

Commentary

Second Universal Definition of Heart Failure: Implications for Prevention, Biomarkers, and Global Clinical Practice

Dipti Tiwari ¹, Chin Shern Lau ^{2,3} and Tar Choon Aw ^{2,3,4,*}¹ Independent researcher, Singapore 469971, Singapore² Department of Laboratory Medicine, Changi General Hospital, 2 Simei Street 3, Singapore 529889, Singapore³ Academic Pathology Program, Duke-National University of Singapore Graduate School of Medicine, Singapore 169857, Singapore⁴ Department of Medicine, Yong Loo Lin School of Medicine, Singapore 119077, Singapore

* Correspondence: tarchoon@gmail.com; Tel.: +65-68504927; Fax: +65-64269507

Abstract

The 2026 AHA/ACC/ESC/WHF Expert Consensus Document on the Second Universal Definition of Heart Failure marks an important recalibration of how heart failure is recognized, classified, and studied. The document retains the central insight of the 2021 First Universal Definition—that heart failure is a clinical syndrome supported by structural, functional, biomarker, or congestion evidence—but moves the field toward earlier detection, etiologic precision, and trajectory-based care. This is a comprehensive commentary on the latest updates from the Second Universal Definition of Heart Failure. Its most visible changes include reaffirmation of the stage A to D continuum, stronger emphasis on pre-heart failure, simplification of ejection-fraction phenotypes into clinically actionable groups, a universal classification of causes, and new language for improvement, remission, recovery, worsening heart failure, and decompensated heart failure. For laboratory medicine, the definition is especially relevant because of its emphasis on natriuretic peptides, cardiac troponins, urine albumin–creatinine ratio, and emerging artificial-intelligence electrocardiography. This commentary reviews the main changes in the second definition, highlights implications for heart failure with preserved ejection fraction, obesity, cardiometabolic disease, global implementation, and frameworks for integrated clinical and laboratory pathways.

Keywords: heart failure; second universal definition; natriuretic peptides; cardiac troponin; HFpEF; obesity; pre-heart failure; biomarkers; laboratory medicine

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1. Introduction

Universal definitions matter because they change the unit of attention. They influence who is counted in epidemiology, who is eligible for trials, which patients trigger quality indicators, and how clinicians explain a disease to patients and families. Heart failure (HF) has long been difficult to define because it is not a single disease, a single imaging measurement, or a single laboratory value. It is a final common clinical syndrome, arising from diverse structural and functional cardiac abnormalities and modified by age, kidney function, body composition, pregnancy, cancer therapy, pulmonary disease, and social context. A definition that is too loose risks overdiagnosis; a definition that is too narrow misses the

patient before hospitalization, before remodeling becomes irreversible, or before a treatable cause is identified.

The First Universal Definition and Classification of Heart Failure, published in 2021, brought much-needed clarity by defining HF as a clinical syndrome with symptoms and/or signs caused by a structural and/or functional cardiac abnormality and corroborated by elevated natriuretic peptide levels and/or objective evidence of pulmonary or systemic congestion [1]. It also renamed stage B as pre-HF, a simple but powerful move that made asymptomatic structural or biomarker disease clinically visible. It is unfortunate that this Universal Definition of Heart Failure has not gained the traction of its close cousin, the Universal Definition of Myocardial Infarction. The 2026 second definition does not discard that foundation. Instead, it updates the language to reflect developments in prevention, imaging, biomarkers, HFpEF, obesity, cardiomyopathy classification, and global health [2].

For a commentary from a laboratory and translational clinical perspective, the most important message is that the second definition is not merely semantic. It asks clinicians and laboratorians to move from a binary mindset—HF present or absent, reduced EF or preserved EF, ischemic or nonischemic—to a staged, etiologic, and longitudinal model. Such a model is more faithful to the biology of HF and better aligned with contemporary preventive therapies. It also forces a careful re-examination of how biomarkers are interpreted: natriuretic peptides are central, but they are not infallible; cardiac troponin is no longer only an acute coronary syndrome test; and urine albumin–creatinine ratio can help capture the cardiovascular–kidney–metabolic substrate that precedes overt HF.

Some cardiologists and many laboratorians remain unaware of the Heart Failure Definition. We should arise and not be left behind. This commentary aims to narrow the gap for laboratorians and clinicians.

2. What Is New in the Second Definition?

The 2026 consensus document highlights five practical shifts. First, it reaffirms HF as a clinical syndrome supported by a constellation of symptoms, signs, structural or functional abnormalities, congestion evidence, and biomarkers, rather than by a single diagnostic test. Second, it strengthens the prevention agenda by re-emphasizing stage A and stage B disease. Third, it moves away from rigid LVEF cutoffs and groups HF into reduced EF, preserved EF, and improved EF categories, while allowing clinicians to consider measurement variability and patient characteristics. Fourth, it proposes a universal classification of HF causes, including ischemic, hypertensive, valvular, arrhythmia-related, infiltrative, infective, inflammatory, toxic, heritable, metabolic and nutritional, pregnancy-related, stress-induced, pulmonary/right-sided, congenital, high-output, other, and idiopathic categories. Fifth, it introduces more explicit trajectory language, distinguishing improvement, remission, recovery, worsening HF, and decompensated HF [2].

These changes are pragmatic. Clinical practice has never been fully captured by a single LVEF threshold. A patient with an LVEF of 39%, 41%, or 50% does not abruptly change disease biology at the moment an echocardiography report crosses a consensus cutoff line. Similarly, patients with HFpEF may have normal natriuretic peptide levels, especially when obesity is present, despite invasive hemodynamic evidence of HF [3,4]. The second definition therefore gives clinicians permission to use judgment while still preserving standard terminology for registries, trials, and guidelines.

The etiologic taxonomy is equally important. The older ischemic versus nonischemic split was necessary and useful for broad categorization but not sufficient for modern care. Cardiac amyloidosis, hypertrophic cardiomyopathy, tachycardia-induced cardiomyopathy, cancer therapy-related cardiomyopathy, Chagas disease, peripartum cardiomyopathy, and obesity-related HFpEF require different diagnostic pathways and may have

cause-targeted therapies. The Second Universal Definition of HF classification avoids overlooking specific treatable causes. For instance, identifying cardiac amyloidosis as the cause of HF prompts targeted evaluation and disease-specific therapy beyond conventional HF treatment, especially the more specific agents against transthyretin (e.g., tafamidis and vutrisiran) in ATTR amyloidosis. Similarly, hypertrophic cardiomyopathy, tachycardia-induced cardiomyopathy, cancer therapy-related cardiomyopathy, and peripartum cardiomyopathy each direct clinicians toward different investigations, surveillance strategies, and treatment pathways. A universal cause framework can also improve not only coding and registry science but also bedside clinical reasoning.

3. From Symptomatic Treatment to Early Detection

Most HF guidelines quite understandably focus on symptomatic HF, where treatment evidence is strongest and patient need is immediate [5–7]. Yet the largest public health opportunity lies before the first HF hospitalization. The Second Universal Definition gives prevention a more prominent stage. Stage A includes individuals with risk factors such as hypertension, diabetes, obesity, atherosclerotic cardiovascular disease, congenital heart disease, cardiotoxin exposure, family history of cardiomyopathy, or pathogenic genetic risk. Stage B (or pre-HF) includes asymptomatic individuals with structural cardiac abnormalities, abnormal cardiac function, elevated natriuretic peptides, or elevated cardiac troponin, particularly in relevant clinical contexts [2]. Identification of Stage B/pre-HF relies on a combination of risk factors, persistent natriuretic peptide or troponin elevation without competing explanations, structural or functional abnormalities on echocardiography, and evidence of increased filling pressures [5].

This language matters because stage B is actionable. The evidence base for prevention is not uniformly overwhelming across all pathways, but it is increasingly persuasive. In diabetes, chronic kidney disease, obesity, and established cardiovascular disease, SGLT2 inhibitors, GLP-1 receptor agonists, blood pressure control, renin–angiotensin system inhibition in selected groups, and mineralocorticoid receptor antagonism in kidney–metabolic disease have shifted the conversation from risk description to risk modification [5–12]. STOP-HF and PONTIAC showed that natriuretic peptide-based screening combined with collaborative care can identify high-risk individuals and reduce cardiac dysfunction or events in selected populations [13,14]. These data do not mean that indiscriminate population screening is ready for prime time. They do suggest that biomarker adoption can help identify patients who deserve closer observation and more aggressive prevention.

A laboratory-centered implementation pathway could begin with high-risk primary care groups: namely, diabetes, chronic kidney disease, obesity, hypertension with left ventricular hypertrophy, prior cardiotoxic chemotherapy, and family history of cardiomyopathy. Natriuretic peptides, cardiac troponin, kidney function, urine albumin–creatinine ratio (UACR), glycemic metrics, and lipid markers should be interpreted together with symptoms, blood pressure, electrocardiography, and imaging. The second definition encourages exactly this integrated view. It should not be reduced to a laboratory reflex rule, but should help laboratories design smarter interpretive comments, risk pathways, and clinician education.

4. Ejection Fraction: Useful, but Not Sovereign

LVEF remains clinically indispensable. It determines eligibility for many therapies and devices, anchors clinical trial evidence, and offers a simple language for communicating cardiac systolic function. The second definition does not minimize its value. Rather, it places LVEF in context. Echocardiographic LVEF has inter-observer and intra-observer variability, differs by imaging modality, and may be influenced by loading conditions; the

measurement uncertainty of LVEF can be as high as 49% [15]. Measurement uncertainty is the term used to convey the notion that there is a range of values around a recorded reading that contains the true value of what is being assessed. There is potential uncertainty when LVEF is estimated using common geometric assumptions and limited short- or long-axis views in echocardiographic practice, especially with 2D echocardiography; the uncertainty is substantially reduced with more accurate 3D approaches. Normal LVEF ranges can also vary by sex, age, and ethnicity. In HFpEF, LVEF is often normal even when filling pressures, myocardial stiffness, vascular reserve, right ventricular–pulmonary coupling, or exercise hemodynamics are abnormal [2].

The simplified grouping into reduced EF, preserved EF, and improved EF has a subtle advantage: it reminds clinicians that HF phenotypes are not fixed identities. While LVEF in a patient with previously reduced EF may improve after guideline-directed medical therapy, they remain biologically vulnerable. The term HF with improved EF is therefore not equivalent to cure. The newer trajectory language—improvement, remission, and recovery—is useful because it separates partial myocardial response from durable normalization. For patients, this may be one of the most important communication points. Feeling better and having a better LVEF should usually lead to continuation of effective therapy and surveillance, not therapeutic complacency.

For trials and registries, moving away from rigid cutoffs could make eligibility more clinically realistic and available. However, it also creates a methodological challenge. If trials use flexible EF categories, they must specify imaging method, timing, baseline therapy, and adjudication rules carefully. Otherwise, a more biologically sensible definition could paradoxically make evidence synthesis harder. The solution is not to return to arbitrary cutoffs but to combine flexible clinical phenotypes with transparent measurement standards.

5. Biomarkers in the New Framework

Natriuretic peptides remain the cornerstone HF biomarkers. BNP and NT-proBNP support diagnosis, help identify higher risk, and guide referral or further imaging when symptoms are nonspecific. They are also attractive for prevention because they often rise before obvious clinical HF. Prior reviews have emphasized their expanding role beyond acute dyspnea, including risk stratification in diabetes and cardiometabolic disease [16]. The second definition reinforces this broader role while also acknowledging a crucial limitation: HF is not excluded in every patient with a low natriuretic peptide concentration.

This caveat is especially relevant in HFpEF and obesity. Obesity is associated with lower natriuretic peptide concentrations, and patients with HFpEF can have normal BNP or NT-proBNP despite abnormal invasive filling pressures and adverse outcomes [3,4]. Therefore, a low natriuretic peptide result should be interpreted against pretest probability, body mass index, kidney function, atrial fibrillation, age, sex, and the acuity of presentation. Laboratory reports that simply label a value as normal may be insufficient in high-risk asymptomatic patients. A more helpful approach is to provide interpretive context: low values reduce the likelihood of HF in many settings but do not reliably exclude HFpEF in obesity or when exertional hemodynamic abnormalities are suspected.

Cardiac troponin deserves similar nuance. High-sensitivity troponin assays have transformed acute myocardial infarction pathways, but chronic low-level myocardial injury is common in structural heart disease, chronic kidney disease, diabetes, hypertension, and HF. Prior work on high-sensitivity troponin has stressed the importance of assay-specific 99th percentile upper reference limits, sex-specific thresholds, analytical imprecision, and clinical context [17]. In the second HF definition, troponin is not a substitute for clinical evaluation; it is a signal of myocardial injury that can identify stage B disease and higher-risk trajectories when combined with imaging and risk factors.

Urine albumin–creatinine ratio (UACR) is another underused component of the HF risk conversation. Albuminuria reflects microvascular, kidney, metabolic, and endothelial disease and is strongly linked to future cardiovascular events. UACR is not a formal diagnostic criterion for Stage B HF in the Second Universal Definition. Rather, UACR is a marker of kidney, endothelial, and cardiometabolic risk that may help identify patients who deserve closer cardiovascular assessment. Many practitioners already use the standard UACR categories from KDIGO (Kidney Disease: Improving Global Outcomes) guidelines for CKD management: 30–300 mg/g as moderately increased and >300 mg/g as severely increased [18]. KDIGO also recommends confirming ACR ≥ 30 mg/g on a random sample with a subsequent first-morning void. In an era of cardiovascular–kidney–metabolic health, the laboratory can help unify what has too often been split into separate disease silos [12]. A practical HF risk panel for selected patients may therefore include NT-proBNP or BNP, high-sensitivity cardiac troponin, estimated glomerular filtration rate, urine albumin–creatinine ratio, HbA1c, and lipids, with reflex pathways to echocardiography or cardiology review when results and clinical context align.

This integrated approach also creates an educational opportunity. Many clinicians learn biomarker interpretation through disease-specific pathways: troponin for myocardial infarction, natriuretic peptides for acute HF, albuminuria for kidney disease, and HbA1c for diabetes. The second HF definition encourages a more holistic interpretation. A patient with mild albuminuria, rising troponin within the reference interval, borderline NT-proBNP, left ventricular hypertrophy, and diabetes may not meet criteria for symptomatic HF, but the pattern should prompt risk modification and surveillance. Laboratories can make this pattern visible through multidisciplinary reporting guidance and clinician-facing education.

6. Obesity, HFpEF, and the Cardiometabolic Substrate

Obesity is one of the areas where the second definition feels particularly timely. It is listed as a stage A risk factor, appears in the universal cause taxonomy under metabolic and nutritional disease-associated cardiomyopathy, and is also discussed as a diagnostic mimic or confounder. This triple emphasis is appropriate. Obesity can predispose to HF through hemodynamic load, systemic inflammation, epicardial and visceral adiposity, insulin resistance, sleep apnea, kidney disease, and pulmonary hypertension. It can also make HF harder to diagnose because dyspnea, edema, deconditioning, and lower natriuretic peptide concentrations can obscure the underlying syndrome.

The accompanying 2026 *European Journal of Heart Failure* expert consensus on guideline-directed medical therapy in patients with HF and obesity is therefore a useful companion document [19]. It emphasizes that obesity is common in HFpEF, alters hemodynamics and biomarker interpretation, and complicates congestion assessment. It also suggests that key HF therapies, including SGLT2 inhibitors, renin–angiotensin system inhibition, mineralocorticoid receptor antagonists, and diuretics when needed, should generally be used according to guideline principles rather than withheld because of body size. The evidence base for beta-blockers in obesity-specific HF populations remains less direct, reflecting older trial designs rather than definitive harm.

Newer anti-obesity pharmacotherapy further changes the landscape. In STEP-HFpEF, semaglutide improved symptoms, physical limitations, and body weight in patients with HFpEF and obesity [9]. In SELECT, semaglutide reduced cardiovascular events in patients who are overweight or obese and with established cardiovascular disease but without diabetes [11]. In SUMMIT, tirzepatide improved outcomes in HFpEF with obesity [10]. These trials strengthen the logic of treating obesity not only as a comorbidity but as a modifiable pathophysiologic driver in selected HF phenotypes. They also show why an

etiologic and trajectory-based definition is clinically useful: the future of HFpEF treatment will likely depend on identifying the dominant biology in each patient.

7. Worsening, Decompensation, Remission, and Recovery

The second definition clarifies several terms that have often been used interchangeably. Worsening heart failure (WHF) refers to progressive deterioration in symptoms, signs, quality of life, biomarkers, imaging, or hemodynamics in someone with a prior HF diagnosis [2,20]. Decompensated HF, by contrast, is defined by the need for therapeutic escalation or rescue therapy and may occur in acute or more gradual settings [21]. This distinction is more than linguistic. It matters for clinical trial endpoints, health-system metrics, and outpatient care. A patient who needs rapid diuretic intensification in the clinic may have a clinically important decompensation even if no hospitalization occurs. Early detection of WHF is important in order to avert further disease progression. WHF is not detected by a single test, but by longitudinal clinical assessment in patients with established HF. The HFA/ESC consensus statement defines worsening HF as worsening symptoms and signs requiring treatment intensification, most often diuretic escalation. Detection may be supported by increasing dyspnea, edema, weight gain, reduced functional capacity, rising natriuretic peptides, renal deterioration with congestion, and imaging or device evidence of increasing congestion [22].

The terms improvement, remission, and recovery also deserve attention. In many chronic diseases, remission implies control rather than eradication. HF should be approached similarly. LVEF improvement, normalized natriuretic peptides, or resolution of congestion may represent a favorable trajectory, but relapse can occur when therapy is withdrawn or when the underlying cause persists. This is particularly relevant for myocarditis, tachycardia-induced cardiomyopathy, peripartum cardiomyopathy, cancer therapy-related cardiomyopathy, and genetic cardiomyopathies. A trajectory framework therefore helps clinicians avoid the misleading phrase stable heart failure. HF may be well controlled, but the patient remains at risk.

8. Global and Equity Implications

A Universal Definition must be globally useful. The second definition explicitly acknowledges geographic variation in HF causes and outcomes. In high-income settings, ischemic heart disease, hypertension, obesity, diabetes, chronic kidney disease, and aging dominate much of the HF burden. In other regions, rheumatic heart disease, Chagas disease, peripartum cardiomyopathy, untreated hypertension, infective causes, and limited access to early diagnostics remain critical. Even within a single country, social determinants shape who receives natriuretic peptide testing, echocardiography, genetic evaluation, specialist referral, and guideline-directed therapy.

This has implications for all laboratories. If natriuretic peptide testing is available only in tertiary centers, the definition will be difficult to operationalize in primary care. If assay cutoffs are imported without understanding local age, ethnicity, obesity, renal function, and disease-prevalence patterns, diagnostic performance may be uneven. If high-sensitivity troponin assays are used without education on chronic myocardial injury, they may create confusion rather than clarity. The goal should therefore be tiered implementation: simple risk-factor recognition in all settings, natriuretic peptide and troponin pathways where available, echocardiography access for high-risk or symptomatic patients, and advanced imaging or genetic testing for selected etiologic questions.

For Singapore and similar health systems, the second definition offers an opportunity to integrate cardiology, endocrinology, nephrology, primary care, and laboratory medicine. Diabetes and chronic kidney disease are common, obesity and central adiposity are

rising, and Asian-specific body-composition patterns can make cardiometabolic risk substantial even at lower body mass index thresholds. A universal definition should not ignore these local realities. Rather, it should provide a common language into which local risk profiles can be translated.

9. Diagnostic Pathways and Practical Cautions

The second definition should not be interpreted as a mandate to test everyone with every available biomarker. Its value lies in matching the intensity of evaluation to the probability and consequences of disease. In a young person with transient dyspnea after a viral illness, normal examination, and low clinical risk, a single low natriuretic peptide may be reassuring. In an older patient with diabetes, chronic kidney disease, atrial fibrillation, obesity, exertional intolerance, and prior chemotherapy, the same result has a different meaning. The clinician should ask whether the test result fits the patient, not whether the patient can be forced to fit the test result. We summarize the diagnostic approach suggested by the Second Universal Definition (see Figure 1). This is not a formal algorithm expressed in the second definition but our proposed strategy derived from the Definition's broader emphasis on integrating clinical assessment, biomarkers, imaging, staging, etiology, and longitudinal patient trajectory.

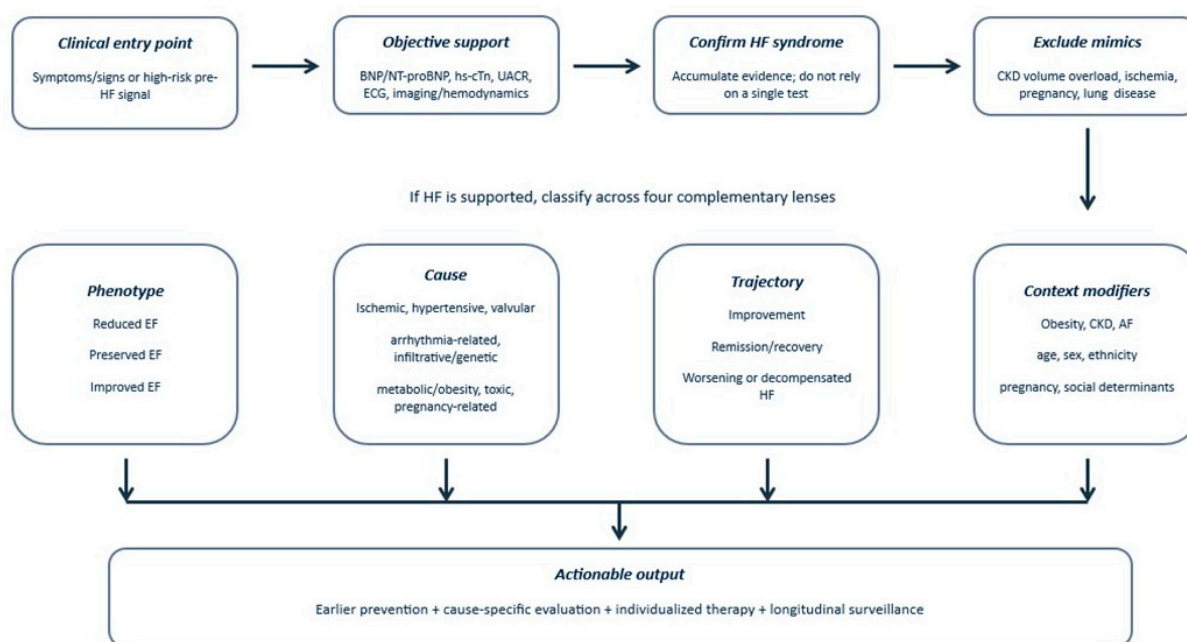


Figure 1. Conceptual framework summarizing the integrated diagnostic and classification approach implied by the Second Universal Definition of Heart Failure.

AI-ECG can detect $EF \leq 35\%$ with AUC of 0.93, sensitivity 86.3% and specificity 85.7% [23]. In a systematic review of AI-ECG for detecting LV systolic dysfunction, the AUC was 0.90, sensitivity 83.3%, and specificity 87.0% [24]. The appeal is obvious: ECGs are inexpensive, widely available, and already embedded in clinical workflows. But AI-ECG should be held to the same standards as other screening tools. Models trained in one population may not perform equally in another; performance may vary by age, sex, ethnicity, comorbidity, device type, and local disease prevalence; and a positive screen must lead to an actionable pathway rather than a diagnostic dead end. Without such pathways, AI may increase testing volume without improving outcomes.

The second definition also has implications for patient communication. The term pre-HF can motivate prevention, but it can also alarm patients who feel well. Clinicians should explain that pre-HF is not inevitable HF; it is a warning sign that risk can often be modified. Similarly, remission should be explained as controlled disease rather than cure. The language of the definition is therefore not only for journals and registries. It should be translated into patient-facing phrases that preserve urgency without fatalism.

10. Trial, Registry, and Quality-Measurement Implications

The definition will likely influence future HF trials. For decades, trials have relied heavily on LVEF thresholds because they are simple, auditable, and linked to prior treatment effects. The second definition does not remove the need for measurable eligibility criteria, but it challenges investigators to define phenotypes more comprehensively. A trial of HFpEF and obesity may need to capture body composition, natriuretic peptide interpretation, exercise capacity, filling pressures, diabetes status, sleep apnea, kidney function, and inflammatory or metabolic features. A trial of infiltrative or heritable cardiomyopathy may need genotype, imaging, and tissue or scintigraphy criteria. One number cannot carry all that biology.

Registries should similarly evolve from diagnosis-only datasets to stage, phenotype, cause, and trajectory datasets. A minimal future HF registry might include stage A to D status, current and historical LVEF, evidence supporting HF diagnosis, natriuretic peptide and troponin values with assay names, kidney function and albuminuria, suspected or confirmed cause, obesity and metabolic status, treatment class, and recent trajectory. Such a structure would allow health systems to identify gaps: patients with stage B disease who never receive follow-up imaging, patients with obesity and dyspnea whose low natriuretic peptides prematurely ended evaluation, or patients with improved EF whose therapy was stopped without monitoring.

Quality measurement must be handled carefully. Measures that reward testing alone may encourage low-value care; measures that focus only on hospitalization miss outpatient worsening and prevention. Better metrics would track whether high-risk patients have appropriate risk-factor control, whether abnormal biomarkers lead to sensible follow-up, whether cause-specific diagnoses are sought when clues are present, and whether patients with known HF maintain evidence-based therapy after improvement. The second definition provides the vocabulary for such measures, but implementation science will determine whether they improve outcomes.

11. Research and Implementation Priorities

Several research questions follow directly from the second definition. First, which combinations of natriuretic peptides, troponin, albuminuria, ECG, imaging, and clinical risk scores best identify stage B disease in diverse populations? Second, how should biomarker thresholds be adapted, if at all, for obesity, kidney disease, atrial fibrillation, age, sex, and ethnicity? Third, can AI-enabled ECG and other digital tools improve early detection without widening diagnostic inequities? Fourth, how should trials enroll patients when LVEF categories are more flexible but regulatory and statistical frameworks still prefer numeric thresholds? Fifth, what is the best patient-facing language for pre-HF, remission, and recovery so that the terms motivate prevention without creating unnecessary anxiety?

Implementation should begin with practical clinical pathways. Laboratories can support these pathways by standardizing reporting units, flagging assay-specific decision limits, adding interpretive comments for obesity and HFpEF, educating clinicians about chronic troponin elevation, and creating reflex recommendations for repeat testing or

imaging only when clinically appropriate. Health systems can support the definition by aligning electronic medical record prompts, registry fields, and quality indicators with stage, phenotype, cause, and trajectory rather than diagnosis codes alone.

A further priority is harmonization of local protocols with international language. Laboratories may already have BNP, NT-proBNP, and troponin decision limits embedded in electronic systems; cardiology services may have separate criteria for echocardiography referral; and diabetes and kidney clinics may have their own thresholds for cardiovascular risk escalation. The second definition can act as the common bridge among these protocols. The immediate task is not to replace every pathway, but to align them so that a high-risk patient is not lost between disease-specific silos.

A concise implementation map is shown in Table 1. Its purpose is not to replace guidelines, but to translate the second definition into the kind of shared clinical and laboratory language that can be used in daily care.

Table 1. Translating the Second Universal Definition into Practice.

Domain	Main Change	Clinical/Laboratory Action
Definition and stages	HF remains a clinical syndrome, but stage A and stage B/pre-HF are emphasized as prevention windows.	Use biomarkers and imaging to support earlier detection in high-risk groups, not only acute dyspnea assessment.
Ejection fraction	Rigid LVEF cutoffs are replaced by reduced EF, preserved EF, and improved EF groupings.	Report LVEF with method and context; avoid treating small numeric differences as categorical biology.
Cause classification	A universal etiologic taxonomy replaces the broad ischemic/nonischemic split.	Prompt cause-directed testing when clinical clues suggest amyloidosis, myocarditis, cardiotoxicity, genetic disease, obesity-related HFpEF, or other specific pathways.
Trajectory	Improvement, remission, recovery, worsening HF, and decompensated HF are separated.	Continue surveillance after LVEF improvement; recognize outpatient therapeutic escalation as clinically meaningful.
Biomarkers	BNP/NT-proBNP and troponin support diagnosis, risk detection, and stage B classification.	Interpret values with obesity, renal function, age, atrial fibrillation, assay characteristics, and pre-test probability.

12. Conclusions

The Second Universal Definition of Heart Failure is best understood as a living framework for earlier, more precise, and more equitable HF care. It preserves the syndromic nature of HF while making room for contemporary biology: cardiometabolic risk, obesity-related HFpEF, genetic and infiltrative cardiomyopathies, biomarker-defined pre-HF, dynamic LVEF trajectories, and global variation in causes. The core strengths of the Second Universal Definition are a move away from rigid EF cutoffs, recognizing HF as a dynamic disease, and adoption of a standardized taxonomy for HF etiology. Its success will depend on whether clinicians, laboratories, researchers, and health systems use it actively. If implemented thoughtfully, the definition can help move HF care upstream, from late recognition after decompensation to early risk detection, cause-specific evaluation, and sustained longitudinal prevention.

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Abbreviations

AHA	American Heart Association
ACC	American College of Cardiology
BNP	B-type natriuretic peptide
CKD	chronic kidney disease
EF	ejection fraction
ESC	European Society of Cardiology
GDMT	guideline-directed medical therapy
HF	heart failure
HFpEF	heart failure with preserved ejection fraction
LVEF	left ventricular ejection fraction
NT-proBNP	N-terminal pro-B-type natriuretic peptide
WHF	World Heart Federation

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