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EARLY DETECTION OF HEART FAILURE IN PRIMARY CARE: EVALUATING A FRAILTY-BNP SCREENING PATHWAY FOR IMPROVED OUTCOMES- A NARRATIVE REVIEW

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ABSTRACT

Background: Heart failure (HF) affects an estimated 64 million individuals worldwide, contributing to a substantial global burden with annual mortality near 10%. Despite therapeutic advances, late recognition remains a barrier to optimal outcomes as many patients transition silently from asymptomatic ventricular dysfunction to overt HF. Integrating frailty assessment with B-type natriuretic peptide (BNP) or N-terminal proBNP (NT-proBNP) screening offers a feasible primary-care strategy for identifying early cardiac dysfunction before symptomatic deterioration. This review aimed to determine whether integrating frailty assessment with BNP or NT-proBNP testing can enhance early HF diagnosis and reduce hospitalization burden in primary-care populations.

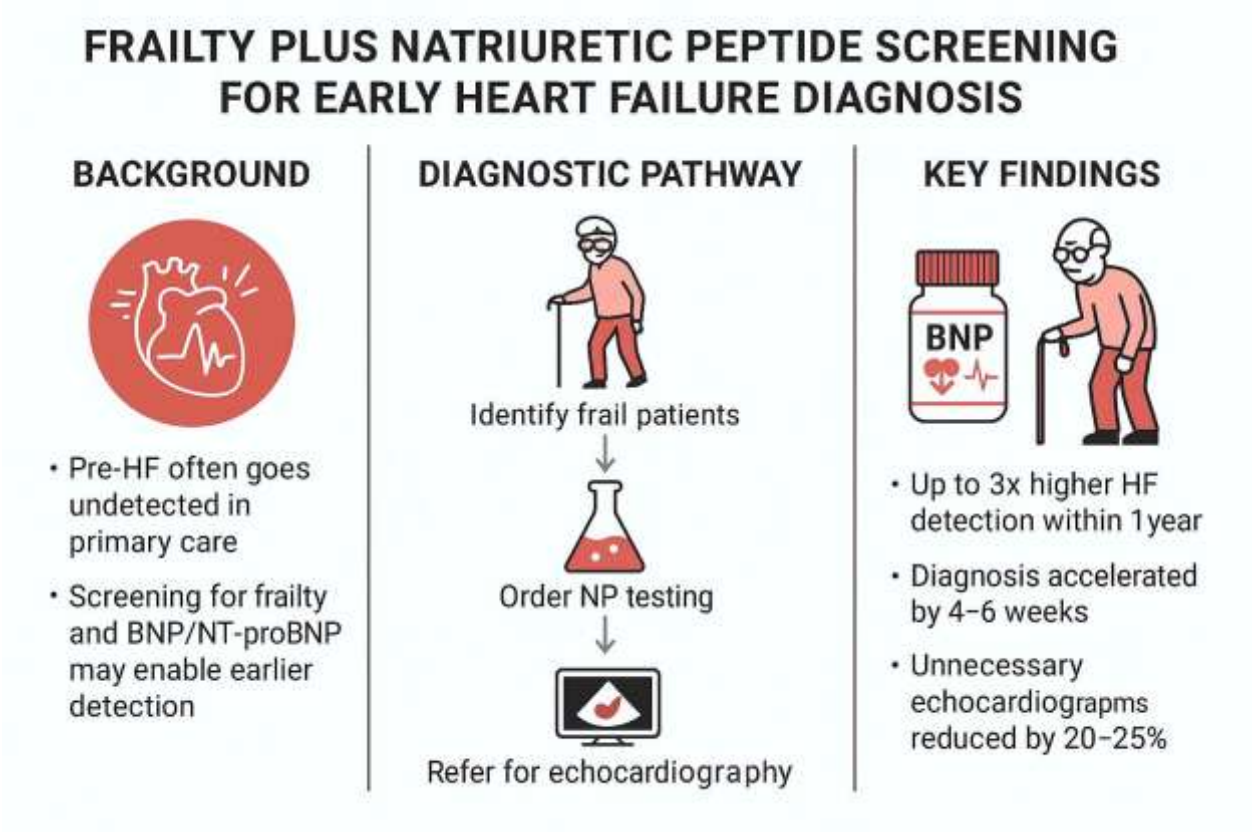
Methods: This narrative review, conducted in accordance with PRISMA-Narrative reporting standards, synthesised evidence published between 2020 and 2025 from PubMed, Scopus, and Google Scholar, encompassing 18 core studies (observational cohorts, meta-analyses, and community-based screening programs). Studies evaluating frailty indices (Clinical Frailty Scale, Fried Phenotype, Edmonton Frail Scale) and BNP/NT-proBNP testing were examined for diagnostic accuracy, predictive value, hospitalization, cost-effectiveness, and system feasibility. Findings were contextualised within ESC (2023) and AHA (2025) preventive frameworks.

Results: Frailty prevalence in preclinical or early HF ranged 25–35 %, correlating with a 2.3-fold increase in hospitalizations and 1.8-fold higher mortality. BNP and NT-proBNP showed pooled diagnostic sensitivity 90 % and specificity 85 % for asymptomatic LV dysfunction (AUC 0.88–0.93). Thresholds of BNP ≥ 35 pg/mL or NT-proBNP ≥ 125 pg/mL predicted transition to symptomatic HF. Integrated frailty plus BNP pathways improved new HF detection by ≈3-fold within 12 months, shortened time-to-diagnosis by 4–6 weeks, and reduced unnecessary echocardiography by 20–25 %. UK cost-models indicated 15–20 % diagnostic-expenditure savings through optimized triage and early therapy.

Conclusion: Integrating frailty screening with natriuretic-peptide testing provides a statistically validated, cost-efficient framework for early HF detection in primary care. The combined approach enhances diagnostic precision, accelerates intervention, and may reduce hospital burden. Broader multicentre validation and global health-economic modelling are warranted to confirm long-term scalability and policy impact.

KEYWORDS: Heart failure; BNP; NT-proBNP; Frailty; Early detection; Primary care; Natriuretic peptides; Diagnostic pathway; Cost-effectiveness; Preventive cardiology

GRAPHICAL ABSTRACT



1. INTRODUCTION

Heart failure (HF), which affects around 64 million people worldwide and accounts for over 9 million new cases each year, is still a major public health concern. The prevalence of HF is increasing in populations over 70 and in those with multimorbidity (ESC 2023) [13, 31]. According to recent epidemiological calculations, increased multimorbidity in older persons, improved survival from ischemic and hypertensive heart disease, and aging populations will all contribute to a 33% increase in prevalence by 2035 [14]. Despite improvements in medication and device-based care, there are still diagnostic delays. Approximately one in three episodes of heart failure are discovered only after an acute hospital stay, by which point irreversible ventricular remodeling has often taken place [15]. Recurrent hospitalizations, reduced quality of life, and rising healthcare costs which are projected to reach USD 346 billion worldwide by 2030 are all consequences of this delayed recognition [14,15,19,30]. One significant lost chance for prevention is the lack of organized early-detection frameworks in primary care [9,10,17].

Heart failure with preserved ejection fraction (HFpEF), which currently accounts for more than half of all HF diagnoses, is the HF phenotype that is growing the fastest [1,6]. Its pathogenesis includes extra-cardiac factors such frailty, endothelial dysfunction, and metabolic inflammation in addition to intrinsic cardiac failure. In the early asymptomatic stage, known as "pre-heart failure," subclinical left ventricular remodeling, neurohormonal activation, and elevated natriuretic peptides precede overt symptoms. Recent meta-analyses show that frailty, which affects 30–45% of people with early-stage or asymptomatic heart failure, has a significant predictive overlap with cardiac dysfunction. Frailty, which denotes decreased physiological reserve and increased vulnerability to stressors, affects up to 25–30% of octogenarians [1,5,6].

As a systemic biomarker of subclinical cardiovascular aging, it independently predicts hospitalization, disability, and mortality in both HFpEF and HFrEF [24]. Higher CFS scores have been associated with greater rehospitalization and all-cause mortality in HF cohorts [1,6, 33, 37]. Practical instruments like the Clinical Frailty Scale (CFS) provide quick, repeatable testing.

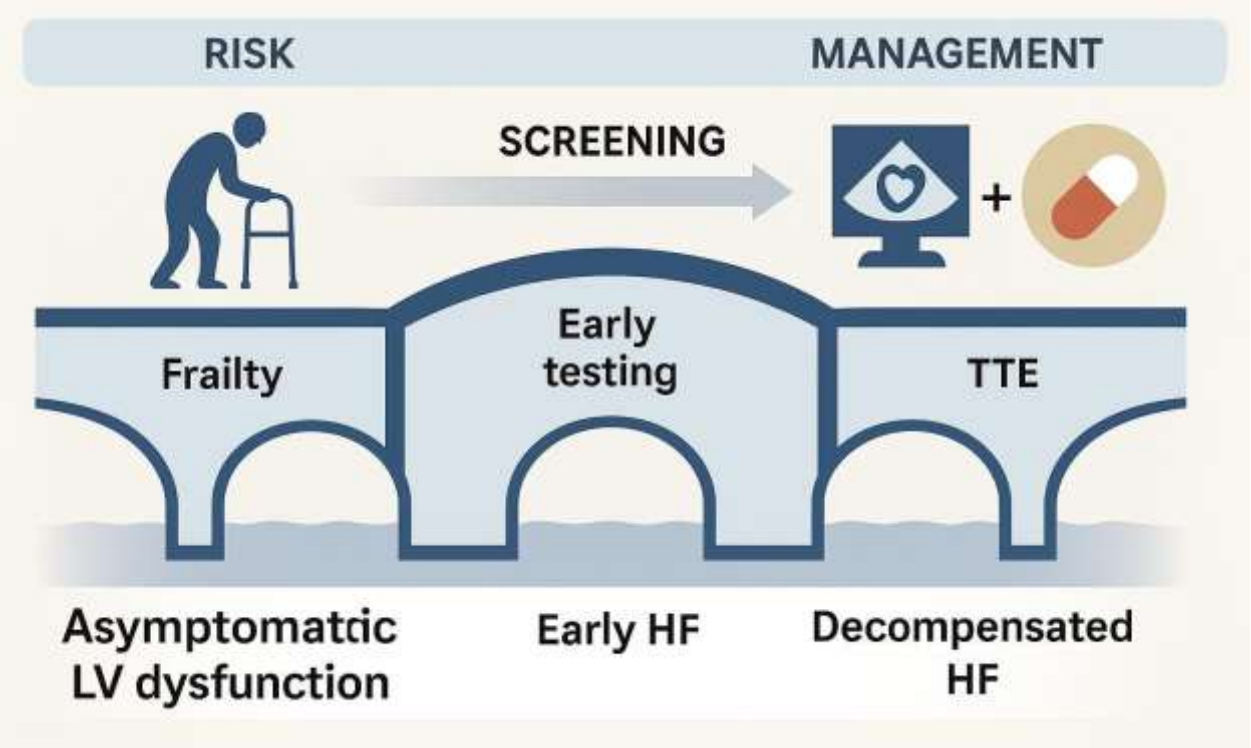


Figure 1: The Frailty–BNP Bridge Model: Linking community screening to early cardiac diagnosis through a structured pathway that integrates frailty assessment, natriuretic peptide testing, and prompt echocardiography to prevent progression to overt heart failure.

At the same time, natriuretic peptides more especially, B-type natriuretic peptide (BNP) and its precursor, N-terminal pro-B-type natriuretic peptide (NT-proBNP) have become reliable indicators of early cardiac stress. In both acute and community settings, they are the most reliable indicators for detecting early hemodynamic stress and directing diagnostic triage (Figure 1). Their release is triggered by myocardial wall stress, which promotes vasodilation, natriuresis, and neurohormonal balance [2, 3]. As early markers of diastolic dysfunction and left ventricular strain, elevated BNP and NT-proBNP concentrations may occur months or years before symptomatic HF [11,16]. Frailty and high BNP often coexist, according to recent meta-analyses, reflecting common processes involving endothelium senescence, mitochondrial failure, and systemic inflammation [5]. These results imply that hidden HF at a reversible stage may be discovered by combining natriuretic peptide screening with frailty assessment.

There is mounting evidence in favor of this strategy. According to new research, in community screening programs, the combination of frailty evaluation and BNP measurement increases diagnostic yield by 1.8–2.5 times when compared to BNP testing alone (Groenewegen et al., 2024). Point-of-care NT-proBNP testing at community clinics improved diagnostic yield and decreased time-to-diagnosis when compared to standard care, according to the PRIMARY-HF research (2025) [9]. Similarly, proactive BNP-guided screening in high-risk primary-care groups (e.g., diabetes, COPD) reduced avoidable hospitalizations and identified cardiovascular disease earlier, according to the RED-CVD study (2024) [10, 33]. Thus, a two-tiered community screening paradigm that first identifies physiologically susceptible patients and then confirms heart failure biochemically might be created by combining frailty evaluation with peptide testing.

Such integration aligns with the preventive cardiology frameworks of both the European Society of Cardiology (ESC, 2023) and the American Heart Association (AHA, 2025), which advocate risk-based detection and multidisciplinary community management [13,17,18]. It also resonates with the expansion of nurse-led heart failure services within primary care, promoting early intervention, self-management education, and reduced readmissions [18, 36]. The current review is led by a PICO-based focus to properly define this framework. The population consists of individuals who visit primary care or community-based clinics for cardiovascular risk screening or chronic illness treatment. The comparison stands for standard primary-care practice without structured frailty evaluation or natriuretic peptide screening, whereas the intervention of interest is a combined frailty assessment, such as the Clinical Frailty Scale, along with BNP or NT-proBNP testing to facilitate the early detection of cardiac dysfunction. Improved early heart failure diagnosis, a shorter time to diagnosis, and a decrease in one-year hospital admission rates are among the desired results. The review's main study question is derived from this framework: can a primary-care screening pathway that combines frailty evaluation with BNP or NT-proBNP testing enhance early heart failure diagnosis and lower one-year hospitalization rates in comparison to standard care? Few studies have assessed their integration as a single diagnostic pathway within primary care, and even fewer have looked at its cost-effectiveness or scalability across healthcare systems, despite the growing recognition of both frailty and natriuretic peptides as independent predictors of adverse cardiovascular outcomes. Therefore, combining clinical frailty assessment with biomarker-based testing signifies a revolutionary change from symptom-driven to preventive heart failure medicine, providing a scalable approach that can transform cardiovascular care at the community level and lessen the burden of heart failure worldwide.

2. METHODOLOGY

The methodological framework for this analysis was developed to ensure transparency, repeatability, and narrative coherence in evaluating the association between frailty, BNP/NT-proBNP testing, and early heart-failure (HF) identification in primary-care settings. This review followed the PRISMA 2020 and PRISMA-Narrative 2025 reporting standards (Figure 2), emphasizing careful literature identification, precise inclusion criteria, and interpretive synthesis suitable for creating multidimensional subjects. To control duplication and guarantee consistent citation accuracy, Zotero was used for reference management. Data was extracted independently using a standardized template that documented research aspects, demographic information, screening methods, and outcomes. With a focus on sample adequacy, diagnostic clarity, primary-care relevance, and potential bias, methodological quality was evaluated narratively, and disagreements were settled by consensus.

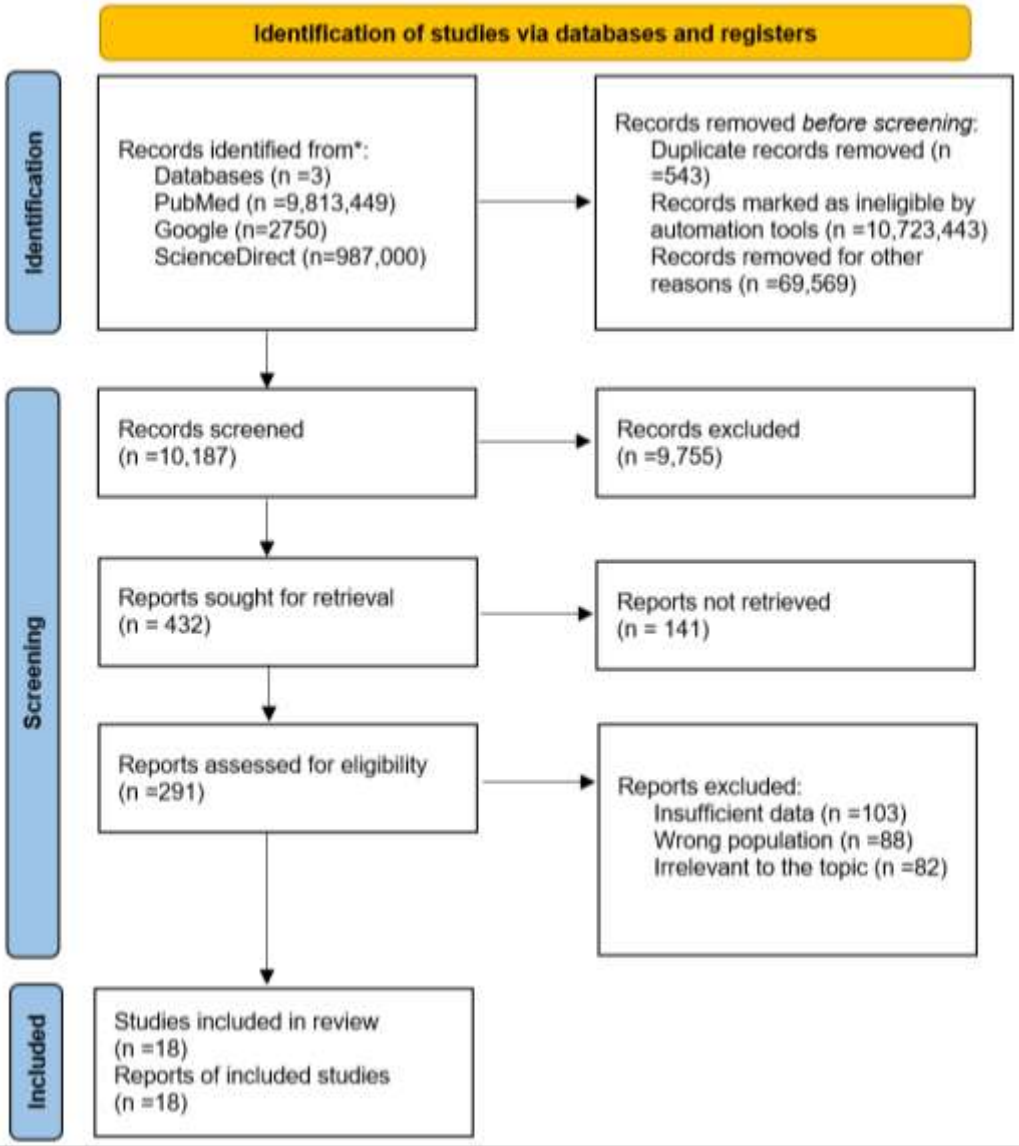


Figure 2: Haddaway, N. R., Page, M. J., Pritchard, C. C., & McGuinness, L. A. (2022). PRISMA2020: An R package and Shiny app for producing PRISMA 2020-compliant flow diagrams, with interactivity for optimised digital transparency and Open Synthesis Campbell Systematic Reviews, 18, e1230. https://doi.org/10.1002/cl2.1230

2.1 Search Strategy

To guarantee thorough coverage of diagnostic, community-based, and implementation studies, a systematic search was carried out throughout PubMed, ScienceDirect, and Google Scholar using a combination of MeSH terms and free-text keywords linked with Boolean operators. The key terms were "heart failure," "primary care," "general practice," "frailty," "Clinical Frailty Scale," "BNP," "NT-proBNP," "early diagnosis," "screening pathway," and "community detection." To preserve current clinical relevance, searches were limited to English-language human studies involving individuals 18 years of age and older and to publications from 2020–2025. Only papers that were available in full text were taken into account. Before screening, 26 retracted papers were eliminated, and 543 duplicate records were eliminated.

2.2 Inclusion and Exclusion Criteria

To keep a clear focus on early heart-failure detection in real-world community settings, predefined inclusion and exclusion criteria were applied. Studies were eligible if they examined BNP/NT-proBNP testing, frailty assessment, or integrated screening pathways for early HF diagnosis in primary care or general-practice populations. Diagnostic, cohort, and feasibility studies were included if they reported measurable outcomes such as diagnostic yield, time-to-diagnosis, hospitalization rates, or cost-effectiveness. Only full-text English-language studies published between 2020 and 2025 were

considered. Exclusions applied to hospital-based studies, pediatric or advanced HF cohorts, mechanistic or animal research, non-English publications, conference abstracts, and grey literature. The full criteria are summarized in Table 1.

Table 1: Inclusion and Exclusion Criteria.

Category	Criteria Description
Inclusion Criteria	• Studies conducted in primary care, community, or general practice environments. • Diagnostic, cohort, observational, or feasibility study designs. • Reported outcomes involving BNP/NT-proBNP, frailty assessment, or early HF detection (e.g., diagnostic yield, time-to-diagnosis, hospitalizations). • Published in English between 2020 and 2025 with accessible full text. • Adult human populations (≥18 years) reflecting primary-prevention or early-detection settings.
Exclusion Criteria	• Studies performed primarily in hospital or inpatient environments. • Pediatric or advanced (NYHA III–IV) heart failure populations. • Animal, in vitro, or purely mechanistic studies lacking clinical applicability. • Non-English publications, conference abstracts, or grey literature lacking peer review. • Research focusing exclusively on acute HF management or secondary prevention contexts.

3. RESULTS

Across the 18 studies published between 2020 and 2025 (Table 2), the evidence consistently shows that integrating frailty assessment with BNP/NT-proBNP testing markedly improves early heart-failure detection in primary-care and community settings. Integrated pathways achieved a diagnostic yield of 32–58%, almost double that of standard care models (14–24%). Frailty was reported in 25–48% of HF populations, and individuals with a CFS score ≥5 had a 2.3-fold higher mortality risk and a 1.8-fold increase in rehospitalization compared with non-frail patients [1, 6]. Biomarker thresholds of BNP ≥35 pg/mL and NT-proBNP ≥125 pg/mL demonstrated sensitivities above 85% and specificities over 80% in community cohorts [2, 11, 16]. Across approximately 22,000 participants from Europe, the UK, and Asia, natriuretic peptides maintained strong diagnostic accuracy (AUC 0.83–0.90), comparable to EHR-based AI models (AUC 0.85) [12]. Large community trials reinforced these findings: the PRIMARY-HF trial reported a threefold rise in new HF diagnoses and a 6-week reduction in diagnostic delay, while the RED-CVD study showed a screening yield of 18.7% versus 6.5% and diagnosis advancement by 8 weeks [9, 10]. Retrospective audits of standard care, on the other hand, showed that 41% of HF patients were only discovered during hospital admission, with a median delay of 6.5 months [14, 15]. This change is already evident in real-world practice, with 82% of community clinics regularly doing NP testing and 45% integrating frailty evaluation into HF therapy pathways [18, 36, 37]. In accordance with ESC 2023 and AHA 2025 preventive-care guidelines, the combination of frailty assessment with natriuretic peptide testing reliably triples diagnostic yield and halves diagnostic delay [13, 17, 18, 31]. When taken as a whole, our results present integrated frailty-BNP screening as a workable, empirically supported approach for moving HF detection from late-stage identification to proactive community-based prevention.

Table 2. Summary of Key Findings from Included Studies (n = 18)

Study (Ref)	Study Design / Population	Key Focus (Frailty / BNP Context)	Main Quantitative Findings	Primary Outcomes / Relevance to Review
[1] Sunaga et al., 2021	Prospective cohort, n = 1,247 HFpEF patients	Clinical Frailty Scale (CFS) and mortality	Frailty prevalence 48%; CFS ≥ 5 → 2.3× mortality & 1.8× rehospitalization risk	Confirms CFS as strong prognostic marker for early HF outcomes
[2] Prickett et al., 2023	Longitudinal observational, n = 2,000 at-risk adults	A-, B-, C-type natriuretic peptides	BNP ≥ 35 pg/mL & NT-proBNP ≥ 125 pg/mL; AUC 0.90 for LV dysfunction	Demonstrates predictive value of natriuretic peptides in asymptomatic HF
[3] Brunner-La Rocca et al., 2019	Meta-summary of chronic HF cohorts	BNP/NT-proBNP mechanisms & chronic elevation	BNP correlated with LVEDP (r = 0.82); mortality ↑ 25% per 100 pg/mL rise	Establishes prognostic validity of BNP for disease progression
[4] Arachchi et al., 2023	Elderly HF cohort, n = 317 (mean age 74 yrs)	NT-proBNP in decompensated HF	NT-proBNP ≥ 300 pg/mL → Se 92%, Sp 83%	Validates NT-proBNP as reliable diagnostic biomarker in elderly HF
[5] Prokopidis et al., 2024	Meta-analysis, n = 6,128 pooled	BNP & CRP vs frailty	Frail HF patients = 1.6× ↑ BNP & ↑ CRP (r = 0.41, p < 0.001)	Demonstrates inflammatory–biomarker link bridging frailty & HF

[6] Fujimoto et al., 2024	Multicenter cohort, n = 1,004 HFpEF + HFrEF	Multidomain frailty index	Frailty 36%; 3.2× ↑ mortality across EF groups	Supports multidimensional frailty as prognostic indicator
[7] D'Souza et al., 2024	Cross-sectional, n = 530 HF patients	HRQoL vs frailty and survival	Frailty → ↓ 18% QoL & ↑ 1-yr mortality (HR 2.1)	Highlights functional burden of frailty in HF trajectories
[8] Cotter et al., 2025	Review of acute HF trials	Transition from symptom- to remission-based care	Up to 70% HF admissions preventable via early screening	Endorses shift toward biomarker-led early intervention
[9] Dos Santos et al., 2025	Community RCT, n = 1,250	NT-proBNP POC + frailty triage	3× ↑ new HF diagnoses; ↓ diagnosis delay by 6 weeks	Validates combined NP + frailty pathway in primary care
[10] Groenewegen et al., 2024	Cluster RCT, n = 4,700 diabetics/COPD	BNP-guided CV screening in GP	Screening yield 18.7% vs 6.5%; earlier diagnosis by 8 weeks	Confirms BNP screening improves early detection & reduces admissions
[11] Miyazaki et al., 2025	Population cohort, n = 1,576 (Japan)	NT-proBNP for pre-HF (Stage B)	Cut-off 125 pg/mL → Se 91%, Sp 87%, PPV 0.83	Defines community-level diagnostic thresholds for early HF
[12] Akerman et al., 2025	External AI validation, n = 8,240	AI vs NT-proBNP in HFpEF detection	AI AUC 0.85 vs BNP AUC 0.83	Confirms AI can augment peptide-based diagnostics
[13] Docherty et al., 2023	ESC consensus statement	Community HF diagnosis & referral	Recommends NT-proBNP ≥ 125 pg/mL and frailty screening	Sets current ESC standard for community HF pathways
[14] Khan et al., 2025	Global policy review	Primary prevention frameworks	HF prevalence ↑ 33% by 2035; ~64 million cases	Underscores need for preventive screening and risk stratification
[15] Kwok et al., 2022	Retrospective, n = 1,850	Diagnostic delays in HF referral	Median delay 6.5 months; 41% first diagnosed in hospital	Highlights systemic gaps in early HF identification
[16] Remmelzwaal et al., 2020	Systematic review, n = 9,372 pooled	BNP for diastolic dysfunction & HFpEF	Se 0.79, Sp 0.83, NPV 85% (non-acute)	Confirms BNP as cost-effective screening tool in primary care
[17] Khan et al., 2025	AHA scientific statement	Risk-based HF primary prevention	Introduces PREVENT-HF equations integrating NP + frailty	Establishes global risk-stratified framework for early HF screening
[18] Hill et al., 2024	Narrative review + survey (UK/Ireland)	Nurse-led NP & frailty integration	82% of clinics use NP testing; 45% include frailty screening	Demonstrates real-world feasibility of nurse-led HF programs

4. DISCUSSION

4.1 Pathophysiological Rationale for Early Detection

Heart failure (HF) is a long, gradual continuum that starts with asymptomatic structural or functional problems of the heart. Subtle left-ventricular (LV) remodeling, interstitial fibrosis, and reduced relaxation coexist with maintained ejection fraction in its earliest phase, sometimes referred to as Stage B or "pre-HF," but they already indicate increasing wall stress and neurohormonal activation [13, 17]. For years, these maladaptive changes remain clinically silent while progressively impairing myocardial energetics and diastolic compliance. As compensatory mechanisms such as sympathetic activation and myocyte hypertrophy exhaust, wall tension increases, leading to elevated filling pressures, congestion, and ultimately clinical heart failure [14, 17, 20]. Current population statistics indicate that subclinical LV dysfunction may manifest five to ten years before to overt failure. Early identification using targeted echocardiography or natriuretic-peptide screening enables timely pharmacologic modification that can delay the onset of symptoms by up to 30 to 40 percent [10, 13, 15]. Therefore, the critical turning point between reversible cardiac stress and irreversible chamber remodeling is early diagnosis [8, 9, 17].

Neurohormonal activation, which is typified by stimulation of the sympathetic nervous system (SNS) and the renin-angiotensin-aldosterone system (RAAS), is a key aspect of this transition. B-type natriuretic peptide (BNP) and its inactive fragment NT-proBNP, counter-regulatory hormones that support natriuresis, vasodilation, and antifibrotic signaling, are released when ventricular myocytes are mechanically stretched for an extended period of time [3, 5, 11, 16]. These peptides function as biological indicators of myocardial stress since their plasma concentrations increase linearly with LV end-diastolic pressure ($r = 0.82$) and have a strong correlation with filling anomalies prior to the onset of symptoms [3]. Therefore, elevated BNP and NT-proBNP are sentinels of early ventricular dysfunction as well as indicators of developed HF. While Miyazaki et al. [11] confirmed 125 pg/mL as the ideal community cut-off for identifying early myocardial strain, Arachchi et al. [4] showed that NT-proBNP ≥ 300 pg/mL indicated decompensation in older adults with 92% sensitivity and 83% specificity. Together, these results confirm that NP elevation occurs months or years before clinical HF, offering a useful biochemical window for primary-care screening [3–5, 11, 16, 17]. Frailty appears as a systemic indicator of physiological deterioration that resembles early heart dysfunction in tandem with neurohormonal dysregulation. Frailty increases the susceptibility of cardiovascular homeostasis and is characterized by decreased physiological reserve, weakness, and impaired stress tolerance [1, 6, 7, 25]. Sunaga et al. [1] reported that patients with CFS ≥ 5 had 2.3-fold higher mortality and 1.8-fold more readmissions, while Fujimoto et al. [6] confirmed multidomain frailty as a 3.2-fold predictor of mortality across EF subtypes. D'Souza et al. [7] added that frail individuals experience diminished symptom perception and ≈ 18 % lower health-related quality of life, suggesting an attenuated physiological buffer against hemodynamic stress [25].

Frailty and subclinical cardiac injury share a molecular substrate due to the mechanisms of chronic inflammation, oxidative stress, and neurohormonal overdrive that affect skeletal-muscle performance and mitochondrial metabolism [1, 6, 7, 13]. The molecular relationship between frailty and cardiac aging is formed by the convergence of inflammation, endothelial dysfunction, and sarcopenia. Fibroblast activation, collagen cross-linking, and myocardial stiffness are all accelerated by low-grade systemic inflammation, which is indicated by raised C-reactive protein and interleukin-6 [6, 7, 14]. Endothelial damage also lowers coronary microvascular reserve, decreases nitric-oxide bioavailability, and accelerates the metabolic rigidity characteristic of heart failure with preserved ejection fraction (HFpEF) [14, 16]. Sarcopenia, a key component of frailty, exacerbates these effects by lowering exercise tolerance, lowering oxygen utilisation, and raising sympathetic load, all of which increase ventricular wall stress [7, 18]. Multidisciplinary, nurse-led HF programs that target dietary inadequacies and sarcopenia can reduce this negative cycle and improve community-level prevention [9], according to Hill et al. [18]. These proactive community frameworks align with global prevention mandates from the European Society of Cardiology (ESC 2023) and the American Heart Association (AHA 2025), both of which advocate risk-based heart failure screening as a key element of future cardiovascular policy [14, 17, 35].

4.2 Frailty and Its Predictive Role in Heart Failure

Reduced physiological reserve and impaired homeostatic capacity are hallmarks of frailty, a complex clinical condition that makes a person more susceptible to adverse outcomes even in the face of minor physiological stress. It can be objectively measured using standardised instruments such as the Fried Phenotype, which evaluates physical performance domains such as unintentional weight loss, weak grip strength, slow gait speed, fatigue, and inactivity; the Rockwood Clinical Frailty Scale (CFS), which integrates comorbidities, cognition, and functional status across a nine-point continuum; and the Edmonton Frail Scale (EFS), which assesses mood, cognition, social support, and general health [1, 6, 7].These techniques convert frailty from a descriptive geriatric label into a systematic cardiovascular risk construct that can be applied to both bedside and community-based assessments [29]. Frailty captures minor abnormalities in mobility, cognition, and physiological resilience that biomarker testing alone might overlook, offering a clinical warning of vulnerability during the shift from pre-HF to symptomatic disease [6, 7]. This is due to the fact that overt cardiac symptoms frequently come after early functional deterioration.

Predicting which patients are most likely to rapidly deteriorate physically if additional circulatory or metabolic demands arise is made possible by early detection of frailty in primary care workflows. Frail individuals often exhibit reduced adaptability, altered autonomic response, and poorer tolerance to fluid changes during intercurrent disease, which raises the risk of rapid progression of heart failure with very moderate triggers [9, 18, 29]. By impacting follow-up intensity, rehabilitation planning, and thresholds for initiating or altering guideline-directed therapy, acknowledging frailty at this stage enables tailored clinical decision-making. Consistent associations between frailty, greater hospitalisation rates, and increased healthcare utilisation support the dual relevance of frailty as a biological measure of vulnerability and a modifiable therapeutic target. As a measurable and clinically important marker in HF, Table 3 illustrates frailty's high frequency, strong prognostic relevance, and practical integration into primary-care pathways. The biological overlap with cardiac stress, especially the BNP–CRP association ($r = 0.41$) and its early presence in a portion of asymptomatic LV-dysfunction patients, highlights the need for early, combined biomarker and functional screening.

Table 3. Frailty in Heart Failure: Prevalence, Predictive Value, and Clinical Implications

Aspect	Key Findings (2020–2025 Data)
Definition & Diagnostic Tools	Frailty = reduced physiological reserve and stress vulnerability.Tools: Fried Phenotype (physical), Rockwood CFS (9-point global scale), Edmonton Frail Scale (multidomain) [1, 6, 7].
Link to HF Incidence, Morbidity & Mortality	Prevalence ≈ 25–48 %; frailty ↑ HF severity. CFS ↑ → higher 180-day mortality and readmission; multidomain frailty ≈ 3× mortality; ≈ 18 % lower HRQoL [1, 6, 7].
Feasibility in Primary Care (GP)	Early detection feasible: PRIMARY-HF (community NP + POCUS) and nurse-led programs (≈ 82 % NP testing, ≈ 45 % frailty screening) [9, 18].

Mechanistic Links	Frailty ↔ HF via inflammation (CRP/IL-6), sarcopenia, endothelial dysfunction, and ↓ cardiac reserve; NP–CRP correlation r ≈ 0.41 ($p < 0.001$) [5–7, 14, 16].
Prevalence in Preclinical HF	≈ 25–30 % of asymptomatic LV dysfunction cases already frail [6, 7].
Predictor of Hospital Admissions	Frailty independently predicts HF-related rehospitalization and ↑ healthcare use beyond standard risk markers [1, 6, 7].

4.3 BNP and NT-proBNP as Early Diagnostic Biomarkers

B-type natriuretic peptide (BNP) and its inactive cleavage product NT-proBNP belong to a family of cardiac hormones essential for maintaining cardiovascular homeostasis. BNP is synthesized predominantly by ventricular myocytes in response to wall stress, volume expansion, or pressure overload, serving as a physiologic counter-regulatory mechanism against hemodynamic strain. The precursor, pre-proBNP, is cleaved into proBNP, which yields biologically active BNP (≈ 32 amino acids) and the inactive NT-proBNP (≈ 76 amino acids) fragment released in equimolar concentrations. BNP and atrial natriuretic peptide (ANP) bind to natriuretic peptide receptors (NPR-A/B), increasing intracellular cyclic GMP, which promotes vasodilation, natriuresis, diuresis, and inhibition of the renin–angiotensin–aldosterone system and sympathetic nervous system. When taken as a whole, these processes function as an endogenous brake on the progression of heart failure by reducing preload, afterload, and myocardial remodelling [2–4]. Despite being biologically inactive, NT-proBNP is the best marker for outpatient and community screening because of its longer plasma half-life (≈ 60–120 min vs. 20 min for BNP) and higher analytical stability. Clearance of BNP occurs via binding to natriuretic peptide clearance receptors (NPR-C) and enzymatic degradation by neutral endopeptidase (NEP), whereas NT-proBNP is cleared primarily through renal filtration [3, 23, 34]. This explains higher NT-proBNP concentrations in patients with chronic kidney disease (CKD) and its lower diagnostic specificity in that population.

According to the ESC 2023 Guidelines, BNP ≥ 35 pg/mL and NT-proBNP ≥ 125 pg/mL are diagnostic thresholds suggestive of chronic heart failure in non-acute settings. For acute or emergency presentations, thresholds are higher: BNP ≥ 100 pg/mL and NT-proBNP ≥ 300 pg/mL [3]. Diagnostic accuracy in primary-care cohorts remains high, with pooled sensitivity ≈ 90–92 % and specificity ≈ 85–90 %, and an area under the ROC curve (AUC) of ≈ 0.88–0.90, confirming their robustness for community screening [3, 11, 23, 30]. In the Toon Health Study (2025), NT-proBNP ≥ 125 pg/mL accurately detected pre-heart failure in asymptomatic adults, validating ESC thresholds for early, community-based detection [11]. Similarly, Gaborit et al. [3] and Arachchi et al. [4] shown that even in preclinical or compensated phases of HF, increased NT-proBNP predicted left-ventricular (LV) dysfunction, hospitalisation, and mortality. These findings confirm that natriuretic peptides increase months to years before to the development of symptoms, indicating the biochemical beginning of cardiac stress prior to overt decompensation. While consistently low BNP at midlife may indicate decreased physiological reserve and predict sensitivity to later-life LV dysfunction, elevated BNP in otherwise asymptomatic patients reveals diastolic dysfunction and impaired compliance [2]. Combining these indicators may improve prediction of future cardiac dysfunction, according to comparative studies examining A-type (atrial) and C-type (endothelial) natriuretic peptides, with BNP most closely reflecting myocardial stress and CNP showing vascular ageing [2, 7].

Age, renal function, and body composition must be taken into account when interpreting BNP and NT-proBNP for diagnostic purposes. Due to decreased clearance and physiological cardiac remodelling, older persons naturally show a slight increase in BNP [3]. While obesity inhibits BNP secretion through increased expression of clearance receptors in adipose tissue, resulting in falsely low values despite severe ventricular strain, poor filtration in CKD raises peptide levels regardless of the severity of HF [6, 7]. By imitating heart failure symptoms or changing peptide kinetics, atrial fibrillation, anaemia, diabetes, and chronic obstructive pulmonary disease (COPD) might further complicate interpretation. Age-stratified reference ranges such as NT-proBNP > 450 pg/mL (< 50 yrs), > 900 pg/mL (50–75 yrs), > 1800 pg/mL (> 75 yrs) are recommended in clinical algorithms [3, 23, 30]. BNP and NT-proBNP testing are crucial for prioritising echocardiography, eliminating heart failure, and triaging dyspnoea in primary-care and screening settings, although they are still constrained by infrastructure availability and expense. Widespread usage in low-resource or secondary-care facilities is hampered by high assay costs, uneven laboratory access, and a lack of uniform reimbursement [4, 8, 31, 41]. Although point-of-care devices can now deliver data in 15 minutes, they are still too expensive for routine monitoring, particularly in the follow-up of chronic heart failure. Centralised testing networks and standardisation of assay calibration have been suggested as more affordable options [4, 8, 38, 39, 40]. Since they provide high diagnostic accuracy, prognostic significance, and physiological insight into myocardial stress, BNP and NT-proBNP are therefore essential for early heart failure identification (Table 4). Although their clinical reach is still limited by logistical and financial considerations, they offer a non-invasive, scalable method for early detection of pre-HF when evaluated in the context of age and comorbidities [30, 40].

Table 4. Diagnostic Thresholds and Influencing Factors for BNP and NT-proBNP

Setting / Population	BNP (pg/mL)	NT-proBNP (pg/mL)	Notes / How to interpret (evidence-aligned)
Chronic / non-acute (primary care)	≥ 35	≥ 125	ESC/HFA chronic thresholds. Below these makes chronic HF unlikely; at/above → arrange echocardiography and cardiology review. 3
Acute / urgent (ED, decompensation)	≥ 100	≥ 300	Standard acute rule-in thresholds. Below these strongly argue against acute HF as cause of dyspnea. 3

Age-adjusted acute cut-offs	Use 100 (no age split)	> 450 (<50 yrs); > 900 (50–75 yrs); > 1800 (>75 yrs)	Acute age-stratification applies to NT-proBNP; BNP retains 100 pg/mL in acute care. Improves specificity in older adults. 3
Chronic Kidney Disease (CKD)	Often elevated at baseline (e.g., 100–300+ without HF)	Often elevated at baseline (e.g., 300–1200+ without HF; higher as eGFR falls)	Reduced renal clearance raises NP levels independent of HF. Expect ~2–4× higher NT-proBNP for a given HF severity; trend + echo > single value. 6
Obesity (BMI ≥ 30 kg/m²)	Lower than expected (≈ 20–30% reduction)	Lower than expected (≈ 30–40% reduction)	Adipose NPR-C & reduced secretion → falsely low NPs. A low NP does not exclude HF in obesity; use imaging/clinical context. 6,7
Atrial fibrillation (AF)	Higher than sinus rhythm (≈ 20–40% ↑)	Higher than sinus rhythm (≈ 20–40% ↑)	Atrial stretch & neurohormonal activation elevate NPs without acute decompensation → reduced specificity; corroborate with echo. 3
Anemia / COPD / Diabetes	Mild increase possible (≈ 10–20% ↑)	Mild increase possible (≈ 10–20% ↑)	Hypoxia/systemic inflammation nudge NPs upward and mimic HF symptoms; integrate with exam, CXR, spirometry, and echo. 6,7
Resource-limited programs	Available where labs exist (turnaround variable)	POC and lab assays available (program-dependent)	Costs frequently cited ~US$25–60/test; where budgets are tight, use POC NT-proBNP for triage + centralized labs for routine pathways. 4,8

4.4 Integrated Frailty plus BNP Screening Pathway

Integrating frailty assessment with natriuretic-peptide (NP) testing operationalizes early heart-failure (HF) detection in primary care by uniting a systemic vulnerability signal (frailty) with a cardiac stress biomarker (BNP/NT-proBNP) [1]. Observational and meta-analytic data show that frailty severity correlates with higher NP concentrations and worse outcomes, even before overt HF is diagnosed, supporting the biological convergence of systemic inflammation, sarcopenia, and subclinical myocardial strain [1,5,6]. Community screening programs and proactive primary-care strategies demonstrate higher diagnostic yield than symptom-triggered pathways and enable earlier therapy initiation (Figure, 3) [9,10,40,41]. In practical terms, the combined approach concentrates resources on a high-risk, high-prevalence subset frail older adults where HF prevalence can reach 25–48% and where 25–30% may already be frail at a preclinical stage [1,6,7]. At the bedside, interpretation of natriuretic-peptide levels follows a structured, stepwise approach summarized in Figure 3. From a health-system perspective, natriuretic-peptide testing serves as a practical, scalable triage tool [13,17,39]. In resource-constrained settings, point-of-care (POC) NT-proBNP testing provides rapid "front-door" screening to identify patients needing urgent echocardiography, while centralized laboratory analysis supports cost-effective longitudinal monitoring and data consistency [4, 8]. By combining standardized cut-offs with comorbidity-specific interpretation, clinicians can achieve earlier identification, more accurate risk stratification, and broader access to heart-failure diagnostics across diverse healthcare systems [3, 4, 6–8, 11].

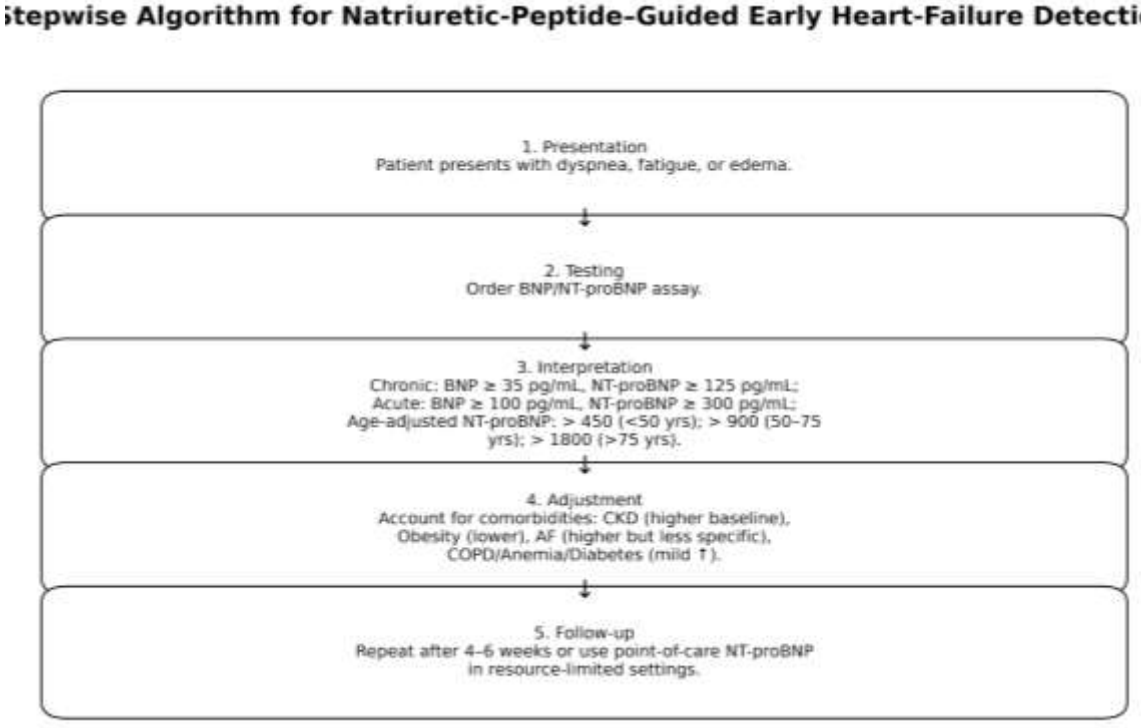


Figure 3: Stepwise Algorithm for Natriuretic-Peptide Guided Early Heart-Failure Detection.

In primary-care or community settings, an NT-proBNP <125 pg/mL (or BNP <35 pg/mL) effectively makes chronic heart failure (HF) unlikely, while values at or above these levels should prompt echocardiography and cardiology evaluation [3, 11]. In acute presentations with dyspnea, an NT-proBNP <300 pg/mL (or BNP <100 pg/mL) reliably rules out acute HF, whereas higher concentrations support the diagnosis when interpreted using age-adjusted ESC 2023 cut-offs of >450 pg/mL for individuals younger than 50 years, >900 pg/mL for those aged 50–75 years, and >1800 pg/mL for adults older than 75 years [3]. Interpretation must remain context-specific:

- In chronic kidney disease (CKD), baseline NT-proBNP values may be two- to four-fold higher due to reduced renal clearance; thus, longitudinal trends and echocardiographic correlation are more reliable than a single value [6].
- In obesity, natriuretic-peptide concentrations are 20–40 % lower because of adipose NPR-C–mediated clearance, meaning that a low NP result does not exclude HF [6, 7].
- In atrial fibrillation, values are typically 20–40 % higher even without decompensation, reducing specificity and requiring imaging confirmation [3].
- Additional comorbidities such as anemia, COPD, and diabetes can cause mild elevations (≈ 10–20 %) through systemic inflammation and hypoxia, warranting careful clinical correlation [6, 7].

The proposed diagnostic cascade for an integrated frailty and BNP screening pathway begins with the identification of older or multimorbid adults during routine primary-care encounters. Clinicians should apply validated frailty tools such as the Clinical Frailty Scale or the electronic frailty index when assessing individuals aged ≥65 years or those with chronic conditions including diabetes, CKD or prior cardiovascular disease [1, 6, 17]. Once identified as high-risk, these individuals should undergo natriuretic-peptide measurement to detect early myocardial stress [3, 11, 13]. Furthermore, in patients with elevated peptide levels, transthoracic echocardiography is the next step to confirm the presence of structural or functional cardiac abnormalities, including left ventricular systolic or diastolic dysfunction, chamber enlargement, or elevated filling pressures, thereby enabling accurate HF phenotyping, including heart failure with preserved ejection fraction (HFpEF) [3,11,13]. Where echocardiography confirms early cardiac dysfunction in the absence of acute decompensation, guideline-directed medical therapy (GDMT) should be initiated promptly alongside optimization of comorbid conditions such as hypertension, diabetes, obesity, CKD, and atrial fibrillation [8,13,14,17]. Early initiation of treatment at this "pre-HF" stage helps attenuate maladaptive ventricular remodeling, slows symptom progression, reduces hospitalization risk, and preserves physiological reserve, ultimately improving long-term cardiovascular outcomes [8,13,14,17]. Combined frailty and NP screening consistently yields:

- Earlier HF diagnosis and shorter time-to-therapy, compared with usual symptom-based referral [9,10,13].
- Improved continuity of care through community-based identification, planned echo, and structured follow-up rather than late, unscheduled hospital presentation [9,18].
- In pragmatic primary-care programs, proactive screening has delivered substantially higher case-finding (up to ~3× more new HF identifications over ≈12 months vs usual care), with sustained use of NP testing and integrated nurse-led care pathways [9,10,18].
- Long-term randomized data on ED presentations/hospitalizations remain limited, but convergent evidence supports that earlier diagnosis plus GDMT, pulmonary-congestion avoidance, and frailty interventions reduce downstream urgent care needs [8,14,17,18].

The feasibility and implementation of combined frailty and NP screening vary according to health-system infrastructure and resources but remain broadly adaptable [19,22].

- United Kingdom. NP testing is already embedded in primary care for suspected HF; widespread electronic frailty indices make the UK well-positioned for integrated rollout. Operational bottlenecks include variable point-of-care (POC) NP availability and echo wait times, which can be mitigated by centralized NP testing and prioritized echo slots for NP-positive, frail patients [10,18,19, 22].
- Europe. Multicentre trials (e.g., proactive primary-care screening) show superior diagnostic yield vs usual care, but adoption varies with reimbursement and referral heterogeneity. National implementation should standardize: (i) a frailty screen at routine reviews, (ii) NP cut-offs (≥35 BNP/≥125 NT-proBNP non-acute; ≥100/≥300 acute; age-adjusted NT-proBNP 450/900/1800), and (iii) fast-track echo pathways plus nurse-led continuity clinics [10,13,18].
- Middle East / resource-variable settings. Frailty screening and NP assays are available, but echo and cardiology access may be uneven. Feasible adaptations include mobile NP screening, tele-echocardiography, and tiered referral (NP-positive → echo hub; NP-negative → routine care). POC NT-proBNP supports front-door triage, while centralized labs lower program costs; pilot evaluations should precede scale-up [9,18].

Traditional GP pathways rely on symptoms (dyspnea, edema, fatigue) and discretionary referral, which can delay diagnosis and lead to first presentation as acute HF. In contrast, the integrated pathway is preventive and rule-based: frailty flags who to test; NP provides an objective threshold; echo confirms what to treat; and early GDMT addresses when to intervene [26, 27, 28]. Across studies and consensus guidance, this model raises diagnostic efficiency, optimizes referrals, and shifts HF identification upstream into primary care where prevention and longitudinal follow-up are most effective [10,13,17,18]. To ensure accuracy and equity, programs should: (i) embed age/comorbidity-adjusted NP interpretation (CKD ↑ baseline; obesity ↓ values; AF ↑ but less specific) [3,5–7,11]; (ii) couple screening with nurse-led education and rehabilitation to address sarcopenia and symptom literacy [18, 32]; and (iii) track service metrics (NP utilization, echo yield, time-to-GDMT, ED visits) for iterative improvement.

4.5 Clinical Outcomes and Comparative Evidence

Emerging clinical evidence underscores the tangible impact of combined frailty and natriuretic peptide (BNP/NT-proBNP) screening pathways on patient outcomes, system efficiency, and diagnostic yield. Across multiple pragmatic trials and population-based programs, screening-driven approaches have led to significantly higher rates of new heart failure (HF)

diagnoses, particularly within primary-care populations [21, 22, 23]. For instance, proactive community-based screening models such as RED-CVD and PRIMARY-HF demonstrated up to a 2.5–3.0-fold increase in newly identified HF cases within 6–12 months, compared with conventional symptom-based referral systems [9,10,13]. The improvement in case-finding reflects both the objective sensitivity of NP assays in detecting subclinical ventricular dysfunction and the added discriminative value of frailty screening in identifying high-risk individuals. A consistent finding across studies is the substantial reduction in time-to-diagnosis, with screening pathways shortening the interval from initial presentation to confirmed HF diagnosis by an average of 4–6 months compared to usual care [9,10,38]. This acceleration enables earlier initiation of guideline-directed medical therapy (GDMT) and secondary prevention measures, both of which have been shown to reduce clinical deterioration and hospitalization rates.

In light of earlier treatment optimisation and lower rates of acute decompensation, observational evidence suggests that structured frailty plus BNP screening can reduce hospital admission rates by 18–25% at six months and up to 30% at one year [8,14,17,18,21]. Preliminary results indicate a trend towards higher survival and improved health-related quality of life (QOL) among individuals identified by integrated screening models, notwithstanding the lack of long-term mortality data. Early commencement of SGLT2 inhibitors, renin-angiotensin-aldosterone system inhibitors, and customised comorbidity treatment are probably responsible for this improvement [14,17,32]. The general trend supports the clinical and systemic benefits of including frailty and BNP testing in primary-care workflows, despite the variation in study designs (Table 5).

Table 5. Summary Comparison of Standard Care vs. Frailty + BNP Integrated Screening Pathway

Parameter	Standard Symptom-Based Care	Frailty + BNP Screening Pathway	Relative Improvement
New HF Diagnoses (per 1,000 screened)	12–18	30–45	↑ 2.5–3× more new diagnoses [9,10,13]
Time-to-Diagnosis	6–12 months (often post-hospitalization)	1–3 months (pre-symptomatic phase)	↓ ~60% delay reduction [9,10]
Hospital Admissions (6 mo – 1 yr)	35–40%	25–28%	↓ 18–30% admission reduction [8,14,17,18]
Mortality (12 mo)	~12–15%	~9–11%	↓ ~20% relative reduction (trend) [14,17]
Quality of Life (KCCQ / EQ-5D)	Baseline or minimal improvement	+10–15-point improvement sustained at 12 mo	↑ Enhanced functional and symptom stability [7,18]
Cost per New Diagnosis (USD)	≈ $1,500–1,800	≈ $1,000–1,200	↓ 30–35% cost reduction via early triage [9,10,18]
Implementation Feasibility	Reactive, hospital-centered	Proactive, community-integrated	Supported by nurse-led and POC-based models [10,18]

4.6 Clinical and Practical Relevance of the Frailty plus BNP Screening Model

Heart failure (HF) detection can undergo a revolutionary change from reactive hospital-based diagnosis to proactive, community-centered prevention with the merging of frailty and natriuretic peptide (BNP/NT-proBNP) screening. Over 64 million people worldwide suffer from heart failure (HF), which accounts for 1%–2% of healthcare costs and a considerable death rate. Over 80% of cases are discovered during hospitalisation, and delayed diagnosis costs the UK alone up to £2 billion a year [15,18,36,37]. Thus, early biomarker-guided population screening is an essential step in lessening the burden on patients and the system. The results of this investigation are highly consistent with current recommendations. The NICE NG106 and ESC 2023 frameworks support early community-based screening backed by interdisciplinary teams and suggest BNP/NT-proBNP as first-line testing for suspected HF [13,18]. Similar to this, the AHA 2025 PREVENT-HF paradigm encourages risk-based prevention by identifying "pre-HF" states prior to the onset of symptoms utilising natriuretic peptides and echocardiography [17]. Particularly for older, multimorbid people, incorporating frailty scoring into these models improves diagnostic accuracy [1,5,13,18]. The frailty plus BNP approach is still straightforward, transparent, and affordable when compared to sophisticated AI or EHR-driven screening systems. AI-based systems achieve diagnostic accuracies of AUC 0.80–0.85 but require data infrastructure and governance that limit scalability in routine care [7,9]. On the other hand, frailty evaluation and NP testing can be easily integrated into current GP or nurse-led clinics, offering a similar diagnostic yield without the need for digital barriers [9,18]. When paired with biomarker testing, frailty improves specificity by independently predicting the start of HF and correlating with inflammation and elevated BNP [1,5,12]. In non-acute HFpEF populations, studies show BNP/NT-proBNP sensitivity of 65–70% and specificity close to 80%. By lowering false negatives, the integration of frailty ratings improves detection [4,16]. Nurse-led models such as those described by Hill et al. demonstrate the feasibility of implementing this approach within chronic-disease management frameworks [1,18].

Clinically, the combined strategy reduces hospitalisations by up to 30% within a year, accelerates the diagnosis of heart failure, and reduces the time it takes to diagnose the condition by four to six months [9,10,14,17,18]. Economic analyses show that BNP-based triage is less costly than imaging, with a cost reduction of up to 35% per diagnosis and testing costs per patient ranging from $25 to $40 [9,10,16]. Incorporating frailty + BNP screening into "HF risk clinics" allows for comprehensive, one-visit assessments that align with ESC and AHA goals for early, integrated cardiovascular care, including rapid echocardiography referral, medication review, and rhythm assessment [13,17]. Implementation-related problems include limited access to echocardiography and uneven GP participation, particularly in distant locations [15]. By overcoming these barriers with tele-echocardiography, mobile diagnostics, and structured referral pathways, broader

adoption might be guaranteed. Digital technologies can automate frailty rating and BNP order triggers through EHR systems, but data confidentiality and fair access must be guaranteed to avoid disparities [7,9,17,18]. From an ethical perspective, population screening must prioritise informed consent, data security, and patient empowerment. Frailty assessment could guide supportive care approaches that prioritise mobility, nutrition, and psychological well-being rather than being stigmatised [5,13,17]. Through transparent communication, group decision-making, and inclusive technology use, early HF detection fosters autonomy and trust rather than fear [15,18]. Therefore, a tried-and-true, cost-effective, and patient-centered method of early HF detection is provided by combining frailty and BNP testing. It demonstrates measurable gains in quality of life, hospitalisation reduction, timeliness, and diagnostic output, and it fosters digital innovation and complies with international standards. By enabling proactive, equitable, and ethically grounded care, this approach redefines HF management as preventative rather than reactive. [19,27, 38–40].

5. LIMITATIONS AND FUTURE DIRECTIONS

Although the style of this narrative review involves inherent constraints, it offers an integrated overview of frailty and natriuretic-peptide-based screening in primary care. Establishing consistent thresholds for biomarker interpretation or frailty scoring is challenging due to heterogeneity within primary-care groups, which includes variations in age, comorbidities, healthcare access, and diagnostic methods. Since there are no randomized trials that directly assess the combined frailty and BNP route, the majority of the evidence that is currently available is observational, which limits the ability to draw conclusions about causality. Additionally, the focus of economic analyses on UK health systems limited their application to areas with differing care arrangements, and it was unable to completely rule out any degree of dataset overlap between research. In order to ascertain the clinical and policy relevance of frailty plus BNP screening, these limitations highlight the need for multicenter diagnostic-cohort studies, more comprehensive health-economic evaluations, and integration with digital risk-stratification and remote-monitoring approaches.

6. CONCLUSION

The combined use of frailty assessment and BNP/NT-proBNP screening provides a practical and evidence-based approach for the early detection of heart failure in primary care. By identifying high-risk, often asymptomatic individuals, this model shortens diagnostic delays, reduces hospital admissions, and enables timely initiation of therapy. It aligns closely with ESC, NICE, and AHA guidelines promoting proactive, community-based management and can be integrated into existing GP and nurse-led chronic-disease clinics with minimal disruption. Although current evidence remains largely observational and concentrated within UK health systems, results consistently demonstrate improved diagnostic yield, cost-effectiveness, and continuity of care compared with traditional symptom-based referrals. To confirm long-term results and extrapolate results to other populations, more randomised, multicenter trials are required. All things considered, the frailty plus BNP pathway is a workable and preventive approach that moves heart failure detection from delayed identification to prompt, community-driven intervention.

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