

# Are there age and sex differences in the investigation and treatment of heart failure? A population-based study

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## SUMMARY

**Background.** Heart failure is a serious, common, and growing problem. Hospital admissions, which account for the bulk of health service costs associated with heart failure, are becoming more frequent.

**Aim.** To determine whether management of heart failure differs by age and sex.

**Method.** A retrospective case note review of prevalent cases in 16 general practices in West London. Five hundred and eighty-three patients (57% women) with a diagnosis of heart failure were reviewed.

**Results.** Mean age of patients with heart failure was 78 years (SD = 9.5) — 74 years at diagnosis (SD = 10) — and was higher for women than men (76 years versus 71 years,  $P < 0.001$ ). In 32% of patients there was no record of a chest X-ray, electrocardiogram, or echocardiogram to support diagnosis. Echocardiography, performed in 34% of patients, was less likely in older patients in both sexes (test for trend  $P = 0.04$  in women and  $0.02$  in men) and, overall, in women (29% compared with 40% of men,  $P = 0.006$ ). Angiotensin-converting enzyme (ACE) inhibitor treatment, recorded in 54% of patients, decreased with age in both sexes ( $P < 0.001$ ) and, on unadjusted data, was more likely in men than in women (61% compared with 49%,  $P = 0.005$ ). On adjustment for age, sex differences in the use of echocardiography and ACE inhibitors were reduced and no longer significant.

**Conclusions.** With increasing age, men and women with heart failure were less likely to have undergone echocardiography or to have received an ACE inhibitor. When account was taken of age, there were no statistically significant sex differences in management; however, because of the demographic distribution of heart failure, women are disproportionately affected by age differences in management. Clinical trials, physician practice, and service developments in heart failure have neglected older people. This balance should be redressed.

**Keywords:** coronary heart disease; hospitals; age bias; sex bias.

## Introduction

HEART failure is a serious, common, and growing problem. Both its incidence and prevalence increase with age, from about 1% of people aged 50 years to 59 years, to 10% of those aged 80 years to 89 years.<sup>1</sup> Heart failure has a profound impact on patients' quality of life<sup>2</sup> and a poor prognosis, with only 25% of men and 38% of women surviving beyond five years.<sup>3</sup> Hospital admissions, which account for the bulk of health service costs associated with heart failure, are becoming more frequent.<sup>4,5</sup> It is increasingly recognised that primary care has a central role in the early detection and treatment of heart failure.<sup>6</sup>

Randomised trials have demonstrated that angiotensin-converting enzyme (ACE) inhibitors improve both quality and quantity of life, although trial participants have been more likely to be younger, male, and hospital-treated compared with prevalent cases in the community.<sup>7-16</sup> European and American guidelines recommend that heart failure be diagnosed with echocardiography and treated with ACE inhibitors;<sup>17-19</sup> however, community-based studies have shown that only a minority of patients receive either of these.<sup>20-23</sup>

Lower rates of investigation and treatment of women and older people with coronary heart disease (CHD) have been widely reported.<sup>24-26</sup> Recently, American studies in hospitalised<sup>27,28</sup> or incident<sup>29</sup> heart failure patients have published similar findings. These issues are important to the National Health Service, particularly in the light of the recent government inquiry into inequalities in health<sup>30</sup> and the setting of national standards for the management of CHD, including heart failure.<sup>31</sup> The objective of the present study, therefore, was to determine whether age and sex influenced the management of the larger pool of prevalent cases of heart failure in the community.

## Method

The study was undertaken in 16 general practices in Kensington & Chelsea and Westminster Health Authority in West London during 1997/1998. Practices were selected from a geographically-defined area (seven out of eight practices participated) or from an administratively-defined group of fundholding practices (15 out of 19 agreed to participate). Data collection in the fundholding practices was stopped after the ninth practice, as the required number of cases had been achieved (see statistical power). All

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the reported results were consistent between the two groups of practices. Four of the 16 practices were single-handed. Two practices did not have any computer system at all and three practices did not keep computerised patient histories (although they did use the computer for repeat prescribing); only one practice kept all patient records on computer.

For the purposes of this study, heart failure was defined pragmatically as a diagnosis of heart failure recorded at any time by a general practitioner (GP) or hospital doctor (discharge summary or letter). Terms that counted as a diagnosis of heart failure included congestive cardiac failure, left ventricular failure, left heart failure, congestive heart failure, and biventricular failure. There was no requirement for minimum signs, symptoms or investigations.

Potential patients with heart failure were identified by searching either computerised disease registers for a diagnosis of heart failure or repeat prescribing lists for a current prescription for a loop or combination diuretic; in addition, GPs were asked to recall from memory additional heart failure patients. This resulted in the identification of 1031 sets of notes, and all written and electronic records of 941 (91%) patients were reviewed by one of two researchers (SH and AR). The remaining notes were missing, owing to death, migration or other reasons. Of those reviewed, 583 patients satisfied the above definition of heart failure.

The following demographic, diagnostic, and treatment data were extracted from the primary care notes of heart failure patients: date of birth; sex; date of diagnosis of heart failure; setting in which the diagnosis was first recorded (general practice, hospital outpatients department, inpatient, accident and emergency [A&E], or other); symptoms and signs; investigations (chest X-ray, electrocardiogram [ECG], or echocardiogram) performed 12 months prior to diagnosis or any time since diagnosis; comorbidity (CHD including myocardial infarction, angina, and coronary revascularisation; hypertension; atrial fibrillation; valvular heart disease; chronic obstructive airways disease [COAD]; and diabetes); inpatient and outpatient visits; prescription of an ACE inhibitor; and adverse reactions or contraindications to ACE inhibitors.

Several items, such as the underlying cause of heart failure, and ethnicity were not collected, as the pilot phase of the study indicated that these were generally not recorded in patient notes.

### *Statistical power and analysis*

Five hundred and fifty cases of heart failure were required in the study in order to have 80% power at the  $P < 0.05$  level to detect a 10% absolute difference in the echocardiography rate between men and women. This assumed equal numbers of men and women with heart failure and that 28% of men would undergo echocardiography.<sup>21</sup> Data were collected in Microsoft Access, and statistical analysis was undertaken using SPSS. Differences in proportions were assessed by chi-square for trend and differences between means by *t*-tests. Age-adjusted proportions were calculated by taking weighted means of the proportions in each age group and differences between age-adjusted proportions were tested using logistic regression. Statistical significance was inferred when the *P*-value was less than 0.05.

## **Results**

### *The prevalence of heart failure*

A total of 583 patients were identified as having a diagnosis of heart failure (57% female). Overall, the prevalence of heart failure was 0.7% (prevalence in males = 0.6%, prevalence in females = 0.8%,  $P = 0.002$ ). The mean age of patients was 78 years (SD = 9.5 years, range = 40 years to 98 years). The preva-

lence of heart failure rose with age, from 0.1% in those aged under 65 years to 4.5% in those aged 65 years and over.

### *The diagnosis of heart failure*

The average age at diagnosis was 74 years (SD = 10 years, range = 32 years to 97 years); this was higher for women (76 years) than for men (71.3 years,  $P < 0.001$ ). Men were more likely to have a comorbid diagnosis of CHD (51% compared with 41% of women,  $P = 0.02$ ), otherwise there was no difference in the proportions of men and women with each comorbidity (Table 1). Sixty-nine patients (12%) had no record of CHD, hypertension, atrial fibrillation, valvular heart disease, COAD or diabetes.

There was no record of a chest X-ray, ECG or echocardiogram being performed to support the diagnosis of heart failure in 189 patients (32%); 349 patients (60%) had a record of a chest X-ray or ECG, and 199 patients (34%) had had an echocardiogram (Table 2). An echocardiogram was less likely in older patients in both sexes (test for trend  $P = 0.02$  in men and 0.04 in women, [Table 3]) and, for unadjusted data, in women than in men (97 [29%] and 102 [40%] respectively,  $P = 0.005$ , [Table 2]). Once data were adjusted for age, the proportions of men and women undergoing echocardiography were not significantly different (Table 2). Of the 199 patients who had a record of an echocardiogram, no results were available for 55 (28%). Of the remaining 144 patients, 55 (38%) showed normal left ventricular function.

Two hundred and ninety-six patients (51%) were diagnosed in primary care and 263 (45%) in hospital (inpatient, outpatient, or A&E). This information was missing for 24 (4%) patients. There was a record of at least one heart failure-related outpatient attendance (i.e. heart failure was a sole or primary reason for the visit) for 290 patients (49%). Hospital admission was more likely in men than women, with age-adjusted proportions of 38% and 27% respectively ( $P = 0.006$ ). For 204 (35%) patients there was no record of a heart failure-related inpatient or outpatient episode; therefore, these patients have had their heart failure managed solely in primary care (Table 2 and Table 3). Of these 204 patients, only 27 (13%) had a record of echocardiography being performed, compared with 172 (45%) of the 379 patients who had been seen in secondary care ( $P < 0.001$ ).

### *ACE inhibitor prescribing*

Overall, 316 patients (54%) had a record of past or current prescription for ACE inhibitors. ACE inhibitor prescribing decreased with increasing age, for both men and women (test for trend  $P = 0.0001$  in men and 0.0009 in women, [Table 4]). On unadjusted data, men were more likely to be prescribed an ACE inhibitor than women (61% of men compared with 49% of women,  $P = 0.005$ ); this difference disappeared once data were adjusted for age.

Patients whose heart failure had been entirely managed in primary care were less likely to have been prescribed an ACE inhibitor (74 [36%] compared with 242 [64%] of patients who had been seen in hospital,  $P < 0.0001$ ). Patients were also more likely to have been prescribed an ACE inhibitor if they had had an echocardiogram (142 [72%] compared with 167 [46%] of those who had not had an echocardiogram,  $P < 0.0001$ ).

Seventy-three patients (13%) had a record of one of the following contraindications to ACE inhibitors: renal impairment, renal failure or peripheral vascular disease; and an adverse effect from an ACE inhibitor was recorded for 48 patients (8%). However, notes were not always clear as to whether adverse effects or contraindications had led to the cessation of an ACE inhibitor — indeed, 42 patients with a recorded contraindication had been prescribed an ACE inhibitor.

**Table 1.** Age and comorbidity of patients with heart failure.

	All patients (n = 583)	Men (n = 253)	Women (n = 330)	P-value men–women (Pearson)
Age (years)	Mean (SD)	Mean (SD)	Mean (SD)	
Current age	78.0 (9.5)	75.0 (9.4)	80.2 (9.1)	<0.0001
Age at diagnosis	74.0 (10.0)	71.2 (9.9)	76.1 (9.5)	< 0.0001
Years since diagnosis	4.0	3.7	4.2	-
Comorbidity	n (%)	n (%)	n (%)	
CHD	263 (45)	129 (51)	134 (41)	0.01
Hypertension	243 (42)	97 (38)	146 (44)	-
Atrial fibrillation	198 (34)	91 (36)	107 (32)	-
Valvular heart disease	73 (13)	31 (12)	42 (13)	-
COAD	148 (25)	72 (29)	76 (23)	-
Diabetes	75 (13)	38 (15)	37 (11)	-

**Table 2.** Numbers (%) of investigations and use of primary and secondary care for patients with heart failure, by sex.

	Crude difference				Age adjusted (%)		
	All (n = 583)	Men (n = 253)	Women (n = 330)	P-value men–women	Men	Women	P-value men–women
Investigations							
Chest X-ray	296 (51)	133 (53)	163 (49)	-	51	49	-
ECG	241 (41)	109 (43)	132 (40)	-	43	39	-
Echocardiography	199 (34)	102 (40)	97 (29)	0.006	38	31	-
None of above	189 (32)	80 (32)	109 (33)	-	32	32	-
Primary/secondary							
Diagnosed in primary care	296 (51)	119 (47)	177 (54)	0.04	48	51	-
Outpatient attendance	290 (50)	128 (51)	162 (49)	-	49	49	-
Inpatient admission	186 (32)	96 (38)	90 (27)	0.006	38	27	0.007
Neither inpatient nor outpatient care	205 (35)	76 (30)	128 (39)	0.02	31	38	-

**Table 3.** Numbers (%) of investigations and use of primary and secondary care for patients with heart failure, by age and sex.

	Men (n = 253) Age group (years)				Women (n = 330) Age group (years)			
	<69 (n = 68)	70–79 (n = 98)	80+ (n = 87)	Test for trend (P)	<69 (n = 41)	70–79 (n = 91)	80+ (n = 198)	Test for trend (P)
Investigations								
Chest X-ray	41 (60)	52 (53)	40 (46)	-	20 (49)	42 (46)	101 (51)	-
ECG	25 (37)	44 (45)	40 (46)	-	13 (32)	41 (45)	78 (39)	-
Echocardiography	31 (46)	46 (47)	25 (29)	0.02	18 (44)	27 (30)	52 (26)	0.04
None of above	19 (28)	28 (29)	33 (38)	-	13 (32)	26 (29)	70 (36)	-
Primary/secondary								
Diagnosed in primary care	28 (41)	43 (44)	48 (55)	-	11 (27)	52 (57)	114 (58)	<0.01
Outpatient attendance	36 (53)	56 (57)	36 (41)	-	20 (49)	49 (54)	93 (47)	-
Inpatient admission	21 (31)	42 (43)	33 (38)	-	17 (42)	16 (18)	57 (29)	-
Neither inpatient nor outpatient care	23 (34)	21 (21)	32 (37)	-	11 (27)	36 (40)	81 (41)	-

## Discussion

In this population-based study of prevalent cases of heart failure, investigation of heart failure with echocardiography and treatment with ACE inhibitors decreased with age. There was little evidence for systematic sex differences in the management of heart failure, although since heart failure is predominantly a condition of older people, and women live longer than men, it is largely women who are affected by these age differences in man-

agement. Since older age is associated with increased risk of hospitalisation and mortality among patients with heart failure,<sup>20,32</sup> the reasons for these age differences in management should be investigated.

There are several possible explanations for the lower rate of ACE inhibitor prescribing in older patients, including doctors' perceptions of benefit, harm, and diagnostic certainty. First, the trials demonstrating the benefits of ACE inhibitors are not representative of patients in the community. Randomised trials have

**Table 4.** Patients with heart failure prescribed an ACE inhibitor, by age and sex.

Age (years)	Men		Women		All patients	
	n	n (%) on ACE inhibitor	n	n (%) on ACE inhibitor	n	n (%) on ACE inhibitor
<65	35	25 (71)	21	15 (71)	56	40 (71)
65–69	33	26 (79)	20	10 (50)	53	36 (68)
70–74	58	39 (67)	40	23 (58)	98	62 (63)
75–79	40	24 (60)	51	32 (63)	91	56 (62)
80–84	47	24 (51)	78	35 (45)	125	59 (47)
85–89	32	14 (44)	77	32 (42)	109	46 (42)
90+	8	2 (25)	43	15 (35)	51	17 (33)
All ages	253	154 (61) <sup>a</sup>	330	162 (49) <sup>a</sup>	583	316 (54)
Test for trend	P = 0.0001		P = 0.0009		P < 0.00001	
Age-adjusted rate	58% <sup>b</sup>		58% <sup>b</sup>		-	

<sup>a</sup>Unadjusted for age, all men compared with all women, P = 0.005; <sup>b</sup>age adjusted rates, no significant differences between men and women.

demonstrated that ACE inhibitors improve both quality and quantity of life, although trial participants<sup>7–16</sup> have been more likely to be younger, male, and hospital-treated compared with prevalent cases in the community.<sup>20–23</sup> In this study, 57% of heart failure patients were female, the average age was 78 years, and 35% were managed wholly in primary care. By contrast, the mean age of patients in trials is more than 15 years younger (the mean age of patients in the CONSENSUS trial<sup>7</sup> at 71 years is exceptional) and no trial has included more than one-third women; all patients are recruited from hospitals. The few studies that have reported results by age show mortality benefits of ACE inhibitors are as great (if not greater) in older patients.<sup>11,33</sup>

Secondly, ACE inhibitors may not be as well tolerated in older people. Published evidence is mixed. One study comparing two ACE inhibitors found that cilazapril was equally well tolerated in patients over and under 65 years of age but that there were more adverse effects from captopril in patients aged over 65 years.<sup>15</sup> Another study concluded that enalapril and captopril were both well tolerated in older patients, although of the 80 patients randomised, 24 were withdrawn due to an adverse event.<sup>34</sup> Our study was unable to draw any conclusions as to the tolerability of ACE inhibitors, as data on adverse events were poorly recorded in patient notes.

Thirdly, there is no clear benefit from ACE inhibitors in the treatment of diastolic heart failure. A recent community-based study estimated that almost half of heart failure patients aged 80 years or over had normal ejection fractions and thus may have heart failure caused by diastolic dysfunction.<sup>20</sup> Echocardiography is recommended to distinguish diastolic from systolic dysfunction;<sup>17,19</sup> however, only 34% of patients identified in our study had undergone echocardiography and this became less likely with age. Patients managed solely in primary care were less likely to have undergone echocardiography than those who had contact with secondary care; in either group, echocardiography was performed in only a minority of patients.

Women were less likely than men to undergo echocardiography or to receive ACE inhibitors on crude comparisons; women were also more likely to have had their heart failure diagnosed in primary care. Many of these differences were explained by age. However, as women were older than men, both at the time of diagnosis of their heart failure (on average 76 years compared with 71 years) and at the time of the study (80 years compared with 75 years), any age-related differences in management affect women disproportionately.

Primary care has a central role in the diagnosis and management of heart failure. Heart failure was diagnosed in primary

care in over half of the patients in this study and was being solely managed in primary care in about one-third. This study included all patients with a record of heart failure (or similar term) in their case notes as a pragmatic definition of what the clinician believed the diagnosis to be. The management consequences of this diagnosis in practice, rather than its veracity, were the subject of this study. This approach differs from that of smaller studies<sup>21,22</sup> that have aimed to reduce diagnostic uncertainty by using a minimum set of symptoms, signs or investigation results to define heart failure (and therefore potentially 're-diagnose' patients). However, these two approaches give broadly comparable results: the prevalence in this study of 4.5% in people aged over 65 years lies between the two estimates from the previous studies (2.8%<sup>21</sup> and 8.1%<sup>22</sup>).

Compared with earlier community-based studies, ACE inhibitor prescribing may have improved. In the present study, 54% of patients had been prescribed an ACE inhibitor, compared with 33% in 1994<sup>22</sup> and 10% in 1988.<sup>21</sup> However, 34% of patients in this study had a record of an echocardiogram as part of the management of their heart failure, little different from the 30%<sup>22</sup> and 28%<sup>21</sup> in previous studies. Current national interest in the provision of 'open access' echocardiography may increase GP access to echocardiography, however further studies are needed to determine whether open access actually translates into higher rates of echocardiography — and, in turn, whether higher rates lead to better patient management. Certainly, the observation that a majority of heart failure patients seen in secondary care have not undergone echocardiography suggests that efforts to increase access should consider secondary as well as primary care.

With increasing age, men and women with heart failure are less likely to undergo echocardiography or be prescribed an ACE inhibitor. Although the extent to which this represents an unfair age bias requires further investigation, it is difficult to avoid the conclusion that clinical trials, physician practice, and service developments in heart failure have — intentionally or otherwise — neglected older people. This balance should be redressed.

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