DISEASE MONITORING OF PATIENTS WITH CHRONIC HEART FAILURE

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As is well known, heart failure in western countries is increasing in prevalence, places a heavy burden on health budgets (accounting for 1–2% of total health care costs), diminishes considerably quality of life, and notwithstanding major advances in management, has a bleak short-term prognosis. Among the challenges facing clinicians is how best to diagnose heart failure. In some patients this presents no problem, especially when symptoms and physical signs are "textbook", an underlying cause is obvious and basic, and simple investigations (chest *x* ray in particular) confirm clinical suspicions. But other patients are more challenging where the presence of obesity or chronic airways disease, for example, can obscure or confuse the clinical picture.

LONG TERM MANAGEMENT OF HEART FAILURE PATIENTS

Once any difficulties regarding the diagnosis of heart failure have been overcome, the question of how best to manage patients in the long term arises. Sad to say, evidence-based guidelines regarding drug treatment (relating to the class of drug and, if in use, the recommended dosage) are not commonly followed in clinical practice. There is evidence that in view of the increasing complexity of pharmacotherapy and the rapid evolution of new interventions (resynchronisation therapy, implantable cardioverter-defibrillators, left ventricular assist devices, for example), patients are best cared for in multidisciplinary specialist heart failure clinics or with careful integration of primary and secondary care. Whatever the clinic setting, attention should be directed to treatment of the underlying disorder (most commonly hypertension or/and coronary artery disease), to correction and avoidance of precipitating factors, to the introduction of non-pharmacological measures including an exercise programme and an educational programme (including dietary advice), and for those who are terminal, to counselling expertise and palliative care.

Regarding drug treatment, there are many areas of uncertainty. For patients whose heart failure results predominantly from diastolic left ventricular diastolic dysfunction, many of whom are elderly, female and hypertensive, there is little guidance from formal controlled studies as to which medications should be used. For those patients with underlying systolic left ventricular dysfunction, by contrast, excellent objective clinical trials in sizeable cohorts give some guidance regarding the use of angiotensin-converting enzyme (ACE) inhibitors (and/or angiotensin receptor blockers, ARBs), selected β-blockers and an aldosterone receptor blocker (spironolactone or eplerenone), all of which have been shown to increase longevity and should be used as a routine in appropriate patients unless there are compelling contraindications. Loop and/or thiazide-type diuretics are also prescribed as a routine despite the fact that there have never been (and probably never will be) placebo-controlled trials to confirm the powerful clinical impression of their efficacy. Digoxin is indicated for control of ventricular rate in a high percentage of patients in whom atrial fibrillation contributes to, or is a complication of, heart failure: its place in the presence of sinus rhythm is less clear where its benefits (reduced hospitalisation rates and improved exercise capacity) must be weighed against the considerable potential for its side effects.

In this article we propose what indices, in our opinion, should be monitored for patients with established chronic heart failure resulting from left ventricular systolic dysfunction—whether they are followed in primary care or in specialty or hospital clinics. Until sound, objective information becomes available, we suggest that with few exceptions, the same indices should be monitored in patients whose chronic heart failure results from underlying diastolic left ventricular failure. We will discuss briefly the potential for plasma values of B-type natriuretic peptide (BNP) to assist in the routine management of patients with chronic heart failure. We emphasise at the outset that what factors should be monitored and with what frequency is, in the absence of objective data and guidance that is consistent among recently published guidelines, open to discussion and dispute.

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WHAT TO MONITOR

Patient understanding (education), history, medications

A comprehensive heart failure education programme, as part of an overall management plan, is a necessary basis for patient compliance with therapy. Accordingly, time should be available at the time of discharge from hospital and at each clinic visit for the patient to clarify any uncertainties to do with his/her disorder, and for the health professional to ensure patient understanding of the rationale for all treatment modalities[1 2] together with the significance of symptoms and signs. Current treatments—both non-pharmacological (dietary sodium restriction, avoidance of liquorice and excessive alcohol, regular moderate exercise) and pharmacological—need regular review as part of this comprehensive management programme (table 1). Such programmes have been clearly shown to improve clinical status and reduce hospitalisation rates.[3]

Symptoms, physical signs and body weight

There is no substitute for a careful history and physical examination. It is obvious that these pivotal indices are better documented when there is adequate time available for well trained health professionals and the facilities permit full examination of each patient's chest, jugular venous pressure (JVP), abdomen and periphery as well as measurement of arterial pressure in the supine and standing positions. Especially useful are accurate measurement of the JVP and auscultation for a third heart sound,[4 5] both benefiting from observer experience (table 1). A low blood pressure that falls further with upright posture points to deterioration in left ventricular function and/or volume depletion, the latter requiring a reduction in diuretic therapy or relaxation of a restricted dietary sodium intake. Uncontrolled hypertension, on the other hand, is one precipitant of hospital readmission for heart failure.

Busy clinics in which time is restricted and where it is impossible to perform an adequate physical examination will lead, inevitably, to inappropriate conclusions and often unnecessary, expensive investigations

Table 1 Clinical indices requiring regular monitoring in patients with chronic heart failure

	Suggested frequency
1. Patient understanding	Every visit
▶ underlying disease, precipitating factors	
▶ medications and dietary sodium—rationale, compliance, toxicity	
2. Symptoms	Every visit
▶ of heart failure	
▶ of precipitating factors/concomitant disorders	
▶ of drug toxicity	
3. Signs	Every visit
▶ heart rate and rhythm, blood pressure supine and standing, JVP, cardiac auscultation, lung fields, abdomen, ankles—other signs as required	
4. Precipitating factors	Every visit
5. Concomitant disorders	Every visit
6. Body weight	Every visit

JVP, jugular venous pressure.

Body weight standardised to time of day and clothing, preferably recorded regularly by the patient at home as well as in the clinic, is useful in detecting sodium and water retention (increased weight) and over-diuresis or cardiac cachexia (weight loss). The potential of non-invasive home telemonitoring (for daily weight, blood pressure, heart rate and rhythm) is exciting.[6]

Concomitant disorders

Since the majority of patients with chronic heart failure are elderly, concomitant diseases are common and, along with medications targeting such diseases, need regular review. Where possible, non-steroidal anti-inflammatory drugs should be avoided in view of their propensity to precipitate heart failure, exacerbate azotaemia, and induce hyperkalaemia—particularly in patients receiving ACE inhibitors or ARBs and aldosterone receptor blockers. Accordingly, the pharmacological management of musculoskeletal/rheumatological disorders in patients with chronic heart failure requires careful thought.

A regular review of factors known to precipitate or exacerbate heart failure and result in unnecessary hospitalisation should be undertaken. Apart from non-adherence to dietary sodium restriction or medication, continuation of smoking,[7] inappropriate use of antiarrhythmics or calcium channel blockers (especially verapamil and diltiazem), myocardial ischaemia, uncontrolled hypertension, arrhythmias, occult infection, pulmonary embolism, thyroid dysfunction, anaemia and worsening cardiac valve lesions need to be considered in a regular, planned manner.[8–10]

Investigations

There are no universally accepted evidence-based guidelines for what laboratory investigations should be utilised and how frequently they should be performed. We suggest that plasma electrolytes and renal function should be measured 3–6 monthly (table 2) and more frequently when there is deterioration in clinical status, with alterations in medication, where there is renal impairment, in patients on high-dose loop diuretics and/or receiving two or more potassium-retaining drugs (ACE inhibitors and/or ARBs, aldosterone receptor antagonists, β-blockers), and if a non-steroidal anti-inflammatory drug (NSAID) is added. Particular attention needs to be paid to plasma concentrations of potassium, creatinine, urea (or blood urea nitrogen, BUN) and sodium. The European Society of Cardiology recommends measuring plasma (or serum) creatinine and potassium every 5–7 days after initiation of treatment with an aldosterone receptor antagonist until values are stable, and 3–6 monthly thereafter.[10] The potentially serious consequences of adding potassium-sparing diuretics without such careful monitoring of renal function and electrolytes is now well publicised. Plasma magnesium should be measured if arrhythmias are a problem. Chest *x* rays need not be routine but, rather, reserved for patients in whom worsening of heart failure is suspected but unproven, and in those whose exacerbation of heart failure is unexplained. A complete blood count is advisable annually as a routine procedure to detect anaemia early, and more frequently where the reason behind worsening cardiac status is unexplained—thinking of anaemia itself or occult infection as a precipitant of heart failure. Thyroid function tests should always be performed when heart failure is

Table 2 Routine investigations for monitoring patients with chronic heart failure

Investigation	Suggested frequency
Plasma creatinine, urea (or BUN), Na, K—Mg if arrhythmias	3–6 monthly*
2. Complete blood count	12 monthly
3. Chest *x* ray	Upon clinical suspicion
4. Electrocardiogram	Upon clinical suspicion
5. Cardiac enzymes	Upon clinical suspicion
6. Echocardiography	Upon clinical suspicion

*Measure plasma creatinine and potassium every 5–7 days upon initiation of spironolactone or eplerenone treatment until the values are stable; then 3–6 monthly.
BUN, blood urea nitrogen; K, potassium; Mg, magnesium; Na, sodium.

first diagnosed and thereafter upon clinical suspicion of hyper- or hypothyroidism or when worsening cardiac status, arrhythmia or hyponatraemia cannot otherwise be explained. Abnormalities in thyroid function are frequently not accompanied by textbook symptoms and signs in the elderly, hence the level of suspicion should always be high. Patients receiving amiodarone require regular, routine measurements of thyroid function.

Serial ECGs, again, are not needed. Rather they should be reserved for those in whom questions relating to cardiac rhythm, exacerbation of myocardial ischaemia or unexplained worsening of heart failure arise.

Likewise, cardiac enzymes (creatine kinase (CK)-MB, troponin T or troponin I) need only be measured where exacerbation of myocardial ischaemia or myocardial infarction is suspected or if worsening of clinical cardiac status is evident without good reason. Diabetics, the elderly and hypertensive patients are most prone to ''silent'' myocardial ischaemia or infarction and cardiac enzymes should be requested early in such patients when worsening heart failure is observed in the absence of a clear precipitating factor.

Re-evaluation of cardiac function by non-invasive or invasive techniques should not be routine in clinical practice. Repeat echocardiography should be carried out where there is uncertainty regarding the status of the cardiac valves, the presence of intra-cardiac clots, and where there is unexplained deterioration in clinical cardiac status. Other special circumstances might call for reassessment of cardiac function (left ventricular ejection fraction and volumes in particular) by echocardiography, radionuclide ventriculography or catheterisation—for example, where unexpected clinical improvement occurs and could result in removal of the patient from the cardiac transplantation list.

Tailoring treatment according to plasma natriuretic peptide values

It is not a new concept that treatment of patients with heart failure might best be accomplished by tailoring treatment, both pharmacological and non-pharmacological, according to some objective measure. Requirements regarding the desirable level of dietary sodium intake and of drug doses differ from patient to patient. For example, elderly patients often cannot tolerate trial-based target doses of ACE inhibitors, β-blockers and ARBs, while patients with azotaemia may need high doses of a loop diuretic to remain oedema-free. Determining optimal diet and drug doses currently depends on assessment of patient clinical status as determined by symptoms and physical signs, and laboratory testing especially for plasma creatinine and urea values. Taking account of these clinical and laboratory results, drug doses are, in general, increased gradually to those used in formal studies which have documented improved mortality and/or morbidity. Whereas this might be accomplished with skill and some objectivity in designer heart failure clinics where health professionals have specialised training and plenty of time to asses each patient, it is unlikely to be possible in the hurly burly of busy general medical, cardiology or primary care clinics. It is in the latter situation, in particular, that an objective measure of cardiac status has the potential to assist in guiding the type and intensity of treatment.

A number of methods and techniques for guiding treatment of patients with chronic heart failure have been assessed. These include clinical and objective haemodynamic indices, and renin profiling. Practical or theoretical limitations have, however, prevented their widespread use in clinical practice.

Another proposed method of guiding treatment involves serial, routine measurements of B-type natriuretic peptide (BNP) or the 1–76 amino acid N-terminal fragment (NT-proBNP) of the precursor 1–108 amino acid prohormone. These

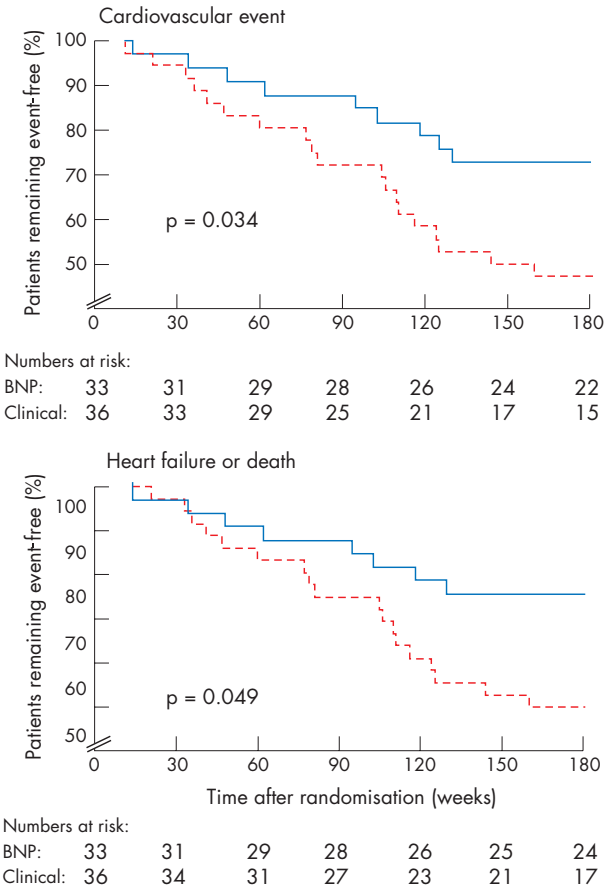

Figure 1 Kaplan–Meier event curves for time to first cardiovascular event (upper panel) and to heart failure event or death (lower panel) in 69 patients with heart failure randomised to drug treatment guided by plasma N-terminal pro-B-type natriuretic peptide (NT-proBNP) (continuous line) or standardised clinical assessment (discontinuous line). Reprinted with permission from Troughton *et al*.[16]

peptides are released from the cardiac ventricles into the circulation according to the degree of stretch of the myocardium, but other factors can also contribute. As cardiac function deteriorates and the ventricles dilate, plasma concentrations of both peptides increase progressively. Accordingly, numerous studies have shown positive associations between circulating BNP and NT-proBNP concentrations on the one hand and the degree of stretch of the left ventricle (or pulmonary wedge pressure) on the other hand. Furthermore, treatment for chronic heart failure which induces a decline in intracardiac pressures results in a parallel fall in plasma concentrations of both peptides. This is so for diuretics (both loop diuretics and spironolactone) and the ACE inhibitors and ARBs. β-blockers may raise natriuretic peptide values in the first few weeks but sustained treatment results in a substantial fall—again in parallel with improved cardiac indices.[11 12] Accordingly a number of workers, including Murdoch and colleagues,[13] have proposed that the management of patients with chronic heart failure might logically be assisted by utilising plasma BNP or NT-proBNP values as a guide, particularly for the intensity of pharmacotherapy. This proposal is strengthened by the observation that changes in plasma concentrations of these peptides over time correspond with parallel changes in objective indices of cardiac function and mortality.[14 15] On the other hand, less enthusiastic views have been expressed by authors who claim the test has severe limitations.

The only way to answer this current uncertainty is to carry out formal controlled studies of drug treatment based on usual clinical care versus treatment guided by BNP or NT-proBNP values. The outcome of such trials, of course, might be quite different according to the clinical setting—for example, whether the study is carried out in clinical research or specialty cardiology clinics or in primary care.

To date, two trials have been completed, one of which was carried out in a single hospital in New Zealand[16] and the other involved patients followed in 21 hospitals in France.[17] Both studies reported that the outcome after 6 months or more favoured natriuretic peptide-guided treatment over "usual care" in regard to total cardiovascular events and time to first cardiovascular event[16] or heart failure events and time to first heart failure event[17] (figs 1 and 2). While the New Zealand study involved only 69 patients[16] and both trials were of brief duration,[16 17] a number of other studies are underway[18] and should provide robust evidence one way or the other.

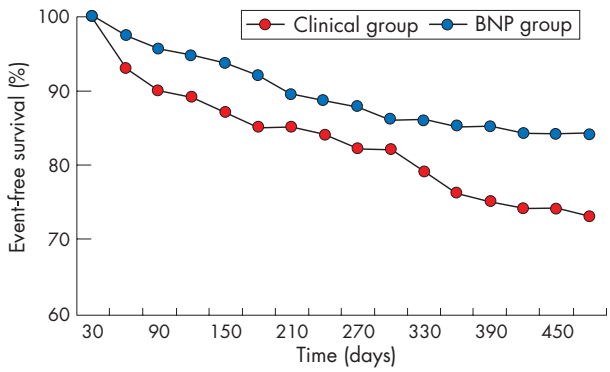

Figure 2 Event-free survival in 220 patients with heart failure whose drug treatment was guided by plasma concentrations of B-type natriuretic peptide (BNP), or by usual clinical criteria. During a median follow-up period of 15 months, there were fewer events (death or hospitalisation for heart failure) in the BNP-guided group than the Clinical group (25 versus 57, $p<0.001$). Reprinted with permission from Jourdain *et al*.[17]

Disease monitoring in chronic heart failure: key points

- Ensure patient understanding: precipitating factors, diet/exercise, medications
- Check patient's symptoms, physical signs, concomitant disease, body weight
- Check medications (especially NSAIDs) for concomitant disorder
- Measure plasma electrolytes 3–6 monthly, complete blood count annually; other investigations only upon clinical suspicion
- Take care on addition of spironolactone (or eplerenone)—measure plasma creatinine and potassium every 5–7 days until the values are stable
- Consider using plasma levels of BNP or NT-proBNP, along with symptoms and physical signs, to guide drug treatment

Meantime, other trials raise the possibility that BNP or NT-proBNP levels might be useful for patient management under other circumstances. For example, an early decline in BNP levels has been proposed as an indicator of recovery of ventricular function during mechanical circulatory support and as a marker of efficacy of long-term cardiac resynchronisation therapy.

The potential for using BNP or NT-proBNP in guiding the treatment of heart failure will require understanding that a number of factors contribute to their plasma levels beyond stretch of the left ventricle and hence the level of left ventricular function/dysfunction. In particular, their levels are generally higher in females than males, are increased in the presence of renal impairment, are elevated in hyperthyroidism and with tachyarrhythmias, and tend to be reduced in the obese. Beyond the above factors, much of the unexplained variation in natriuretic peptide levels between individuals is attributable to genetic factors.[19]

SUMMARY

Monitoring of patients with chronic heart failure requires recognition that "disease management programmes" for such patients need to be multifaceted with intensive patient education, optimisation of the therapeutic regimen and ongoing surveillance.[2 6 20] In the absence of objective data, and since the various guidelines for managing patients with chronic heart failure do not provide uniform instructions, we have here given our personal view on what factors should be monitored, and how frequently. The vital question of optimisation of treatment is at present an uncertain goal wherein it is unclear whether drug doses should be directed according to completed trials or whether it is better to tailor treatment to some objective index of cardiac function in the individual patient. We declare our optimism regarding the place of BNP and NT-proBNP in individualising pharmacological treatment. The issue will become clear upon completion of several ongoing trials.

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REFERENCES

1 **Lainscak M**, Keber I. Patients' knowledge and beta blocker treatment improve prognosis of patients from a heart failure clinic. *Eur J Heart Fail* 2006;**8**:187–90.

2 **van der Wal MHL**, Jaarsma T, Moser DK, *et al*. Compliance in heart failure patients: the importance of knowledge and beliefs. *Eur Heart J* 2006;**27**:434–40.

► **Compliance with medications and non-pharmacologic indices was shown to relate to patient knowledge of the disorder (assessed on a formal knowledge scale) in elderly patients with heart failure.**

3 **Fonarow GC**, Stevenson LW, Walden JA, *et al*. Impact of a comprehensive heart failure program on hospital readmission and functional status of patients with advanced heart failure. *J Am Coll Cardiol* 1997;**30**:725–32.

4 **Butman SM**, Ewy GA, Standen JR, *et al*. Bedside cardiovascular examination in patients with severe chronic heart failure: importance of rest or inducible jugular venous distension. *J Am Coll Cardiol* 1993;**22**:968–74.

► **Useful, practical study demonstrating that examination of the JVP, at least by a cardiologist, provides an accurate index of left heart pressures in patients with severe chronic heart failure.**

5 **Marcus G**, Vessey J, Jordan MV, *et al*. Relationship between accurate auscultation of a clinically useful third heart sound and level of experience. *Arch Intern Med* 2006;**166**:617–22.

6 **Cleland JGF**, Louis AA, Rigby AS, *et al*. Noninvasive home telemonitoring for patients with heart failure at high risk of recurrent admission and death. The Trans-European Network-Home-Care Management System (TEN-HMS) Study. *J Am Coll Cardiol* 2005;**45**:1654–64.

7 **Suskin N**, Sheth T, Negassa A, *et al*. Relationship of current and past smoking on mortality and morbidity in patients with left ventricular dysfunction. *J Am Coll Cardiol* 2001;**37**:1677–82.

► **Demonstration that current smoking is a powerful independent predictor of morbidity and mortality in patients with left ventricular dysfunction. Smoking cessation substantially decreased morbidity and mortality in such patients. As the accompanying editorial states: ''It is never too late'' (to stop smoking).**

8 **Michalsen A**, Konig G, Thimme W. Preventable causative factors leading to hospital admission with decompensated heart failure. *Heart* 1998;**80**:437–41.

► **Important findings, substantiated by subsequent studies, that an unacceptable percentage (54% here) of hospitalisations for acute decompensation of pre-existing heart failure are caused by potentially preventable factors, including lack of adherence to the medical regimen, coronary ischaemia, arrhythmia, uncontrolled hypertension or inadequate pre-admission treatment.**

9 **Tsuyuki RT**, McKelvie RS, Arnold JMO, *et al*. Acute precipitants of congestive heart failure exacerbations. *Arch Intern Med* 2001;**161**:2337–42.

10 **The Task Force for the diagnosis and treatment of CHF of the European Society of Cardiology**. Guidelines for the diagnosis and treatment of Chronic Heart Failure: full text (update 2005). *Eur Heart J* 2005;**26**:1115–40.

► **Excellent, detailed guidelines for the diagnosis and management of chronic heart failure. For those unable to find time to scrutinise all of this substantial document, a useful brief review is provided in *Heart* 2006;92:437–40.**

11 **Fung JWH**, Yu CM, Yip G, *et al*. Effect of beta blockade (carvedilol or metoprolol) on activation of the renin-angiotensin-aldosterone system and natriuretic peptides in chronic heart failure. *Am J Cardiol* 2003;**92**:406–10.

► **Demonstration that β-blockers for heart failure have little effect, or a stimulatory effect, on plasma natriuretic peptide values in the short-term (4 weeks), but have a substantial inhibitory action in the longer term (12 and 52 weeks) as left ventricular function improves.**

12 **Frantz RP**, Olson LJ, Grill D, *et al*. Carvedilol therapy is associated with a sustained decline in brain natriuretic peptide levels in patients with congestive heart failure. *Am Heart J* 2005;**149**:541–7.

13 **Murdoch DR**, McDonagh TA, Byrne J, *et al*. Titration of vasodilator therapy in chronic heart failure according to plasma brain natriuretic peptide concentration: randomized comparison of the hemodynamic and neuroendocrine effects of tailored versus empirical therapy. *Am Heart J* 1999;**138**:1126–32.

14 **Gackowski A**, Isnard R, Golmard J-L, *et al*. Comparison of echocardiography and plasma B-type natriuretic peptide for monitoring the response to treatment in acute heart failure. *Eur Heart J* 2004;**25**:1788–96.

15 **Latini R**, Masson S, Wong M, *et al*. Incremental prognostic value of changes in B-type natriuretic peptide in heart failure. *Am J Med* 2006;**119**:70.e23–30.

► **Important evidence that changes in plasma BNP over time in patients with heart failure caused by left ventricular function are of prognostic value.**

16 **Troughton RW**, Frampton CM, Yandle TG, *et al*. Treatment of heart failure guided by plasma aminoterminal brain natriuretic peptide (N-BNP) concentrations. *Lancet* 2000;**355**:1126–30.

► **Pilot study from a single hospital showing that drug treatment of chronic heart failure guided by plasma values of NT-proBNP was superior to ''usual care'' that was based on conventional clinical and laboratory criteria.**

17 **Jourdain P**, Funck F, Gueffet P, *et al*. Benefit of BNP plasma levels for optimizing therapy: The Systolic Heart Failure Treatment Supported by BNP Multicenter and Randomised Trial (STARS-BNP). *J Am Coll Cardiol* 2005;**45**(Suppl A):3A.

► **Similar style of study to that of Troughton *et al* above (reference 15) but in a larger cohort—with a similar outcome favouring treatment guided by circulating BNP values. The full report of this study is awaited.**

18 **Vasan RS**. Expanding indications for natriuretic peptides: importance of better new (research) protocols. *Am Heart J* 2004;**148**:743–6.

► **A useful editorial article discussing the current status of natriuretic peptides in the diagnosis, evaluation and management of heart failure. Studies in progress to determine the usefulness of these peptides in guiding drug treatment are listed.**

19 **Wang TJ**, Larson MG, Levy D, *et al*. Heritability and genetic linkage of plasma natriuretic peptide levels. *Circulation* 2003;**108**:13–6.

20 **Yu DSF**, Thompson DR, Lee DTF. Disease management programmes for older people with heart failure: crucial characteristics which improve post-discharge outcomes. *Eur Heart J* 2006;**27**:596–612.

► **Review of the literature which points to the desirability of developing multifaceted disease management programmes in order to achieve the best possible outcomes (hospital readmissions and mortality) in elderly patients with heart failure.**