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Overdiagnosis of heart failure in primary care:

a cross-sectional study

Abstract

Background
Access to echocardiography in primary care is limited, but is necessary to accurately diagnose heart failure (HF).

Aim
To determine the proportion of patients with a GP's diagnosis of HF who really have HF.

Design and setting
A cross-sectional study of patients in 30 general practices with a GP's diagnosis of heart failure, based on the International Classification of Primary Care (ICPC) code K77, between June and November 2011.

Method
Electronic medical records of the patients' GPs were scrutinised for information on the diagnosis. An expert panel consisting of two cardiologists and an experienced GP used all available diagnostic information, and established the presence or absence of HF according to the criteria of the European Society of Cardiology (ESC) HF guidelines.

Results
In total, 683 individuals had a GP's diagnosis of HF. The mean age was 77.9 (SD 11.4) years, and 42.2% were male. Of these 683, 79.6% received cooperative care from a cardiologist. In 73.5% of cases, echocardiography was available for panel re-evaluation. Based on consensus opinion of the panel, 434 patients (63.5%, 95% confidence interval [CI] = 59.9 to 67.1) had definite HF, of which 222 (32.5%, 95% CI = 30.9 to 34.1) had HF with a reduced ejection fraction (HFrEF), 207 (30.3%, 95% CI = 29.0 to 31.6) had HF with a preserved ejection fraction (HFpEF), and five (0.7%, 95% CI = 1.2 to 2.6) had isolated right-sided HF. In 17.3% of cases (95% CI = 14.4 to 20.0), the panel considered HF absent, and in 19.2% (95% CI = 16.3 to 22.2) the diagnosis remained uncertain.

Conclusion
More than one-third of primary care patients labelled with HF may not have HF, and such overdiagnosis may result in inadequate patient management.

Keywords
cross-sectional studies; health professionals; heart failure; multiple deprivation; primary care; resilience; rurality.

INTRODUCTION

Heart failure (HF) is a chronic progressive disease mainly affecting older people.[1] Pharmacological treatment, devices, and HF management programmes can reduce morbidity and mortality in patients who have HF with reduced ejection fraction (HFrEF).[1] In this study the authors defined HFrEF as symptoms and/or signs suggestive of heart failure, and a left ventricular ejection fraction (LVEF) ≤45% with echocardiography. In patients who have HF with preserved ejection fraction (HFpEF) clear evidence-based disease-modifying treatment is still lacking, but, importantly, symptoms may be reduced with adequate titration of diuretics during periods of fluid retention.[1] This study defined HFpEF as symptoms and/or signs suggestive of heart failure, and an LVEF >45% plus structural or functional abnormalities with echocardiography.[1]

The diagnosis of non-acute HF is primarily initiated in primary care, but this diagnosis is notoriously difficult without echocardiography, especially in the early stages of the disease, in the obese, older people, and in patients with chronic obstructive lung disease.[2,3] Additional investigations with natriuretic peptides and referrals for echocardiography are needed, and have increased in primary care over the past decade.[4,5] GPs tend to follow the recommendations of existing guidelines that advocate considering referral for echocardiography of individuals with suggestive symptoms and signs who in addition have natriuretic peptide levels above the exclusionary threshold.[1] Nevertheless, this strategy has not been completely implemented yet,[2,4,6] resulting in the risk of over- and underdiagnosis of HF if GPs consider the clinical assessment only. Multiple studies have mentioned underdiagnosis of HF in primary care,[3,7–11] but exact data on overdiagnosis in this setting are lacking.[11]

The authors wanted to quantify overdiagnosis of HF in primary care, and therefore evaluated whether patients with a GP's diagnosis of HF really had HF according to an expert panel that applied the criteria of the European Society of Cardiology (ESC) HF guidelines. Additionally, the study determined which patient characteristics were associated with referral for echocardiography.

METHOD

Design and study population

The authors performed a cross-sectional study in 30 general practices in and around Amersfoort, a town in the middle of the Netherlands. Around 70 000 individuals were enlisted in these practices in 2010. Notably, all citizens in the Netherlands are enlisted with a GP, irrespective of cooperative care by a specialist, except for those living in nursing homes. Those

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How this fits in

The diagnosis of non-acute heart failure is primarily initiated in primary care, but this diagnosis is notoriously difficult without echocardiography, especially in the early stages of the disease. Multiple studies have mentioned underdiagnosis of HF in primary care. The authors wanted to quantify overdiagnosis of HF in primary care. The results show that around one in six patients with a GP's diagnosis of HF are misclassified, and such overdiagnosis brings the risk of inappropriate patient management.

eligible for inclusion in the study were community-dwelling individuals with a GP's diagnosis of HF (International Classification of Primary Care [ICPC] code K77) registered during at least two encounters to prevent including those who had been accidentally misclassified.[12] The GPs' electronic medical records (EMRs) and specialists' letters of patients were scrutinised for information on demographics, medical history, medication, comorbidities, laboratory tests, and results of echocardiography between June and October 2011. In November 2011, all participating GPs received a letter recommending completion of the diagnostic work-up of any of their patients labelled with HF who had not yet undergone echocardiography to confirm the diagnosis and to help discriminate heart failure with reduced ejection fraction from heart failure with preserved ejection fraction, as recommended in the Dutch general practice guidelines on HF.[13] The current study is a cross-sectional analysis of the baseline characteristics of all 683 patients labelled with HF. Those with a definite HF diagnosis, established by an expert panel ($n = 434$), then participated in a cluster-randomised trial. In this cluster-randomised trial, the 30 GP practices were randomised either to a one-day training course on the diagnosis and drug management of HF, or to usual care. The GPs working in the 15 GP practices of the intervention arm received a second reminder on the relevance of echocardiography.[14]

Cooperative care of patients by both a GP and cardiologist was pragmatically defined as any contact with the cardiologist (outpatient clinic visit or cardiac hospitalisation) in the 18 months before the assessment.

Definition of heart failure

An expert panel composed of two cardiologists and a GP with expertise in HF determined the presence or absence of HF (definite HF, possible HF, or no HF) during consensus meetings using all available diagnostic information, including echocardiography. Available echocardiograms were re-evaluated. The panel based the diagnosis of HF on the criteria laid out in the ESC HF guidelines, that is, signs and symptoms suggestive of HF, and objective evidence of structural or functional cardiac abnormality related to ventricular dysfunction in rest with echocardiography.[1] Disagreement between panel members was solved by discussion and a majority vote. In participants lacking information on natriuretic peptides and echocardiography the panel decided between no HF and possible HF, apart from patients who had been hospitalised for an episode of acute HF — they were diagnosed as 'definite HF' by the panel. Patients with definite HF were further classified based on echocardiography as HFrEF, HFpEF, or isolated right-sided HF. For HFrEF the LVEF had to be ≤45%. For HFpEF, the LVEF had to be >45%, in the presence of a composite of echocardiographic indices of diastolic dysfunction or structural abnormalities (left ventricular hypertrophy or left atrial enlargement). For isolated right-sided HF, the LVEF had to be >45%, and the estimated systolic pulmonary artery pressure >40 mmHg, with the absence of evident left ventricular dysfunction or valvular disease.[1]

Data analysis

To compare groups the authors used Student's *t*-tests or Mann–Whitney *U* tests for continuous variables, and the χ^2 test for categorical variables. The authors compared patients with definite, no, and possible HF. They also compared patients who received cooperative care from a cardiologist with those who had no cooperative care from a cardiologist, and patients who had HFrEF with those who had HFpEF. The association between patient characteristics and referral for echocardiography was assessed using multivariable logistic regression analysis to identify independent predictors for referral. All analyses were done with SPSS version 20.0.

RESULTS

Baseline characteristics of the 683 patients with a GP's diagnosis of HF are presented in Table 1. The mean age was 77.9 (SD 11.4) years, 42.2% were male, and 79.6% received cooperative care from a cardiologist. A total of 77 (17.8%) patients had been hospitalised for acute HF. The expert panel was able to use the results of natriuretic peptide

Table 1. Characteristics of 683 patients with a GP's diagnosis of heart failure who have been categorised by an expert panel into definite heart failure, possible heart failure, and no heart failure

	Definite HF, % (*n* = 434)	Possible HF, % (*n* = 131)	No HF, % (*n* = 118)
Mean age, years (SD)	77.2 (10.9)	83.9 (9.5)	74.1 (12.6)
Male sex	46.9	33.6	34.7
Cooperative care by a cardiologist	91.7	44.3	74.6
Comorbidities			
Angina pectoris	18.4	15.3	17.8
Prior myocardial infarction	32.5	18.3	17.8
Atrial fibrillation	48.4	37.4	21.2
Stroke or TIA	13.8	22.1	13.6
COPD	20.0	19.1	18.6
Renal insufficiency (eGFR<30 mL/min/1.73 m^2)	9.7	13.7	4.2
Hypertension	54.6	45.0	58.5
Diabetes mellitus	32.7	26.7	19.5
Additional investigations			
Natriuretic peptide measurements[a]	71.0	68.7	64.4
Echocardiography[a]	92.6	15.3	67.8
Natriuretic peptides or echocardiography[a]	97.5	74.8	83.9
Drug prescriptions			
Diuretics	75.1	74.0	61.0
ACE inhibitors	50.5	40.5	44.1
ARBs	15.2	11.5	11.0
Beta-blockers	56.0	42.0	44.1
MRAs	28.1	16.8	13.6
Digoxin	23.5	20.6	10.2

[a]*Results available to the panel. ACE inhibitors = angiotensin-converting enzyme inhibitors. ARBs = angiotensin receptor blockers. COPD = chronic obstructive pulmonary disease. eGFR = the calculated glomerular filtration rate according to the modification of diet in renal diseases (MDRD) formula. HF = heart failure. MRAs = mineralocorticoid receptor antagonists. SD = standard deviation. TIA = transient ischaemic attack.*

measurements in 69.3% of the patients, and echocardiography in 73.5%.

In total, 118 (17.3%, 95% CI = 14.4 to 20.0) patients had no HF according to the panel, and 131 (19.2%, 95% CI = 16.3 to 22.2) patients had possible HF.

The 139 patients who received care from a GP only were significantly older (81.5 versus 76.9 years, *P*<0.001), had less prior myocardial infarction (10.8 versus 31.4%, *P*<0.001), had had echocardiography less often (30.9 versus 84.4%, *P*<0.001), and were less often prescribed an angiotensin-converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) (43.9 versus 61.8%, *P*<0.001) and mineralocorticoid receptor antagonists (MRAs) (15.1 versus 25.6%, *P* = 0.009) than the 544 patients who received cooperative care from a cardiologist (Table 2).

Multivariable analysis showed that younger age, prior myocardial infarction, and prescription of ACE-I/ARBs were independent predictors of referral for echocardiography (Table 3).

The 434 (63.5% of the 683 patients with a GP's label of HF, 95% CI = 59.9 to 67.1) patients with definite HF can be divided into 222 (32.5%, 95% CI = 30.9 to 34.1%) with HFrEF, 207 (30.3%, 95% CI = 29.0 to 31.6%) with HFpEF, and five (0.7%, 95% CI = 1.2 to 2.6) with isolated right-sided HF. Considering the ejection fraction only, the 434 patients with definite HF can be divided as follows: 33.9% had an LVEF <40%, 21.2% had an LVEF of 40–50%, 36.4% had an LVEF >50%, and in 8.5% an LVEF had not been recorded.

Comparing the 222 patients with HFrEF with the 207 with HFpEF showed that those with HFrEF were younger (74.5 versus 79.9 years, *P*<0.001), more often male (57.2% versus 37.7%, *P*<0.001), and had more often had a prior myocardial infarction (47.7% versus 16.4%, *P*<0.001). Those with HFpEF more often had a history of hypertension (64.7% versus 45.5%, *P*<0.001), atrial fibrillation (62.3% versus 35.6%, *P*<0.001), and stroke/TIA (17.9% versus 9.9%, *P* = 0.02) than those with HFrEF (Table 4).

DISCUSSION

Summary

This study demonstrated that among 683 patients with a GP's diagnosis of HF the

Table 2. Characteristics of 683 patients with a GP's diagnosis of heart failure, divided into patients receiving GP care only, and patients who received cooperative care from a cardiologist

	GP care only, % (*n* = 139)	Cooperative care from cardiologist, % (*n* = 544)	*P*-value
No HF, according to the panel	21.6	16.2	0.13
Possible HF, according to the panel	52.5	10.7	<0.001
Definite HF, according to the panel	25.9	73.1	<0.001
Mean age, years (SD)	81.5 (12.4)	76.9 (11.4)	<0.001
Male sex	36.7	43.6	0.14
Comorbidities			
Angina pectoris	10.8	19.5	0.02
Prior myocardial infarction	10.8	31.4	<0.001
Atrial fibrillation	36.7	42.8	0.19
Stroke	10.1	9.2	0.75
COPD	20.1	19.5	0.86
Hypertension	53.2	53.5	0.96
Diabetes mellitus	25.2	30.3	0.23
eGFR<60 mL/min/1.73 m^2	33.1	38.2	0.26
Additional investigations			
Natriuretic peptides measurements[a]	70.5	68.9	0.72
Echocardiography[a]	30.9	84.4	<0.001
Drug prescriptions			
Diuretics	71.2	72.8	0.71
ACE inhibitors or ARBs	43.9	61.8	<0.001
Beta-blockers	38.1	54.6	0.01
MRAs	15.1	25.6	0.009
Digoxin	15.8	19.3	0.35

[a]Results available to the panel. ACE inhibitor = angiotensin-converting enzyme inhibitor. ARB = angiotensin receptor blocker. COPD = chronic obstructive pulmonary disease. eGFR = the calculated renal flow according to the modification of diet in renal diseases (MDRD) formula. MRAs = mineralocorticoid receptor antagonists. SD = standard deviation.

Table 3. Multivariable association between patient characteristics and referral for echocardiography in 683 patients with a GP's diagnosis of heart failure

	Adjusted odds ratio (95 % CI)
Age, per year	0.98 (0.96 to 0.99)
Male sex	1.19 (0.85 to 1.65)
Hypertension	1.01 (0.74 to 1.39)
Angina pectoris	1.00 (0.66 to 1.52)
Prior myocardial infarction	1.73 (1.19 to 2.49)
Atrial fibrillation	1.35 (0.98 to 1.86)
Diabetes mellitus	0.91 (0.64 to 1.29)
COPD	1.02 (0.69 to 1.52)
Renal insufficiency (eGFR<30 mL/min/1.73 m^2)	1.23 (0.70 to 2.16)
Mild renal impairment (eGFR between 30 mL/min/1.73 m^2 and <60 mL/min/1.73 m^2)	1.04 (0.73 to 1.47)
Natriuretic measurements performed	1.29 (0.94 to 1.79)
Diuretic prescription	1.21 (0.84 to 1.73)
ACE inhibitor or ARB prescription	1.42 (1.03 to 1.96)
Beta-blocker prescription	1.04 (0.75 to 1.44)

ACE inhibitor = angiotensin-converting enzyme inhibitor. ARB = angiotensin receptor blocker. COPD = chronic obstructive pulmonary disease. eGFR = the calculated renal flow according to the modification of diet in renal diseases (MDRD) formula.

diagnosis could not be confirmed in 17.3% of the cases, and another 19.2% were classified as 'possible' HF by an expert panel. Younger age and prior myocardial infarction, and prescription of ACE-I/ARBs, were independently related to referral for echocardiography. Of the 434 (63.5%) patients with panel-confirmed HF, 222 (32.5%) had HFrEF, 207 (30.3%) HFpEF, and five (0.7%) isolated right-sided HF. Patients with HFrEF in this study were prescribed ACE-I/ARBs in 69.4% of cases, beta-blockers in 59.0%, and MRAs in 31.5%. These prescription rates are low compared with large drug randomised controlled trials, but are in line with other observational studies of real-life patients.[15–18] Moreover, prescription rates of disease-modifying drugs in HFrEF have been on the increase since the beginning of 2000.[6,17,18] Around one in six patients with a GP's diagnosis of HF are misclassified, and such overdiagnosis brings the risk of inappropriate patient management. There is room for improvement in the diagnostic work-up of suspected cases of heart failure, importantly including the use of natriuretic peptides to select those needing echocardiography to confirm the diagnosis and type of heart failure.

Comparison with other literature

To the best of the authors' knowledge, this is the first study to provide exact data on the overdiagnosis of HF in primary care. Moreover, among those with established HF it also provides the exact percentages of cases with preserved and reduced ejection fraction. When considering these results, one has to bear in mind that patients could receive cooperative care from a cardiologist for diagnoses other than HF (such as, rhythm disorders, valvular disease, and ischaemic heart disease). Moreover, some of these patients could have been referred by a GP under the suspicion of HF (and were already labelled with ICPC code K77)without being confirmed by the cardiologist, and thus may have remained incorrectly labelled as HF (ICPC code K77) in the EMR of the GP.

Previous studies have reported that HF could be established in 14 to 72% of patients referred to an open-access facility or cardiologist.[16,19–21] However, patients in these studies could also have been referred for analysis of a heart murmur, or for other cardiac causes of breathlessness.

Other studies have reported how often GPs performed additional investigations in suspected cases of HF. Electrocardiography (36 to 53%) and chest X-ray (20 to 50%) were performed in a minority of cases.[22] At the beginning of the 21st century, just 12% of the

Table 4. Comorbidities and drug prescription of 434 patients with panel-confirmed heart failure, divided into those with reduced and preserved ejection fraction[a]

	HFrEF, % (*n* = 222)	HFpEF, % (*n* = 207)	*P*-value
Mean age, years (SD)	74.5 (11.3)	79.9 (8.7)	<0.001
Male sex	57.2	37.7	<0.001
Comorbidities			
Angina pectoris	14.0	23.7	0.10
Prior myocardial infarction	47.7	16.4	<0.001
Atrial fibrillation	35.6	62.3	<0.001
Stroke or TIA	9.9	17.9	0.02
COPD	20.7	18.8	0.56
Renal insufficiency (eGFR <30 mL/min/1.73 m^2)	9.9	9.7	0.75
Hypertension	45.5	64.7	<0.001
Diabetes mellitus	33.3	31.4	0.67
Drug prescriptions			
Diuretics	76.6	73.4	0.45
ACE inhibitors or ARBs	69.4	53.6	<0.001
Beta-blockers	59.0	52.7	0.15
MRAs	31.5	24.6	0.13
Digoxin	15.3	26.6	0.01

[a]Five (1.2%) patients with isolated right-sided HF are not included in this table. ACE inhibitors = angiotensin-converting enzyme inhibitors. ARB = angiotensin receptor blocker. COPD = chronic obstructive pulmonary disease. eGFR = the calculated glomerular filtration rate according to the modification of diet in renal diseases (MDRD) formula. HFpEF = heart failure with a preserved ejection fraction. HFrEF = heart failure with a reduced ejection fraction. MRAs = mineralocorticoid receptor antagonists. SD = standard deviation. TIA = transient ischaemic attack.

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Ethical approval

The study complied with the Declaration of Helsinki and was approved by the Regional Medical Ethics Committee (Verenigde Commissies Mensgebonden Onderzoek — VCMO) of four hospitals in the Utrecht region, including the Meander Medical Center in Amersfoort in the Netherlands (NL29397.100.10).

Provenance

Freely submitted; externally peer reviewed.

Competing interests

The authors have declared no competing interests.

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patients labelled with HF and managed by a GP only had undergone echocardiography.[5] In this study, 45.2% of 683 patients had undergone echocardiography at the start of the study, and this number increased to 73.5% after two reminders to consider referral for echocardiography. Irrespective of the past decade's increase in referrals for echocardiography of cases suspected of HF, there is still ample room for improvement. Multiple studies show that certainty about the diagnosis and knowing the type of HF greatly helps to improve the management of these patients.[11,23] Moreover, previous studies have shown that patients with HF with missing LVEF results are older, are prescribed less required HF medication, and show more comorbidity and worse prognosis.[24] A postal survey in the UK in 2008 showed that direct access to echocardiography facilities was available for 72% of the GPs of the responding primary care trusts.[4] Apart from availability of echocardiography, stimulation can substantially improve referral for echocardiography, as shown by these results, with an increase of 28.3% after two reminders.

Strengths and limitations

A strength of this study is that it is the first to evaluate whether HF really is present in a representative sample of community-dwelling individuals who have a GP's diagnosis of HF. The authors used an expert panel to evaluate all available data for these people, and if an echocardiogram was available it was re-evaluated. An expert panel diagnosis such as this is considered superior to the diagnosis of a single cardiologist during everyday practice, and previous studies have shown high reproducibility of such a panel diagnosis of HF.[3,7]

To answer the research question the authors had to use routine care data. Such data, however, are renowned for missing or incomplete diagnostic work-ups. As a result, the panel had to classify 26.5% of the patients without access to echocardiographic results. The percentage of echocardiography performed may on the one hand have been underestimated in this study because in some cases it may not be adequately registered in the GP's EMR. On the other hand, overestimation is possible because the authors stimulated GPs to perform echocardiography. Importantly, however, this procedure did not affect the validity of the estimate of those with a GP's label of HF — those who really had heart failure — because this estimate was based on those with a GP's diagnosis of heart failure when the data were extracted from the EMR.

In this study, the authors used the cut-off value of 45% for the LVEF to distinguish between HFrEF and HFpEF. Alternative thresholds exist to define HFpEF, and 50% has also been recommended.[25]

In 19% of the subjects, the panel could not make a definite diagnosis of HF, and this was merely due to the absence of echocardiography. Although heart failure essentially is a clinical diagnosis, structural and functional cardiac abnormalities should be established to relate the non-specific symptoms and signs suggestive of heart failure to a cardiac origin.

Implications for practice

To facilitate the diagnostic pathway for primary care patients suspected of HF, easy access to echocardiography should become more widely available. Furthermore, optimisation of cooperative care with a cardiologist and HF outpatient clinic could promote drug use and result in more intensive up-titration of drugs. Previous studies have shown that the substitution of care from the HF outpatient clinics to primary care is safe and feasible for patients with HFrEF. However, this must be after they have been carefully and adequately up-titrated with evidence-based treatment.[26–28]

REFERENCES

1. McMurray JJ, Adamopoulos S, Anker SD, *et al.* ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: the Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur J Heart Fail* 2012; **14(8):** 803–869.
2. Hobbs FD, Korewicki J, Cleland JG, *et al.* The diagnosis of heart failure in European primary care: The IMPROVEMENT Programme survey of perception and practice. *Eur J Heart Fail* 2005; **7(5):** 768–779.
3. Rutten FH, Moons KG, Cramer MJ, *et al.* Recognising heart failure in elderly patients with stable chronic obstructive pulmonary disease in primary care: cross sectional diagnostic study. *BMJ* 2005; **331(7529):** 1379.
4. Murphy JJ, Chakraborty RR, Fuat A, *et al.* Diagnosis and management of patients with heart failure in England. *Clin Med* 2008; **8(3):** 264–266.
5. Rutten FH, Grobbee DE, Hoes AW. Differences between general practitioners and cardiologists in diagnosis and management of heart failure: a survey in every-day practice. *Eur J Heart Fail* 2003; **5(3):** 337–344.
6. Remme WJ, McMurray JJ, Hobbs FD, *et al.* Awareness and perception of heart failure among European cardiologists, internists, geriatricians, and primary care physicians. *Eur Heart J* 2008; **29(14):** 1739–1752.
7. Boonman-de Winter LJ, Rutten FH, Cramer MJ, *et al.* High prevalence of previously unknown heart failure and left ventricular dysfunction in patients with type 2 diabetes. *Diabetologia* 2012; **55(8):** 2154–2162.
8. van Riet EE, Hoes AW, Limburg A, *et al.* Prevalence of unrecognized heart failure in older persons with shortness of breath on exertion. *Eur J Heart Fail* 2014; **16(7):** 772–777.
9. van Mourik Y, Bertens LC, Cramer MJ, *et al.* Unrecognized heart failure and chronic obstructive pulmonary disease (COPD) in frail elderly detected through a near-home targeted screening strategy. *J Am Board Fam Med* 2014; **27(6):** 811–821.
10. Davies M, Hobbs F, Davis R, *et al.* Prevalence of left-ventricular systolic dysfunction and heart failure in the Echocardiographic Heart of England Screening study: a population based study. *Lancet* 2001; **358(9280):** 439–444.
11. Fonseca C. Diagnosis of heart failure in primary care. *Heart Fail Rev* 2006; **11(2):** 95–107.
12. Okkes I, Jamoulle M, Lamberts H, Bentzen N. ICPC-2-E: the electronic version of ICPC-2. Differences from the printed version and the consequences. *Fam Pract* 2000; **17(2):** 101–107.
13. Hoes AW, Voors AA, Rutten FH, *et al.* The Dutch College of General Practitioners guideline on heart failure. (In Dutch). *Huisarts Wet* 2010; **53:** 368–389.
14. Valk MJ, Hoes AW, Mosterd A, *et al.* Rationale, design and baseline results of the Treatment Optimisation in Primary care of Heart failure in the Utrecht region (TOPHU) study: a cluster randomised controlled trial. *BMC Fam Pract* 2015; **16(1):** 130.
15. Calvert MJ, Shankar A, McManus RJ, *et al.* Evaluation of the management of heart failure in primary care. *Fam Pract* 2009; **26(2):** 145–153.
16. Braun V, Heintze C, Rufer V, *et al.* Innovative strategy for implementing chronic heart failure guidelines among family physicians in different healthcare settings in Berlin. *Eur J Heart Fail* 2011; **13(1):** 93–99.
17. Bongers FJ, Schellevis FG, Bakx C, *et al.* Treatment of heart failure in Dutch general practice. *BMC Fam Pract* 2006; **7:** 40.
18. Bosch M, Wensing M, Bakx JC, *et al.* Current treatment of chronic heart failure in primary care; still room for improvement. *J Eval Clin Pract* 2010; **16(3):** 644–650.
19. Rao A, Walsh J. Impact of specialist care in patients with newly diagnosed heart failure: a randomised controlled study. *Int J Cardiol* 2007; **115(2):** 196–202.
20. Khunti K. Systematic review of open access echocardiography for primary care. *Eur J Heart Fail* 2004; **6(1):** 79–83.
21. Cancian M, Battaggia A, Celebrano M, *et al.* The care for chronic heart failure by general practitioners. Results from a clinical audit in Italy. *Eur J Gen Pract* 2013; **19(1):** 3–10.
22. Kelder JC, Cramer MJ, van Wijngaarden J, *et al.* The diagnostic value of physical examination and additional testing in primary care patients with suspected heart failure. *Circulation* 2011; **124(25):** 2865–2873.
23. Fuat A, Hungin AP, Murphy JJ. Barriers to accurate diagnosis and effective management of heart failure in primary care: qualitative study. *BMJ* 2003; **326(7382):** 196.
24. Poppe KK, Squire IB, Whalley GA, *et al.* Known and missing left ventricular ejection fraction and survival in patients with heart failure: a MAGGIC meta-analysis report. *Eur J Heart Fail* 2013; **15(11):** 1220–1227.
25. Paulus WJ, van Ballegoij JJ. Treatment of heart failure with normal ejection fraction: an inconvenient truth! *J Am Coll Cardiol* 2010; **55(6):** 526–537.
26. Peters-Klimm F, Muller-Tasch T, Remppis A, *et al.* Improved guideline adherence to pharmacotherapy of chronic systolic heart failure in general practice — results from a cluster-randomized controlled trial of implementation of a clinical practice guideline. *J Eval Clin Pract* 2008; **14(5):** 823–829.
27. Schou M, Gislason G, Videbaek L, *et al.* Effect of extended follow-up in a specialized heart failure clinic on adherence to guideline recommended therapy: NorthStar Adherence Study. *Eur J Heart Fail* 2014; **16(11):** 1249–1255.
28. Luttik ML, Jaarsma T, van Geel PP, *et al.* Long-term follow-up in optimally treated and stable heart failure patients: primary care vs. heart failure clinic. Results of the COACH-2 study. *Eur J Heart Fail* 2014; **16(11):** 1241–1248.