Heart failure (HF) is a complex clinical syndrome characterised by the reduced ability of the heart to pump and/or fill with blood.1,2 From a physiological point of view, HF can be defined as an inadequate cardiac output to meet metabolic demands or adequate cardiac output secondary to compensatory neurohormonal activation (generally manifesting as increased left ventricular filling pressure).3 HF has recently been classified into three subtypes, namely HF with reduced ejection fraction (HFrEF), HF with preserved ejection fraction (HFpEF) and HF mid-range ejection fraction (HFmrEF), according to the ejection fraction, natriuretic peptide levels and the presence of structural heart disease and diastolic dysfunction.3

HF has been defined as a global pandemic, since it affects around 26 million people worldwide.4 In 2012 it was responsible for an estimated 4.2 million people with HF, with an estimated prevalence of 1.3 %.12 Similarly in Spain showed HF prevalence steadily increasing from 895 per 100,000 population per year in 2000 to 2,126 cases in 2007, with higher rates in men than women. The prevalence of HFpEF was higher than that of HFrEF; in the former rates were higher in women, while in the latter they were higher in men. The overall HF prevalence significantly increased with ageing, particularly among patients >64 years and with HFpEF.7 In Germany in 2006 the prevalence of HF was 1.6 % in women and 1.8 % in men, with numbers increasing considerably with advancing age.4 In Sweden in 2010 the crude prevalence of HF was 1.8 % and was similar in men and women, but after adjustment for demographic composition the estimated rate was 2.2 %, with a weak decrease in temporal trend in women but not men between 2006 and 2010.9 A recent survey reported HF prevalence of 1.44 % in Italy, with rates increasing with the ageing of the population.10 HF is also an important health problem in Asia, and its prevalence seems to be even higher compared to Western countries, ranging between 1.3 % and 6.7 %.11 Currently in China there are 4.2 million people with HF, with an estimated prevalence of 1.3 %.12,13 In Japan around 1 million people have the condition, accounting for 1 % of the population.14–16 In India the estimates range between 1.3 and 4.6 million, which translates to a prevalence of 0.12–0.44 %, although this may be underestimated.17 In Southeast Asia 9 million people have HF; with a prevalence of 6.7 % in Malaysia and 4.5 % in Singapore.18,19 In South America the HF prevalence is 1 % and in Australia it ranges between 1 % and 2 %, similar to Western countries (see Figure 2).19,20 Although aetiologies and clinical characteristics have been studied in Sub-Saharan Africa,21 there are actually no population studies providing insight into prevalence or incidence.22 Few studies have evaluated the different trends in HFrEF and HFpEF prevalence and there are currently no data on the emerging HFmrEF
Epidemiology

than treatment of the risk factors, such as hypertension, diabetes are multifactorial and complex and there is no known prevention other (i.e. early revascularisation) appear to be effective in reducing the

Currently every year in US there are still 915,000 new cases of HF, accounting for an incidence approaching 10 per 1,000 population after 65 years of age. At 40 years of age the lifetime risk of developing HF is one in five and at 80 the remaining lifetime risk of developing HF remains at 20 %, despite the shorter life expectancy. In Portugal the EPICA study reported an incidence of 1.3 cases per 1,000 population per year for those aged ≥25 years, increasing to 8.8 per 1,000 population at ≥65 years and 11.6 per 1,000 population at ≥85 years, with 1.75-fold higher rates in males versus females. In UK, however, the overall incidence rate was 4.4 per 1,000 population per year in men and 3.9 per 1,000 women, with rates doubling every 5 years after the age of 55. In Spain between 2000 and 2007 the overall incidence of HF increased from 2.96 to 3.90 cases per 1,000 population per year, with a higher incidence among men (0.2 cases per 1,000 population per year). Notably, the incidence of HFpEF surpassed that of HFrEF by 0.24 cases per 1,000 population per year. There were 0.32 more HFpEF cases per 1,000 population per year in men; whereas HFrEF was 0.17 cases per 1,000 population per year higher in women. However, when observing the trends over time, in 2007 the rise in overall incidence of HF plateaued, with HFpEF rates starting to slowly decrease in 2005 while HFrEF was still increasing. In Germany in 2006 the age- and gender-standardised incidence of HF was 2.7 cases per 1,000 population per year, with rates being higher in men than women (2.3 versus 3.1 cases per 1,000 population per year). These incidences more than doubled in each of the higher age categories in both genders. The Prevention of Renal and Vascular End-stage Disease (PREVEND) study that enrolled all 28–75-year-old inhabitants of Groningen (85,421 subjects) in the Netherlands in 1997–8 and followed them until the end of 2009 reported an overall HF incidence of 4.4 %, with 34 % of new-onset cases classified as HFpEF and 66 % as HFrEF. In Sweden in 2010 the incidence of HF was 3.1 cases per 1,000 population per year, and was similar in women and men; however, after adjustment for demographic composition the estimated incidences were revised to 3.7 in women and 3.9 in men, with a decreasing temporal trend of 0.9 cases per 1,000 population per year in absolute terms between 2006 and 2010. In Asia there are fewer data about the incidence of HF. In China every year 500,000 new HF cases are diagnosed, accounting for an incidence of 0.9 %, whereas in India there are 0.5–1.8 million new cases per year (an incidence of 0.05–0.17 %), which again may be underestimated. In South America the incidence of HF, according to a single population study, is 199 cases per 100,000 person-years (see Figure 2). The demographic and clinical characteristics of HF have been widely described in Europe and the US, and have been shown to differ considerably between HFpEF and HFrEF; with further variation according to the populations enrolled and the definitions of HFpEF and HFrEF adopted. In particular, it has emerged that HFpEF patients are more likely to be women and older, obese, with a higher New York Heart Association (NYHA) class and cardiovascular comorbidities (such as hypertension, diabetes, atrial fibrillation, valvular disease) and non-cardiovascular comorbidities (such as anaemia, chronic kidney disease, chronic pulmonary disease, hypothyroidism, cancer, peptic ulcer and psychiatric disorders); whereas coronary artery disease is the main determinant of HFrEF. Recently, HFrEF has been recognised as a potentially distinct entity and the few observations available suggest that its characteristics are generally intermediate between those of HFpEF and HFrEF: a high prevalence of comorbidities as in HFrEF (i.e. hypertension, diabetes, atrial fibrillation, chronic

category. Data are heterogeneous and also depend on the definition used for HFpEF and HFrEF, but it might be that about half of HF patients have HFpEF and half HFrEF, with the proportion of individuals with HFpEF increasing, particularly if more unselected populations are considered (see Figure 3). HFpEF could be dominant in driving the overall HF prevalence, since in the past 20 years secular trends have reported an increasing proportion of patients with HFpEF but relatively stable or even decreasing rates with HFrEF (see Figure 4); thus it is expected that by 2020 65 % of patients hospitalised for HF will have HFpEF. Notably, the increase in HF prevalence observed worldwide may not necessarily be linked with an increase in HF incidence, which has been reported to be stable or even decreasing in several studies, particularly in women. The ageing of the population, together with improved HF survival due to the advancement in treatments and diagnostic technology could explain the increase in prevalence, whereas the reduction in incidence (due to prevention programmes) may be determined by lower severity and better treatment of acute coronary syndromes. In addition to this, the risk factors for HFpEF are multifactorial and complex and there is no known prevention other than treatment of the risk factors, such as hypertension, diabetes and obesity; whereas prevention and early treatment strategies (i.e. early revascularisation) appear to be effective in reducing the risk and severity of acute myocardial infarction. These observations may explain a reduction in the incidence of HFpEF but increasing incidence of HFrEF and HFrEF.
Most studies describing HF characteristics have been performed in North America and Europe; however the phenotypes of HF patients could be different in other regions due to different aetiologies, comorbidities, economic and health care systems. One study showed that in Africa HF patients are younger than in other regions, with most being NYHA class III/IV and having valve disease.\textsuperscript{41} Half of these HF patients are male and 29 \% have HFrEF. The leading causes of HF in Africa are hypertensive heart disease and dilated cardiomyopathy.\textsuperscript{41-43} In Asia the proportion of patients in NYHA class III/IV is similar to that in NYHA class II.\textsuperscript{17,44} Coronary artery disease is the leading HF aetiology. More than half of the HF population is male and has hypertension, and HFrEF is present in 41 \% of patients.\textsuperscript{17,44} It is notable that in Japan ischaemic aetiology is still lower than in Western countries.

It has, however, increased over time, and the HFrEF prevalence ranges between 34 \% and 68 \%.\textsuperscript{44} Middle Eastern HF patients are also young, and are more likely to be male. There is a high prevalence of several comorbidities as such obesity, diabetes, hypertension, hyperlipidaemia and valve disease, but only 10–30 \% of the population has HFrEF. Coronary artery disease is the main cause of HF in the Middle East.\textsuperscript{45} In South America the most common cause of HF is coronary artery disease. More than half of HF patients are male and have hypertension, and around half have dyslipidaemia and valve disease.\textsuperscript{45} In Australia HF patients are more likely to be male and the leading HF aetiology is coronary artery disease; HFrEF is present in 25 \% of cases.\textsuperscript{45}

**Outcomes**

HF outcomes have been extensively investigated in the US. The Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients With Heart Failure (OPTIMIZE-HF) study enrolling 20,118 patients with HFrEF and 21,149 with HFrEF (EF >40 \%) reported no differences between HFrEF and HFrEF in 60–90-day mortality (9.8 \% versus 9.5 \%) and rehospitalisation (29.9 \% versus 29.2 \%), but higher in-hospital mortality in those with HFrEF (3.9 \%) versus HFrEF (2.9 \%). When the comparison between HFrEF (EF >50 \%) and HFrEF (EF 40–50 \%) was performed, no differences in outcomes were observed.\textsuperscript{46} Similarly, the Get With The Guidelines (GWGT) registry that enrolled 15,716 patients with HFrEF, 5,626 with HFrEF and 18,897 with HFrEF observed 37.5 \%, 35.1 \% and 35.6 \% mortality at 1 year respectively, with no differences in risk after several adjustments. The 1-year HF hospital readmission rates were 30.9 \%, 28.4 \% and 24.3 \% in HFrEF, HFrEF and HFrEF, respectively, but there was a higher risk in HFrEF and HFrEF compared with HFrEF.\textsuperscript{46} The Management Predischarge Process for Assessment of Carvedilol Therapy for Heart Failure (IMPACT-HF) study reported that >50 \% of patients were discharged with unresolved symptoms, and within 60 days half had worsening symptoms, a quarter were re-hospitalised and >10 \% died.\textsuperscript{47} The Canadian Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study enrolling 1,570 patients with HFrEF and 880 with HFrEF reported no differences in mortality at 30 days (7.1 \% and 5.3 \%, respectively) and 1 year (25.5 \% and 22.2 \%, respectively). Similarly, for HFrEF and HFrEF there were no differences between HF readmissions at 30 days (4.9 \% and 4.5 \%, respectively) and at 1-year (16.1 \% and 13.5 \%, respectively).\textsuperscript{48}

In Europe, the EuroHeart Failure Survey II, which enrolled 3,580 patients hospitalised for HF, overall in-hospital mortality was 6.4 \%.\textsuperscript{50,51} Recently, in the European Society of Cardiology Heart Failure Long-Term (ESC-HF-LT) registry that enrolled 12,440 patients with acute and chronic HF from 21 European and/or Mediterranean countries, the 1-year mortality rate was estimated to be 23.6 \% for acute HF and 6.4 \% for chronic HF; whereas the rates for the combined endpoint of mortality or HF hospitalisation within 1 year were 36 \% for acute HF and 14.5 \% for chronic HF. Mortality rates ranged across the different regions from 21.6 \% to 36.5 \% for acute HF and from 6.9 \% to 15.6 \% for chronic HF.\textsuperscript{52}

Fewer studies have evaluated outcomes in other world regions. Thirty-day mortality reported in China was 5.3 \%, while it was 3.9 \% in Taiwan.\textsuperscript{53} In Singapore, in a cohort of 15,774 HF patients followed from 1991 to
Since many episodes of worsening of HF are treated by modifying oral therapy or by temporary intravenous treatments in community departments without hospital admission, ambulatory care has a role in HF management. The Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure (PARADIGM-HF) trial recently showed that episodes of outpatient treatment-intensification could significantly contribute to accrue a target number of endpoints in an event-driven trial. According the most recent US reports, in 2011 there were 553,000 emergency department visits and 257,000 outpatient department visits for HF; whereas in 2012 there were 1,774,000 physician office visits with a primary diagnosis of HF.48 No similar estimates are available in Europe, but the quality of outpatient care has been evaluated by the ESC–HF–LT registry, which reported only 3.2–5.4 % non-adherence to guideline-suggested drugs, although enrolment in this registry was highly selective.49 A report from the nationwide and generalisable Swedish Heart Failure Registry suggests poor treatment utilisation, particularly of mineralocorticoid receptor antagonists and device therapy.50

Quality of life in HF is worse than in many other chronic diseases.51 Indeed, a national registry in Sweden has reported that 66,318 and 59,535 premature life-years are lost due to HF compared to 55,364 and 64,533 due to cancer in men and women, respectively.52 In the Candesartan in Heart Failure: Assessment of Reduction in Mortality and Morbidity (CHARM) trial, health-related quality of life was similarly impaired in patients with HFpEF and HFrEF (41.1 versus 40.8) and independent factors were associated with worse health-related quality of life in both populations (female gender, younger age, higher body mass index, lower systolic blood pressure, greater symptom burden and worse functional status).53

Limitation

The current review reports data from studies with different designs and settings, thus the prevalence, incidence and outcome rates might not be fully comparable.

Conclusion

Dataindicate that HF is a major and growing public health problem worldwide. Even though the incidence of HF is stable, the prevalence is going to rise because of the ageing population and improvements in treatment. This will cause further increases in hospitalisation rates and, consequently, in health care costs. HF is a common disease not only in Europe and the US, but worldwide. The switch toward a Western lifestyle in developing countries may be contributing to a real HF pandemic. Phenotyping of HFpEF and HFrEF, testing existing drugs and developing novel interventions for these categories represents an important future challenge. Currently HFpEF and HFrEF are poorly investigated, particularly in developing countries, and there are no effective therapies. In order to reduce the number of hospitalisations and related costs, appropriate treatments are needed and further epidemiological registries are required to better characterise the HF population and improve trial design.
the incidence of and survival with heart failure. JAMA. 2002;287:1937-40. DOI: 10.1001/jama.287.20.1937

29. Najafi F, Jamrozik K, Dobson A. Understanding the ‘complexity of heart failure in acute presentations’. influence of the effects of heart failure. Eur Heart J 2009;30:1833-41. DOI: 10.1093/eurheartj/epp242

30. Roger VL, Weston SA, Redfield MM, et al. Trends in heart failure incidence and survival in a community-based population. JAMA 2004;292:348-50. DOI: 10.1001/jama.292.3.348

31. Heidenreich PA, Albert NM, Allen LA, et al. American Heart Association Advocacy Committee; Council on Arteriosclerosis, Thrombosis and Vascular Biology; Council on Cardiovascular Radiology and Intervention; Council on Clinical Cardiology; Council on Epidemiology and Prevention; Stroke Council. Forecasting the impact of heart failure in the United States: a policy statement from the American Heart Association. Circ Heart Fail 2011;4:606-19. DOI: 10.1161/HFH.0b013e31829130a9

32. Joumah G, Hammad N, Eltoum S, et al. Time trends in incidence and mortality of acute myocardial infarction, and all-cause mortality following a cardiovascular prevention program in Sweden. PLoS One 2012;7:e104201. DOI: 10.1371/journal.pone.0010420

33. Johansson S, Wallander MA, Ruigomez A, et al. Incidence of newly diagnosed heart failure in UK general practice. Eur J Heart Fail 2013;15:221-30. DOI: 10.1093/eurjhf/hft063

34. Brouwers FP, De Boer RA, van der Harst P, et al. Incidence and epidemiology of new onset heart failure with preserved vs. reduced ejection fraction in a community-based cohort: 11-year follow-up of PREVEND. Eur J Heart Fail 2013;15:1424-34. DOI: 10.1093/eurjhf/hft073

35. Goffdinner JS, McClelland RS, Marshall R, et al. Outcome of community-based care of acute heart failure: influences of left ventricular systolic function. The Cardiovascular Health Study. Am J Med 2002;113:83-91. DOI: 10.1016/S0002-9343(01)00803-5

36. Cheng RK, Coo M, Neely ML, et al. Outcomes in patients with heart failure with preserved, borderline, and reduced ejection fraction in the Medicare population. Am J Cardiol 2014;114:956-63. DOI: 10.1016/j.amjcard.2014.07.078

37. Gheorghe M, Filipides G, De Luca L, et al. Congestion in acute heart failure: a comparison of clinical and biomarker targets of evaluation and treatment. Am J Med 2009;120:53-60. DOI: 10.1016/j.amjmed.2008.09.011

38. Bhatia RS, Tu JV, Lee DS, et al. Outcome of heart failure with preserved ejection fraction in a population-based study. N Engl J Med 2006;355:260-9. DOI: 10.1056/NEJMoa051530

39. Niemann MS, Brutsaert D, Dickenstein K, et al. EuroHeart Survey Investigators; Heart Failure Association; European Society of Cardiology. Are hospitalized or ambulatory heart failure patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12,440 patients from the EuroHeart Failure Survey (EHFS). Eur J Heart Fail 2004;6:83-91. DOI: 10.1016/j.ejhf.2003.12.003

40. Nordskag TD, Jorgesen M, Th Christensen K, et al. Synergistic versus diastolic heart failure in community practice: clinical features, outcomes in hospital, and potential role of left ventricular hypertrophy inhibitors. Am J Med 2000;109:605-13. PMID: 1199679

41. Solomon SD, Anavekar N, Skali H, et al. Cardiometabolic predictors of hospitalization with heart failure in the Medicare population. Circulation 2005;112:1378-84. DOI: 10.1161/CIRCULATIONAHA.105.561432

42. He K, Burkhoff D, Long MX, et al. Comparison of ventricular structure and function in Chinese patients with heart failure and heart failure with preserved, and reduced, borderline, and preserved ejection fractions. J Am Coll Cardiol 2007;49:186-91. DOI: 10.1016/j.jacc.2006.07.024

43. Kapoor Jr, Kapoor R, Lu C, et al. Precipitating clinical factors, heart failure characterization, and outcomes in patients hospitalized with heart failure with reduced, borderline, and preserved ejection fraction. J Am Coll Cardiol 2014;64:672. DOI: 10.1016/j.jacc.2014.01.075

44. Dekbari H, Reo K, Zhu J, et al. INTER-CHF Investigators. Heart failure in Asia, the Middle East and South America: The INTER-CHF study. Int J Cardiol 2016;204:183-41. DOI: 10.1016/j.ripc.2016.02.017

45. Lee R, Chan SP, Chan YH, et al. Impact of race on morbidity and mortality in patients with congestive heart failure: a study of the multiracial population in Singapore. Int J Cardiol 2009;134:42-9. DOI: 10.1016/j.ijcard.2007.12.037. PMID: 18372360

46. Yum YJ, Yoo BS, Lee JW, et al. Treatment performance measures affect clinical outcomes in patients with acute systolic heart failure: initial results from the Heart Failure Registry. Cardiovasc Drug Rev 2012;30:151-8. DOI: 22343915

47. Tsuchihashi-Makaya M, Hamaguchi S, Kinugawa S, et al. Clinical characteristics and outcomes of heart failure patients: observations from the Gulf acute heart failure registry (Gulf AHR). Eur J Heart Fail 2015;17:915-22. DOI: 10.1002/ejhf.1868

48. Hobbs FD, Kenkre JE, Roalfe AK, et al. Impact of heart failure therapy on survival of hospitalised patients with heart failure and reduced vs preserved ejection fraction. Report from the Japanese Cardiac Registry of Heart Failure (JCR-HF). J Card Fail 2009;15:1893-900. PMID: 1944216

49. Rajkomar A, Salo N, Takaro T; Investigators of the Acute Decompensated Heart Failure Syndromes (ATTEND) Registry Association of age and baseline systolic blood pressure with outcomes in patients hospitalized for acute heart failure syndromes. Int J Cardiol 2015;191:100-6. DOI: 10.1016/j.ijcard.2015.04.258. PMID: 25965613

50. Teng TH, Katzenellenbogen MH, Hung L, et al. Rural urban differences in 30-day and 1-year mortality following first-ever heart failure hospitalisation in Western Australia: a population-based study using data linkage. BMJ Open 2016;6:e004474. DOI: 10.1136/bmjopen-2013-004474

51. Micali AE, Eshik GD, Coats AI. The epidemiology of heart failure in Australia. Int J Cardiol 2007;118:370-4. DOI: 10.1016/j.ijcard.2007.06.050

52. Okumura N, Jung FS, Gong J, et al. PARADIGM-HF Investigators and Committees. Importance of clinical worsening of heart failure treated in the outpatient setting: evidence from the Prospective Comparison of ARNI With ACEI to Determine Impact on Global Mortality and Morbidity in Heart Failure Trial (PARADIGM-HF). Circulation 2016;133:2254-62. DOI: 10.1161/CIRCULATIONAHA.115.021698

53. Maggioni AP, Anker SD, Dahlstrom U, et al. Heart Failure with preserved ejection fraction: clinical features, outcomes and medical disorders and a representative adult population. Eur Heart J 2015;36:1733-4. DOI: 10.1093/eurjhf/het133. PMID: 23978433

54. Thoverson T, Bensen L, Dahlstrom U, et al. Use of evidence-based therapy and survival in patients with heart failure treated in accordance with European Society of Cardiology guidelines? Evidence from 12,440 patients from the EuroHeart Failure Survey (EHFS). Eur J Heart Fail 2013;15:783-9. DOI: 10.1002/ejhf.1064

55. Hobbs FD, Kenkre E, Roalfe AK, et al. Impact of heart failure and left ventricular systolic dysfunction on quality of life: a comparison study of common chronic cardiac and medical disorders and a representative adult population. Eur Heart J 2002;23:1867-76. PMID: 12445536

56. Stewart E, Little EV, Krakowitl RA, et al. Population impact of heart failure and the most common forms of cancer: a study of 116 309 hospital cases in Sweden (1998 to 2004). Cardiovasc Journals Cardiovasc Journals Outcomes 2005;9:13-22. DOI: 10.1161/CIRCOUTCOMES.110.957371

57. Lam CS, Donal K, Kragh-Krainer E, et al. CHARM Investigators. Characterization of heart-related quality of life in heart failure patients with preserved versus low ejection fraction in the CHARM. Eur Heart J 2007;28:9-51. DOI: 10.1093/eurheartj/eht016

58. Bonta EG, Redfield MM. Diastolic and systolic heart failure are distinct phenotypes within the heart failure spectrum. Circulation 2013;128:1806-13. DOI: 10.1161/CIRCULATIONAHA.110.943638

59. Tzanas A, Papadopoulos E, Tzoufi A, et al. Heart failure with preserved ejection fraction: a comparison study of common chronic cardiac and medical disorders and a representative adult population. Eur Heart J 2002;23:1867-76. PMID: 12445536