

**Chronic heart failure: management of chronic heart failure in
adults in primary and secondary care**
A clinical guideline for the NHS in England and Wales

APPENDIX J: EVIDENCE TABLES

**Section 7.2: Pharmacological treatment of heart failure
due to LV systolic dysfunction -
Dosing, Sequencing, Communication and Adherence**

Pharmacological therapy
Dosing and sequencing

Experimental Studies

Paper	Packer, M., Poole-Wilson, P. A., Armstrong, P. W., Cleland, J. G., Horowitz, J. D., Massie, B. M., Ryden, L., Thygesen, K., & Uretsky, B. F. 1999, "Comparative effects of low and high doses of the angiotensin-converting enzyme inhibitor, lisinopril, on morbidity and mortality in chronic heart failure. ATLAS Study Group", <i>Circulation</i> , vol. 100, no. 23, pp. 2312-2318.
Description	Randomised controlled trial
N=	n=3164, low dose =1596, high dose =1568 Age =64 yrs, Male =80%, LV ejection fraction =23%, NYHA class II =16%, class III =77%, class IV =7% International
Intervention	Lisinopril was given orally at either 2.5 to 5.0 mg/day or at 32.5 to 35.0 mg/day as a continuous therapy
Outcomes	The primary endpoint was all cause mortality, with secondary endpoints of cardiovascular mortality, and also mortality and hospitalisation (for various reasons) in combination, and safety was monitored by adverse reactions including cause for cessation all to a median of 45.7 months
Results	<ul style="list-style-type: none"> • There were no significant differences in the rates of all cause or cardiovascular mortality between the dosing groups, this held when transplants were included or excluded • There was a significantly greater decrease in mortality and hospitalisation with high dose lisinopril Vs low dose 79.7% Vs 83.8%, HR 0.88 (95% CI 0.82 – 0.96) (p=0.002), this was regardless of age, sex, HF aetiology, LV ejection fraction, or NYHA class. • The reduction in mortality and HF hospitalisation was even more marked between the groups in favour of the high dose HR 0.85 (p<0.001). • There was no significant difference in the rates of fatal and non-fatal MI and hospitalisation for angina. • Blood pressure declined 2.3 mm Hg more in the high than the low dose group (p<0.001), but there was little change in heart rate in either group. • Patients in the high dose group experienced dizziness, hypotension, worsening renal function, and hyperkalaemia more frequently than in the low dose group, although side effect did not lead to more cessation of medication 17% and 18% respectively. These figures must be treated with caution given the 4% exclusion across the trial of patients with a history of ACEi intolerance.
Comments	The results of this study are widely applicable to the general HF population except those who are ACEi intolerant, or have had a recent ischaemic event An increase in dose may reduce the risk of death and hospitalisation even if there is no improvement in functional status
Reference	75

Paper	Erbel, R., Meyer, J., Diefenbach, C., Delorme, G., Bourdarias, J. P., Vernant, P., Lellouche, D., Mattioli, G., Barbieri, A., & Installe, E. 1987, "A dose-response study of intravenous enoximone in congestive heart failure", <i>American Journal of Cardiology</i> , vol. 60, no. 5, pp. 31C-36C.
Description	Randomised controlled trial
N=	n=60, 0.25mg/kg =12, 0.5 mg/Kg =13, 1.0mg/Kg =14, 1.5 mg/Kg =10, 2.0mg/Kg =11. Age ~59 yrs, Male =78%, Ischaemic origin of HF =42%, NYHA class II =3%, class III =47%, class IV =50%. Europe
Intervention	Intravenous infusion of enoximone at 0.25 / 0.5 / 1.0 / 1.5 / 2.0 mg/Kg as one off dose over =10 secs
Outcomes	Various haemodynamic variables recorded at 15, 30, 60, 90, and 120 mins from dose then hourly until 8 hours, with haematology and ECG measurements at 24 hours
Results	<ul style="list-style-type: none"> • There were no dose related effects on heart rate. • Systolic blood pressure was not affected by enoximone, but diastolic pressure was significantly reduced at 30 mins with the 2.0mg/Kg dose (11% decrease) (possibly due to higher baseline levels) • In terms of cardiac index, enoximone increased mean index in all groups with generally a dose relationship for magnitude of change and duration • Statistically significant decreases in pulmonary artery diastolic pressure were observed for 1 hour with 0.25 mg/kg but for 3 hours with 2.0mg/Kg • There were no significant differences in the frequency of adverse reaction reported between dose groups • Blood samples taken before and after enoximone administration showed no changes in biochemical or haematological values.
Comments	Results are applicable to most HF patients except those with uncontrolled tachyarrhythmias, valvular disease, or hepatic, haematological, or renal disease It is possible that at 2.0mg/Kg a plateau had been reached for efficacy with regard to cardiac index The authors suggest a 0.5mg/Kg starting dose.

Paper	Francis, G. S. & Rucinska, E. J. 1989, "Long-term effects of a once-a-day versus twice-a-day regimen of enalapril for congestive heart failure", <i>American Journal of Cardiology</i> , vol. 63, no. 8, pp. 17D-21D.
Description	Randomised controlled trial
N=	n=88, 20mg once a day =? 10mg twice a day =? For total population within the study 142 of which 88 were invited into the double blind phase Age =63 yrs, Male =76%, Ischaemic origin of HF =58%, LV ejection fraction =32%, NYHA class II =23%, class III =63%, class IV=7% USA and Puerto Rico
Intervention	Oral doses of enalapril at 20mg or twice daily dose at 10mg was given with 2 week titration for 16 weeks
Outcomes	Symptomatic response by NYHA class evaluation was recorded at intervals to 48 weeks as was Exercise duration and LV ejection fraction. Adverse events were also documented
Results	<ul style="list-style-type: none"> • There were no significant changes in NYHA class between the dosing groups • There were no significant differences between the positive effect on exercise duration exhibited by the two dosing groups • There were decreases in blood pressure after the first titration doses of enalapril in both groups but the difference between the groups was not significant
Comments	The study includes a broad selection of HF patients in its population so the results can be widely The data indicate no differences between the once and twice daily dosing of enalapril in HF patients

Paper	Tang, W. H., Vagelos, R. H., Yee, Y. G., Benedict, C. R., Willson, K., Liss, C. L., & Fowler, M. B. 2002, "Neurohormonal and clinical responses to high- versus low-dose enalapril therapy in chronic heart failure. [erratum appears in J Am Coll Cardiol 2002 Feb 20;39(4):746.]", <i>Journal of the American College of Cardiology.</i> , vol. 39, no. 1, pp. 70-78.
Description	Randomised controlled trial
N=	n=75, 40mg/day dose =37, 5mg/day dose =38 Age =51.5 yrs, Male =82%, LV ejection fraction =21%, NYHA class II =3%, Class III =90%, class IV =7% USA
Intervention	A dose of enalapril (oral) at 40 mg/day was compared to 5 mg/day in patients with mild to severe HF for 6 months
Outcomes	Changes to neurohormone levels of plasma AT-II or serum aldosterone or ACEi activity, as well as changes from baseline in NYHA class, exercise duration, and a composite event outcome of hospital admission / death / increased use of diuretics) were all evaluated at 6 weeks
Results	<ul style="list-style-type: none"> • The only significant difference between scores for the two dose groups was in serum ACEi activity with significantly lower concentrations in the high dose group Vs low dose group in comparison of respective trough and peak values (p<0.05 for both comparisons) • There was no significant difference in the level of post-dose (peak) plasma AT-II of serum aldosterone. • There were no statistically significant differences between plasma norepinephrine and epinephrine levels in both intra and inter group comparisons. • Overall there was no significant differences between the groups in terms of NYHA class and cardiopulmonary exercise test results. • There were nearly twice as many patients reaching the composite endpoint in the low dose group, but the difference was statistically significant (p=0.061) • There was a non significant trend towards a reduction in LV end diastolic dimension within the high dose group • There were more reported adverse events and death requiring withdrawal from the trial in the low dose group than the high dose group • Once daily dose of enalapril might not have provided the expected neurohormonal suppression
Comments	There was one baseline difference in patient characteristics between the groups with the low dose group having 45% patients with an aetiology of ischaemic cardiomyopathy as opposed to 24% in the high dose arm Results are widely applicable to HF patients, except those with recent MI A long period of ACEi treatment and well advanced disease in the population may explain the high aldosterone escape even in the high dose group Results noted may not be observed with different dosing regimes or other ACEi drugs
Reference	76

Paper	Uretsky, B. F., Shaver, J. A., Liang, C. S., Amin, D., Shah, P. K., Levine, T. B., Walinsky, P., Lejemtel, T., Linnemeier, T., & Rush, J. E. 1988, "Modulation of hemodynamic effects with a converting enzyme inhibitor: acute hemodynamic dose-response relationship of a new angiotensin converting enzyme inhibitor, lisinopril, with observations on long-term clinical, functional, and biochemical responses", <i>American Heart Journal</i> , vol. 116, no. 2 Pt 1, pp. 480-488.
Description	Randomised controlled trial
N=	n =55, 2.5 mg lisinopril =17, 5.0 mg lisinopril =20, 10.0 mg lisinopril =17. No details regarding missing patient. Age =59yrs, Male =84%, NYHA class II =2%, NYHA class III =40%, NYHA class IV =55%, Ischaemic HF origin =49%, duration of CHF =3.3yrs USA
Intervention	Intervention of either 2.5 / 5.0 / 10.0mg of lisinopril per day, on top of digoxin and diuretics in compensated HF patients
Outcomes	For the acute haemodynamic monitoring, Heart rate, right arterial pressure, pulmonary artery pressure, capillary sedge pressure, systemic arterial pressure, and cardiac output were all measured every 2 hours for 12 hours then every 4 hours for 24 hours. With target response being a 25% decrease in capillary wedge pressure, or 25% increase in cardiac index
Results	<ul style="list-style-type: none"> • There were no significant differences in the mean peak pulmonary capillary wedge pressure between the 3 groups, and similarly the percentage of patients reaching the 25% decrease was not significantly different between the groups • The peak increase in the cardiac index was significantly greater in the 10.0mg group (0.49 L/min/m²) than in the 5.0mg group (0.29 L/min/m²) and 2.5mg group (0.20 L/min/m²) (p<0.05 for both comparisons). Also the percentage of patients reaching the 25% increase endpoint was larger in the 10.0mg group (53%) than the 5.0 or 2.5 mg group (18% and 14% respectively) (p<0.05 for both comparisons) • At the 10 hour time point the fall in heart rate was significantly greater in the 10.0mg group 74 BPM than in the 2.5mg group 82 BPM. • Mean arterial blood pressure fell in each study group but the fall was greater in the 10.0 mg group than the 2.5 mg group at 4, 6, 8, 10, and 12 hours • There were no significant changes to stroke work index from baseline or between groups
Comments	<p>The was only one baseline difference between the three study arms with more women receiving the 5mg dose (n=7) compared to the 2.5 or 10mg dose (n=1 each)</p> <p>No other vasodilator therapy was allowed for at least 3 days prior to study entry and stable digoxin and diuretics were required for 3 days prior to the haemodynamic study</p> <p>Different doses can produce differing haemodynamic responses with this ACEi although this may not be extrapolated to others within this class</p> <p>Once total enzyme inhibition has been achieved, larger doses of this or other ACEi cannot be expected to improve haemodynamics further.</p> <p>The findings are applicable to most HF patients except those with Renal, hepatic, haematological, or allergic disorders.</p>

Non-experimental studies

Paper	McMurray, J., Cohen-Solal, A., Dietz, R., Eichhorn, E., Erhardt, L., Hobbs, R., Maggioni, A., Pina, I., Soler-Soler, J., Swedberg, K., & Clinical, R. 2001, "Practical recommendations for the use of ACE inhibitors, beta-blockers and spironolactone in heart failure: putting guidelines into practice", <i>European Journal of Heart Failure</i> , vol. 3, no. 4, pp. 495-502.
Description	Review / consensus recommendations
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • It is recommended that the ACEi is initiated first, followed by a B blocker. • If patients cannot be up-titrated to target doses it is suggested that lower doses of both treatments are still likely to be of value to the patient. • STEP 1 initiate ACEi in patients with NYHA class I-IV congestive HF <p>Drug <i>Starting dose (mg)</i> <i>Target dose (mg)</i></p> <p>Captopril 6.25 thrice daily 50-100 thrice daily</p> <p>Enalapril 2.5 twice daily 10-20 twice daily</p> <p>Lisinopril 2.5-5.0 once daily 30-35 once daily</p> <p>Ramipril 2.5 once daily 5 twice daily or 10 once daily</p> <p>Trndolapril 1.0 once daily 4 once daily</p>

<p>Double the dose at not less than 2 weekly intervals Monitor blood chemistry for urea and K⁺ and blood pressure ACEi induced cough rarely requires treatment discontinuation An increase in creatinine of up to 50% above baseline, or up to 3mg/dl which ever is the smaller is acceptable An increase in K⁺ to =6.0 mmol/l is acceptable</p> <ul style="list-style-type: none">• STEP 2 Initiate B blocker inpatients with stable NYHA class I-IV (and as early as possible in the course of disease) <p>Drug <i>Starting dose (mg)</i> <i>Target does (mg)</i></p> <p>Bisoprolol 1.25 once daily 10 once daily</p> <p>Carvedilol 3.125 twice daily 25-50 twice daily</p> <p>Metroprolol CR/XL 12.5-25 once daily 200 once daily</p> <p>Double the dose at not less than 2 weekly intervals Monitor HR, BP, clinical status (symptoms, signs, especially signs of congestion, body weight) Check blood chemistry 1-2 weeks after initiation and final dose titration If increasing congestion double dose of diuretic and / or halve dose of b blocker If <50 BPM and worsening symptoms halve dose of B blocker, or if severe deterioration stop B blocker (rarely needed) If dizziness, light headedness and / or confusion and a low blood pressure reconsider need for nitrates, calcium channel blockers and other vasodilators</p>
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<p>Results Cont'd</p>	<ul style="list-style-type: none"> • STEP 3 requires the addition of second line therapy for those patients with persisting signs and symptoms of HF (NYHA class III-IV) with spironolactone and digoxin <p>Drug <i>Starting dose (mg)</i> <i>Target dose (mg)</i></p> <p>Spironolactone 25 once daily 25-50 once daily</p> <p>Check blood chemistry at 1, 4, 8, and 12 weeks then 6, 9, 12 months and 6 monthly thereafter If K⁺ rises to between 5.5 and 6.0 mmol/l or creatinine rises to 2.4mg/dl reduce dose to 25mg on alternate days and monitor blood pressure closely If K⁺ rises to >6.0 mmol/l or creatinine to >4.0 mg/dl stop spironolactone and seek specialist advice It is important to avoid other K⁺ retaining drugs such as K⁺ sparing diuretics and nephrotoxic agents</p> <p>Digoxin may still have a special role in the patient with atrial fibrillation when the rapid control of ventricular rate is needed, which cannot be achieved with cautious up-titration of B blockers. Initial treatment with digoxin should not preclude subsequent introduction of a B blocker</p>
<p>Comments</p>	<p>A paper aimed at giving practical guidance to non-specialists to support the implementation of evidence based therapy for heart failure There is unreasonable concern about the possible adverse effects of drugs such as hypotension and renal insufficiency, and doses used in clinical practice has been lower than the doses used in trials which have been shown to have survival benefits These step-wise set of clinical recommendations for each drug come out of a meeting of clinicians with expertise in the diagnosis and management of heart failure. The paper acts as a tool to facilitate the implementation of current guidelines rather than an updated replacement of these The paper covers the initiation and maintenance of four drugs (ACEi, B Blockers, Spironolactone, and Digoxin) calling on evidence from the major trials n=35 references</p>
<p>Reference</p>	<p>98</p>

Paper	Packer, M. 1989, "The clinical significance of nitrate tolerance in patients with chronic heart failure.", <i>European Heart Journal</i> , vol. 10, no. Suppl A, pp. 20-25.
Description	Review
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Trials have shown the development of tolerance to isosorbide dinitrate in patients with angina, and similarly when nitro glycerin is given by transdermal or intravenous route in HF patients tolerance develops to the haemodynamic effects of the drugs within 24-48 hours. • When nitro glycerin or isosorbide dinitrate is given intermittently tolerance can be avoided as long as doses are separated by 8-12 hours • In chronic heart failure responsiveness to nitrates is restored when therapy is withdrawn for 12-14 hours, but not for 2-4 hours • Solutions to tolerance build up include administering the drugs once twice or three times a day only, the importance of continuous 24 hr haemodynamic benefits in treating HF are not yet known. Alternatives include the concurrent use of a sulphyryl compound but long-term safety and efficacy are not known, or with an agent that interferes with the activation of endogenous neuro-hormones.
Comments	<p>A review to explain both the mechanisms that may lead to interventions that will overcome the development of tolerance and enhance efficacy of long term nitrate therapy in HF patients n=48 references USA author Based on evidence from clinical trials with some note made of study quality and findings well referenced in the text The increase in cardiac output with the administration of nitrates is usually small unless high doses are used, or given to patients with a low baseline index or with severe mitral and aortic regurgitation. There is little known about how or when to use nitrates in patients with chronic heart failure Only a few controlled studies are available, and most of these only evaluated small numbers of patients for brief follow up periods</p>

Paper	Pearson, G. J., Cooke, C., Simmons, W. K., & Sketris, I. 2001, "Evaluation of the use of evidence-based angiotensin-converting enzyme inhibitor criteria for the treatment of congestive heart failure: opportunities for pharmacists to improve patient outcomes", <i>Journal of Clinical Pharmacy & Therapeutics</i> , vol. 26, no. 5, pp. 351-361.
Description	Case series / audit
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • 58% of patients admitted had a diagnosis of HF recorded but only 39.1% of these had previously received an ACEi • Of all the patients discharged from hospital with a diagnosis of HF only 68.1% were discharged on an ACEi. Of the 44 discharged without an ACEi 25 had no reasons for it not being given, while 19 had reasons stated. (renal failure n=6, hypotension n=6, ACEi induced cough n=4, headache nausea and vomiting n=1, ACEi induced rash n=2). • Alternative vasodilators were prescribed in 23 of the 44 patients without ACEi. • Of the 94 patients discharged on ACEi only 40.4% were discharged on recommended target doses. • Males were more likely to be given an ACEi OR 2.43 (95% CI =1.04 – 5.81), and patients on concomitant diuretics OR 0.25 (0.10 – 0.62) or digoxin OR 0.18 (0.05 – 0.58) were less likely to be discharged with an ACEi • These findings are far removed from clinical trials where between 80 and 90% of patients with HF can tolerate ACEi. • Overall 20.3% of the eligible patients with HF were not receiving either an ACEi or a vasodilator alternative on discharge. • While considerable effort and resources are being put into the utilisation of newer therapies (B blockers and spironolactone) for the treatment of heart failure, the use of proven efficacious therapies (ACEi) continues to be sub optimal.
Comments	<p>n=138 patients Canada</p> <p>A retrospective case audit to evaluate the prescribing of ACEi and the dose prescribed for a consecutive series of patients.</p> <p>A drug use evaluation tool was developed from the literature, with clinical pharmacists practising in cardiology and with local academic cardiologists. The tool encompassed such factors as indications, contraindications, dosages, dosage frequency, drug interactions, outcomes of therapy for efficacy and toxicity, and was piloted and refined.</p> <p>For patients who were not receiving an ACEi on discharge the reason for not prescribing was recorded where documented</p> <p>Multiple regression analysis were undertaken using sex, age, history of HF, previous ACEi use, concomitant medication, contraindications, serum creatinine, and LV ejection fraction as variables</p>

Communication and adherence to therapy

Experimental studies

Paper	Mullen, P. D., Green, L. W., & Persinger, G. S. 1985, "Clinical trials of patient education for chronic conditions: a comparative meta-analysis of intervention types.", <i>Preventive.Medicine.</i> , vol. 14, no. 6, pp. 753-781.
Description	Systematic review
N=	n=70 studies, n=4 in HF number of participants not stated
Intervention	Various information and or counselling systems, categories in to 9 groupings
Outcomes	1. Knowledge effect 2. Drug errors 3. Clinical effect
Results	<ul style="list-style-type: none"> • Effect size of intervention on Knowledge strongly positive (0.42 – 1.13) (except for patient package insert) • Intervention on drug use errors all suggest strong to middle benefit (0.3- 0.5) (except for patient package insert) • No data on clinical effect
Comments	Small studies included Different outcome assessment times No description of patient variables at baseline Outlying studies removed
Reference	223

Paper	Serxner, S., Miyaji, M., & Jeffords, J. 1998, "Congestive heart failure disease management study: A patient education intervention", <i>Prevention & Management of Congestive Heart Failure</i> , vol. 4, no. 3, pp. 23-28.
Description	Randomised controlled trial
N=	n=109, education=55, conventional care=54 Age =71 yrs, Male =48%, More than one third of the patients were not confident in their ability to manage their condition and rated their health as poor at baseline USA
Intervention	An intervention of a individualised set of educational material every 3-4 weeks post discharge, relating to the need for continued compliance, printed education materials on HF medications, risk factors, and behavioural health issues. The intervention group were also sent a video on HF and a weight graph to track daily weight. Patients in the control arm received typical fact sheets on the patient conditions and medications on discharge
Outcomes	A telephone administered survey was undertaken with patients (or carers) to assess knowledge about HF, attitudes, self-efficacy, and outcomes behaviour, after discharge and at 6 months. In addition hospitalisation for HF was surveyed, also to 6 months
Results	<ul style="list-style-type: none"> • Significantly ($p < 0.02$) more patients in the intervention group reported cutting back on salt intake was important in managing their health (88%) than in the control group (59%). Similarly more patients in the education group (96%) reported making positive dietary changes because of their heart condition than those in the control group (78%) ($p < 0.01$) • In analysis of covariance between pre and post intervention survey results patients within the intervention group reported forgetting medication less frequently than those in the control group ($p < 0.05$) • Patients in the intervention group improved in their confidence to self manage their condition (an improvement of 0.4 points on a five point scale, while those in the control group reported no improvement in this outcome over 6 months. • Self reported assessment of overall health suggested that patients in the intervention group thought themselves healthier than those in the control group after 6 months, with correction for baseline score, ($p < 0.05$) • There were twice as many total readmissions for HF among patients in the control group (43 events) than in the intervention group (21 events).

Comments	<p>There were no significant differences between demographic or results on pre-test survey items at baseline, although no data was collected on the clinical status of the patients</p> <p>The lack of assessment of clinical status of patients at baseline could have introduced confounding factors (?) effects of intervention</p> <p>The lack of definite blinding within the study could have lead to more positive outcomes being recorded in the self reporting outcomes among patients who believed they were in the intervention arm ↗ effect.</p> <p>Some outcomes causally linked to the intervention and thus positive outcomes not surprising</p> <p>No details on drop out rates, if the patients who responded less in the placebo group dropped out more frequently then protocol analysis would overstate ↗ treatment effect</p> <p>Patients without access to telephones, or who were discharged to a skilled nursing facility were excluded form the study.</p> <p>A minimal intervention was implemented to demonstrate what could be achieved with modest resources.</p> <p>Not clear what element of the intervention derived the outcome benefits with increased contact from the medical profession likely to improve most of the outcomes reported on, over and above the impact of the education materials</p> <p>Patients reported not being able to use or understand the weight graph</p> <p>Not clear what benefit the intervention would have long term once education ceased</p>
Reference	241

Paper	Stewart, M. A. 1995, "Effective physician-patient communication and health outcomes: a review.", <i>CMAJ.</i> , vol. 152, no. 9, pp. 1423-1433.
Description	Systematic review
N=	Number of participants not stated
Intervention	Trained physicians Vs not trained
Outcomes	1. Physiological status 2. Functional status 3. Symptom resolution 4. Emotional status
Results	<ul style="list-style-type: none"> • Few trials showed a benefit of intervention of training • All but one study failed to adjust for baseline patient characteristics
Comments	Generalised population Various outcomes
Reference	227

Paper	Brown, S. A. 1990, "Studies of educational interventions and outcomes in diabetic adults: a meta-analysis revisited", <i>Patient Education & Counseling</i> , vol. 16, no. 3, pp. 189-215.
Description	Systematic review
N=	n=82 studies, number of participants not stated
Intervention	Many intervention methods broken down by which discipline led
Outcomes	1. Knowledge effects 2. Self care behaviour effects 3. Metabolic control 4. Psychological outcomes
Results	<ul style="list-style-type: none"> • Reporting of size estimates not useful as a means of comparison • Studies are not statistically heterogeneous • Knowledge of medication principles shown to improve, but a knowledge composite score was not improved
Comments	A good quality review in terms of bias limitation
Reference	224

Paper	Balas, E. A., Jaffery, F., Kuperman, G. J., Austin Boren, S., Brown, G. D., & Pinciroli, F. 1997, "Electronic communication with patients: evaluation of distance medicine technology.", <i>JAMA</i> , vol. 278, no. 2, pp. 152-159.
Description	Systematic review
N=	n=80 studies, number of participants not stated
Intervention	6 groups including telephone and/or computer reminders/communication Vs control group
Outcomes	Various across studies: - Appointments made - Self and pharmacy drug reporting - Rates of vaccinations
Results	<ul style="list-style-type: none"> • Effects in hypertension of patients taking a monthly supply: Telephone prompt = 64% Mailed prompt = 65% Control = 58% • Medication compliance – nurse telephone reminder increased pharmacy score • Cardiovascular disease – telephone call to refill medications increased the mean number of compliant patients
Comments	No meta-analysis
Reference	225

Paper	Ptacek, J. T. & Eberhardt, T. L. 1996, "Breaking bad news. A review of the literature.", <i>JAMA</i> , vol. 276, no. 6, pp. 496-502.
Description	Systematic review
N=	n=67 studies, number of participants not stated
Intervention	Various communication strategies
Outcomes	- Patient satisfaction - Physician stress
Results	<ul style="list-style-type: none">• Majority of the evidence is not empirical• Even some positive messages in all but terminal illness diagnosis• Diagnoses that fail to match one's expectations may have more severe impact
Comments	
Reference	226

Paper	Forster, A., Smith, A., Knapp, P., House, A., & Wright, J. 2001, "Information provision for stroke patients and their caregivers.", <i>Cochrane Library</i> no. 3.
Description	Systematic review
N=	n=17 studies, number of participants not stated
Intervention	Information and education by: - Leaflets - Booklets - Manuals - Lectures
Outcomes	2 primary: - Knowledge about stroke and severity - Impact on health especially mood 8 secondary including compliance with treatment / rehabilitation
Results	<ul style="list-style-type: none"> • Knowledge improved with information and/or education – especially with both • Some improvement in depression with education intervention. • No effect of intervention in three trials • Only chance findings on effect on quality of life • No significant modification of health related behaviours
Comments	A good quality study Small studies included

Paper	Walsh, R. A., Girgis, A., & Sanson-Fisher, R. W. 1998, "Breaking bad news. 2: What evidence is available to guide clinicians?", <i>Behavioral.Medicine</i> , vol. 24, no. 2, pp. 61-72.
Description	Systematic review
N=	n=10 studies, number of participants not stated
Intervention	<ul style="list-style-type: none"> - Information sheets - Education - Cassette of consultation
Outcomes	<ul style="list-style-type: none"> Varied across papers - Psychological outcome - Patient satisfaction - Knowledge
Results	<ul style="list-style-type: none"> • Only significant findings for effectiveness of information provision in patient satisfaction, • No effect on psychological outcome • Some studies showed that patients' knowledge improved
Comments	<p>A descriptive review. Disparate studies. Suggests further research for</p> <ul style="list-style-type: none"> - Supplementing physician consultation with others - Need for psychometrically robust performance scales - Modifiable elements of bad news consultation

Paper	Jaarsma, T., Halfens, R., Tan, F., Abu-Saad, H. H., Dracup, K., & Diederiks, J. 2000, "Self-care and quality of life in patients with advanced heart failure: the effect of a supportive educational intervention", <i>Heart & Lung</i> , vol. 29, no. 5, pp. 319-330.
Description	Randomised controlled trial
N=	n=186 Age=72yrs, Male =79%, LV ejection fraction =34% Holland
Intervention	Intensive education by nurse on recognition of symptoms , and card with warning signs
Outcomes	Self rated agency (scale) Self rated behaviour (scale) Quality of life: functional capacity scale, symptoms questionnaire, psychological adjustment, overall well-being
Results	<ul style="list-style-type: none"> • Self care (reported): 14 intervention vs. 12 control. p = 0.001 • Some improvement in well-being and psychological adjustment but not significant.
Comments	Outcomes are unclear. High dropout

Paper	Varma, S., McElnay, J. C., Hughes, C. M., Passmore, A. P., & Varma, M. 1999, "Pharmaceutical care of patients with congestive heart failure: interventions and outcomes", <i>Pharmacotherapy</i> , vol. 19, no. 7, pp. 860-869.
Description	Randomised controlled trial
N=	n=83 Age =76, Male =41%, NYHA class (mean)=2.15 UK
Intervention	Education programme from pharmacist and patient information leaflet.
Outcomes	Many outcomes including: 1) MLHF Quality of life 2) 2 minute walk test 3) Compliance
Results	<ul style="list-style-type: none"> • 2-minute walk test: 90.3m intervention vs. 64.2m control at 6 months (p = 0.03) • MLHF quality of life: 15.6 intervention vs. 25.7 control at 9 months (p = 0.04) • Compliance: 10 intervention vs. 3 control (p = 0.039)
Comments	Pilot study High dropout rate

Paper	Linne, A. B., Liedholm, H., & Israelsson, B. 1999, "Effects of systematic education on heart failure patients' knowledge after 6 months. A randomised, controlled trial", <i>European Journal of Heart Failure</i> , vol. 1, no. 3, pp. 219-227.
Description	Randomised controlled trial
N=	n=130 Age=70yrs, Male=66%, NYHA I-III =100% Sweedden
Intervention	Nurse and pharmacist education with interactive CD programme
Outcomes	Knowledge of care
Results	<ul style="list-style-type: none"> • Knowledge score was 17.2 intervention vs. 12.9 control at 6 months (95% CIs: 16.6 – 18.9 intervention, 11.7 – 14.1 control) (p = 0.0051)
Comments	No pre-test of knowledge or educational capacity

Paper	Mohide, E. A., Whelan, T. J., Rath, D., Gafni, A., Willan, A. R., Czukar, D., Campbell, I. B., Okawara, G. S., Neimanis, M., & Levine, M. N. 1996, "A randomised trial of two information packages distributed to new cancer patients before their initial appointment at a regional cancer centre", <i>British Journal of Cancer.</i> , vol. 73, no. 12, pp. 1588-1593.
Description	Randomised controlled trial
N=	n=304 Age=63yrs, Male =40%, All cancer patients Canada
Intervention	1) New patient information pack 2) Mini-new patient information pack 3) No information
Outcomes	1) Brief symptom inventory 2) Sherer Self-efficacy scale 3) General sensitivity index
Results	• No significant effects in depression, anxiety, or general severity index. p>0.5 for all outcomes
Comments	Not significant and no outcomes of concordance and outcome except quality of life

Paper	Ong, L. M., Visser, M. R., Lammes, F. B., van, D., V, Kuenen, B. C., & de Haes, J. C. 2000, "Effect of providing cancer patients with the audiotaped initial consultation on satisfaction, recall, and quality of life: a randomized, double-blind study", <i>Journal of Clinical Oncology</i> , vol. 18, no. 16, pp. 3052-3060.
Description	Randomised controlled trial
N=	n=201 Age =54yrs, Male =18%, Prognosis of less than 5 years =27% Holland
Intervention	Use of a tape of consultation for patients
Outcomes	1) Recall 2) Quality of life 3) Satisfaction
Results	<ul style="list-style-type: none"> • Recall: mean difference 10-40 • Satisfaction: mean difference 2.39 (1 week) • Quality of life: mean difference ~ 5 • Recall 95%CI: 4 – 75 (p<0.001) • Satisfaction 95%CI: 1.5 – 5.6 (p<0.05)
Comments	Older patients showed more recall than young with intervention. Young patients showed more satisfaction with intervention Low numbers of men and patients with poor prognosis.

Paper	Bruera, E., Pituskin, E., Calder, K., Neumann, C. M., & Hanson, J. 1999, "The addition of an audiocassette recording of a consultation to written recommendations for patients with advanced cancer: A randomized, controlled trial", <i>Cancer</i> , vol. 86, no. 11, pp. 2420-2425.
Description	Randomised Controlled Trial
N=	n=71 Characteristics of participants not stated, all lung cancer patients Canada
Intervention	Cassette recording of consultation and information versus information only.
Outcomes	3 self-reporting scales. 1 test. 1 effectiveness of cassette questionnaire
Results	<ul style="list-style-type: none"> • Usefulness of the clinic: mean difference 1.0 (8.7 vs. 7.7) (p = 0.04) • Total score on : mean difference 8.0 (88 vs. 80) (p = 0.02)
Comments	Significant against a control with greater knowledge. Assessing physicians 2nd visit post MDT Dropouts probably not systematic i.e. death, technical problems

Paper	Mant, J., Carter, J., Wade, D. T., & Winner, S. 1998, "The impact of an information pack on patients with stroke and their carers: a randomized controlled trial", <i>Clinical Rehabilitation</i> , vol. 12, no. 6, pp. 465-476.
Description	Randomised controlled trial
N=	n=93 Age =73yrs, Male =23%, Hospital admissions =7%, Living at home =30% UK
Intervention	Use of information pack for patients and carers
Outcomes	1) Knowledge of disease 2) Satisfaction 3) Patient's behaviour
Results	<ul style="list-style-type: none"> • Significant effect on 2nd of 11 questions in the knowledge questionnaire: "Is a stroke caused by sudden mental shock?" • Odds ratio: 2.9 (adjusted) (p = 0.05)
Comments	Information packs not individualised. 75% of intervention group recognised information packs No record of whether they had been lost

Paper	Maggs, F. M., Jubb, R. W., & Kemm, J. R. 1996, "Single-blind randomized controlled trial of an educational booklet for patients with chronic arthritis", <i>British Journal of Rheumatology</i> , vol. 35, no. 8, pp. 775-777.
Description	Randomised controlled trial
N=	n=150 Age=57yrs, Male=31% UK
Intervention	Information booklet versus information booklet and instruction
Outcomes	1) patient knowledge 2) quality of life scales
Results	<ul style="list-style-type: none"> Increase in knowledge: group 2: mean +5.84, SD +5.27 (p < 0.01) group 3: mean +7.5, SD +5.36 (p < 0.01)
Comments	Reporting of p-value for effect on increased knowledge not clear

Paper	Frederikson, L. G. & Bull, P. E. 1995, "Evaluation of a patient education leaflet designed to improve communication in medical consultations", <i>Patient.Education.& Counseling.</i> , vol. 25, no. 1, pp. 51-57.
Description	Randomised controlled trial
N=	n=80 From all clinics in a general practice UK
Intervention	1) A patient guide to consultations 2) Short leaflet 3) Given in appendix
Outcomes	Quality of consultation rated by doctor on 3 point scale
Results	• Significant association between intervention and good communication. $\chi^2 = 4.71$ (p < 0.05)
Comments	Small sample. No patient ratings.

Paper	Sandler, D. A., Mitchell, J. R., Fellows, A., & Garner, S. T. 1989, "Is an information booklet for patients leaving hospital helpful and useful?", <i>BMJ</i> , vol. 298, no. 6677, pp. 870-874.
Description	Randomised controlled trial
N=	
Intervention	Patient discharge leaflet / booklet of treatment details and intent
Outcomes	Knowledge of treatment regime by questionnaire
Results	<ul style="list-style-type: none"> • Knowledge of drugs: 86% intervention vs. 47% control (p < 0.001)* • Knowledge of treatment frequency: 95% intervention vs. 58% control (p < 0.001)* • Knowledge of reason for treatment: 85% intervention vs. 42% control (p < 0.001)* (* - with reference to booklet)
Comments	Strong evidence of effectiveness even when recall from memory was tested without reference to booklets. No difference in knowledge of consultant's name. 40% of intervention group brought all drugs to clinic when requested. Indication of intent for prescription was useful for patients and GPs
Reference	240

Paper	Tattersall, M. H., Butow, P. N., Griffin, A. M., & Dunn, S. M. 1994, "The take-home message: patients prefer consultation audiotapes to summary letters.", <i>Journal of Clinical Oncology</i> , vol. 12, no. 6, pp. 1305-1311.
Description	Randomised controlled trial
N=	Number of participants not stated
Intervention	Audiotape of consultation versus letter.
Outcomes	1) Recall of information 2) Anxiety & depression
Results	<ul style="list-style-type: none"> No significant effect on outcomes
Comments	Missing data from copy obtained No significant differences in outcomes. Strong preference for audiotape: $\chi^2 = 16.5$ ($p < 0.001$)

Paper	Lorig, K. R., Mazonson, P. D., & Holman, H. R. 1993, "Evidence suggesting that health education for self-management in patients with chronic arthritis has sustained health benefits while reducing health care costs", <i>Arthritis & Rheumatism.</i> , vol. 36, no. 4, pp. 439-446.
Description	Cohort study
N=	n=848 Age =64yrs, Male =20% USA
Intervention	Inclusion in self-management programme Vs control
Outcomes	Frequency of visits to physician Depression Pain
Results	<ul style="list-style-type: none"> • Intervention group 15-20% decline in pain and a decrease in frequency of visits to physician • Significant difference between control and intervention groups
Comments	Combined sub-groups of intervention arm

Non-experimental studies

Paper	Parker, P. A., Baile, W. F., de Moor, C., Lenzi, R., Kudelka, A. P., & Cohen, L. 2001, "Breaking bad news about cancer: patients' preferences for communication", <i>Journal of Clinical Oncology</i> , vol. 19 , no. 7, pp. 2049-2056
Description	Observational study – Patient questionnaire
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Top ratings (4.53 – 4.72 out of 5) for items relating to physician expertise • Even the lowest rated factors rated 2.5 out of 5 representing moderate importance of these • Patients gave less weight to how the information was given
Comments	<p>Cross sectional study looking at how a diagnosis is broken by 1) Content 2) Support 3) Facilitation Outcomes of patient preferences Only measured at one point in time (opinions may change) Set in specialist centre – findings may not transpose to other settings Cross section of HF population (60% women) at least one month since diagnosis of various cancers Those who chose not to participate (1.5%) may have had stronger views Responses referenced to a test of patient response types (Miller Behavioural Style Scale) 92 % return rate</p>
Reference	234

Paper	Jenkins, V., Fallowfield, L., & Saul, J. 2001, "Information needs of patients with cancer: results from a large study in UK cancer centres", <i>British Journal of Cancer</i> , vol. 84, no. 1, pp. 48-51.
Description	Observational study – Patient questionnaire
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • 87% want as much info as possible • 1.9% did not want to know they had cancer • Significantly more over 70's happy to leave details to the doctor (P<0.0001) • No differences in preference between treatment intent patients are being given (lends towards cross applicability) • 99% of respondents thought it absolutely need to know / nice to know about side effects
Comments	<p>Study of results from a patient preference questionnaire, concerning what info should be given</p> <p>Rated by 1) Absolute need 2) Nice to have 3) Do not need</p> <p>15% did not consent to participate, (those who did so may represent individuals who are keener to have info) no details of drop out rate</p> <p>Cross section of the population, preferences analysed against age (> 70 years) and sex</p> <p>In 34 hospitals from teaching to small district</p>
Reference	229

Paper	Baile, W. F., Buckman, R., Lenzi, R., Glober, G., Beale, E. A., & Kudelka, A. P. 2000, "SPIKES-A six-step protocol for delivering bad news: application to the patient with cancer", <i>Oncologist.</i> , vol. 5, no. 4, pp. 302-311.
Description	Comment
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Communication skill can be taught and are retained • Training can help physician handle to topic
Comments	<p>Application of a 'bad news' protocol American oncologists rated their ability in breaking bad news as good / very good (53%) fair (39%) poor (8%) Protocol covers four areas to be included in a consultation – Gathering info from patient - Providing intelligible info – Reduce emotional impact – developing a strategy / treatment plan Steps to facilitate this Setting up interview – privacy / involving others Perception – what does the patient know Initiation – do you / how do you want to know? Knowledge – use common language Emotions – assess emotions / identify / and give reasons for Strategy – goals for patient / symptom control Not based on empirical data Efficacy for patients not tested</p>
Reference	236

Paper	Faulkner, A., Maguire, P., & Regnard, C. 1994, "Breaking bad news--a flow diagram", <i>Palliative.Medicine</i> , vol. 8, no. 2, pp. 145-151.
Description	Comment
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Up to 80% of patients know that their disease is advanced or recurring • Patient may have looked at signs and symptoms and put them in a pattern • Give patient time and space to absorb bad news before looking at treatment
Comments	<p>Health professional should always remember and accept that a relative will know the patient best Patient should be allowed to have whom they wish at the consultation, and say if they are comfortable with the location No empirical evidence ¾ of all references from the author of the paper No account of whether useful for patients Hard to say if transferable to HF patients.</p>

Paper	Silani, V. & Borasio, G. D. 1999, "Honesty and hope: announcement of diagnosis in ALS.", <i>Neurology</i> , vol. 53, no. 8:Suppl 5, pp. S37-S39, discussion S40-S42.
Description	Comment
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Very important to tell patients about support and information services • Physicians find end of life issues difficult as may impinge on own fears of mortality • Inform in a quiet, private room, with who patient wants present and be ready to stop if needed • Shown differences in regional practices in Japan
Comments	<p>Minimum information - name and nature of the disease, available therapies and side effects and unconventional treatments</p> <p>Information sheet can reinforce information in consultation</p> <p>ALS study is relevant, as it is a chronic condition with breathing problems</p> <p>No evidence basis as yet</p>

Paper	Girgis, A. & Sanson-Fisher, R. W. 1995, "Breaking bad news: consensus guidelines for medical practitioners.", <i>Journal of Clinical Oncology</i> , vol. 13, no. 9, pp. 2449-2456
Description	Consensus guidelines
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Only 35% of doctors felt competent at interactional skills, including breaking bad news • Uninformed patients may seek poor advice and are more likely to be non-compliant with treatment • Denial is a valid coping strategy, so not always valid to give full disclosure • Only one person should be responsible for breaking bad news ? to other studies • Physicians should: assess understanding; give facts; allow feelings; give time; review (24 hours); explain treatment options; advise on support services; document in case notes
Comments	<p>Guideline based on review of literature Medline 1973-1993 4 RCTs in 261 papers identified 28 members on consensus panel 100 patients questioned Do physicians' thoughts equal patients' perspectives? Difficult to define useful and appropriate outcomes for RCTs on effectiveness A needs assessment instrument maybe required Trial sensitive to population confounders</p>
Reference	238

Paper	Girgis, A. & Sanson-Fisher, R. W. 1998, "Breaking bad news. 1: Current best advice for clinicians.", <i>Behavioral.Medicine</i> , vol. 24, no. 2, pp. 53-59.
Description	Consensus guidelines (update)
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • More than 40% of 358 cancer patients reported that their expectations of being fully informed were unmet • ¾'s of surgeons surveyed in Australia rated skill in breaking bad news important or very important in being a good surgeon • Do not give test results singly on a one by one basis unless patient knows there is more to come • Ensure the GP is informed • Use trained interpreters where necessary • Be concise in documenting discussion
Comments	<p>Little progress on empirical evidence since guideline first drawn Admit that consensus is only 4B grade evidence High agreement between care givers and patients on importance of guideline Differences in short and long term effects on patients psychological outcomes makes trial difficult to focus</p>

Paper	Radziewicz, R. & Baile, W. F. 2001, "Communication skills: breaking bad news in the clinical setting.", <i>Oncology Nursing Forum</i> , vol. 28, no. 6, pp. 951-953.
Description	Opinion
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Clinician fear that sharing unfavourable information may cause harm • Often lack of practice or skill • Well delivered information can in the long term lead to an increase in patient satisfaction, compliance and coping • SPIKES protocol - Stick to the facts • Don't push for details • Avoid giving advise of what to do
Comments	<p>Author written widely Little use in terms of patient outcomes – compliance and quality of life No empirical evidence</p>
Reference	237

Paper	Hinds, C., Streater, A., & Mood, D. 1995, "Functions and preferred methods of receiving information related to radiotherapy. Perceptions of patients with cancer", <i>Cancer Nursing</i> , vol. 18 , no. 5, pp. 374-384.
Description	Before and after trial
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Pre-treatment most seek information regarding participation – Post treatment regarding preparation • Once treatment is almost completed new informational needs emerge • More men than women use information for preparatory function (27% vs. 13%) • No significance of information function across age, education, socio-economic status • Some people have different information needs over and information needs change over time, so need to tailor information given
Comments	<p>Recruitment of population from one arm of an existing study</p> <p>Small samples n = 21 – 36</p> <p>Information categories designed form responses rather than pre-meditated</p>
Reference	232

Paper	Mushlin, A. I., Mooney, C., Grow, V., & Phelps, C. E. 1994, "The value of diagnostic information to patients with suspected multiple sclerosis.", <i>Archives of Neurology</i> , vol. 51, no. 1, pp. 67-72.
Description	Before and after study
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Health status – no change • Current perception – no significant change • Future outlook – Pre-test = 63%; Post-test = 58% (p<0.02) • Uncertainty – Pre-test = 50%; Post-test = 40% (p<0.01) • Anxiety – fell less than patients expected • Value of information – ratio of years in perfect health/life expectancy increased by 4% • Patients without clear diagnosis were more anxious than they were expecting, clarity more important than a positive diagnosis • Patients feel better off even when health outlook is worse, would be willing to experience considerable discomfort rather than wait for diagnosis
Comments	<p>Study to examine if diagnostic test improves patient outcomes by questionnaire pre and post-test</p> <p>Surveyed pre and post-diagnostic test. No errors but bias on knowing previous scores</p> <p>Used validated scales consistently</p> <p>Low numbers</p> <p>Expected anxiety perhaps not a valuable outcome measure</p>
Reference	235

Paper	Walden, J. A., Dracup, K., Westlake, C., Erickson, V., Hamilton, M. A., & Fonarow, G. C. 2001, "Educational needs of patients with advanced heart failure and their caregivers", <i>Journal of Heart & Lung Transplantation</i> , vol. 20, no. 7, pp. 766-769.
Description	Observational; questionnaire
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Educational needs highly similar for patient and carers, so can educate them together • Three most common needs in both groups - Hope for good quality of life • Honest explanation • Receive information for emergencies • Needs rated least important - Appearance post-transplant, Employment, Instruction on sexual activity
Comments	<p>Small sample Preferences for education type may change over time (particularly for those rated least important) Hard to extrapolate findings to outside transplant arena</p>
Reference	230

Paper	Buetow, S., Goodyear-Smith, F., & Coster, G. 2001, "Coping strategies in the self-management of chronic heart failure", <i>Family Practice</i> , vol. 18, no. 2, pp. 117-122.
Description	Observational – texts of interview
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Stories can bring messages alive by being – affective; cognitive; behavioural; affirmative; temporal • Four coping strategies identified – Avoidance; disavowal; denial; acceptance • Disavowal = register and acknowledge reality but, palliate strain by disassociation of awareness from personal impact • Disavowal most common response (except in >65's diagnosed 3+ years ago) – coping through disavowal supports hope • Not influenced by severity or sex
Comments	<p>Small sample, however drop out unimportant as study is a qualitative review Qualitative judgement of coping procedure – could check with patient Changes in coping procedure over time not fully discussed Clear intent Not included patients with known diastolic failure</p>

Paper	Simpson, S. H., Farris, K. B., Johnson, J. A., & Tsuyuki, R. T. 2000, "Using focus groups to identify barriers to drug use in patients with congestive heart failure", <i>Pharmacotherapy</i> , vol. 20, no. 7, pp. 823-829.
Description	Observational patient survey
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Estimated 50% of patients who are prescribed life long therapies stop concordance after 1 year • Non-concordance puts patients at increased risk of more severe illnesses, hospitalisation and death • Aids to concordance with drugs • Confidence in health care providers (improves when relationship is established) • Patient knowledge – more likely to concord when purpose of drug is known • Experience with drugs – regular times for taking • Social support - spouses, family members informed and educated • Ease of communication (including pamphlets and brochures, wallet cards for emergency). • Patients recognise that physicians strive to give best possible information, but meaning can be lost in translation to lay language • Intelligent non-concordance – shows disease control • Concordance changes over time
Comments	<p>All participants are volunteers so it may not be a representative sample (keener, more concordant sample)</p> <p>Mean age of sample (67.5 years ± 12) older than average population</p> <p>55% men</p> <p>Four focus groups (3 heart failure; 1 general population)</p> <p>Total n = 26</p> <p>Structured questions and four item compliance questionnaire</p>
Reference	239

Paper	Rogers, A. E., Addington-Hall, J. M., Abery, A. J., McCoy, A. S., Bulpitt, C., Coats, A. J., & Gibbs, J. S. 2000, "Knowledge and communication difficulties for patients with chronic heart failure: qualitative study", <i>BMJ</i> , vol. 321, no. 7261, pp. 605-607.
Description	Qualitative survey
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Good general description of heart failure • Many patients felt symptoms a fact of getting older • Half of participants wanted to discuss death and dying but it wasn't stimulated in consultation • Various reasons why patients believed doctors did not tell them as much as they wished to hear • Participants reported difficulties getting to hospitals and clinic rooms • RCP recommendations for information and audio-visual provision
Comments	<p>Low sample (n=30) – adopted to gain wide spectrum, appropriate for qualitative survey Does not aim to produce findings that are that are necessarily representative for a larger population Average age 69 years 67% men LV ejection fraction 33.1% Recruited from outpatient clinics and wards Coding of responses duplicated</p>
Reference	239

Paper	Luniewski, M., Reigle, J., & White, B. 1999, "Card sort: an assessment tool for the educational needs of patients with heart failure", <i>American Journal of Critical Care</i> , vol. 8, no. 5, pp. 297-302.
Description	Observational patient survey
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Participants with 12 + years of education rated information on disease and management as most important • 11 participants with no previous admission rated information on risk factors and future of disease most important • Class IV HF rated information on 'what's wrong with my heart', medication and side effects most important • Physicians matched any of pt's top 3 – 34% of the time • Nurses matched top one – 23% of the time • Nurses matched least important – 30% of the time • Sorting may help to stimulate educational needs debate
Comments	<p>Blinding of duplication of preference sorting by health care professionals Small sample (n=30); participants 33 – 82 years; 60% male Participants reported that the number of cards was overwhelming No measure of the spread of opinion Sorting of patients preferences repeated by physician and by nurse to test matching Significance of matches not stated</p>
Reference	233

Paper	Cline, C. M., Bjorck-Linne, A. K., Israelsson, B. Y., Willenheimer, R. B., & Erhardt, L. R. 1999, "Non-compliance and knowledge of prescribed medication in elderly patients with heart failure.", <i>European Journal of Heart Failure</i> , vol. 1, no. 2, pp. 145-149.
Description	Observational study – patient survey
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • 27% of participants classified to be non-concordant • 23% only, remember receiving information 30 days earlier • Average number of drugs participants taking = 7.5 ± 3.3 • A number of patients still taking medication that they had been instructed to discontinue • Physicians poor at assessing patient concordance • No gold standard for measuring compliance
Comments	<p>Small sample Intervention perhaps not significant - but well defined High polypharmacy – previously shown to be poor predictor of compliance Age and gender similar to national population Average NYHA class of HF = 2.5 ± 0.9 Assessor blind</p>

Paper	Ni, H., Nauman, D., Burgess, D., Wise, K., Crispell, K., & Hershberger, R. E. 1999, "Factors influencing knowledge of and adherence to self-care among patients with heart failure", <i>Archives of Internal Medicine</i> , vol. 159, no. 14, pp. 1613-1619.
Description	Observational study – Patient questionnaire
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> • Majority of patients had received self care information, yet as many as 40 % reported knowing little or nothing about HF • Thus a need for ongoing patient education, and need for effective communication • Increase in knowledge is not always accompanied by changes in self care behaviour • Adherence may be improved by targeting specific patient populations • Hospitalisation increases self care knowledge either by increased contact with health care professionals, or increased motivation from a life threatening event.
Comments	<p>From an academic medical centre, 113 participants from 120 that were approached (94.2%) Age 51 66% male Knowledge of self care and adherence to self care measured by an assessor by a specifically designed scale, and demographic characteristics surveyed Clinical data extracted from charts and electronic patient database with duplication (K=0.8) Multiple linear regression analysis to examine factors predictive of knowledge, and of adherence Assessment surveys may not be reproducible Patients were from a specialised heart failure centre, and had more advanced heart failure than general HF population (generalisability low) Did not assess the mental state of study patients at baseline Patients tend to over-report healthy behaviours so health related behavioural problems may be worse than stated</p>
Reference	231

Paper	Horan, M., Barrett, F., Mulqueen, M., Maurer, B., Quigley, P., & McDonald, K. M. 2000, "The basics of heart failure management: Are they being ignored?", <i>European Journal of Heart Failure</i> , vol. 2, no. 1, pp. 101-105.
Description	Observational Study
N=	
Intervention	
Outcomes	
Results	<ul style="list-style-type: none"> Lack of knowledge could adversely influence compliance and lead to high readmission rate within 3 months seen in this study
Comments	<p>80 patients in study at university hospital (13 excluded with either wrong diagnosis, or death n=2) To assess management practices, and to assess patient knowledge of their condition Demographic data from patients chart including prior history of HF and previous admissions Questionnaire to assess knowledge of diagnosis in n=43 with prior history of HF Medication noted on admission and discharge Patients under care of cardiologist received expert guidance more frequently than with internal medicine care 32% Vs 19% (P=0.002) Only 37% understood that their problem related to heart dysfunction 2/3 did not know their medication Only 15% knew the action of their medication None understood or had been advised about regular weight measurement 1/2 understood that exercise important but only 20% exercised regularly Not possible in the study to get info on why strategies were or were not used Did not evaluate carer understanding of heart failure Generalisable population of HF patients (Age 73 yrs)</p>

Improving adherence to drug therapy

Experimental Studies

Paper	Haynes, R. B., McDonald, H., Garg, A. X., & Montague, P. 2002, "Interventions for helping patients to follow prescriptions for medications", <i>Cochrane Library</i> no. 2.
Description	Systematic Review
N=	RCTs =33 (35 reports) of which 12 relate to non communication strategies n=2571 patients included in trials looking at interventions other than communication Population characteristics varied across the studies,, no demographic inclusion criteria, any patient who was prescribed a medication for a medical disorder
Intervention	The articles that related to interventions of interest to this guideline included automated telephone patient monitoring (2 trials) manual telephone follow up (1) simplified dosing regime (3) reminders (4) 'reminder' pill packaging (1) dose dispensing units of medication and medication charts (1) Vs no treatment in a variety of medical conditions
Outcomes	Outcomes of compliance are recorded for all papers although definition of compliance is not defined, and measured at a variety of time points
Results	<ul style="list-style-type: none"> • Automated telephone reminders proved to be effective in improving medication adherence when adjusted for age, sex, and baseline adherence in one trial (p<0.05) and with a combined intervention of education call and nurse follow up in another trial fewer adherence problems were reported (p<0.003) • Simplifying medication regimes appeared to be effective in improving adherence to medication in 2 studies, with a twice rather than four times daily regimen providing 95% and 85% compliance respectively (p<0.01), and a once versus twice daily dose of enalapril study using electronic medication monitoring reported a higher percentage of doses taken in the once daily regime (p<0.001) • Recommendations. <p>Simpler treatment regimes can sometimes improve adherence (and treatment outcomes) for both long and short term treatments There is no evidence that poor adherence can be 'Cured' and thus efforts to improve adherence must be maintained for as long as the treatment is needed</p>

Comments	<p>Many trials have used self-reported outcomes of compliance, which have been shown to overestimate adherence and could blur any differences between intervention groups and control.</p> <p>Attempts to increase adherence can have adverse effects including loss of privacy and autonomy, and more frequent adverse drug effects if treatment is being taken in higher doses.</p> <p>Many of the multiple intervention studies could not easily replicate the increased attention effect in control arms that was found in the active intervention</p> <p>The efficacy of the interventions included in this review to improve adherence to medication can be seen to be relevant to this guideline despite coming from a range of care settings, however the efficacy to improve patient outcomes cannot be satisfactorily transferred from non HF trials</p> <p>A thorough review of methodology used with inclusion criteria assessed independently by two or more reviewers, and explicit inclusion criteria pre-stated. Owing to differences across studies in venues, clinical disorders, interventions, adherence measures, and outcome measures a quantitative summary of findings was not made</p> <p>A thorough update on literature search from previous review including Medline, Cinahl, Healthstar, Psychlit, Sociofile, IPA, Embase, and Cochrane library, which is in keeping with the wide clinical scope of the review. Authors of included trials were also contacted to suggest other published or unpublished trials</p>
Reference	168
Studies included	Too many to describe here please check with original reference

Paper	Claxton, A. J., Cramer, J., & Pierce, C. 2001, "A systematic review of the associations between dose regimens and medication compliance", <i>Clinical Therapeutics</i> , vol. 23, no. 8, pp. 1296-1310.
Description	Systematic Review
N=	n=76 studies, n=? patients Patients taken from a wide therapeutic area from cancer, cardiovascular, fertility, infectious diseases, general medical, psychiatry, and respiratory management USA reviewers of International trials
Intervention	The use of varying dose frequency therapies from once to four times a day were compared
Outcomes	The compliance with the regimen in terms of the appropriate number of doses that were taken each day, or whether dose timings were within 25% of the target time
Results	<ul style="list-style-type: none"> • The overall rate of compliance was 71% (SD =17%) across all trial • Comparisons across dose regimens showed that compliance was significantly higher with once daily regimens versus 3 times or 4 times daily regimens with 79% compliance (SD =14%) compared to 65% compliance (SD =16%) (p=0.008) and 51% compliance (SD 20%) (p<0.001) respectively • Also dosing with twice daily medication was more often complied with than at 4 times daily 69% Vs 51% (p=0.001) • There were no significant differences between once and twice daily regimens • Although there was a trend for patients to take once daily therapies at the correct time of day (74%) more than with 2 doses (58%) or 3 doses (46%) there were too few studies available to make any statistical comparisons
Comments	<p>The complexity of the regimen is inversely related to compliance across the spectrum of therapeutic classes. The results suggest that once or twice daily dosing regimens should be prescribed wherever possible to aid compliance and therefore theoretically improve outcomes.</p> <p>Patients were not blind to the use of EM Multiple reports by several authors The studies included were not discernable from the main reference list Clinical heterogeneity on terms of classification of compliance All trials are equally weighted Trial results are compared by analysis of variance only</p>
Reference	169
Studies included	Too many to describe here please check with original reference

Paper	Newell, S. A., Bowman, J. A., & Cockburn, J. D. 1999, "A critical review of interventions to increase compliance with medication-taking, obtaining medication refills, and appointment-keeping in the treatment of cardiovascular disease.", <i>Preventive Medicine</i> , vol. 29, pp. 535-548.
Description	Systematic Reviews and Meta-analyses
N=	n=6 trials for compliance analysis n=397 patients Age =53 – 69yrs, Male =20 – 86%, USA trials
Intervention	A range of interventions are considered both individual and in overall programmes. In terms of the studies concerning drug compliance the strategies encompassed reducing dose frequency, supplying the medication as confectionary, a multiple strategy intervention, involving tailored behavioural and education counselling for patients, or a multiple strategy intervention involving home visits with counselling, written communication schedules, education materials, and compliance –enhancing packaging
Outcomes	The outcomes of the primary trials are all related to compliance rates, although the rate at which compliance was stated to have been achieved is not stated. Follow up was for between 1 month and 2 years
Results	<ul style="list-style-type: none"> • The only two interventions that were reviewed to be tentatively recommendable were reducing dose frequency, and one of the multiple strategy interventions of which one intervention was the use of 7 day dose packaging • Other strategies including behavioural and educational counselling were not recommended for or against • The provision of medication in confectionary form was tentatively recommended against as the primary trial did not show statistical significance in improved compliance
Comments	<p>It is difficult to rate the value of the non-communication interventions in aiding compliance amongst multifaceted programmes. The ability to make confident recommendations was hampered by a number of limitations within the primary studies</p> <p>Wide variation in the nature of the interventions, outcome measures, length of follow-ups, and presentation of results so no meta analysis was attempted.</p> <p>A literature search of Medline, Healthplan, and Psychlit was undertaken from 1985 to date and the bibliographies of all relevant papers were searched for additional papers. Health related government and non government bodies and additional organizations and companies were approached to locate unpublished trials, and finally an expert on compliance literature and an expert on cardiovascular literature were consulted on the final list of papers</p> <p>A thorough discussion of the methods used was given.</p>
Reference	170
Studies included	Miller (1990), Burris (1991), Miller (1989), Miller (1988), Sweeney (1991), Burrelle (1986)

Paper	Rich, M. W., Gray, D. B., Beckham, V., Wittenberg, C., & Luther, P. 1996, "Effect of a multidisciplinary intervention on medication compliance in elderly patients with congestive heart failure", <i>American Journal of Medicine</i> , vol. 101, no. 3, pp. 270-276.
Description	Randomised Controlled Trial
N=	n=156, multidisciplinary intervention =80, or normal care =76 Age =80yrs. Male =33%, NYHA class =2.4 (mean), LV ejection fraction =45% USA
Intervention	A multifaceted intervention of a 15 page teaching guide, daily nurse visits before discharge with importance of compliance emphasised, patients were seen by a dietician and by a social services representative, with each patient's medication being reviewed by a geriatric cardiologist, and specific recommendations made to simplify and consolidate the regimen by minimising the number of drugs and dosing frequencies, Vs normal treatment for 30 days
Outcomes	The primary outcomes were medication compliance both by the percentage of pills being taken correctly for each medication determined, and also the total number of pills taken correctly was divided by the total number of pills that should have been taken, to 30 days. Clinical outcomes of readmission were also recoded for each patient to 90 days. Demographic and clinical baseline variables were related to outcomes by multiple regression analysis
Results	<ul style="list-style-type: none"> • Patients randomised to the study intervention had significantly better compliance than control group by both means of compliance evaluation. For method 1 (% pills taken correctly for each drug) the compliance was 87.9% in the intervention group and 81.1% in the normal treatment (p=0.003), for the 2nd method (% of total pills that should have been taken) the compliance was 87.5% for the intervention group, and 80.9% for the control group (p=0.004). • There was a marked increase in the number of patients achieving a compliance rate of 90% or greater (p=0.032). • Independent predictors of medication compliance that were seen across both outcome evaluation methods were allocation to intervention group, and not living alone. • There was a readmission rate of 28.9% in the intervention group and 22.5% in the control group, but the readmissions per patient and hospital days reduced were not significantly different between groups. • Medication compliance was not predictive of readmission by univariate or multivariate analysis
Comments	<p>Difficult to extract the effects of any particular facet of the multidisciplinary intervention on compliance</p> <p>Compliance rates across the study were high</p> <p>The number of medications taken (median 5) was not associated with compliance rates</p> <p>Study was small</p> <p>Use of pill counts to evaluate compliance</p> <p>All analyses were undertaken using the intention to treat principle</p>

Paper	Fulmer, T. T., Feldman, P. H., Kim, T. S., Carty, B., Beers, M., Molina, M., & Putnam, M. 1999, "An intervention study to enhance medication compliance in community-dwelling elderly individuals", <i>Journal of Gerontological Nursing</i> , vol. 25, no. 8, pp. 6-14.
Description	Randomised Controlled Trial
N=	n=48, telephone =15, videophone =17, control =18 Age =74yrs, Years of education =9yrs, white =15%, black =31%, other =54%, all congestive HF as primary or secondary diagnosis USA
Intervention	Once daily telephone or videophone call (mon –fri) of usually 3-5 mins to ask whether patients had taken their medication the previous day for 6 weeks compared to usual treatment
Outcomes	The mean level of compliance across patients in each arm was evaluated at 6 weeks and additionally at 2 weeks after the intervention phase, The SF-36 and Minnesota living with heart failure QOL scales were also administered at baseline and at 8 weeks
Results	<ul style="list-style-type: none"> • There was a significant difference between the compliance rates at 8 weeks (2 weeks after the end of the intervention) with a 24% drop in compliance among the normal treatment arm compared to a 2% fluctuation (both positive and negative) in the telephone and videophone arms (p<0.05). • There was no significant difference in the efficacy of the telephone and videophone interventions to alter compliance. • There was a significant difference in the Minnesota living with heart failure score at week 8 (p<0.001) though given the size of the sample this has to be treated with caution
Comments	<p>The effect on overall symptom management should be investigated in the future</p> <p>The benefits of telephone or videophone intervention lasted into 2 weeks beyond the end of the study period when reminders were no longer given</p> <p>High refusal to participate rate</p> <p>Individuals who take their medication from special pill boxes rather than the bottle could not be included in this study due to limitations of technology</p> <p>The MEMS recording systems provides a very accurate record of compliance with medication using a micro-chip to record how often bottles are opened</p> <p>Use of MEMS in control group raises compliance at baseline across all groups</p>