PORTHOS
ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

PORTHOS

The Portuguese Heart Failure Prevalence Observational Study

novas evidências

Sociedade Portuguesa de CARDIOLOGIA

AstraZeneca

NOVA MEDICAL SCHOOL

On behalf of the PORTHOS Investigators

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Clinical Trials.gov Registration number NCT05434923

HF Prevalence

How to diagnose HFpEF in the community?

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Heart failure with preserved ejection fraction: everything the clinician needs to know

Patricia Campbell, Frans H Rutten, Matthew MY Lee, Nathaniel M Hawkins, Mark C Petrie

*"There are **no modern prospective, population-based studies** using natriuretic peptides and detailed echocardiography to assess the true prevalence of HFpEF".*

*"If such a study were to be conducted, especially **with a liberal interpretation of the ESC's definition of HFpEF**, it is possible that the prevalence of HFpEF would be **much higher** than currently cited".*

The Lancet. February 14, 2024 https://doi.org/10.1016/S0140-6736(23)02756-3

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Objectives

OBJECTIVES

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Primary Objective:

- **Estimate the prevalence of HF among Portuguese adults aged 50 years and older.**

Secondary Objectives:

- Determine the prevalence of **HF phenotypes** according to the LVEF
- Determine **age and sex-specific** HF prevalence rates

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Methods

METHODS

Population and sampling

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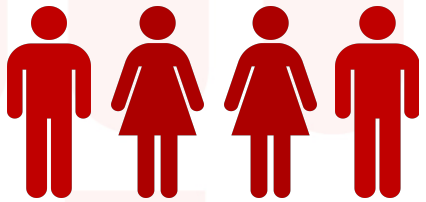
Portuguese citizens
Age ≥50 years

~ 4 260 272, Census 2011
~ 4 677 908, Census 2021



Inclusion criteria

- **Mainland Portugal**
- **Registered in the National Health Service (>99% of the population)**
- **Informed consent**

Exclusion criteria

- Living in an institution (e.g., nursing homes, prisons, military facilities)
- Being unable to speak and understand Portuguese
- Any disability limiting study participation

Participants will be selected through a **multistage sampling methodology**, using the National Health Service (SNS) registry as the sampling frame. Subjects aged 50 + registered in the Primary Care Centres Groups (ACES) will be **stratified by age and gender** and **selected randomly**.

Baptista R, Silva Cardoso J, Canhão H, et al. Portuguese Heart Failure Prevalence Observational Study (PORTHOS) rationale and design – A population-based study. *Rev Port Cardiol*. 2023;42(12):985-995.

METHODS

Case definition

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HFrEF

- **Self-reported** fatigue, shortness of breath, orthopnea or edema (≥NYHA II accessed by a structured questionnaire)
- **NT-proBNP ≥125 pg/mL**
- **LVEF ≤40%**

HFmrEF

- **Self-reported** fatigue, shortness of breath, orthopnea or edema (≥NYHA II accessed by a structured questionnaire)
- **NT-proBNP ≥125 pg/mL**
- **LVEF 41-49%**

HFpEF

- **Self-reported** fatigue, shortness of breath, orthopnea or edema (≥NYHA II accessed by a structured questionnaire)
- **NT-proBNP ≥125 pg/mL**
- **LVEF ≥50% and validating HFA-PEFF** diagnostic algorithm up to Step E with score **≥5 points***

*** HFA-PEFF score ≤ 1 points excludes HFpEF.**
2–4 points is considered indeterminate diagnosis and, therefore, not diagnostic of HFpEF

Baptista R, Silva Cardoso J, Canhão H, et al. Portuguese Heart Failure Prevalence Observational Study (PORTHOS) rationale and design – A population-based study. *Rev Port Cardiol*. 2023;42(12):985-995.

METHODS

Sampling

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Participants will be selected through a **multistage sampling methodology**, using the National Health Service (SNS) registry as the sampling frame.

First stage:
Primary sampling units (PSU) - geographical areas corresponding to Primary Care Centres Groups (ACES).

Of the 55 ACES in Portugal, 12 PSU will be selected considering their rural (<100 people per km^2), semi-urban (100 to 500people per km^2) or urban (>500 people per km^2) characteristics.

The number of PSU to be selected by region will be proportional to the size of resident population aged 50 years or above.

PSU will be selected within each ARS region by simple random sampling without replacement using the ‘‘sampling’’ package of R statistical software.

Second stage:
Subjects aged 50 years old or over registered in the ACES will be stratified by age and gender and selected randomly.

METHODS

Study design

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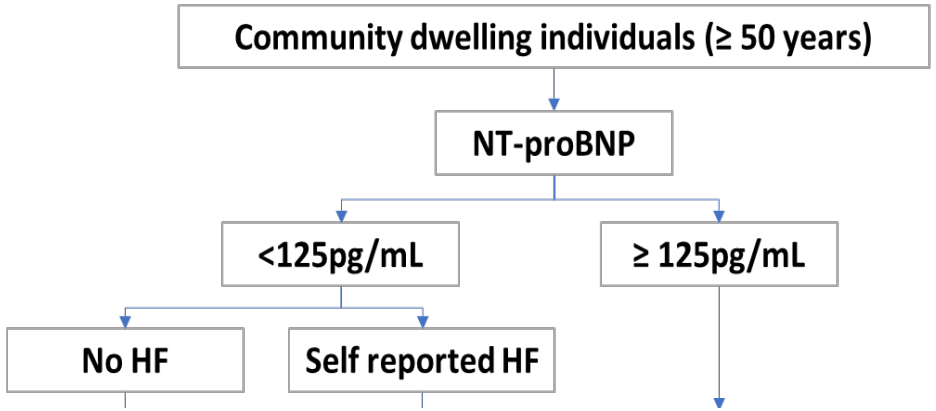

Stage 1

HF screening

- Quality of Life (EQ-5D)
- BP, HR, BMI, waist circumference
- Sociodemographic questionnaire
- 1 lead ECG (AF screening)
- BIOBANK (FMUC) (serum, plasma, DNA and RNA aliquots)

METHODS

Study design

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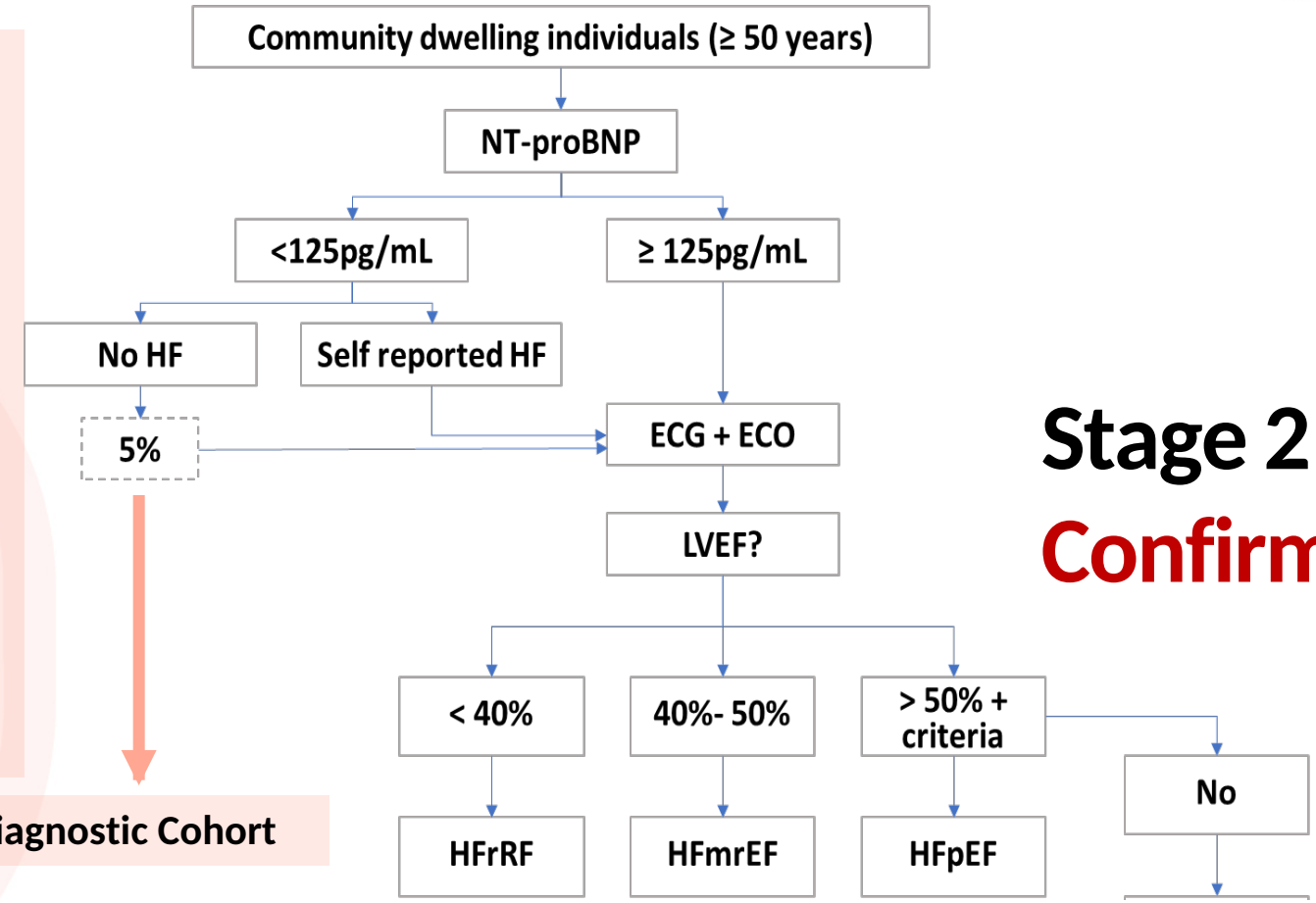
1. **Symptoms and KCCQ**
2. **Comorbidities and medical therapy**
3. **12 lead ECG**
4. **Blood tests** (HbA1c,serum creatinine, hsTn, hsCRP, liid profile)
5. **Comprehensive TTE**

- EACVI protocol
- Central lab (GE-EchoPac)
- Validation by a EACVI certified cardiologist



Stage 2
Confirmatory

METHODS

Study design

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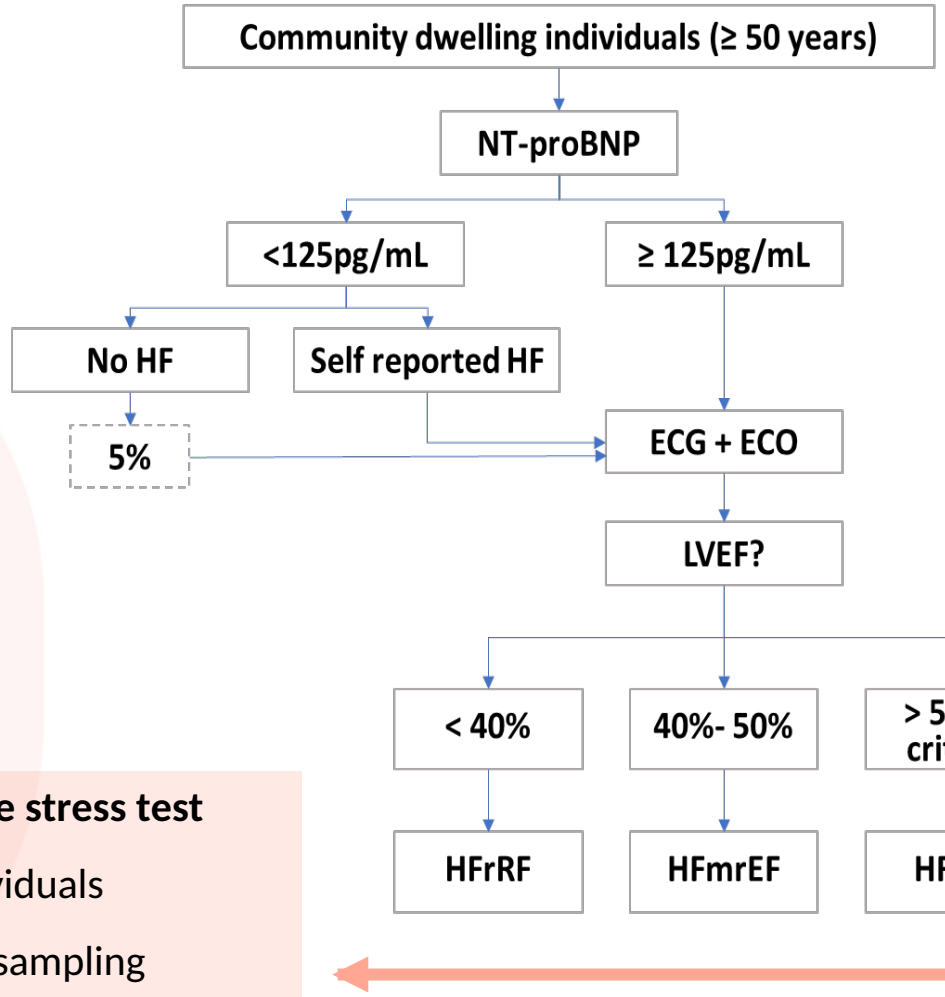


Stage 3

Exploratory

TTE exercise stress test

- ~50 individuals
- random sampling
- 2 centres

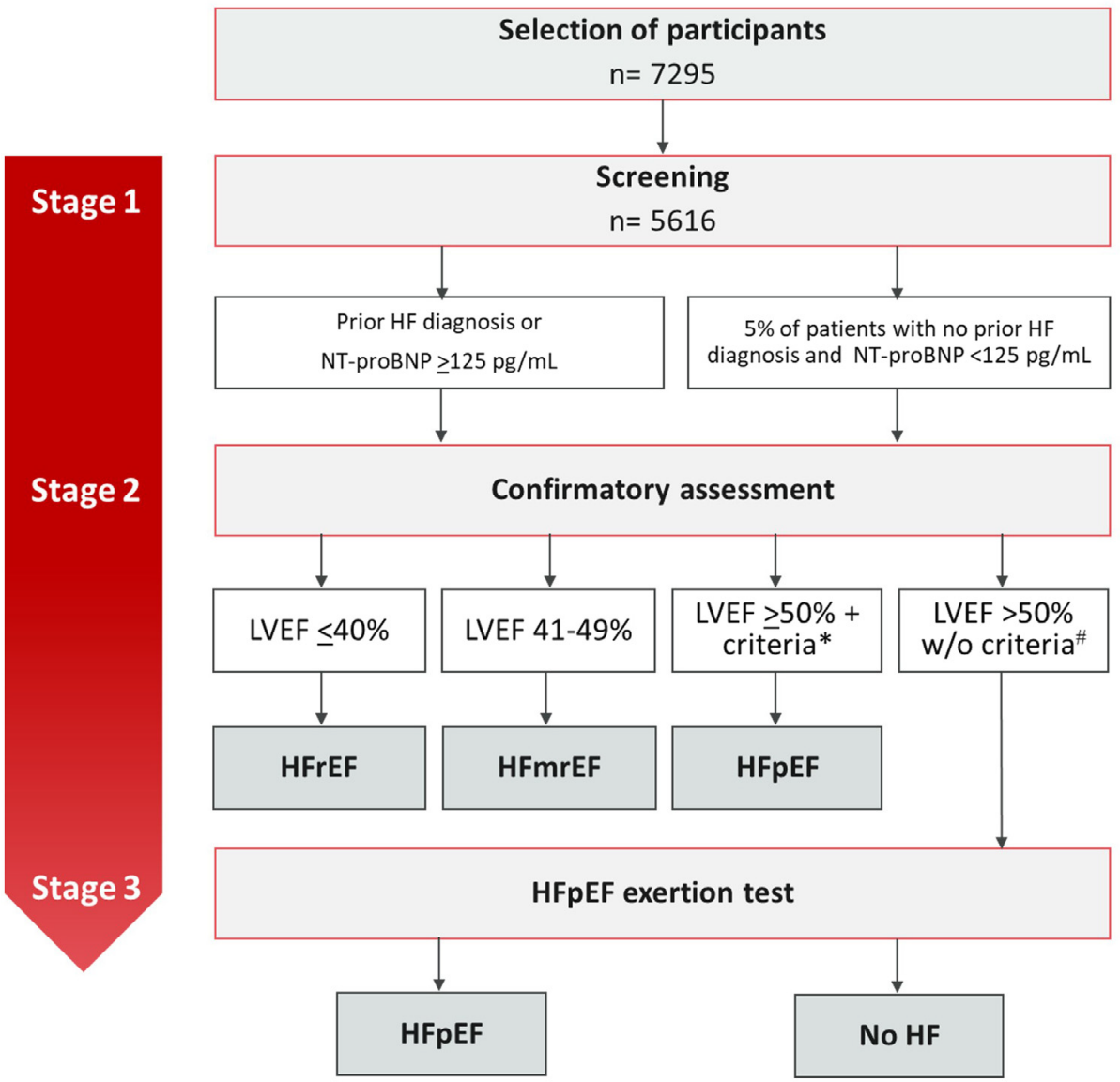
(north and south)

METHODS

Sample Size

Sample size

Sample size calculation was based on the **expected prevalence of HF of 2.5%,** with an absolute precision of 0.5% and design effect of 1.5 to account for clustering



- Invitation to participate
- Oral consent
- Outpatient visit schedule

- Written consent
- Vital signs and body measurements
- NT-proBNP assessment
- Sociodemographic questionnaire
- EQ-5D questionnaire
- 1-lead electrocardiogram

- KCCQ questionnaire
- 12-lead electrocardiogram
- Ecocardiography
- Medical history and treatments
- Laboratory assessments

- Echocardiographic diastolic stress test

*validation of the HFA–PEFF diagnostic algorithm up to Step E with a total score ≥5 points

validation of the HFA–PEFF diagnostic algorithm up to Step E with a total score 2-4 points

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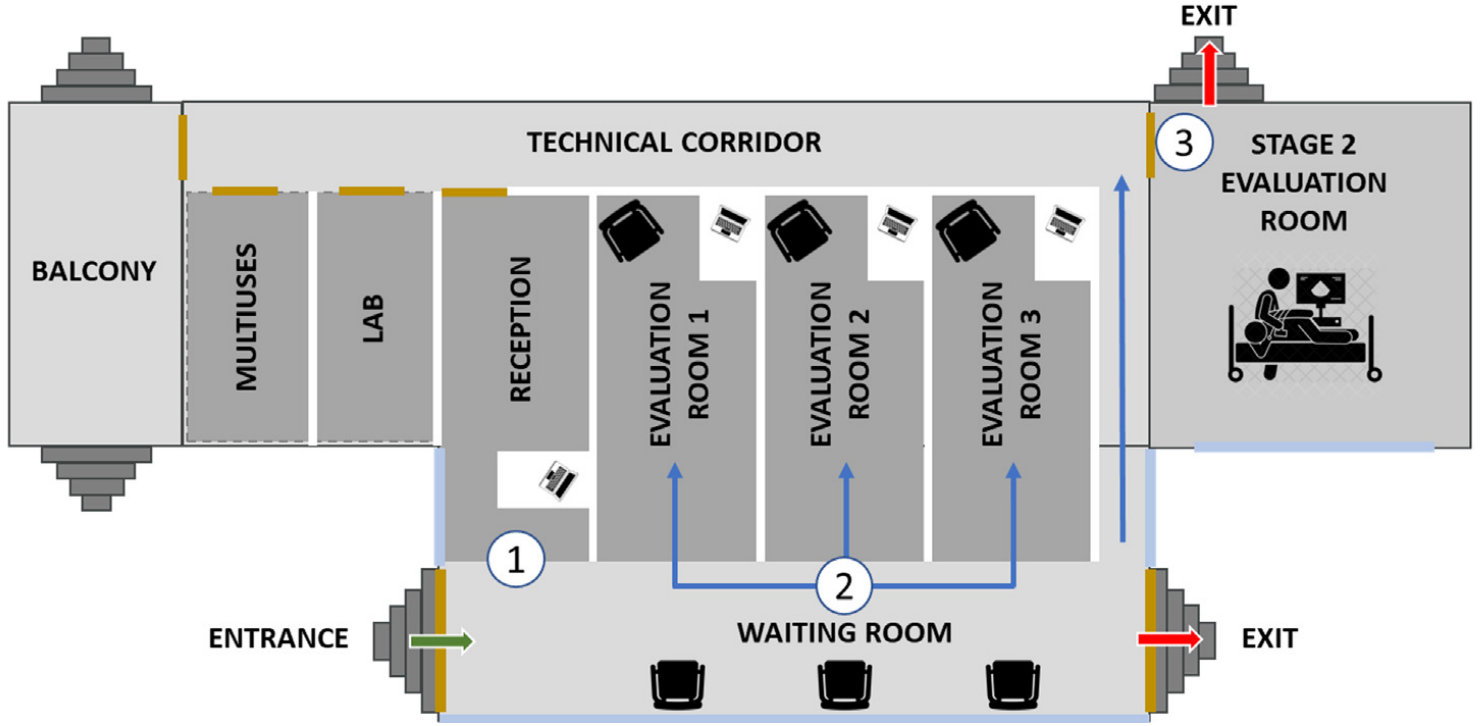
The PORTHOS Mobile Clinic

A

B



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Results

RESULTS

The PORTHOS cohort versus the Portuguese Census 2021

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	PORTHOS n = 6 189	Census 2021 age ≥ 50 years n = 4 677 908
Sex		
Men	2.774 (44.8%)	1.981.950 (42.4%)
Women	3.415 (55.2%)	2.695.958 (57.6%)
Age (years)		
50-59	2.098 (33.9%)	1.491.780 (31.9%)
60-69	1.812 (29.3%)	1.377.940 (29.5%)
70 +	2.279 (36.8%)	1.808.188 (36.7%)
NUTS II (region)		
Norte	2.375 (38.4%)	1.700.375 (36.3%)
Centro	1.062 (17.2%)	875.067 (18.7%)
Lisboa e Vale do Tejo	2.181 (35.2%)	1.611.899 (34.5%)
Alentejo	303 (4.9%)	270.340 (5.8%)
Algarve	268 (4.3%)	220.227 (4.7%)

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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Eligible population:
Mainland Portuguese 50+
n= 4 677 908 (Census 2021)

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

Eligible population:
Mainland Portuguese 50+
n= 4 677 908 (Census 2021)

↓ **multistage sampling methodology**

Contact attempts

***n*= 18 969**

←

Reasons for not participating in the study:
Not contactable (n=2859)
Not Eligible (n=2523)
Refused (n=7398)

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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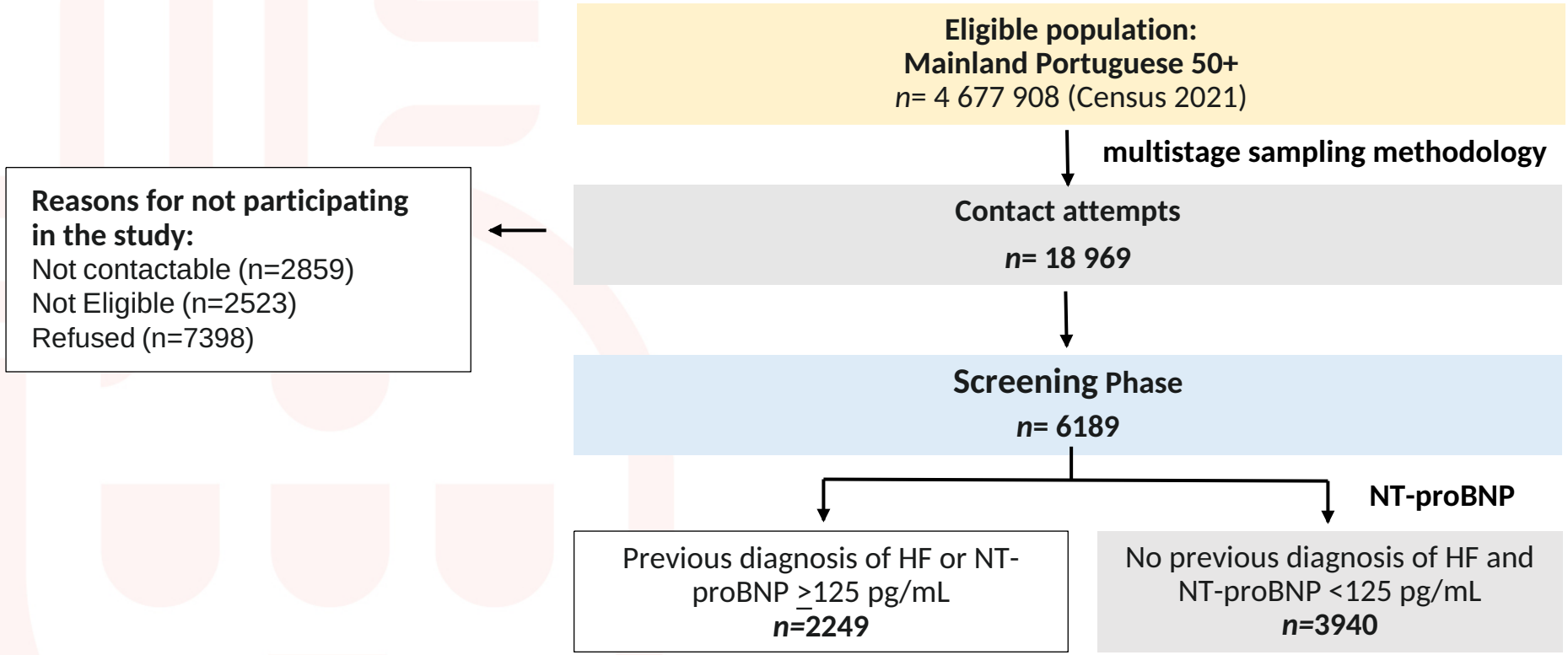

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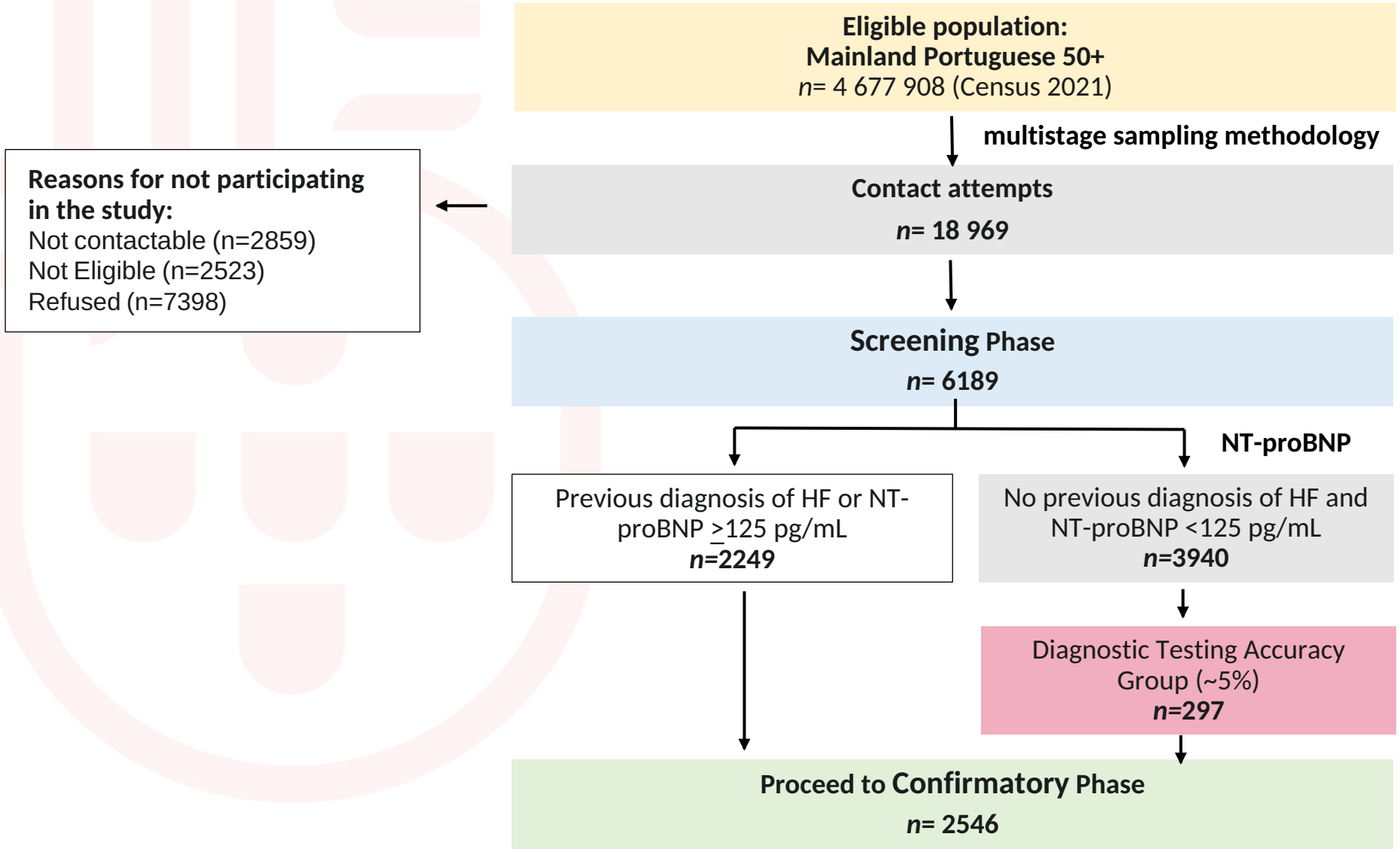

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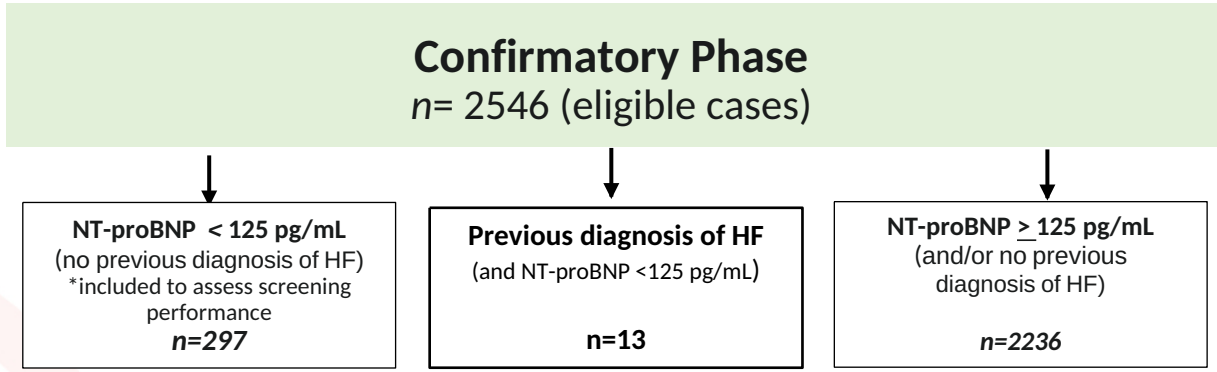

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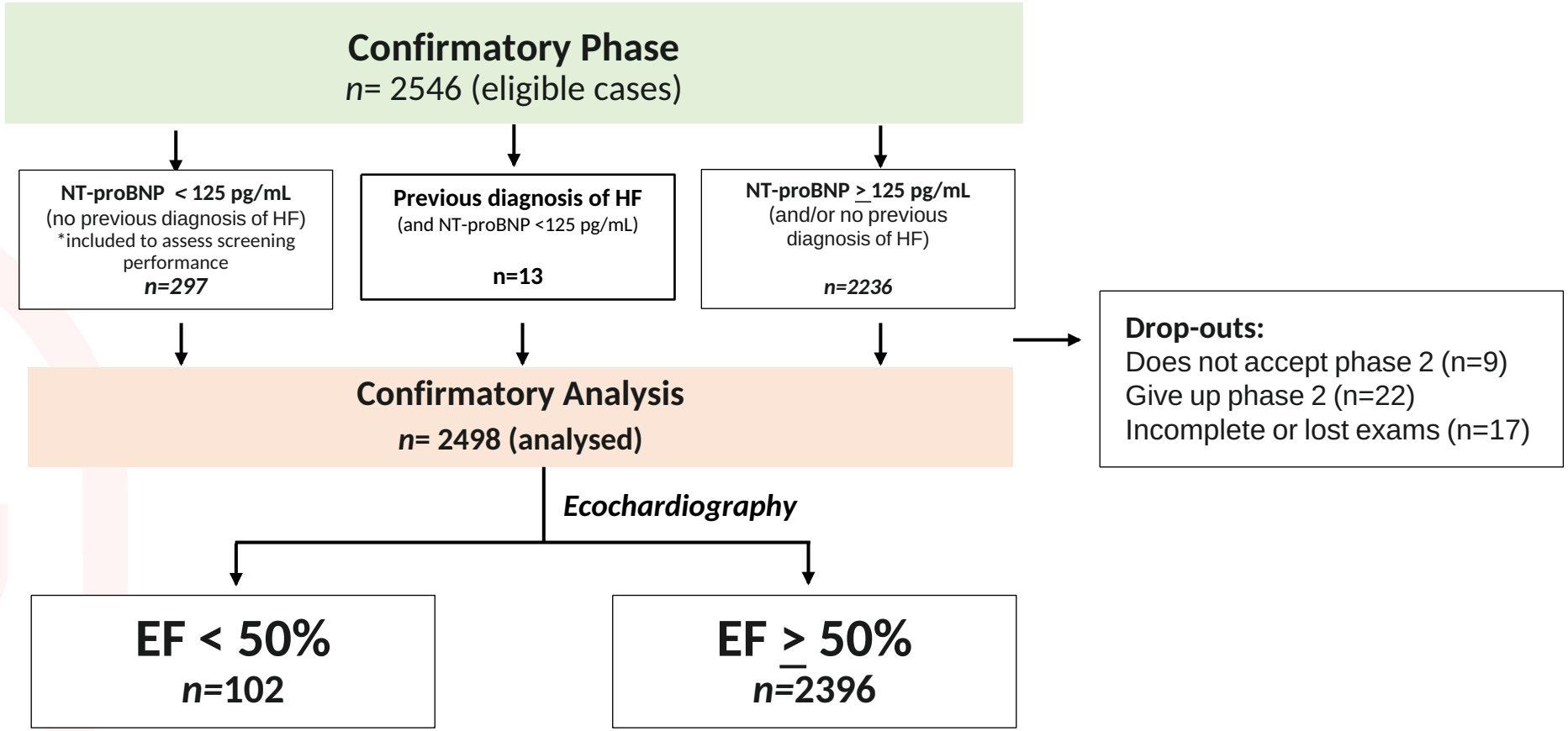

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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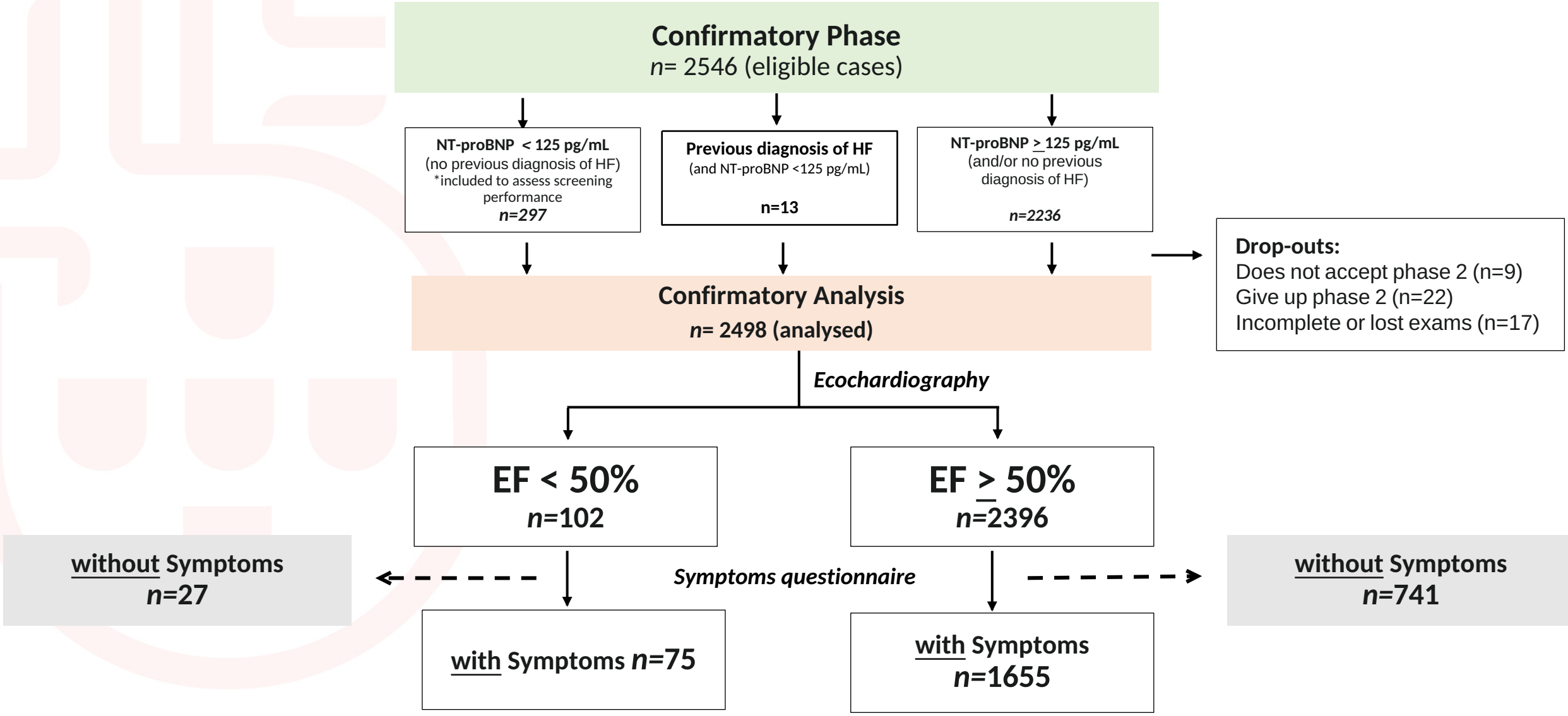

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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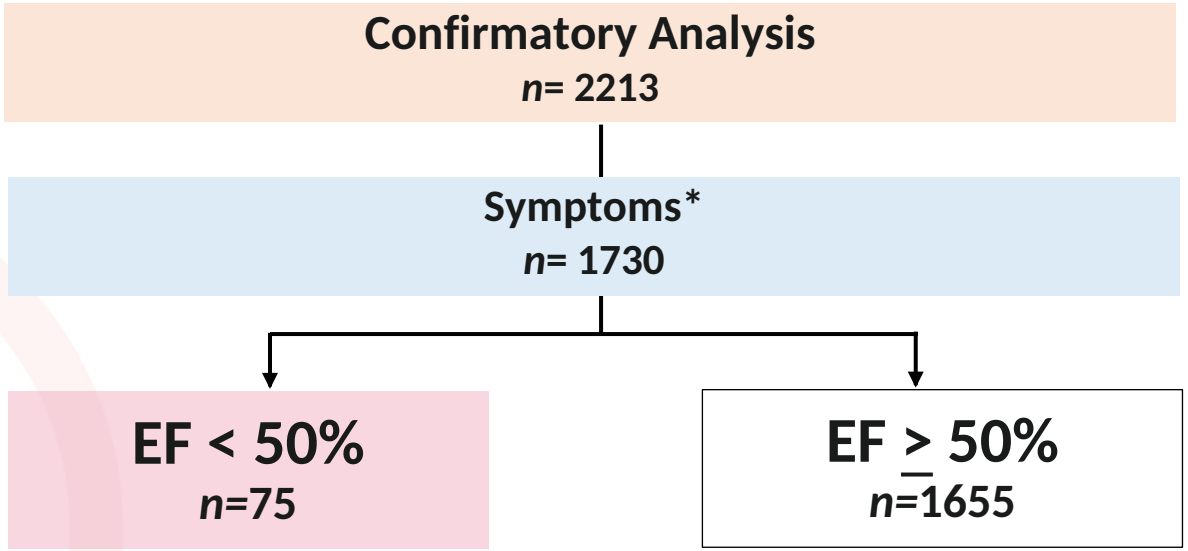

*** Consider presence of symptoms of HF if at least one of :**
NYHA class ≥ 2
Edema ≥ 3
Dyspneia at rest ≥ 3
Orthopnea ≥ 3

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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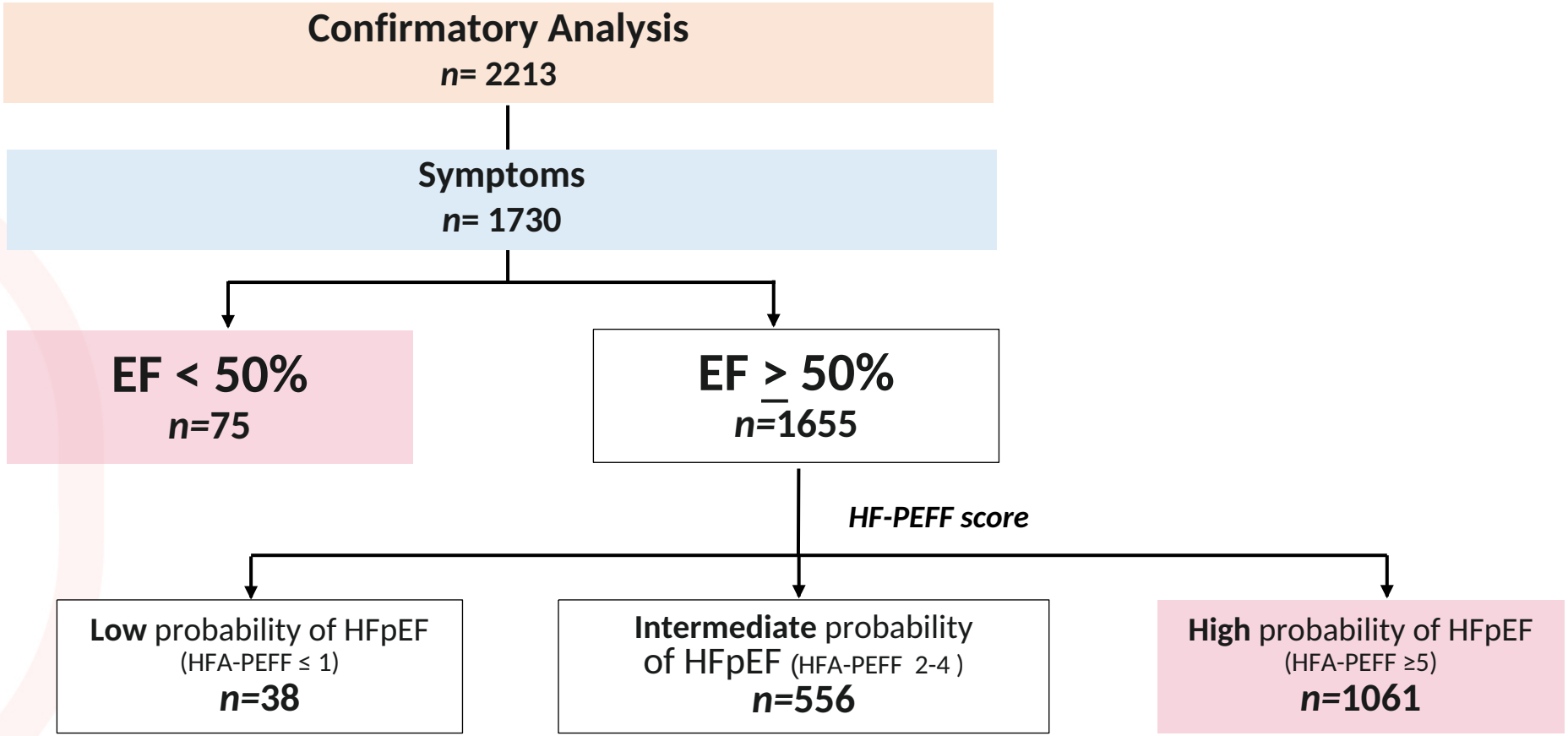

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

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Estimated HF Prevalence
n=1136
16.54% (14.88 – 18.35%)

HFrEF	HFmrEF	HFpEF
n=23	*n*=52	*n*=1061
0.35 % (0.23 – 0.55%)	**0.97 %** (0.49 – 1.91%)	**15.22 %** (13.73 – 16.84%)
HFrEF Prevalence	HFmrEF Prevalence	HFpEF Prevalence

RESULTS

Estimated Prevalence in individuals 50+ living in Mainland Portugal

PORTHOS
ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

Estimated HF Prevalence
***n*=1136**
16.54% (14.88 – 18.35%)

HFrEF	HFmrEF	HFpEF
***n*=23**	***n*=52**	***n*=1061**

1.32 % (0.72 – 2.20%)

HFrEF + HFmrEF Prevalence

15.22 % (13.73 – 16.84%)

HFpEF Prevalence

RESULTS

Sensitivity analysis excluding: Primary Valvular Heart Disease*

PORTHOS
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Estimated HF Prevalence
***n*=1037**
15.66% (14.03 – 17.44%)

HFrEF	HFmrEF	HFpEF
n=20	*n=46*	*n=971*

1.27 % (0.73 – 2.19%)

HFrEF + HFmrEF Prevalence

14.39 % (12.94 – 15.98%)

HFpEF Prevalence

* **Valvular Heart Disease** (VHD): moderate to severe primary valvular disease: n=150 (3.45%)

RESULTS

Sensitivity analysis excluding: HFpEF mimics*

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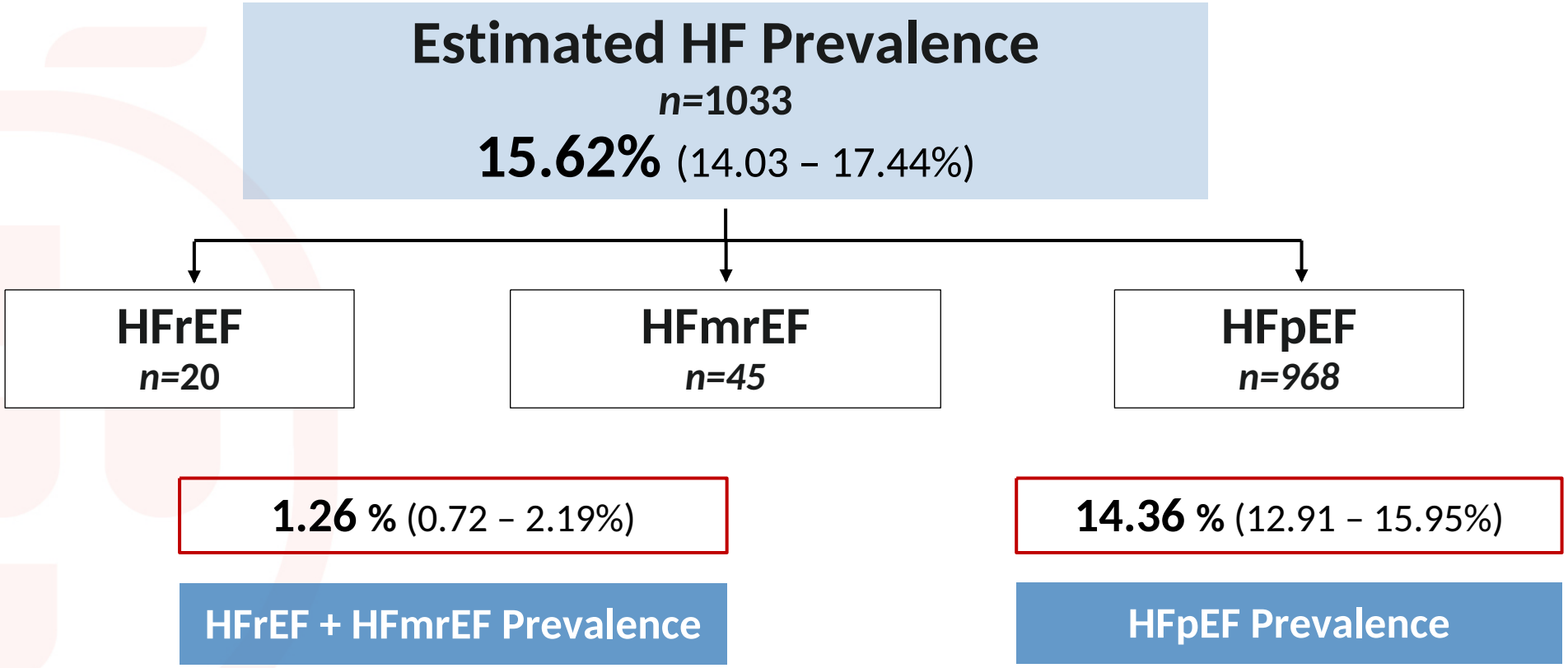

* **HFpEF mimics**: VHD, infiltrative cardiomyopathy, hypertrophic cardiomyopathy, pericardial disease, or high-output HF

RESULTS

Sensitivity analysis excluding: Atrial Fibrillation/Flutter*

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Estimated HF Prevalence
***n*=1033**
15.52% (13.90 – 17.29%)

HFrEF	HFmrEF	HFpEF
n=17	*n=36*	*n=980*

1.26 % (0.72 – 2.19%)

HFrEF + HFmrEF Prevalence

14.47 % (13.01 – 16.06%)

HFpEF Prevalence

* **Atrial fibrillation/flutter**: confirmed in 12 lead ECG

RESULTS

HF Prevalence by sex and age

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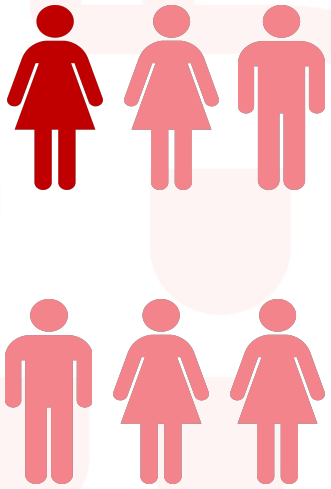
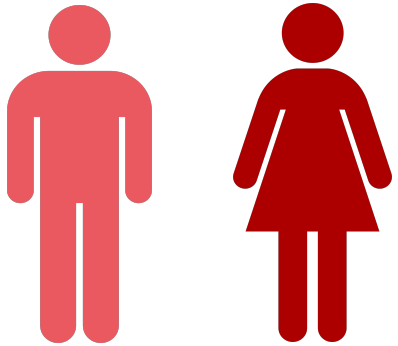
773 726 patients



1 out of 6
with 50+ live with HF

Prevalence by sex (%)

Men: n=206 916; Women: n=566 690



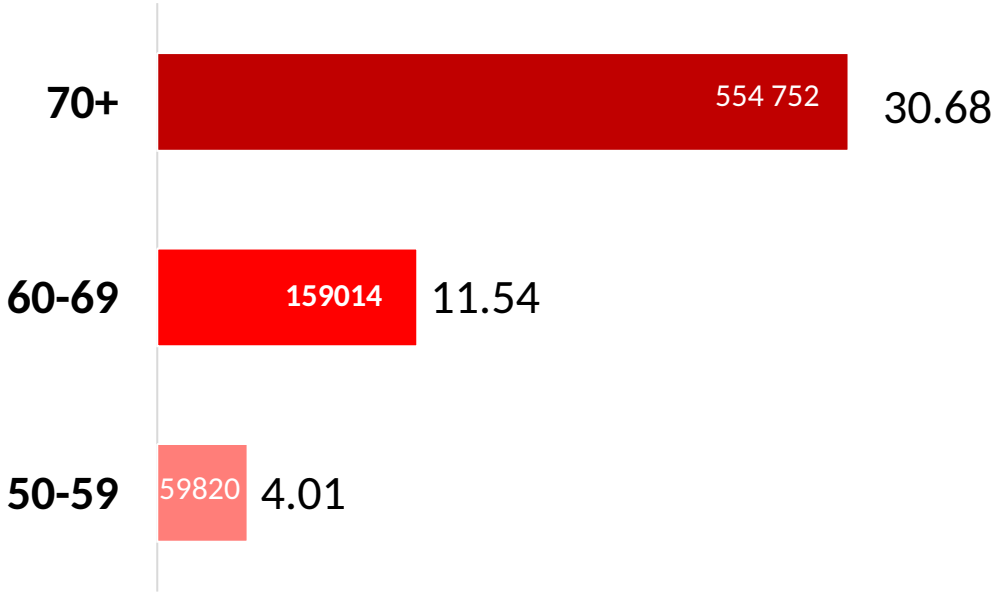
10.44%
(8.78; 12.37)

21.02%
(18.43; 23.87)

Crude OR*: 2.28
(95%CI:1.77; 2.94; p< 0.001)

* ref men

Prevalence by age (%)



60-69 OR: 3.12** (95%CI:1.71; 5.70; p< 0.001)

70+ OR: 10.58** (95%CI:5.91; 18.85; p< 0.001)

** ref 50-59 y

RESULTS

Prior HF diagnosis

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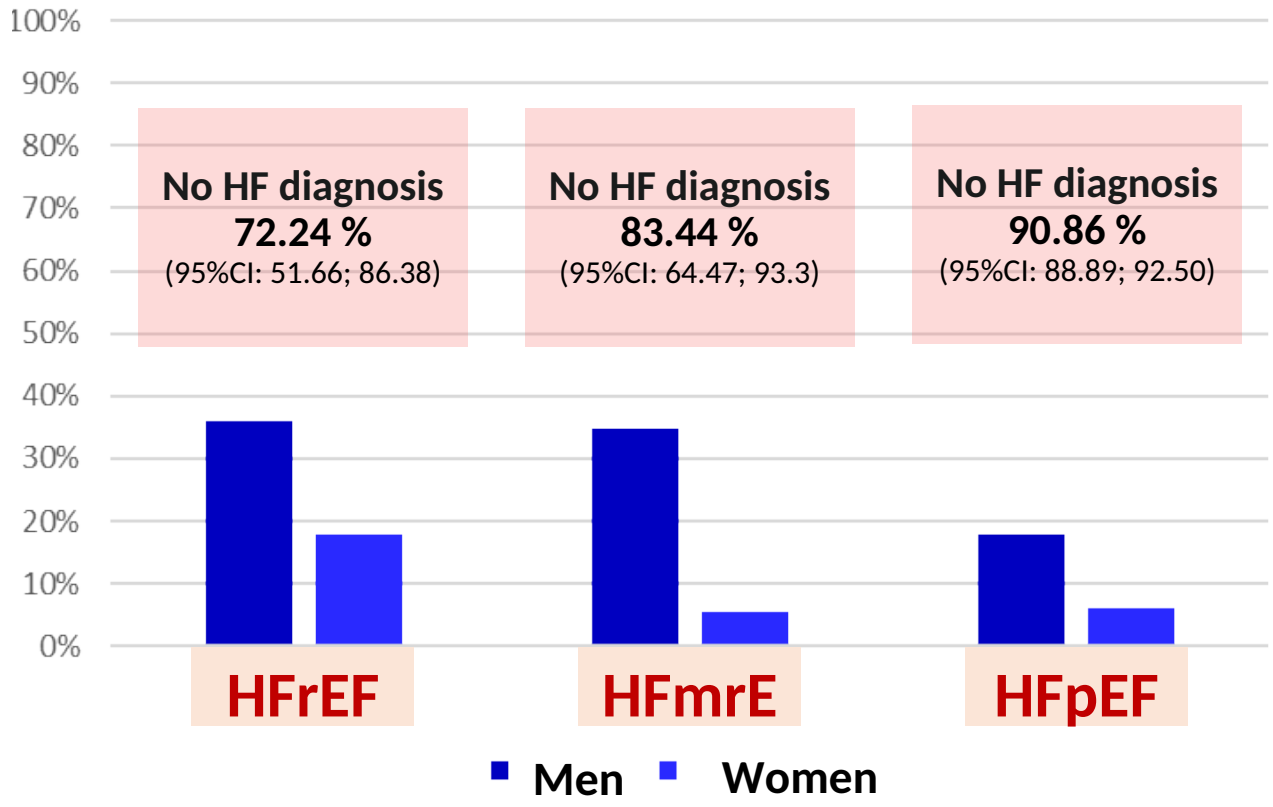
Estimated Prevalence of no previous diagnosis of HF
90.02 %
(95%CI:88.04; 91.71)

9 out of 10 patients were unaware of their condition

Self-reported previous diagnosis of HF (%)



Undiagnosed cases is higher in **women** and in the **age group of 70 and older**

RESULTS

Demographic and clinical characteristics

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ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

	NT-proBNP≥125 pg/mL No HF diagnosis n=1362	HFrEF + HFmrEF (EF<50%) n=75	HFpEF (EF ≥50%) n=1061
Age 70+ (%)	32.1%	42.9%	74.2%
Female (%)	54.5%	57.7%	74.6%
Obesity (BMI ≥30 kg/m^2) (%)	26.9%	28.6%	30.5%
Type 2 DM (%)	16.6%	22.3%	25.4%
Arterial hypertension (%)	47.2%	83.6%	76.0%
Previous MI (%)	2.4%	22.6%	6.5%
Atrial fibrillation (%)	13.8%	22.3%	7.4%
NYHA III-IV	7.8%	50.8%	24.1%

RESULTS

Biochemical and imaging biomarkers

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	NT-proBNP≥125 pg/mL No HF diagnosis n=1362	HFrEF + HFmrEF (EF<50%) n=75	HFpEF (EF ≥50%) n=1061
eGFR mL/min/1.73 m², median [P25-P75]	89.4 [76.92-101.65]	78.03 [66.81-85.11]	75.42 [59.44-90.04]
NT-proBNP (point of care) pg/mL, median [P25-P75]	60 [59-110]	449 [126-825]	277 [183-499]
Ejection fraction (%), median [P25-P75]	63.45 [60.01-66.81]	42.33 [39.5-45.3]	63.25 [49.43-67.19]
Left atrial volume index mL/m², median [P25-P75]	40.39 [34.56-44.94]	52.12 [50.27-63.10]	46.31 [41.67-53.5]
E' septal m/s, median [P25-P75]	0.07 [0.06-0.09]	0.07 [0.05-0.08]	0.06 [0.05-0.07]
E/e' median [P25-P75]	8.06 [6.82-8.99]	9.26 [5.74-12.43]	10.74 [9.01-13.10]

RESULTS

Sample characteristics

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	HFrEF + HFmrEF (EF<50%) n=75	HFpEF (EF ≥50%) n=1061
Age 70+ (%)	42.9%	74.2%
Male sex (%)	42.3%	25.4%
Obesity (BMI 30+ kg.m^{-2}) (%)	28.6%	30.5%
Type 2 DM (%)	22.3%	25.4%
Arterial hypertension (%)	83.6%	76.0%
Previous MI (%)	22.6%	6.5%
Atrial fibrillation (%)	22.3%	7.4%
NYHA III-IV (%)	50.8%	24.1%

RESULTS

Sample characteristics

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	HFrEF + HFmrEF n=75	HFpEF n=1061
eGFR mL.min.1.73 m^{-2}, median [P25-P75]	78.03 [66.81-85.11]	75.42 [59.44-90.04]
NT-proBNP (point of care) $ng.L^{-1}$, median [P25-P75]	449 [126-825]	277 [183-499]
Ejection fraction (%) median [P25-P75]	42.33 [39.8-45.53]	63.25 [59.43-67.19]
Left atrial volume index $mL.m^{-2}$, median [P25-P75]	52.12 [50.27-63.10]	46.31 [41.67-53.5]
E' septal $m.s^{-1}$, median [P25-P75]	0.07 [0.05-0.08]	0.06 [0.05-0.07]
E/e' median [P25-P75]	9.26 [5.74-12.43]	10.74 [9.01-13.10]

RESULTS

Results of the KCCQ questionnaire: HF vs non-HF

	Non- HF	HF	Crude ß	Crude	Adjusted ß	Adjusted
	1363	*n*=1136	Non-HF vs HF [95% CI]	p-value Non-HF vs HF	Non-HF vs HF [95% CI]	p-value Non-HF vs HF
KCCQ Summary scores (0-100)						
Clinical, (mean ± sd)	**92.72** (11.25)	**79.84** (17.84)	-16.208 (-18.192; -14.225)	<0.001	-10.201 (-12.452; -7.951)	<0.001
Overall, (mean ± sd)	**92.33** (10.80)	**79.13** (17.31)	-15.028 (-16.711; -13.346)	<0.001	-9.401 (-11.454; -7.348)	<0.001

Adjusted for: gender, age strata, NUTSII, education level, employment status, BMI, smoking habits, alcohol consumption and number of chronic diseases

RESULTS

Results of the KCCQ questionnaire: HFrEF/HFmrEF vs HFpEF

PORTHOS
ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

	HF *n*=1136	HFrEF/ HFmrEF n=75	HFpEF n=1061	Crude ß HFrEF or HFmrEF /HFpEF [95% CI]	Crude p-value HFrEF or HFmrEF /HFpEF	Adjusted ß HFrEF or HFmrEF /HFpEF [95% CI]	Adjusted p-value HFrEF or HFmrEF /HFpEF
KCCQ Summary scores (0-100)							
Clinical, (mean ± sd)	79.84 (17.84)	**79.44** (17.51)	**79.87** (79.87)	-0.659 (-6.553; 5.234)	0.826	-3.555 (-8.477; 1.368)	0.157
Overall, (mean ± sd)	79.13 (17.31)	**75.18** (16.20)	**79.47** (17.37)	-4.268 (-7.907; -0.629)	0.022	-4.981 (-9.399; -0.562)	0.027

Adjusted for: gender, age strata, NUTSII, education level, employment status, BMI, smoking habits, alcohol consumption and number of chronic diseases

RESULTS

NYHA class and KCCQ score according to HF-PEFF score

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ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

	EF >= 50 + symptoms or previous diagnosis (*n*=1655)	Low probability (*n*=38)	Intermediate (n=*556*)	High probability (n=1061)
NYHA class, n (%)				
Class I	201 (12.75)	8 (21.81)	81 (12.83)	112 (9.63)
Class II	1096 (70.19)	28 (71.84)	372 (71.48)	696 (66.29)
Class III	329 (16.17)	2 (6.35)	92 (15.11)	235 (22.10)
Class IV	29 (0.89)	-	11 (0.58)	18 (1.99)
KCCQ Summary scores (0-100)				
Clinical, mean (sd)	86.83 (15.02)	93.02 (11.91)	88.74 (13.16)	79.87 (17.88)
Overall, mean (sd)	86.30 (14.67)	93.11 (8.05)	88.07 (13.20)	79.47 (17.37)

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Conclusion

CONCLUSIONS

PORTHOS
ESTUDO DE PREVALÊNCIA DE INSUFICIÊNCIA CARDÍACA EM PORTUGAL

We used a **contemporary definition of HF** according to the ESC/Universal Definition of HF criteria and HFA-PEFF score for those with symptoms + NT-proBNP ≥125 pg/mL and EF ≥ 50%.

Primary objective:

The **estimated prevalence of HF** in the population **50+** in mainland Portugal was **16.54%** (14.88 – 18.35%).

Secondary objectives:

HFpEF is the dominant phenotype, with an estimated prevalence of **15.22 %** (13.73 – 16.84%).

9 out of 10 patients were **unaware** of their condition.

Prevalence in **women is 2.3 times higher** than in men.

There is a steep increase with age, reaching **~30% in those 70+.**

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We are deeply grateful to all participants of the PORTHOS study

PROMOTORES

Sociedade Portuguesa de CARDIOLOGIA

AstraZeneca

NOVA MEDICAL SCHOOL

COM O ALTO PATROCÍNIO DE SUA EXCELÊNCIA O Presidente da República

PARCEIROS

MARIA

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MISSÃO CONTINENTE

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