

# Evaluation of a combined symptom-based questionnaire and capillary natriuretic peptides testing for early detection of heart failure: a Heart Failure Awareness Days nationwide screening study (DEPIC FR)

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## Aims

Early diagnosis of heart failure (HF) remains challenging, as symptoms are often nonspecific or absent. We aimed to evaluate the performance of a two-step screening strategy combining a symptom-based questionnaire—based on the acronym EPOF (dyspnoea, weight gain, oedema, fatigue in French)—and capillary NT-proBNP fingerstick testing to identify individuals with elevated cardiovascular risk or preclinical HF.

## Methods and results

We screened 2481 adults without known HF during a nationwide, community-based campaign held in 21 hospital cardiology centres across France. All participants underwent capillary NT-proBNP testing using a point-of-care assay. A threshold of >125 pg/mL, per European Society of Cardiology guidelines for ruling out HF in ambulatory settings, was exceeded in 419

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individuals (16.9%), of whom 36.5% were asymptomatic. Conversely, 30.5% of those with NT-proBNP  $\leq$ 125 pg/mL reported at least one symptom.

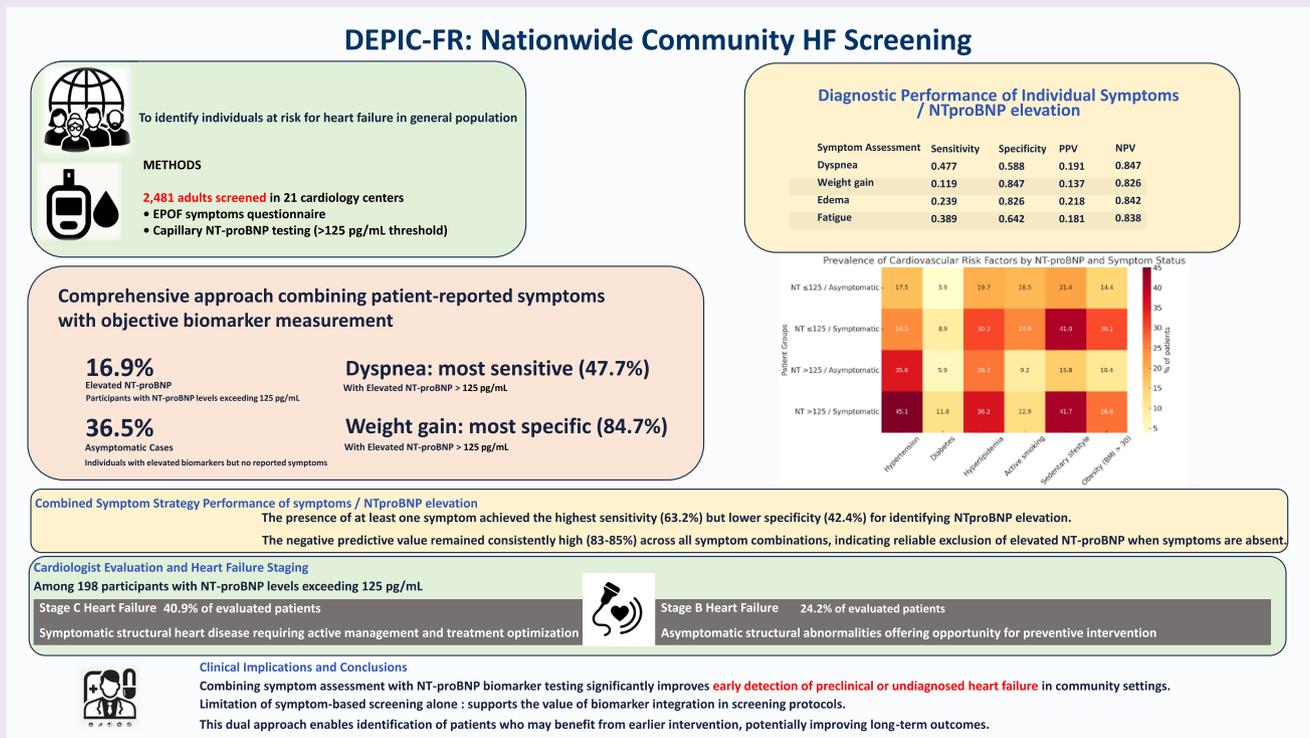
Symptom-based screening alone had limited diagnostic accuracy for detecting NT-proBNP  $>$ 125 pg/mL. The presence of  $\geq$ 1 symptom yielded a sensitivity of 63.2% and a specificity of 42.4%. Dyspnoea was the most sensitive symptom (47.7%), while weight gain had the highest specificity (84.7%). In contrast, the absence of both symptoms and NT-proBNP elevation was associated with a high negative predictive value (85.4%).

Among the 198 participants with NT-proBNP  $>$ 125 pg/mL who underwent cardiologist-led evaluation, 40.9% were classified as symptomatic HF (Stage C) and 24.2% as preclinical HF (Stage B).

## Conclusion

Combining symptom assessment with NT-proBNP testing improves early identification of at-risk individuals and may help uncover a significant proportion of undiagnosed or early-stage HF.

## Graphical abstract



## Keywords

Heart failure screening • NT-proBNP • Primary care • Clinical symptoms

## Key Learning Points

### What is already known:

- Early diagnosis of heart failure (HF) in the community remains challenging due to the nonspecific nature of symptoms.
- NT-proBNP measurement is recommended by European Society of Cardiology guidelines for HF diagnosis in ambulatory settings but is rarely implemented in community screening campaigns.

### What this study adds:

- A simple, symptom-based questionnaire (EPOF-questionnaire: dyspnoea, weight gain, oedema, fatigue) combined with capillary NT-proBNP testing identifies individuals at risk of preclinical or undiagnosed HF.
- This two-step screening approach could help improve early detection and management of HF at the population level.

## Introduction

Heart failure (HF) is frequently underdiagnosed in its early stages, particularly in community settings where access to imaging is limited and symptoms may be nonspecific. Delays in diagnosis contribute to missed therapeutic opportunities, avoidable hospitalizations, and excess mortality.<sup>1–3</sup> In France, as in many European countries, a substantial proportion of HF cases remain unrecognized, especially among older adults and patients managed in primary care.

The European Society of Cardiology (ESC) recommends to ground a HF diagnosis on the presence of typical symptoms, elevated natriuretic peptides, and structural or functional cardiac abnormalities.<sup>4</sup> However, symptoms such as dyspnoea or fatigue are frequently attributed to non-cardiac causes, and echocardiography is not always readily available in frontline care.<sup>5</sup> As a result, early-stage HF is often undetected, particularly in populations at higher risk such as women and the elderly.<sup>6,7</sup>

To raise awareness and support early identification, national educational campaigns in France have promoted the use of the acronym 'EPOF'—dyspnoea, weight gain, peripheral oedema, and fatigue in French—as a practical symptom-based tool targeting the general population and primary care providers.<sup>1</sup> Although widely disseminated to identify patients with acute HF, the diagnostic performance of EPOF-questionnaire in real-world screening remains untested across the spectrum of HF stages in community populations.

NT-proBNP has emerged as a validated biomarker for risk stratification and for guiding the diagnostic work-up of HF.<sup>5,8</sup> In ambulatory care, a threshold of 125 pg/mL is recommended by the ESC guidelines to rule out HF in patients with symptoms suggestive of the disease.<sup>4</sup> Point-of-care capillary NT-proBNP testing offers rapid, low-complexity implementation in out-of-hospital settings, and has shown strong correlation with venous assays.<sup>9</sup>

Combining symptom-based screening with NT-proBNP measurement may offer a pragmatic, scalable approach to improve early detection of HF in the general population.<sup>10,11</sup> However, the individual and combined diagnostic value of these tools remains poorly characterized in large-scale screening campaigns.

The present study aimed to evaluate the diagnostic performance of EPOF-questionnaire symptoms and NT-proBNP fingerstick testing—used alone or in combination—for the early identification of individuals at risk of HF in adults without known HF. This screening campaign was part of the national Heart Failure Awareness Days (HFA Days), an annual initiative led by the Heart Failure Association of the ESC (HFA-ESC). This specific national initiative was endorsed by the French Society of Cardiology and supported by public health authorities. The campaign aimed to raise awareness of HF among the general population, encourage early recognition of symptoms, and promote screening in community settings. We also sought to characterize the clinical and echocardiographic profiles of patients identified through this dual-step screening strategy.

## Methods

### Trial design and oversight

DEPIC FR (Dépistage de l'Insuffisance Cardiaque en France) was a prospective, multicentre, cross-sectional screening study conducted in France between September 2024 and January 2025. The study was coordinated by the Heart Foundation (Vincennes, France) and carried out in 21 cardiology centres, including both public and private hospitals. Each site organized a one-day screening campaign following a standardized protocol. The study was approved by the national ethics committee (Comité de Protection des Personnes Ouest 5; ID-RCB: 2024-A00447-40) and conducted in accordance with the Declaration of Helsinki. The Heart Foundation acted as the sponsor and had no role in study design, data collection, or data analysis. All investigators vouch for the accuracy and completeness of the data. This screening initiative was conducted in the context

of the French HFA Days, a coordinated effort to promote public engagement, improve recognition of early symptoms, and mobilize cardiology services across the country. The campaign involved national and local media coverage, press conferences, distribution of educational materials, and active collaboration with general practitioners and pharmacists. A detailed overview of the campaign structure and communication tools is available in the [Supplementary material online, appendix](#).

### Study participants

Participants were recruited through a public awareness campaign conducted during the weeks before the screening day, when individuals were invited to undergo HF screening at hospitals across France. This campaign relied on local press, social media, general practitioner outreach, and promotion through cardiology networks. Eligible participants were adults aged 18 years or older, affiliated with the French national health insurance system, and without a known history of HF. Individuals under legal protection or unable to provide informed consent were excluded. All participants provided written informed consent before enrolment.

### Screening procedure

On the screening day, each hospital hall hosted a designated screening space, structured into three zones: an information desk; a confidential consultation area where staff collected medical history, obtained informed consent, provided results, and referred participants to a cardiologist if needed; and a dedicated space for biological testing. Each participant underwent capillary NT-proBNP measurement using a fingerstick point-of-care assay (LumiraDx NT-proBNP; Roche Diagnostics, Basel, Switzerland). This method requires a small capillary blood sample and yields results within minutes. It has previously demonstrated good correlation with venous NT-proBNP levels,<sup>9</sup> supporting its use in out-of-hospital screening environments. Participants also completed a standardized symptom questionnaire assessing four clinical features suggestive of HF—dyspnoea, peripheral oedema, fatigue, and recent weight gain. These items correspond to the French acronym EPOF (Essoufflement, Prise de poids, Oedèmes, Fatigue); throughout the manuscript, we refer to this tool as the EPOF-questionnaire. Additional clinical information was collected, including age, sex, body weight and height, cardiovascular risk factors, comorbidities, and medication use.

### Follow-up of NT-proBNP-positive individuals

Participants with a capillary NT-proBNP value greater than 125 pg/mL, i.e. NT-proBNP-positive individuals, were encouraged to consult a cardiologist in routine care. A summary report containing the NT-proBNP result and the symptom profile was provided to facilitate the follow-up. Cardiologists were asked to complete a standardized case report form including clinical evaluation, echocardiographic parameters, and classification according to the ESC HF staging system. As the screening was conducted outside the patients' healthcare pathway and without access to their medical records, participants with NT-proBNP >125 pg/mL were invited to consult a cardiologist in routine care. This approach preserved medical autonomy, and respected healthcare system regulations and ethical committee advice not to interfere with the patients' medical pathway. A standardized report was provided to facilitate referral to a cardiologist, but follow-up evaluation was not mandatory within the study protocol. As such, no formal diagnostic classification (e.g. ESC staging) could be applied to the full cohort, and the analysis of screening performance [including negative predictive value (NPV)] was based on NT-proBNP >125 pg/mL as the predefined screening threshold, not on confirmed HF diagnosis. In the subgroup of patients who underwent cardiologist-led evaluation, ESC 2021 criteria were used to classify HF stages and assess clinical profiles.

### Study outcomes and statistical analyses

The primary objective of the study was to evaluate the diagnostic performance of symptom-based screening in identifying individuals with elevated NT-proBNP levels (>125 pg/mL), which served as a proxy for suspected or preclinical HF in the general screened population. Sensitivity, specificity, positive predictive value (PPV), and NPV were calculated for each symptom and for predefined combinations, using NT-proBNP >125 pg/mL as the reference threshold for positivity in the primary analysis.

In the subgroup of participants who underwent full cardiologist evaluation ( $n = 198$ ), the cardiologist's final classification—based on clinical examination, echocardiographic findings, and ESC 2021 criteria—was considered the diagnostic reference standard.

Secondary objectives included estimating the prevalence of NT-proBNP  $>125$  pg/mL in the overall population, comparing the clinical characteristics of symptomatic and asymptomatic participants, and identifying the cardiovascular profile of individuals with NT-proBNP elevation but no symptoms. Of note, diagnostic classification into ESC 2021 HF stages (Stages A, B, and C) was only possible in the subgroup of patients who underwent a full cardiologist-led evaluation with echocardiography ( $n = 198$ ). In the overall population, NT-proBNP  $>125$  pg/mL was used as a predefined screening threshold for descriptive and performance analyses, but does not constitute a diagnostic confirmation of HF.

Statistical analyses were performed using R software (version 4.3.0). Continuous variables were reported as means  $\pm$  standard deviations and compared using Student's *t*-tests or one-way analysis of variance. Categorical variables were reported as counts and percentages, and compared using  $\chi^2$  tests. A heatmap was generated to visualize the prevalence of cardiovascular risk factors—including hypertension (HTA), diabetes, dyslipidemia, obesity [Body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>], and coronary artery disease—across four subgroups defined by crossing NT-proBNP level ( $\leq 125$  or  $>125$  pg/mL) and symptom presence (yes/no). A *P*-value  $<0.05$  (two-tailed) was considered statistically significant.

## Results

### Patient characteristics according to NT-proBNP threshold

A total of 2481 individuals were included in the screening campaign, with a mean age of  $55 \pm 14$  years, and 72% were women. The distribution of capillary NT-proBNP values is shown in [Figure 1](#). The median NT-proBNP concentration was 55 pg/mL [IQR: 50–97], with 60.4% of participants having values between 50 and 75 pg/mL. A total of 419 participants (16.9%) had NT-proBNP values  $>125$  pg/mL. Their baseline characteristics are described in [Table 1](#). Compared to those with NT-proBNP  $\leq 125$  pg/mL, they were significantly older (66.6 vs. 52.0 years,  $P < 0.001$ ), more likely female (78.1% vs. 71.3%,  $P = 0.006$ ), and more likely had cardiovascular comorbidities, including hypertension (41.6% vs. 21.5%,  $P < 0.001$ ), diabetes (9.6% vs. 6.8%,  $P = 0.05$ ), and coronary artery disease (6.1% vs. 2.3%,  $P < 0.001$ ). They also had higher rates of hyperlipidaemia (32.5% vs. 25.8%), while active smoking (11.5% vs. 22.2%) and obesity (20.8% vs. 23.5%) were less frequent in the NT-proBNP  $>125$  pg/mL group. Sedentary lifestyle was equally prevalent in both groups (31.9% vs. 32.6%). Individuals with NT-proBNP  $>125$  pg/mL were also more frequently followed-up by a cardiologist (44.4% vs. 22.9%,  $P < 0.001$ ), and to have had a cardiologist follow-up before the study (44.4% vs. 22.9%,  $P < 0.001$ ). Of note 4% of participants had NT-proBNP levels  $>300$  pg/mL.

### Symptoms profile and diagnostic performance

Symptoms potentially related to HF were reported by 1453 individuals (58.6% of the population), while 1028 (41.4%) were asymptomatic. Among symptomatic individuals, 575 participants (23.2%) reported only one symptom, 543 (21.9%) reported two, 226 (9.1%) reported three, and 109 (4.4%) presented all four predefined symptoms. The most frequently reported symptom was dyspnoea (42.3%), followed by fatigue (36.3%), peripheral oedema (18.5%), and recent weight gain (14.7%).

Compared to asymptomatic individuals, symptomatic participants were slightly older (55.1 vs. 53.7 years) and more likely had cardiovascular comorbidities, including hypertension (30% vs. 20%), diabetes (10% vs.  $<1\%$ ), and more frequent cardiologist follow-up (30% vs. 20%). Importantly, although symptoms were associated with a higher burden of cardiovascular risk factors, a substantial proportion of asymptomatic individuals also presented underlying risk markers.

To assess the clinical utility of symptoms in community screening, we evaluated their ability to identify individuals with NT-proBNP  $>125$  pg/mL—a threshold recommended by ESC guidelines for rule-out testing in ambulatory settings. The performance of individual and combined symptoms in detecting elevated NT-proBNP is reported in [Table 2](#). Dyspnoea showed the highest sensitivity (47.7%) and a NPV of 84.7%, while weight gain was the most specific symptom (84.7%) but had low sensitivity (11.9%). The presence of at least one symptom increased sensitivity (63.2%) but remained poorly specific (42.4%). Conversely, the combination of all four symptoms was rare (4.3%) but highly specific (95.6%), albeit with low sensitivity and PPV (16.5%).

### Cross-classification by NT-proBNP level and symptom status

To better characterize the population flagged by the screening strategy, we stratified participants according to NT-proBNP level ( $\leq 125$  vs.  $>125$  pg/mL) and the presence or absence of EPOF symptoms. This yielded four subgroups: (1) NT-proBNP  $\leq 125$  pg/mL and asymptomatic, (2) NT-proBNP  $\leq 125$  pg/mL and symptomatic, (3) NT-proBNP  $>125$  pg/mL and asymptomatic, and (4) NT-proBNP  $>125$  pg/mL and symptomatic. This cross-classification was used to explore whether NT-proBNP, as recommended by ESC guidelines for ambulatory triage, could help identifying individuals with a high cardiovascular risk profile, even in the absence of typical symptoms.

The characteristics of the four cross-classified subgroups are summarized in [Table 3](#). As expected, individuals in the NT-proBNP  $>125$  pg/mL and symptomatic group were the oldest (mean age 66.4 years) and had the highest overall burden of cardiovascular risk factors. In this group, 45.1% had hypertension, 11.8% type 2 diabetes, 26.8% obesity, and 38.2% reported hyperlipidaemia. Interestingly, participants with elevated NT-proBNP but no reported symptoms (group 3) displayed a comparable risk profile, with a similar mean age (66.9 years), and high rates of hypertension (35.6%), hyperlipidaemia (30.4%), and ischaemic heart disease (7.7%).

In contrast, symptomatic individuals with normal NT-proBNP values (group 2) had a younger age (52.5 years), and while they reported more symptoms, they had lower prevalence of objective cardiovascular risk factors—hypertension (24.5%), obesity (32.4%), and diabetes (8.9%)—than their NT-proBNP-positive counterparts.

[Figure 2](#) presents a heatmap displaying the prevalence of major cardiovascular risk factors across the four groups. The colour gradient highlights the additive burden of risk in biomarker-positive groups, regardless of symptom status, reinforcing the potential utility of NT-proBNP in revealing otherwise unrecognized cardiovascular risk.

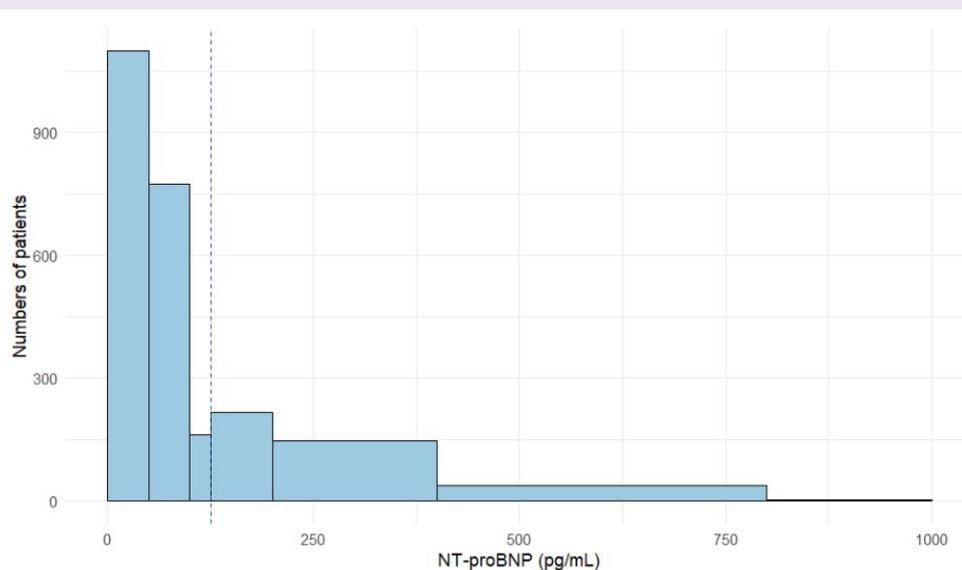
### Cardiologist-led assessment in a subset of NT-proBNP-positive individuals

Among the 419 participants with capillary NT-proBNP  $>125$  pg/mL, ultimately, only 198 participants returned complete follow-up data after consultation, and 185 of them had confirmed venous NT-proBNP values  $>125$  pg/mL.

The correlation between the two methods was excellent (Pearson's  $r = 0.91$ ; intraclass correlation coefficient = 0.81), with minimal bias on Bland–Altman analysis (mean difference  $-9.6$  pg/mL). These results confirm the reliability of capillary NT-proBNP testing in ambulatory and community-based settings.

The ESC 2021 classification enabled further phenotypic stratification. A total of 27 participants (13.6%) were classified as Stage A (no symptoms or structural cardiac abnormalities), 48 (24.2%) as Stage B (asymptomatic with structural abnormalities), and 81 (40.9%) as Stage C (symptomatic HF with structural abnormalities).

Interestingly, a distinct group of 42 participants (21.2%) reported typical HF symptoms and had elevated NT-proBNP, but no detectable structural cardiac abnormalities on echocardiography. These individuals



**Figure 1** Distribution of NT-proBNP values (capillary testing). Histogram showing the distribution of capillary NT-proBNP concentrations in 2481 individuals without known heart failure. Bars reflect predefined clinically relevant intervals, resulting in unequal bin widths. The vertical dashed line indicates the European Society of Cardiology-recommended rule-out threshold of 125 pg/mL for ambulatory patients.

**Table 1** Baseline characteristics of patients according to the NT-proBNP level

Characteristics	NT-proBNP ≤ 125 (n = 2062)	NT-proBNP > 125 (n = 419)	P-value*
Age, years (mean ± SD)	52.0 ± 13.9	66.6 ± 13.2	<0.001
Female sex, n (%)	1468 (71.3%)	324 (78.1%)	0.006
Weight, kg (mean ± SD)	74.7 ± 16.6	70.3 ± 15.4	<0.001
BMI, kg/m <sup>2</sup> (mean ± SD)	26.5 ± 5.8	25.8 ± 5.4	0.013
Previous follow-up by a cardiologist, n (%)	463 (22.9%)	182 (44.4%)	<0.001
Hypertension, n (%)	432 (21.5%)	169 (41.6%)	<0.001
Diabetes, n (%)	138 (6.8%)	40 (9.6%)	0.050
Dyslipidemia, n (%)	524 (25.8%)	134 (32.5%)	0.006
History of coronary artery disease, n (%)	45 (2.3%)	24 (6.1%)	<0.001
Active smoking, n (%)	453 (22.2%)	48 (11.5%)	<0.001
Sedentary lifestyle, n (%)	659 (32.6%)	129 (31.9%)	0.83
Dyspnoea, n (%)	849 (41.4%)	198 (48.9%)	0.006
Peripheral oedema, n (%)	359 (17.6%)	100 (24.0%)	0.002
Fatigue, n (%)	738 (36.0%)	163 (39.3%)	0.23
Recent weight gain,*** n (%)	316 (15.4%)	50 (12.1%)	0.093

\*Statistical comparisons were made using Student's *t*-test or  $\chi^2$  test, as appropriate. Significance thresholds:

\*\**P* < 0.001; *P* < 0.01; *P* < 0.05.

\*\*\*More than 2 kg in less than 48 h.

—referred to as 'Symptoms only'—fall outside the ESC staging system, which requires imaging findings for classification beyond Stage A.

Among structural abnormalities, the most frequent finding was left atrial enlargement, with a mean indexed left atrial volume (LAVi) of  $34 \pm 13$  mL/m<sup>2</sup>,<sup>15,16</sup> whereas only 8% of the participants had atrial fibrillation.

Despite identification of symptomatic patients with echocardiographic abnormalities (Stage C), only 18% received at least one

guideline-recommended HF therapy, including SGLT2 inhibitors, loop diuretics, or mineralocorticoid receptor antagonist (MRAs).

## Discussion

In this nationwide community-based screening initiative conducted as part of the 2025 HFA Day in France, 16.9% of participants without

**Table 2** Diagnostic performance of symptoms in indemnifying NT-proBNP > 125 pg/mL

Test	Sensitivity	Specificity	PPV	NPV
Symptoms including in the questionnaire				
Dyspnoea	0.477	0.588	0.191	0.847
Weight gain	0.119	0.847	0.137	0.826
Oedema	0.239	0.826	0.218	0.842
Fatigue	0.389	0.642	0.181	0.838
Combination of symptoms				
≥1 symptom	0.632	0.424	0.182	0.85
≥2 symptoms	0.403	0.656	0.192	0.844
≥3 symptoms	0.146	0.867	0.182	0.833
All 4 symptoms	0.043	0.956	0.165	0.831

Performance metrics (sensitivity, specificity, PPV, and NPV) were calculated using NT-proBNP >125 pg/mL as the screening threshold, in accordance with ESC recommendations for ambulatory settings. These values do not reflect a diagnostic assessment of heart failure, which was only performed in the cardiologist-evaluated subgroup. PPV, positive predictive value; NPV, negative predicted value.

known HF had a capillary NT-proBNP concentration >125 pg/mL. While this proportion exceeds the expected prevalence of clinically diagnosed HF in the general population—estimated between 1% and 2% overall and up to 10% in individuals over 70 years of age<sup>2,12</sup>—it does not reflect confirmed HF diagnoses, but rather a biomarker-based identification of individuals potentially at risk.

Among the 419 participants with NT-proBNP > 125 pg/mL, a subset of 198 underwent full clinical and echocardiographic assessment by a cardiologist. Based on ESC staging criteria, 13.6% were classified as Stage A (risk factors only, no symptoms or structural abnormalities), 24.2% as Stage B (asymptomatic with structural abnormalities), and 40.9% as Stage C (symptomatic HF with structural abnormalities). An additional 21.2% presented with symptoms and NT-proBNP elevation but no echocardiographic abnormalities—highlighting a ‘Symptoms only’ group not currently captured by the ESC staging system.

These findings are consistent with previous population-based studies such as ICPS2 and Handicap-Santé,<sup>1,12</sup> which also revealed a high burden of subclinical cardiac abnormalities in individuals without a formal HF diagnosis. Our study further demonstrates that combining a brief symptom questionnaire with capillary NT-proBNP testing can uncover a wide spectrum of at-risk individuals in the general population—many of whom would not have been identified through symptoms or clinical evaluation alone. This initiative also illustrates the public health potential of HF Awareness Days not only to raise awareness but to enable large-scale cardiovascular screening through a pragmatic and reproducible model.

## Reliability and feasibility of capillary NT-proBNP testing

From an implementation perspective, our findings confirm both the feasibility and reliability of capillary NT-proBNP testing in community settings. In the subgroup with paired venous and capillary samples, the agreement between the two methods was excellent, with strong correlation coefficients and minimal bias. These results are consistent with previous studies demonstrating that point-of-care NT-proBNP testing can be performed accurately outside hospital environments, including ambulatory and primary care settings.<sup>9,12</sup> The fingerstick assay used in our study offers several practical advantages: it requires only a small capillary blood sample, yields results within minutes, and can be performed by trained non-laboratory personnel. These attributes make capillary NT-proBNP testing particularly well-suited for

population-level screening and outreach initiatives, including those conducted in primary care, pharmacies, and public health campaigns. Its simplicity, speed, and high patient acceptability position it as a scalable and actionable tool for early detection strategies targeting individuals who may otherwise remain undiagnosed.

## Diagnostic performance of NT-proBNP vs. symptoms

Despite their central role in clinical assessment, symptoms alone showed limited accuracy in detecting individuals with elevated NT-proBNP levels. Among the four symptoms assessed, dyspnoea was the most sensitive for identifying participants with NT-proBNP >125 pg/mL, although its performance remained suboptimal. Conversely, weight gain demonstrated higher specificity but was infrequently reported. Overall, individual symptoms and their combinations lacked sufficient diagnostic precision to reliably identify early or preclinical cardiac involvement. In contrast, NT-proBNP testing—used alone or alongside symptom assessment—proved more effective for detecting individuals at risk.

Our findings confirm that relying solely on symptom-based screening is inadequate to detect individuals with elevated NT-proBNP levels or early cardiac involvement, a limitation already described in real-world studies of diagnostic delay.<sup>1,2</sup> In our cohort, over one-third of participants with NT-proBNP >125 pg/mL reported no symptoms, despite being older and carrying a higher burden of cardiovascular risk factors, including hypertension and ischaemic heart disease, than symptomatic individuals with normal NT-proBNP levels.

This biomarker-positive but asymptomatic subgroup likely represents a silent high-risk population, undetectable through symptoms alone. Heatmap analysis confirmed that their comorbidity profile was comparable to, or even greater than, that of symptomatic individuals, supporting the hypothesis that NT-proBNP reveals latent cardiovascular risk missed by clinical evaluation alone.<sup>4,6,10</sup> These data strongly argue for measuring NT-proBNP levels independently of symptoms, to detect cardiac dysfunction at earlier stages.

While NT-proBNP >125 pg/mL is not diagnostic of HF by itself, its use as a triage biomarker—especially when combined with structured symptom assessment—may help uncover a broader population with unrecognized cardiovascular disease. Conversely, the absence of both symptoms and biomarker elevation was associated with a high NPV (85.4%), supporting the use of this dual-negative profile to safely rule out significant cardiac involvement in community-based screening.<sup>3,5,6</sup>

## Added value of NT-proBNP testing in asymptomatic individuals

Among participants with NT-proBNP >125 pg/mL, 36.5% reported no EPOF symptoms. Although asymptomatic, these individuals were older and presented a substantial burden of cardiovascular risk factors such as hypertension and ischaemic heart disease. Their biomarker elevation—despite the absence of overt symptoms—suggests early or subclinical cardiac stress, rather than isolated traditional risk.

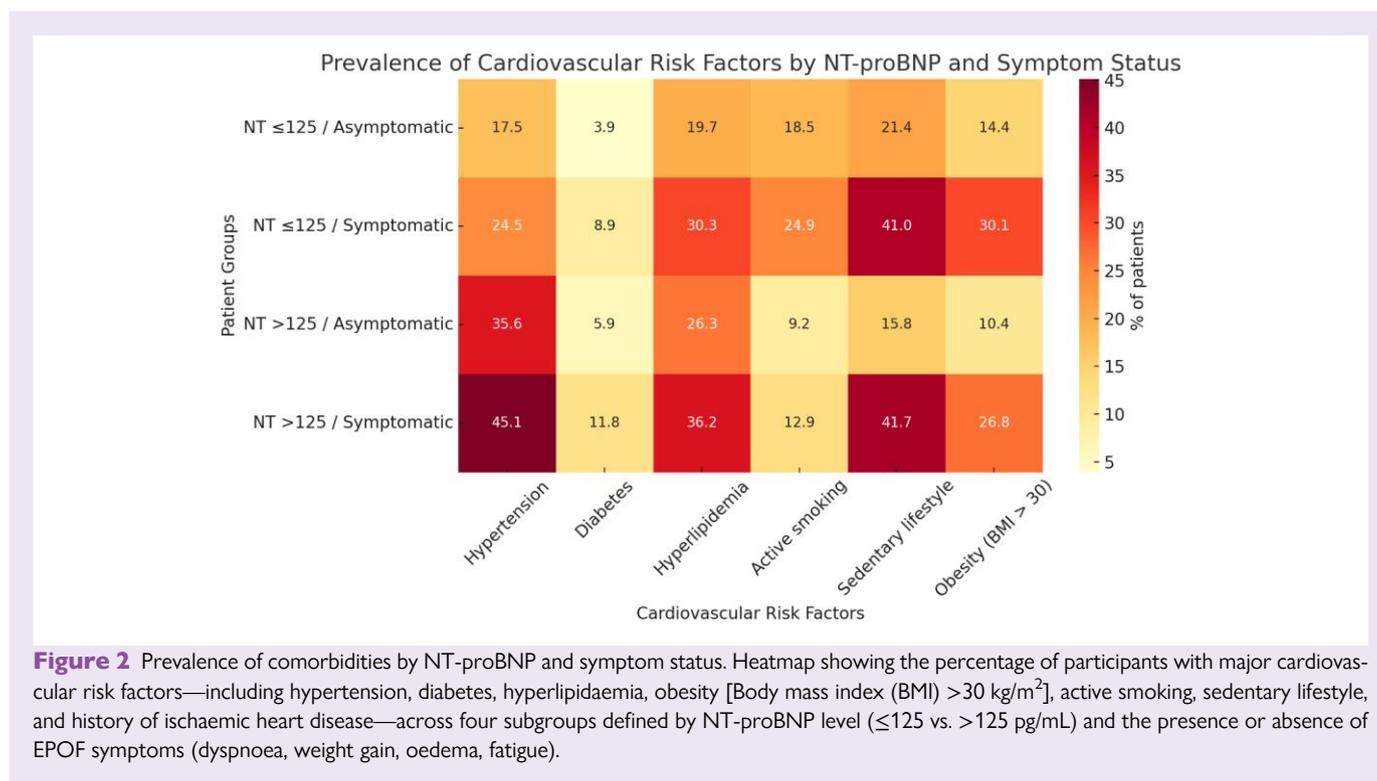
This phenotype aligns with previous evidence that NT-proBNP can detect myocardial stress before structural remodelling or symptom onset occurs.<sup>7,8,11</sup> As illustrated in the heatmap, their comorbidity profile was comparable to—or even more pronounced than—that of symptomatic participants, supporting the utility of NT-proBNP to uncover latent cardiac involvement that may otherwise go unnoticed.<sup>4,6,10</sup>

The heatmap analysis further supported this interpretation, showing that these asymptomatic but biomarker-positive individuals had comorbidity profiles comparable to, or exceeding, those of symptomatic patients.<sup>4,6,10</sup> This highlights their potential risk and the value of biomarker-based detection strategies in identifying such individuals for closer follow-up or preventive care.

**Table 3** Cross-comparison of groups based on the NT-proBNP level and the presence of symptoms

NT-proBNP (pg/L) symptoms	≤125 asymptomatic	≤125 symptomatic	>125 asymptomatic	>125 symptomatic	P-value
Age	51.3 (14.4)	52.5 (13.6)	66.9 (12.6)	66.4 (13.6)	<0.001
Weight	71.5 (15.1)	77.0 (17.3)	67.5 (13.3)	71.9 (16.3)	<0.001
Height	168.1 (9.2)	166.4 (8.5)	166.7 (8.6)	163.8 (7.8)	<0.001
BMI	25.3 (4.7)	27.7 (5.6)	24.2 (4.3)	26.8 (5.6)	<0.001
Cardiologist <sup>a</sup>	19.3%	25.6%	46.0%	43.5%	<0.001
HTA	17.5%	24.5%	35.6%	45.1%	<0.001
Diabetes	3.9%	8.9%	5.9%	11.8%	<0.001

<sup>a</sup>To receive follow-up care from a cardiologist.



**Figure 2** Prevalence of comorbidities by NT-proBNP and symptom status. Heatmap showing the percentage of participants with major cardiovascular risk factors—including hypertension, diabetes, hyperlipidaemia, obesity [Body mass index (BMI) >30 kg/m<sup>2</sup>], active smoking, sedentary lifestyle, and history of ischaemic heart disease—across four subgroups defined by NT-proBNP level (≤125 vs. >125 pg/mL) and the presence or absence of EPOF symptoms (dyspnoea, weight gain, oedema, fatigue).

Although cardiologist follow-up was more frequent in individuals with NT-proBNP >125 pg/mL, this variable likely reflects underlying cardiovascular risk—particularly hypertension and coronary artery disease. Given the strong overlap between follow-up and comorbidities, no independent comparison was made between followed and non-followed patients to avoid redundancy and misinterpretation.<sup>13,14</sup>

### Added value of a combined screening strategy and practical implications

The combination of NT-proBNP testing with a brief symptom questionnaire offers a pragmatic and scalable screening strategy. While symptoms alone lacked specificity and failed to identify a substantial proportion of at-risk individuals, NT-proBNP testing revealed early biochemical signs of cardiac stress, including in asymptomatic individuals. Conversely, participants with both normal NT-proBNP and no symptoms had a high NPV, suggesting that this combination may safely exclude significant cardiac dysfunction in low-risk individuals. These findings support a two-step approach: initial screening using capillary

NT-proBNP and symptom assessment, followed by referral for echocardiography and cardiologist evaluation in cases of NT-proBNP >125 pg/mL and/or ≥2 symptoms. This strategy is consistent with ESC recommendations for the early detection of HF,<sup>4,5</sup> and mirrors models used successfully in interventional studies such as St Vincent's Screening to Prevent Heart Failure study (STOP-HF) and NT-proBNP selected PreventiON of cArdiaC events in a population of diabetic patients without a history of cardiac disease (PONTIAC), where biomarker-guided care improved outcomes in high-risk populations.<sup>13,14</sup> Such an approach may optimize healthcare resource utilization while improving early identification and management of HF.

### Clinical evaluation of NT-proBNP-positive patients confirms diverse heart failure phenotypes

Cardiologist-led evaluation in a subset of NT-proBNP-positive participants revealed a broad spectrum of HF phenotypes. While 40.9% were

classified as Stage C and 24.2% as Stage B according to the ESC 2021 criteria,<sup>4</sup> a substantial proportion of patients could not be clearly staged despite presenting symptoms and biomarker elevation. Specifically, 21.2% of evaluated individuals had symptoms suggestive of HF and NT-proBNP >125 pg/mL, but no echocardiographic abnormalities or structural heart disease. These ‘Symptoms only’ patients fall outside the current ESC classification framework, which requires objective cardiac changes for diagnosis, yet their clinical presentation raises concern for early or subclinical HF.

The presence of this intermediate phenotype highlights a possible gap in current classification systems and suggests the need for staging tools that integrate biomarkers and symptoms—even in the absence of overt structural changes. Longitudinal studies are needed to determine whether these individuals progress towards structural heart disease, and whether early intervention may be beneficial.<sup>11</sup>

Left atrial enlargement, measured as indexed LAVi, was the most frequent echocardiographic abnormality in this cohort, with a mean value of  $34 \pm 13$  mL/m<sup>2</sup>. LAVi is a sensitive marker of chronically elevated filling pressures and early diastolic dysfunction, particularly relevant in HFpEF, whereas only 8% of the participants had atrial fibrillation reported. Its high prevalence supports its inclusion as a key imaging parameter in future screening algorithms.<sup>15,16</sup>

Despite identification of patients fulfilling diagnostic criteria for HF, treatment rates remained low: only 18% of Stage C patients received guideline-recommended therapy. This underscores the need for structured follow-up pathways post-screening, to ensure timely initiation of disease-modifying treatments.<sup>14</sup>

The experience of this HFA Days 2025 initiative combining information and screening of HF in France has proven to be highly successful, both in terms of public outreach and professional engagement. The strong mobilization of media, social networks, and healthcare teams due to the proposition of a nationwide HF screening demonstrated that such an initiative can generate a significant impact on awareness, education, and early detection of HF. Given these encouraging results, the replication of this model in other European countries appears both feasible and desirable.

## Study limitations

Several limitations should be acknowledged. First, the cross-sectional design precludes evaluation of longitudinal outcomes and prognostic impact. Future follow-up will be necessary to determine whether early identification via NT-proBNP screening leads to improved clinical trajectories. Second, symptoms were self-reported and not standardized through clinician assessment, introducing potential reporting bias. Third, only a subset (198 of 419) of participants with NT-proBNP >125 pg/mL underwent full cardiac evaluation, possibly reflecting selection bias. Fourth, echocardiographic assessments were performed locally without core-lab validation. Fifth, conditions known to affect NT-proBNP levels independently of HF (e.g. renal dysfunction, anaemia, pulmonary disease) were not systematically collected in the screening setting, which may have influenced biomarker interpretation. Finally, while the screening campaign reached a large number of individuals, its setting in specialized centres may limit generalizability to routine primary care. Nonetheless, the high participation of women and older adults suggests good external relevance.

Despite these limitations, this study provides real-world evidence supporting the use of NT-proBNP-based screening as a practical tool for early identification of HF in the general population.

## Conclusion

In this large-scale community screening initiative, a simple two-step strategy combining symptom assessment and capillary NT-proBNP testing enabled the identification of individuals with previously

unrecognized HF or at increased cardiovascular risk. The approach proved both feasible and clinically valuable, revealing a substantial number of asymptomatic participants with biomarker elevation and risk factor burden. Incorporating echocardiographic markers such as LAVi may further refine risk stratification in selected individuals. These findings support the integration of NT-proBNP-based screening into population-level strategies for the early detection of HF and related cardiovascular conditions.

## Supplementary material

Supplementary material is available at *European Heart Journal—Quality of Care and Clinical Outcomes* online.

## Author contributions

Emmanuelle Berthelot (MD (Conceptualization [lead]; Formal analysis [lead]; Funding acquisition [supporting]; Investigation [equal]; Methodology [equal]; Writing—original draft [lead])), Nathan Mewton (MD PhD (Investigation [equal]; Writing—original draft [supporting])), François Roubille (MD PhD (Investigation [equal]; Writing—review & editing [equal])), Damien Logeart (MD PhD (Investigation [equal])), Nicolas Mensancal (MD PhD (Investigation [equal])), Annabelle Jagu (MD (Investigation [equal])), Anne Celine Martin (MD PhD (Investigation [equal])), Lise Legrand (MD (Investigation [equal])), Charles Fauvel (MD (Investigation [equal])), Erwan Donal (MD PhD (Investigation [equal])), Gianluigi Savarese (Writing—review & editing [equal]), Amina Rakisheva (MD PhD (Investigation [equal])), Marco Metra (MD PhD (Writing—review & editing [supporting])), Marie Fertin (MD (Investigation [equal])), Frederic Mouquet (MD (Investigation [equal])), Emmanuelle Vermes (MD (Investigation [equal])), Jerome Costa (MD (Investigation [equal])), Mathieu Chacornac (MD (Investigation [equal])), Didier Romain (MD (Investigation [equal])), Marie-France Seronde (MD PhD (Investigation [equal])), Barnabas Gellen (MD (Investigation [equal])), Benoit Lequeux (MD (Investigation [equal])), Michel Galinier (MD PhD (Investigation [equal])), Florence Canoui Poitrine (MD PhD (Investigation [equal])), Olivier Lairez (MD PhD (Investigation [equal])), Jean Michel Tartièrre (MD PhD (Investigation [equal])), Mounira Kharoubi (Project administration [lead]), and Thibaud Damy (MD PhD (Conceptualization [lead]; Formal analysis [equal]; Funding acquisition [lead]; Investigation [equal]; Methodology [lead]; Resources [lead]; Supervision [lead]; Writing—review & editing [equal]))

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## Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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