic reforms in health care affordability, AI oversight, and digital inclusion must accompany scientific progress to prevent widening disparities in cardiovascular health. By aligning technological breakthroughs with ethical governance, we can move beyond innovation toward true impact.

A UNIFIED ROADMAP: PREVENTION, ACCESS, IMPLEMENTATION, AND EQUITY

Reducing cardiovascular mortality on a national scale requires a comprehensive, equity-driven strategy that integrates prevention, broad access to innovation, and responsible scientific advancement. Although biomedical breakthroughs continue to transform cardiovascular care, their true value will depend on how effectively they are implemented—and whether they reach those most at risk.

First, future progress must prioritize primary and primordial prevention. This includes expanding and enhancing screening programs for the early detection of cardiovascular risk factors and disease. Strengthening the primary care workforce and improving health care infrastructure—particularly in underserved and rural communities—are essential to ensuring that preventive services are both available and accessible. Expanding access to mobile health clinics and telehealth platforms will further improve reach, especially in areas with limited traditional health care facilities.

Second, ensuring that novel therapies are both affordable and accessible is critical. This will require expanding Medicaid and Medicare coverage to reduce financial barriers and promoting value-based pricing models that tie cost to measurable patient benefit.

Third, we must enhance the implementation of both preventive and therapeutic innovations. To do so, stakeholders—including clinicians, patients, policymakers, and industry leaders—should be engaged early in the development process to anticipate barriers to adoption. Investments must be directed toward the infrastructure, workforce training, and operational support needed to

transition discoveries from research settings into real-world clinical outcomes.

Fourth, improving health equity must be at the heart of any national strategy. This includes addressing longstanding systemic disparities that disproportionately affect marginalized populations by ensuring access to nutritious foods and safe spaces for physical activity. Enhancing health education through culturally relevant, community-based partnerships can also foster trust and support behavior change.

Last, we must foster a sustainable and ethical ecosystem for scientific innovation. This means advancing research in ways that maximize benefit while minimizing unintended harm. As AI becomes increasingly integrated into cardiovascular care, oversight frameworks and formal training for health care providers will be essential to ensure that these technologies are deployed responsibly and equitably.

Dr Eugene Braunwald's recent recommendations—to strengthen our investment in basic science, broaden access to cardiovascular advancements, and elevate prevention as a clinical and public health priority—offer a clear and timely vision for the path ahead.²⁹ Our analysis affirms these principles and emphasizes the urgent need for a unified, future-focused strategy to ensure that scientific progress translates into measurable improvements in cardiovascular health for all.

ARTICLE INFORMATION

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Disclosures

None.

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