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Does case management for patients with heart failure reduce unplanned hospital admissions? A systematic review and meta-analysis

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ABSTRACT

Objectives

This systematic review aims to extend our knowledge of the effectiveness and cost- effectiveness of case management (CM) for patients with heart failure (HF) in reducing unplanned admissions.

Setting

CM interventions initiated either whilst as an inpatient or on discharge from acute care hospitals including the emergency department, or in the community and then continuing on in the community.

Participants

Adults with a diagnosis of HF and resident in Organisation for Economic Co-operation and Development countries.

Intervention

CM based on nurse co-ordinated multi-component care of individual patients which is applicable to the primary care based health systems.

Primary and secondary outcomes

The primary outcomes of interest were unscheduled secondary care and cost effectiveness. Secondary outcomes were primary health care resources.

Results

Twenty-two studies were included: 17 RCTs and five controlled trials. Seventeen of these studies described hospital-initiated CM and five described community-initiated CM of HF. Hospital -initiated CM showed a reduced risk of readmission (rate ratio 0.77 [0.63, 0.94] p=0.01) and length of hospital stay (mean difference -1.28 days [-2.03,-0.53] p=0.0008) in favour of CM compared to usual care. Nine trials described cost data of which six reported no difference between CM and usual care. Data from three of five trials of community-initiated CM showed no differences in risk of admission compared to the usual care group (rate ratio 1.08 [0.62, 1.87] p=0.8). Data from some individual studies suggests that family involvement and education/self-management are likely to be important in CM but this was not demonstrated in sub-group analysis.

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Conclusions

Hospital-initiated CM can be successful in reducing unplanned hospital readmissions for HF and length of hospital stay for people with HF. Limited data suggest no difference in costs between usual care and CM. There were limited data for community-initiated CM which suggested it does not reduce hospital admission.

Protocol registration

No

Strengths of review

- High quality systematic review
- Interventions examine nurse-led multicomponent care of heart failure patients
- Focus on use of resources specific to heart failure

Limitations of review

- Community-initiated case management trials were limited in quantity and were mostly of low quality.
- Lack of cost data in most trials

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INTRODUCTION

Applying current prevalence figures to population estimates suggests that more than 550,000 individuals (more than 308,000 men and slightly fewer than 250,000 women) in the UK are living with heart failure (HF).[1] Quality and Outcome Framework (QOF) data supports this: in 2012/13 just over 480,000 patients were recorded as having heart failure.[2] The average age of HF patients in general practice in the UK is 77 years.[3]

Prior to 1990, 60–70% of patients died within 5 years of diagnosis, and admission to hospital with worsening symptoms was a regular and recurrent event.[4-6] Effective treatment has improved care, with a relative reduction in hospitalization in recent years of 30–50%, and smaller but significant decreases in mortality.[4-6]

More than £6.8 billion was spent on treating all cardiovascular disease within the NHS in England in 2012/13 with 63% of these costs coming from within secondary care and 21% within primary care. Within secondary care, non-elective inpatient admittance for cardiovascular disease, i.e. emergency admissions, had the greatest expenditure with £1,925 million.[1]

Case management (CM) is the process of planning, coordinating and reviewing the care of an individual. We used the definition cited by the King's Fund in the UK 'A collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual's and family's comprehensive health needs through communication and available resources to promote quality cost-effective outcomes.'[7] The NHS has used less-intensive approaches than the traditional US model, for example, through the use of nurses to support older people and those with long-term conditions at home.[8] In this review we have focused on CM based on nurse co-ordinated multi-component care of patients which is applicable to the primary care based health systems such as that in the UK.

Previous research suggests that whilst CM is not effective in reducing unplanned hospital admissions for the general older/elderly population, the evidence for patients with HF is promising.[9,10] Therefore this review aimed to a) update the evidence of the effectiveness and cost-effectiveness of interventions by examining both randomised and non-randomised controlled trials and b) to better understand the potential success of CM by examining the components of tested interventions.

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METHODS

Search

Databases and registries

A search strategy was developed using keywords for the electronic databases according to their specific subject headings or searching structure. The search strategy was run from 1985 – 2012 in the OVID databases - Medline®, Excerpta Medica Database (Embase), Cumulative Index to Nursing and Allied Health Literature (CINAHL®), PsycINFO® on the 2nd July2014. (Appendix one) The search strategy was modified to search internet sites such as the Agency for Healthcare Research and Quality (AHRQ) and the King's Fund. A pragmatic update of these searches was conducted on the 20/11/15 using the same search strategy and run in Medline and Medline in process only.

Other sources

Once the included papers were determined, both backwards (reference list of paper) and forwards citation searching (via google scholar) was performed to identify any other potentially relevant studies. All authors of included studies in the field were contacted with data queries and to identify additional relevant studies.

Eligibility criteria:

Randomised controlled trials, and other controlled studies (controlled trials, controlled before and after studies, analytic cohorts, comparative studies) were included as determined by our eligibility criteria. CM interventions needed to be initiated either whilst as an inpatient or on discharge from acute care hospitals including the emergency department (ED), or in the community, and then continue on in the community. Only studies including adults with HF in Organisation for Economic Co-operation and Development (OECD) countries were included as the outcomes were more likely to be comparable for synthesis, and relevant to the UK situation.[11] Studies were included as long as one of the outcomes of interest was unscheduled secondary care [unplanned hospital admissions/readmissions, ED attendance, length of hospital stay] as well as related cost and cost effectiveness of the interventions. Other outcomes of interest were primary health care resources e.g. GP visits, visits to other primary care health professionals or services and prescriptions. Studies written in any language were considered if there was an English abstract.

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Reference management and study selection

EndNote and Excel were used to manage the references. Duplicates were removed from the Endnote file. References underwent a two stage process of screening using the inclusion and exclusion criteria by two reviewers independently (AH, AK, RJ). Firstly, a screen of titles and abstracts (if abstract available) and secondly screening of the full paper was conducted. Where there was continued disagreement between reviewers about including or excluding a paper, a third reviewer made the final decision (SP or RJ).

In addition to the included quantitative intervention papers, we identified relevant reviews from the search. Any potentially relevant conference proceedings were followed up, firstly by searching in Medline to see if the study had been published. If the study was not published, the authors were contacted where possible to check if the studies were likely to be published within the work frame of this review.

Data extraction

Data were extracted into a custom-designed table which included description of trial type, participants, intervention, controls, outcome measures and results. Based on the Kings Fund definition of case management we devised taxonomy of intervention components.[8] (table 1) As part of this data extraction process, the intervention and control treatments were also described by their component parts e.g. monitoring signs and symptoms using the framework of the CM definition.

Quantitative data concerning the outcomes of interest were extracted into the Cochrane Revman software. The Cochrane risk of bias tool was used to record trial bias.[12] This process was performed by one author and checked by a second. (AH, AK) Any disagreements were resolved by discussion and if necessary with a third author. (RJ, SP)

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Data analysis

Trials were divided as previously described by Huntley *et al* 2013 into hospital-initiated CM and community-initiated CM.[9] Where there were data from three or more studies, effect sizes were calculated and presented in forest plots as rate ratios (admissions) or mean differences (length of stay) using Revman software. If the heterogeneity of the combined data was greater than 50%, a random effects model was used for analysis.

We conducted sensitivity analysis in response to the risk of bias assessment of studies, removing high risk of bias studies as appropriate; the results of both analyses are presented.[13] We conducted subgroup-analysis to explore the effects of CM duration (3,6 and 12 months plus) on hospital admission and LOS. There was insufficient detail in trials to perform sub-analysis by severity of HF or intensity of intervention.

Data were assessed narratively in respect of the components of interventions using the CM definition cited above as guidance.[8] (table 1) In addition, where possible subgroup-analysis was conducted in Revman in which interventions with components of interest were compared with those that did not have these components.

RESULTS

The systematic review yielded 22 studies with data published over 32 papers of which 17 were RCTs and five were CTs. [14-45] No relevant studies were identified in the pragmatic update search. Seventeen of these studies described hospital-initiated CM[14,15,17,18,20-24,26-28,31,32,] and five described community-initiated CM of HF.[38,42-45]

Profile of patients (table 2)

The range of female participants in the trials was 1-58%, but the majority of trials had relatively even gender divide. Co and multi-morbidity were common. Eight of the 22 trials gave no detail on ethnicity of participants; in four studies the trialists used white/non-white and English speaking/non-English speaking categories. In the remaining 10 studies, a fuller profile was described. Twelve of the 22 trials were conducted in the USA and the ethnicity profile reflected that including Spanish speaking/Hispanic, American Indian, Black, African American, Asian and White participants.

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The majority of trials described the severity of HF using New York Heart Association (NYHA) classification. Twelve of the trials gave a breakdown of numbers or percentages in the I-IV classes with some trials only giving numbers of participants for the III and IV class. In these trials the percentage range of III and IV class patients was 6-98%. Four trials gave mean and median values of NYHA status, one trial used the APR-DRG severity of illness scale, and five trials did not describe disease severity.

Profile of interventions (table 1)

The majority of studies (n=15) described the intervention being delivered by a case manager/ specialist nurse with no specific mention of other health professionals, and the remaining seven studies described a case manager/speciality nurse working as part of a multi-disciplinary team.
All but two studies compared CM with usual care although the control group was not always described. The two remaining studies were comparative: one RCT comparing CM with specialist clinics and one RCT comparing CM with telemedicine plus CM. [32,42,]
The duration of the CM interventions in the studies was 1-24 months with the majority having a 3 or 6 month duration. The majority of studies were conducted face to face or a combination of in-person and by phone. Four interventions were conducted purely by phone.[21,22,26, 42] Outcomes were measured to match the total duration of intervention in the majority of studies. For many of the studies the intensity of interventions was not stated explicitly. When intensity was described it was always a tapered approach after an initial intensive period.

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Risk of bias (Figure 2a&b)

The degree of risk of bias was starkly different between the RCTs and CTs. All five of the CTs were rated at high risk or unknown risk for most domains.[35,36,37, 44,45] The majority of the RCTs were rated at low risk for most domains with the exception of the domain of blinding of the participants and personnel which is not applicable to this type of intervention. Three RCTs were assessed as at high risk for at least one domain: both Hancock and Wade gave no description of the randomisation process or allocation concealment, Riegel 2002 was randomised at physician level and patients were chosen by physician preference.[21, 42,43] Four of the five community-initiated trials (2RCTs and 2CTs) were assessed to be at high risk of bias, and in some studies did not present usable data. [35-37,42]

All the intervention studies reported unplanned hospital admissions [14-45] and 17 reported number of days in hospital.[14, 15, 17, 18, 20-22, 24, 26-28, 35, 38, 42-45] There were few data on A and E attendance and primary care resource use. However, only some of the data could be used in meta-analysis with the main reasons being that data were presented in different formats where neither confidence intervals, standard errors nor raw data were given. Due to heterogeneity of data all analysis was conducted using a random effects model.

Unplanned HF (re)admissions data (figure 3)

Hospital-initiated CM

Thirteen of hospital-initiated CM trials had data that could be used in the meta-analysis. Overall the data showed the rate ratio of readmissions was 0.77 [95% CI 0.63, 0.94] p=0.01 I^2 =69% in favour of hospital- initiated CM. (figure 3a) A sensitivity analysis was conducted, removing Riegel 2000 (high risk CT) and 2002 (RCT with high risk for randomisation domain) which had a minimal effect on the rate ratio and heterogeneity 0.77 [0.61, 0.96] p=0.02 I^2 =68%.[21,35] Sub-analysis looking at 3, 6 and 12-18 month data did not produce a clear time-related effect which is most likely due to heterogeneity within and between studies.(figure 3b,c,d). There was one hospital-initiated CM trial which compared CM with specialist clinics which reported no differences in hospital readmissions between the two groups.[32]

Community initiated CM

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Of the four community initiated trials comparing admissions between CM with usual care, two reported no significant differences[38,43] and two reported statistically significant reductions in favour of CM.[44,45] Data were available from three of these trials for meta-analysis and showed no significant differences in admissions between groups, (rate ratio 1.08 [0.62,1.87] p=0.8 I^2 =78% (figure 3e).[38,44,45] One further trial compared CM, with telehealth and CM and reported no differences in admissions but data were not presented.[42]

Length of hospital stay (LOS) (figure 4)

Hospital-initiated CM

Nine of the hospital-initiated CM trials had data that could be used in a meta-analysis. Overall the data showed that LOS was reduced in the CM group compared to usual care mean difference (MD) -1.28 days [-2.03,-0.53] p=0.0008 I^2 =68%. (figure 4a) A sensitivity analysis was conducted removing Riegel 2000 and 2002 which had an important effect on the rate ratio and heterogeneity MD -1.76 [-2.29,-1.23] p<0.00001 I^2 = 14%. [21,35] Sub-analysis looking at 3, 6 and 12-18 month data suggests this effect is short-term (first 3 months) but a longer time-related effect was difficult to assess due to lack of data.(figure 4b,c,d).

The one study comparing CM with specialist clinic care, reported that CM patients accumulated 592 and clinic patients 547 *all-cause* hospitalizations (p = 0.087) associated with 3067 versus 4410 days of hospital stay (p < 0.01 for rate and duration of hospital stay).[32]

Community initiated CM

Of the 4 community initiated trials comparing CM with usual care, two did not report LOS [38, 43] one reported median values in favour of CM[44] and the remaining one reported a mean reduction in LOS. [45] (table 2). The one comparative trial between community-initiated CM , and telehealth and CM did not report any useful data.[42]

Intervention components (table 2 and appendix 2)

Fourteen intervention components were identified and grouped as per the CM definition in methods and prevalence determined for both hospital and community –initiated CM studies with a usual care control group (table 2). [7]

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Hospital-initiated CM (appendix2)

Data from individual studies which contained components of either family involvement or education/self-management showed an overall reduction in hospital readmissions in comparison with usual care. They also showed a reduction in hospital readmissions observationally in comparison with interventions which did not contain these components. However, analysis comparing the studies in which the component was present with those in which the component was absent did not yield any statistically significant differences. (appendix 2a &b) The same calculations for medication review, referral to other services, and assessment of home environment, CM meetings and patient-directed access did not indicate any specific effect of these components of hospital- initiated CM on rates of admission. (appendix 2 c-e)

Community initiated CM

There were insufficient data to conduct any subgroup-analysis on any of the remaining components of hospital-initiated CM, community initiated studies or the length of stay data.

Outpatient health care resources

Only six of the included studies measured outpatient resource use. In some studies, outpatient resource data were all-cause and not HF-specific. In some studies primary and secondary use was combined.[23,24,35,38,42, 45] Two of these studies also reported ED attendance.[23, 42] All but one of these studies reported no difference between intervention and control group for these measures with the exception of Lowery which showed a statistically significant greater use of outpatient resources in the usual care group (optional primary care visits 1yr 16.75(13.62),10.43(9.6) p<0.001 , 2yr 14.27(11.98),9.35(9.97) p<0.001).[45]

Costs

Nine of the seventeen hospital initiated trials described cost comparison data. Of these, six reported no statistically significant difference between CM (3 or 6 month duration) and usual care.[17,18,22,24,35,26] and three reported costs in favour of CM although data from Stauffer was brief.[15,32,37] One of these was 12-18 months[32] and two were 3 months in duration. It was difficult from the intervention

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descriptions to determine their intensity. There were no cost data reported from the community-initiated trials.

DISCUSSION

This systematic review confirms that hospital-initiated CM can be successful in reducing unplanned hospital readmissions, and reducing length of stay in hospital in the short term for people with HF. There were only five community-initiated CM studies of which four were at high risk of bias. Limited data shows no effect of community-initiated CM on hospital admissions. A minority of trials report cost comparisons with usual care and most of those show no difference. There were limited data on the effect of CM on other health care resources. Observational intervention component data suggests that care providing family involvement and education/self-management are likely to be important in case management but these observations did not stand when subjected to subgroup analysis.

Many factors are likely to modify the effect of CM on use of emergency care seen in these studies. It is generally accepted that CM is more appropriate for people with severe HF and poorer general health. However it was difficult to compare the health status of the study participants in both hospital-initiated and community-initiated trials as in some studies there was little detail, others gave median and mean figures for NYHA status, and the presentation format and detail of co-morbidities varied.

Seventeen studies described hospital-initiated CM and five described community initiated CM of heart failure although often the participants were identified via hospital clinic records. Overall the meta-analysis showed that a positive effect of CM on readmissions and hospital length of stay. This may be explained by the fact that in most of the trials the participants were identified via hospital contact and therefore were likely to have had a recent exacerbation of their HF and to be at increased risk of re-admission in the post-discharge period. In addition, it is likely that interventions are acting at a time of highest risk as reflected by HF mortality in first year of diagnosis.[4] Therefore once they were assessed and given extra support they were stable for a period of time. Previous work by Roland et al 2005 suggests that admission rates in people aged 65 with two or more emergency admissions in 12 months fall in subsequent years without any intervention and account for fewer than 10% of admissions in the following year and thus effectiveness of admission avoidance schemes cannot be judged by tracking admission rates without careful comparison with a control group.[46] The data from

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trials of community-initiated CM was lacking both in the number of studies , and the fact there were limited useable data that showed no effect on unplanned hospital admissions. It is likely that these patients were likely to be in more stable health.[41]

A meta-review of a wide range of HF disease management programs by Savard 2011 reports that nine previous systematic reviews (2001-2009) identified significant reductions in HF admissions with reductions in risk ranging from 30-56%.[47] However the authors caution that these reviews are limited by inadequate reporting in the population, setting, intervention and comparator components. They report that reviewers have not taken into account statistical, clinical and methodological heterogeneity in interventions.[47] Our review focussed specifically on CM avoiding some of these limitations and indicates a reduction in HF admissions with hospital-initiated CM in the range of 10-30%.

Wakefield *et al* in 2013 looked at common components of a range of HF care programs focusing mainly on disease management and education investigated in RCTs, and 10/35 of the discussed studies were included in our review.[48] They described patient education, symptom management by health professionals and by patients, and medication adherence strategies as the most commonly occurring elements of care. A literature review by Jaarsma 2012 looked at 70 'home care' controlled studies (mostly RCTs) which encompassed 9 of our included CM studies covering a wide range of approaches such as telemedicine, hospital at home and health buddies for patients with HF.[49] They identified a multi-disciplinary team, continuity of care, care plans, optimising titration of medication, education/counselling of patients and caregivers and increased access as important.
In order to understand why our meta-analysis reported that the specific approach of CM was successful in reducing admissions and length of stay we also conducted component analysis. Our analysis agreed with the above reviews that patient education/self-management is significant but also flagged up the importance of family involvement. The magnitude of effect was not so convincing for medication review (appendix 2c) but it was difficult from the study description to distinguish between medication management and formal reviewing of medication by either the CM or pharmacist.

Previous systematic reviews have investigated the role of the lay caregiver in HF patient management.[50-52] These suggest that better relationship quality and communication were related to reduced mortality, increased health status and less distress and improved patient self-care outcomes.

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Our review adds to this evidence base by suggesting that more family involvement in CM may also reduce unscheduled secondary care.

Education about HF and about its pharmacological and non-pharmaceutical treatment has been well-reviewed both as an individual approach and as part of complex interventions, and is considered to be essential for improving many patient outcomes. [49, 53,54]A recent mixed method study, suggests asking patients with HF to write down their learning needs before the education increases their chances of receiving education based on their individual needs.[55] Qualitative interviews with health professionals caring for HF patients suggest that communication with, and education by specialist nurses facilitated by continuity of care is essential to good care of HF patients. The authors also highlight the role of the specialist nurse in multi-disciplinary team communication and functioning; essentially describing the role of the specialist nurse as a case manager.[56]

Our review of CM suggests that the evidence for its cost-effectiveness is lacking with most studies that have performed cost comparisons with usual care show no advantage. Previous work by de Bruin et al 2001 looked at cost effectiveness of disease management for a range of chronic conditions and concluded that the data is most positive for HF with 5 out of the 8 included studies showing cost-effectiveness.[57]

Strengths and limitations

The contribution of our high quality systematic review to the above is that we have focused on CM which is based on nurse co-ordinated multi-component care of patients which is applicable to the primary care based health systems such as that in the UK. We have focused on HF admissions and length of stay as opposed to all-cause data which many of the previous reviews have used.

By examining the components of CM we have a profile of the components most likely to lead to the success of CM of patients with heart failure in terms of reducing admissions and hospital length of stay. Our review has high-lighted the potential importance of family involvement and education/self-management.

The limitations of this review are that majority of the community-initiated CM studies were of low quality with the exception of one low risk RCT, and provided limited data for meta-analysis. This was counteracted by the fact that the hospital-initiated studies comprised of predominantly community-

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based case management. There is a lack of cost data and analysis in the included papers. This point needs to be emphasised for future trials. It is possible that cost effectiveness will be more likely with intervention for patients with more severe HF.

CONCLUSIONS

Hospital-initiated CM reduces unplanned hospital admissions, and length of stay for people with HF in the short term. Cost data is limited. There were limited data for community-initiated CM which suggested it does not reduce hospital admission. Further research is needed to determine the individual components of CM that contribute to reduced admissions.

Contributorship statement

Alyson Huntley. Main systematic reviewer, worked across all stages of the review from inception to completed draft.

Rachel Johnson. Cardiology and primary care expertise. Worked on screening, selection of studies, commenting on analysis, and development and checking of final document content.

Anna King. Second reviewer, involved in screening, selection, data checking and commenting on developing and final document content.

Richard Morris. Statistical expertise, advising on data analysis and commenting on the developing and final document content.

Sarah Purdy. Primary care and admission avoidance expertise. Advised throughout project, third reviewer for screening process and commenting on the developing and final document content.

Competing interests

None declared

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Data sharing statement

Full data extraction tables and data analysis files are available on request

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Table 1: Components of CM interventions

Definition & total prevalence of Components of CM interventions	Number of hospital-initiated CM vs. usual care with component present (total studies=16)	Number of community-initiated CM vs. usual care with component present (total studies=4)
Assessment /Evaluation		
Monitoring signs & symptoms (n=18) Encompasses general care of CHF patients which is likely to include establishing a relationship with patient over visits, physical and cardiac status checking, lifestyle assessment, general medication check and screening tests e.g. depression, dementia	**14**	**4**
Medication review (n=8) Review and adjustment of medication by experienced case manager (nurse), pharmacist, GP or consultant often using a combination of these health professionals.	**6**	**2**
Assessment of home environment (n=4) Assessment carried out by case manager to identify any issues or potential issues with home environment e.g. stairs	**4**	**0**
Planning		
CM meetings/feedback to other HPs (n=5) Group meetings of health professionals involved in CHF patients care with the aim of reporting on and planning for patients care.	**3**	**2**
Appointment organisation (n=2) Case manager checking medical appointments, ensuring ability to go etc.	**2**	**0**
Advance care planning (n=1)	**1**	
Facilitation		
Education/self-management (n=18) Educating CHF patients about their condition, treatment and what to expect. The aim of this is to assist self-management (care with assistance of health professionals) and self-care (patient engaging in activities to promote their health and well-being).	**15**	**3**
Patient–directed access (n=6) The ability of CHF patients to initiate care from the case manager or case management service.	**6**	**0**
Care co-ordination		
Referral to …. (n=14) When the case manager refers the patient to other health or social care professionals, this can be GP hospital consultant, social care or tests.	**11**	**3**
Advocacy for options & services		
Equipment (n=4) Provision of items to assist patient's health care such as pill counters, weighing scales and measured water bottles.	**3**	**1**
Physical therapy (n=1) CHF patient receiving physical therapy/rehabilitation	**1**	**0**
Support group (n=1) CHF attending or being offered the opportunity of a support group.	**1**	**0**
Other		
Family involvement (n=9) When the case manager involves the patient's family in terms of information, education or involvement e.g. goal setting in patients' care or active monitoring	**8**	**1**
Emotional support (n=1) Case manager providing emotional support to CHF patient.	**0**	**1**

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Table 2: study characteristics of intervention studies

Study n=randomised Recruitment/setting	Baseline characteristics of participants: CM vs. usual care	Intervention	Control
Hospital Initiated CM - RCTs			
Rich[14] **1993** USA n=98 randomised Patients ≥70 yrs admitted to medical wards of Jewish Hospital at Washington University Medical Centre were screened for congestive HF.	**Age** 80(6.3),77.3(6.1) yrs p=0.04 **% Female:** 60.3, 47.1% **Ethnicity:** White 46,57.1% **Disease Status:** Mean NYHA status 2.7(1.1),3.0(1.0)	**Non-pharmacological comprehensive multidisciplinary treatment strategy** (n=63) ***Components of intervention at home:*** Monitoring signs& symptoms Medication review (nurse) Education /Self-management support Assessment of home environment Patient directed access to study personnel	**Usual care** (n=35) **Components of intervention:** Visits by home nurse
Rich [15] **1995** USA n=285 randomised As above for Rich 1993 .	**Age:** 80.1(5.9),78.4(6.1) yrs p=0.02 **% Female:**68,59% **Ethnicity:** Non-white race 52,59% **Disease Status:** Mean NYHA class 2.4(1.0),2.4(1.1)	**Nurse-directed multidisciplinary intervention** (n=142) As above for Rich 1993	**Usual care** (n=140) As above for Rich 1993
Stewart [17] **1998** Australia n=97 randomised Patients were recruited whilst admitted to a large tertiary hospital	**Age:** 76 (11), 74(10) yrs **% Female:**55,48% **Ethnicity:** Non-English speaking 20.4,18.75% **Disease Status:** NYHA II 49,50% III 47,42% III 4,4%	**Home-based intervention** (n=49) **Components of intervention at home:** Monitoring signs& symptoms Education (pharmacist)/self-management support Medication review (pharmacist) Referral to GP Family involvement Equipment	**Usual care** (n=48) **Components of intervention:** Disease management
Stewart [18,19] **1999** Australia n=200 randomised Patients admitted to a tertiary referral hospital	**Age:** 75.2(7.1),76.1(9.3) **% Female:** 35,41% **Ethnicity:** Primary language not English 32,32 **Disease Status:** NYHA II 42,48 III 46,43 IV 12,9	**Multidisciplinary home base intervention (n=100)** **Components of intervention at home:** Monitoring signs& symptoms Referral to other health & social care Appointment organisation Assessment of home environment Family involvement Education/self-management support Medication review (nurse/GP/cardiologist)	**Usual care (n=100)** **Components of intervention:** Contact with other health and social professionals Appointment with GP or cardiac clinic or both
Blue[20] **2001** UK n=165 randomised Patients admitted as an emergency to the acute medical ward of the hospital	**Age:** (SD)74.4(8.6),75.6(7.9)yrs **% Female:** 36,49% **Ethnicity:** Not reported **Disease Status:** NYHA II 19(23), 16(20) III 28(34), 33 (42) IV 36 (43), 30(38) **Co or Multi-morbidity:** Angina 40(49), 38(45) Past MI 41 (51), 46(55) Diabetes 15(19), 15(18) Chronic lung disease 18(22),23(27) Hypertension 42(52), 36(43) AF 42(52), 29(35) Valve disease 12(15),15(18)	**Specialist nurse intervention** (n=82) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Referral to other health & social care Appointment organisation Medication review (nurse, cardiologist)	**Usual care** (n=75) **Components of intervention:** GP care
Riegel[21] **2002** USA n=281 physicians randomised Patients admitted at 2 Southern California hospitals.	**Age:** 72.52(13.05), 74.63(12) **% Female:**46.2,53.9 **Ethnicity:**(Primary language) English 91(70), 168(73.7) Spanish 35 (26.9), 58(25.4) **Disease Status:** NYHA II 2.3,3.6 III 35.9, 38.4 IV 61.7,58.0	**Telephonic case management** (n=130) **Components of intervention at home:** Monitoring signs& symptoms Self-management support Referral to other HPs (includ.GP) & social care Family involvement	**Usual care** (n=228) **Components of intervention:** Not known
Laramee[22] **2003** USA n=287 randomised Patients admitted to hospital for CHF were screened.	**Age:** 70.6(11.4), 70.8(12.2) yrs. **% female:** 42,50% **Ethnicity:** Not reported **Disease Status (SD):** NYHA I 10(7),35(26) II 76(55),47(36) III 50(36),46(35) IV 3(2),4(3) Note P<0.001	**Case management** (n=131 data available) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement Equipment Patient–directed access to CM	**Usual care** (n=125 data available) **Components of intervention:** Not known

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De Busk[23] **2004** USA n=462 randomised Patients who were admitted with a provisional diagnosis of HF from Kaiser Permanente medical centres in California	**Age:** <60yrs 15,14%, 6-70yrs 22,24%,70-80yrs 40,37%, >80yrs 21,26% **% Female:**52,45% **Ethnicity:** American Indian 0,1% Asian 4,8% Black 2,2% White 5,6% Hispanic 3,3% **Disease Status:** NHYA I-II 50,50% III-IV 50,50%	**Case management** (n=228) **Components of intervention at home:** Monitoring signs& symptoms Education /Self-management support CM meetings/feedback to other health providers	**Usual care** (n=234) **Components of interventions:** not known
Naylor [24,25] **2004** USA n=239 patients randomised Patients aged 65yrs+ admitted to 6 study hospitals from home with a diagnosis of HF were screened for participation.	**Age:** 76.4(6.9),75.6(6.5) **% Female:**60, 56% **Ethnicity:** African American 34,38%**,** White 66, 62% **Disease Status:** Functional Status (Moinpur C 1992) Personal 17.1(5.8),16.9(5.8) Social 8.4(2.6),8.6(2.6) Total 25.5(8),25.4(7.8)	**Transitional care intervention with advanced practice nurses (APNs)** (n=118) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement CM meetings/feedback to other health providers Patient–directed access to CM	**Usual care** (n=121) **Components of intervention:** Care from standard home care services Patient–directed access to home care services
Riegel[26] **2006** San Diego USA n=135 randomised Self-identified Hispanics were identified at 2 community hospitals close to US-Mexico border	**Age:** 71.6910.8),72.7(11.2) **% Female:**58,49.2% **Ethnicity:** Hispanic patients Speak/read only Spanish 60.9,65.1% **Disease Status:** NYHA II 17.4,20% III 44.9,47.7% IV 37.7,32.3%	**Telephonic case management** (n=69) **Components of intervention at home:** Monitoring signs& symptoms self-management support Referral to other HPs (includ.GP) & social care Family involvement	**Usual care** (n=65) **Components of intervention:** Disease management Information
Thompson[27] **2005** UK Randomisation was at GP practice level Patients recruited from 2 North of England general hospitals following an admission	**Age:** 73(14),72(12) **% Female:**38,27% **Ethnicity:**No details **Disease Status:** NYHA III &IV 76,73%	**Clinic & home based intervention** (n=58) **Components of intervention at home:** Monitoring signs& symptoms Education/self-management support Family involvement *In outpatient clinic* Monitoring signs& symptoms Education/self-management support Family involvement Referral to other health and social care	**Usual care** (n=48) **Components of intervention at home:** unknown
Jaarsma [28,29] **2008** The Netherlands n=1049 randomised All patients had been admitted to hospital with symptoms of HF	**Age:** 71(11),70(12),72(11) **% Female:**34,39,40% **Ethnicity:** No detail **Disease Status:** NYHA II 51,48,54% III 47,48,42% IV3,4,4%	**Basic nurse support** (n=340) **Components of intervention:** *Outpatients* Education /Self-management support Patient directed access to HF nurse **Intensive nurse support** (n=344) **Components of intervention at home:** Patient directed access to HF nurse Referral to other health & social care Education/Self-management support Equipment	**Usual care group (n=339)** **Components of intervention:** Disease management
Brotons[31] **2009** Spain n=283 randomised Patients were recruited by well-trained nurses at 2 university hospitals	**Age:** 76.6(7.5),76(8.9)yrs. **% Female:**54.2,56.1% **Ethnicity:** Not reported **Disease Status:** NHYA I 42.4,55.4% II 52.1,37.4% III 4.9,5.8% IV 0.7,1.4%	**Home based intervention** (n=144) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Medication review (nurse, physician, cardiologist) Referral to physician or cardiologist as necessary	**Usual care** (n=139) **Components of intervention:** not known
Stewart [32] **2012** WHICH trial Australia n=280 randomised Patients admitted to participating hospitals were screened for study eligibility	**Home vs. Clinic** **Age:** 70 (15), 73(13) yrs **% Female:**27,28% **Ethnicity:** No details **Disease Status:** NYHA II or III 83,88% Months since CHF diagnosis 34.6(55.3),44.8(71.0)	**Home based intervention** (n=143) **Components of intervention at home:** Monitoring signs& symptoms Family involvement CM meetings/feedback to other health providers Referral to other health or social care Assessment of home environment Medication review (nurse, pharmacist, physician, cardiologist)	**Clinic-based intervention** (n=137) **Components of intervention:** *In clinic* Disease management Assessment of home environment Family involvement? Referral to other health or social care CM meetings/feedback to other health providers
Hospital Initiated CM - CTS			
Riegel[35] **2000** USA n=240 were randomised Patients were recruited from 5 hospitals following a hospitalisation for HF.	**Age:** 74.44 yrs. (10.65), 70.77 (11.77) **% female:**55, 55% **Ethnicity:** No details **Disease Status:** NYHA I 19.2,24.2% II 26.7,18.3% III 43.3,44.2% IV 10.8,13.3%	**Multidisciplinary disease management (DM)** (n=120) **Components of intervention at home:** Monitoring signs& symptoms Support group Referral to specialist RN visits	**Usual Care** (n=120) **Components of intervention at home:** Disease management

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Russell[36] **2011** USA n=447 Patients were referred from a single large not-for-profit general medical and surgical hospital	**Age:**79.4(10.7),79.9(10.7) **% Female:**55.6,57.6 (numbers) **Ethnicity:** White non-Hispanic 56.9,58.4 African-American 17.0,16.5 Hispanic 14.8,14. Asian/other 11.2,10.7 **Disease Status:** Patients with a primary or secondary diagnosis of CHF	**Transitional care service** (n=223) **Components of intervention at home:** Self-management support Referral to other health & social care Assessment of home environment CM meetings/feedback to other health providers Advance care planning Physical therapy	**Usual home care services** (n=224) **Components of intervention at home:** Nurse visits Physical therapy (44.6) Home health aide service (27.7)
Stauffer[37] **2011** USA n=140 Patients were screened for eligibility within 48 hours of hospital admission	**Age:** 78.9(8.3), 81.4(8.3) **% Female:**58.1, 54.8% **Ethnicity:** Hispanic ethnicity 7.1,3.6% **Disease Status:** APR-DRG severity of illness 1 5.4,1.2% 2 44.6,31% 3 37.5,57.1% 4 12.5,10.7%	**Nurse-led transitional care intervention** (n=56) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement Referral (Assessing availability of social care) Patient directed access to study personnel	**Control group** (n=84) **Components of interventions:** unknown
Community-initiated CM-RCTs			
Peters-Klimm [39] **2010** Germany n=199 at randomisation Recruitment was via general practice by mail.	**Baseline characteristics of participants: CM,UC** **Age:** 70.4yrs (10.0), 68.9 (9.7) **% Female**:29, 26% **Ethnicity:** No details **Disease Status:** NYHA I 1(1.0), 5 (5) II 63 (64.9),67 (67) III 33 (34),27 (27) IV 0, 1(1.0) Mean yrs. with CHD 6.2(4.6) (n=79),6.8(6.3)(n=74	**Case management** (n=97) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Medication review (CM/GP) Referral to GP	**Usual care** (n=100) **Components of control intervention:** Disease management Education
Wade[42] **2011** USA n=2,200 were randomised Aetna Medicare Advantage members with medical & pharmacy benefits were identified through analysis of claims	**Age:** 75.8, 77.7 yrs. **% female:** No detail **Ethnicity:** Black/African American 24,20.4% **Disease Status (SD):** No detail	**Case management** (n=152) **Components of intervention at home:** Referral to other health & social care Equipment	**Tele health with case management (THCM) (n=164)** **Components of intervention:** Disease management Education Referral to other health & social care
Hancock [43] **2012** UK n=28 randomised Residents from 33 of 35 long-term residential & nursing homes	**Age:** 85.1 (6.7), 81.8 (7.1)yrs **% Female:**56%, 58% **Ethnicity:**100% white British **Disease Status:** I:II:III:IV 10:1:4:1, 5:4:1:1	**Case management** (n=16) **Components of interventions at home:** Monitoring signs and symptoms Education CM meetings/feedback to other health providers Medication review (CM/GP/cardiologist)	**Routine GP-led care** (n=12) **Components of intervention:** Disease management
Community –initiated CM -CCTs			
Bonarek- Hessamfar [44] **2008** France n=362 Compared patients included prospectively from Jan 1st 2004- Dec 31st 2005 from GP list	**Age:** Median 78, 80 yrs. **% Female:** No details **Ethnicity:** No details **Disease Status:** NHYA Median of III, IV	**Co-ordinated care via multidisciplinary network** (n=129) **Components of intervention at home:** Monitoring signs& symptoms Education (diet) Physical therapy CM meetings/feedback to other health provider.	**Usual care** (n=233) **Components of intervention:** not known
Lowery[45] **2012** USA n=1043 Intervention implemented in 4 Midwest VA medical centres from the same region & one affiliated outpatient clinic and 2 VA medical centres served as control.	**Age:** 65.4(0.51),67.4(0.45) yrs. **% female:**1, 1% **Ethnicity:** White 71.2,79.9% Black 24,16.1% Other 4.8,4.0% **Disease Status:** No details	**Nurse-practitioner-led disease management model** (n=457) **Components of intervention at home:** Location was lead tertiary centre, other medical centres (some primary care) or one affiliated outpatient clinic. Monitoring signs& symptoms Education /Self-management support Referral to other health & social care Family involvement	**Usual care** (n=510) **Components of intervention:** not known

Key : AF atrial fibrillation, CHF Chronic heart failure, COPD chronic obstructive pulmonary disease, CM case management or case manager, HOCM/RCM Hypertrophic Obstructive/Restrictive Cardiomyopathy, GP general practitioner, UC usual care, NYHA, LV left ventricular SNF skilled nursing facility, PAD peripheral arterial disease,

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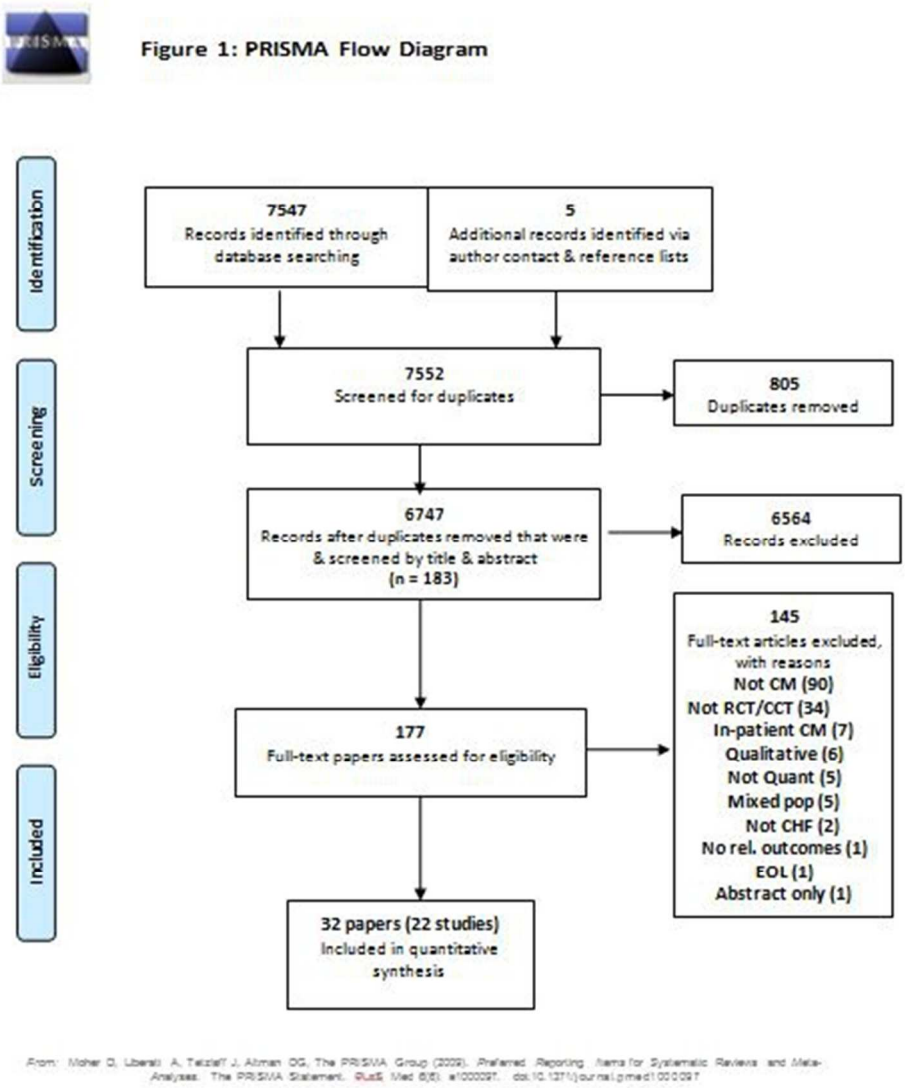

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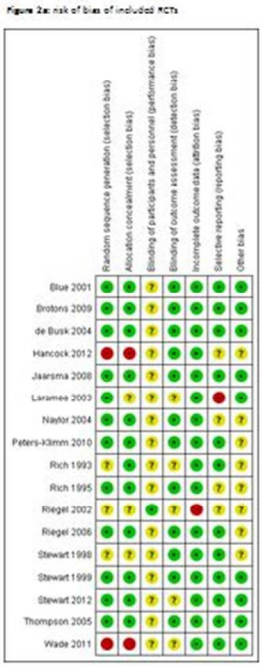

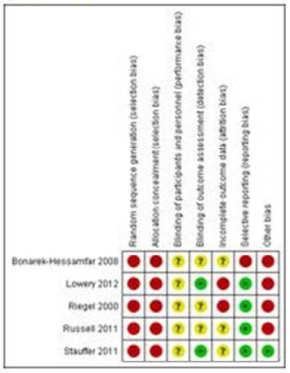

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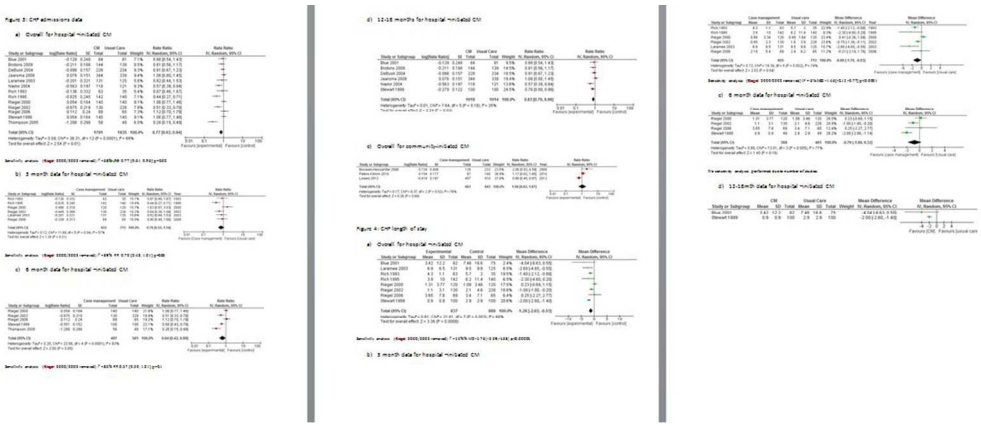

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Appendix 1:

Database: Medline In-process - Current week, Medline 1950 to present

Search Strategy:

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1 randomized controlled trial.pt. (376608)
2 random$.tw. (717987)
3 control$.tw. (2630023)
4 intervention$.tw. (556397)
5 evaluat$.tw. (2214967)
6 or/1-5 (5041451)
7 Qualitative Research/ (20094)
8 semi-structured questionnaire.mp. (1162)
9 observation methods.mp. (152)
10 Observation/mt [Methods] (635)
11 Nvivo.mp. (639)
12 interview/ (25018)
13 Personal Narratives/ (877)
14 Focus Groups/ (16824)
15 patient experience*.mp. (8525)
16 or/7-15 (70071)
17 exp Heart Failure/ (87270)
18 exp Heart Failure, Diastolic/ (496)
19 exp heart failure, systolic/ (789)
20 exp Ventricular Dysfunction/ (26332)
21 chronic heart failure.mp. (11341)
22 congestive heart failure.mp. (33082)
23 cardiac failure.mp. (10151)
24 LV dysfunction.mp. (2827)
25 left ventricular dysfunction.mp. (9373)
26 left ventricular impairment.mp. (188)
27 diastolic impairment.mp. (121)
28 systolic impairment.mp. (93)
29 or/17-28 (135885)
30 exp Case Management/ (8326)
31 exp Patient Care Planning/ (52319)
32 organisation of care.mp. (367)
33 community matron.mp. (44)

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34 "Continuity of Patient Care"/ (14497)
35 Community Health Nursing/ (18371)
36 transit* care.mp. (580)
37 Interdisciplinary Communication/ (10602)
38 Patient Discharge/ (18977)
39 discharge plan.mp. (176)
40 exp Patient Care Management/ (535496)
41 Comprehensive Health Care/ (6078)
42 exp Managed Care Programs/ (38918)
43 Primary Health Care/ (54234)
44 Community Health Services/ (26923)
45 General Practitioners/ (1943)
46 Family Practice/ (60223)
47 Physicians, Family/ (14745)
48 multidisciplinary.mp. (44988)
49 or/30-48 (674050)
50 6 or 16 (5094326)
51 29 and 50 (47009)
52 49 and 51 (2590)
53 52 not (case report/ or case study/ or letter/ or editorial/ or expert opinion.mp.) (2489)
54 53 not (Algeria$ or Egypt$ or Liby$ or Morocc$ or Tunisia$ or Western Sahara$ or Angola$ or Benin or Botswana$ or Burkina Faso or Burundi or Cameroon or Cape Verde or Central African Republic or Chad or Comoros or Congo or Djibouti or Eritrea or Ethiopia$ or Gabon or Gambia$ or Ghana or Guinea or Keny$ or Lesotho or Liberia or Madagasca$ or Malawi or Mali or Mauritania or Mauritius or Mayotte or Mozambiq$ or Namibia$ or Niger or Nigeria$ or Reunion or Rwand$ or Saint Helena or Senegal or Seychelles or Sierra Leone or Somalia or South Africa$ or Sudan or Swaziland or Tanzania or Togo or Ugand$ or Zambia$ or Zimbabw$ or China or Chinese or Hong Kong or Macao or Mongolia$ or Taiwan$ or Belarus or Moldov$ or Russia$ or Ukraine or Afghanistan or Armenia$ or Azerbaijan or Bahrain or Cyprus or Cypriot or Georgia$ or Iran$ or Iraq$ or Israel$ or Jordan$ or Kazakhstan or Kuwait or Kyrgyzstan or Leban$ or Oman or Pakistan$ or Palestin$ or Qatar or Saudi Arabia or Syria$ or Tajikistan or Turkmenistan or United Arab Emirates or Uzbekistan or Yemen or Bangladesh$ or Bhutan or British Indian Ocean Territory or Brunei Darussalam or Cambodia$ or India$ or Indonesia$ or Lao or People's Democratic Republic or Malaysia$ or Maldives or Myanmar or Nepal or Philippin$ or Singapore or Sri Lanka or Thai$ or Timor Leste or Vietnam or Albania$ or Andorra or Bosnia$ or Herzegovina$ or Bulgaria$ or Croatia$ or Estonia or Faroe Islands or Greenland or Liechtenstein or Lithuani$ or Macedonia or Malta or maltese or Romania or Serbia$ or Montenegro or Slovenia or Svalbard or

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Argentina$ or Belize or Bolivia$ or Brazil$ or chile or Chilean or Colombia$ or Costa Rica$ or Cuba or Ecuador or El Salvador or French Guiana or Guatemala$ or Guyana or Haiti or Honduras or Jamaica$ or Nicaragua$ or Panama or Paraguay or Peru or Puerto Rico or Suriname or Uruguay or Venezuela or developing countr$ or south America$).ti,sh. (2413)

55 54 not animal/ (2393)

56 remove duplicates from 55 (2335)

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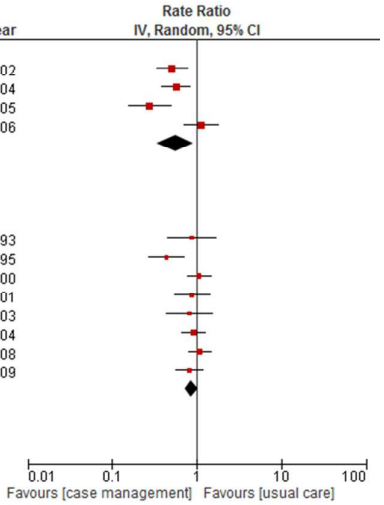
Appendix 2: Subgroup-analysis by intervention component- hospital initiated studies

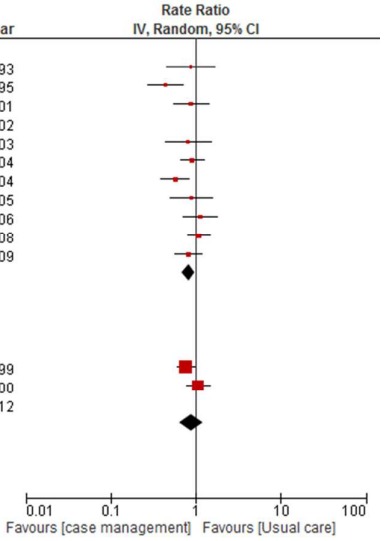
a) Family involvement

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.12.1 CM & FI							
Riegel 2002	-0.675	0.219	130	228	25.9%	0.51 [0.33, 0.78]	2002
Naylor 2004	-0.563	0.197	118	121	26.9%	0.57 [0.39, 0.84]	2004
Thompson 2005	-1.288	0.298	58	48	22.3%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	24.9%	1.12 [0.70, 1.79]	2006
Subtotal (95% CI)			**375**	**462**	**100.0%**	**0.56 [0.34, 0.92]**	
Heterogeneity: Tau² = 0.20; Chi² = 14.07, df = 3 (P = 0.003); I² = 79%							
Test for overall effect: Z = 2.30 (P = 0.02)							
1.12.2 CM minus FI							
Rich 1993	-0.136	0.332	63	35	6.5%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	10.2%	0.44 [0.27, 0.71]	1995
Riegel 2000	0.054	0.164	140	140	16.6%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	82	75	10.1%	0.88 [0.54, 1.43]	2001
Laramee 2003	-0.201	0.321	131	125	6.8%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	17.4%	0.91 [0.67, 1.23]	2004
Jaarsma 2008	0.076	0.151	344	339	18.0%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	14.4%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1274**	**1227**	**100.0%**	**0.87 [0.72, 1.04]**	
Heterogeneity: Tau² = 0.03; Chi² = 11.41, df = 7 (P = 0.12); I² = 39%							
Test for overall effect: Z = 1.54 (P = 0.12)							
Test for subgroup differences: Chi² = 2.64, df = 1 (P = 0.10), I² = 62.2%							



b) education & self-management

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.20.1 Education and self-management							
Rich 1993	-0.136	0.332	63	35	5.9%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	9.1%	0.44 [0.27, 0.71]	1995
Blue 2001	-0.129	0.248	84	81	8.9%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228		Not estimable	2002
Laramee 2003	-0.201	0.321	131	125	6.2%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	14.6%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	11.7%	0.57 [0.39, 0.84]	2004
Thompson 2005	-0.1288	0.298	58	48	6.9%	0.88 [0.49, 1.58]	2005
Riegel 2006	0.112	0.24	69	65	9.3%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	15.0%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	12.3%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1381**	**1327**	**100.0%**	**0.82 [0.68, 0.98]**	
Heterogeneity: Tau² = 0.03; Chi² = 15.46, df = 9 (P = 0.08); I² = 42%							
Test for overall effect: Z = 2.17 (P = 0.03)							
1.20.2 No education and self-management							
Stewart 1999	-0.279	0.122	100	100	55.4%	0.76 [0.60, 0.96]	1999
Riegel 2000	0.054	0.164	140	140	44.6%	1.06 [0.77, 1.46]	2000
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**240**	**240**	**100.0%**	**0.88 [0.63, 1.21]**	
Heterogeneity: Tau² = 0.03; Chi² = 2.65, df = 1 (P = 0.10); I² = 62%							
Test for overall effect: Z = 0.79 (P = 0.43)							
Test for subgroup differences: Chi² = 0.14, df = 1 (P = 0.71), I² = 0%							



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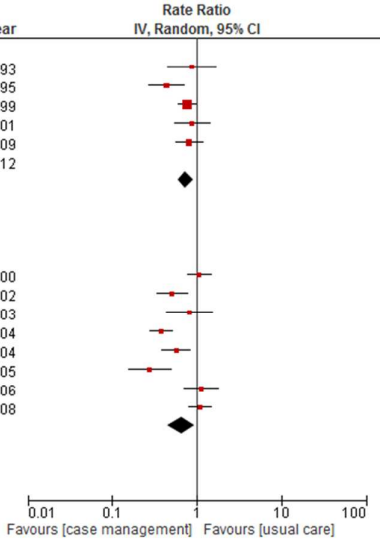
c) medication review

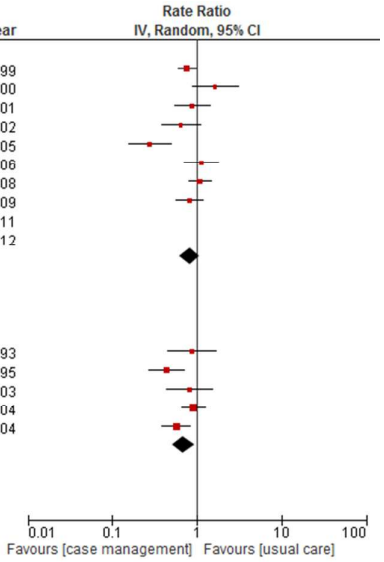
Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.19.1 Medication review							
Rich 1993	-0.136	0.332	63	35	9.3%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	15.4%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	37.5%	0.76 [0.60, 0.96]	1999
Blue 2001	-0.129	0.248	84	81	15.1%	0.88 [0.54, 1.43]	2001
Brotons 2009	-0.211	0.188	144	139	22.7%	0.81 [0.56, 1.17]	2009
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**533**	**495**	**100.0%**	**0.73 [0.59, 0.91]**	
Heterogeneity: Tau² = 0.02; Chi² = 5.56, df = 4 (P = 0.23); I² = 28%							
Test for overall effect: Z = 2.87 (P = 0.004)							
1.19.2 No medication review							
Riegel 2000	0.054	0.164	140	140	13.6%	1.06 [0.77, 1.46]	2000
Riegel 2002	-0.675	0.219	130	228	12.5%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.201	0.321	131	125	10.5%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.98	0.157	228	234	13.7%	0.38 [0.28, 0.51]	2004
Naylor 2004	-0.563	0.197	118	121	13.0%	0.57 [0.39, 0.84]	2004
Thompson 2005	-1.288	0.298	58	48	10.9%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	12.1%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	13.8%	1.08 [0.80, 1.45]	2008
Subtotal (95% CI)			**1218**	**1300**	**100.0%**	**0.66 [0.45, 0.95]**	
Heterogeneity: Tau² = 0.23; Chi² = 47.20, df = 7 (P < 0.00001); I² = 85%							
Test for overall effect: Z = 2.26 (P = 0.02)							



Test for subgroup differences: Chi² = 0.26, df = 1 (P = 0.61), I² = 0%

d) Referral to other services

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.16.1 Referral to others							
Stewart 1999	-0.279	0.122	100	100	16.4%	0.76 [0.60, 0.96]	1999
Riegel 2000	0.486	0.318	120	120	9.4%	1.63 [0.87, 3.03]	2000
Blue 2001	-0.129	0.248	84	81	11.7%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.445	0.268	120	120	11.0%	0.64 [0.38, 1.08]	2002
Thompson 2005	-1.288	0.298	58	48	10.1%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	12.0%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	15.4%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	0	14.0%	0.81 [0.56, 1.17]	2009
Russell 2011	0	0	0	0		Not estimable	2011
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**1039**	**873**	**100.0%**	**0.82 [0.63, 1.08]**	
Heterogeneity: Tau² = 0.10; Chi² = 24.27, df = 7 (P = 0.001); I² = 71%							
Test for overall effect: Z = 1.43 (P = 0.15)							
1.16.2 No referral							
Rich 1993	-0.136	0.332	63	35	13.7%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	19.6%	0.44 [0.27, 0.71]	1995
Laramee 2003	-0.201	0.321	131	125	14.3%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	28.3%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	24.1%	0.57 [0.39, 0.84]	2004
Subtotal (95% CI)			**682**	**655**	**100.0%**	**0.69 [0.51, 0.93]**	
Heterogeneity: Tau² = 0.06; Chi² = 8.13, df = 4 (P = 0.09); I² = 51%							
Test for overall effect: Z = 2.47 (P = 0.01)							



Test for subgroup differences: Chi² = 0.73, df = 1 (P = 0.39), I² = 0%

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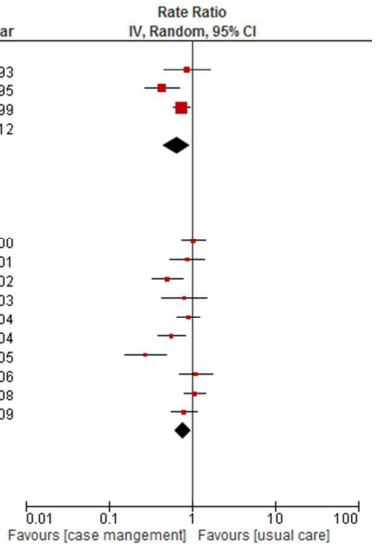
e) Assessment of home environment

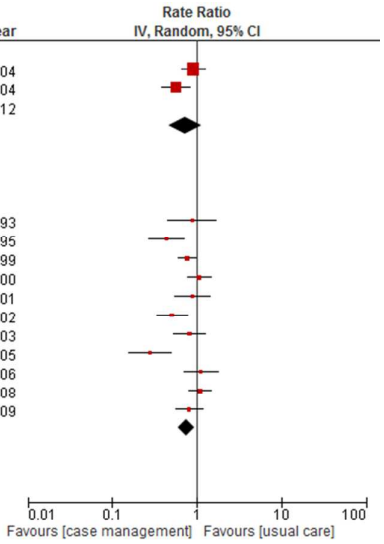
Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.18.1 Home assessment							
Rich 1993	-0.136	0.332	63	35	21.5%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	30.3%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	48.2%	0.76 [0.60, 0.96]	1999
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**305**	**275**	**100.0%**	**0.66 [0.45, 0.96]**	
Heterogeneity: Tau² = 0.06; Chi² = 4.50, df = 2 (P = 0.11); I² = 56%							
Test for overall effect: Z = 2.15 (P = 0.03)							
1.18.2 No home assessment							
Riegel 2000	0.054	0.164	140	140	11.6%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	84	81	9.0%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228	9.9%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.21	0.321	131	125	7.1%	0.81 [0.43, 1.52]	2003
DeBusk 2004	-0.098	0.157	228	234	11.9%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	10.6%	0.57 [0.39, 0.84]	2004
Thompson 2005	-1.288	0.298	58	48	7.7%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	9.3%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	12.1%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	10.9%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1446**	**1520**	**100.0%**	**0.77 [0.61, 0.97]**	
Heterogeneity: Tau² = 0.09; Chi² = 29.37, df = 9 (P = 0.0006); I² = 69%							
Test for overall effect: Z = 2.21 (P = 0.03)							



Test for subgroup differences: Chi² = 0.46, df = 1 (P = 0.50), I² = 0%

f) Case management/health professional meetings

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.21.1 CM/HP meeting							
DeBusk 2004	-0.098	0.157	228	234	53.3%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	46.7%	0.57 [0.39, 0.84]	2004
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**346**	**355**	**100.0%**	**0.73 [0.46, 1.15]**	
Heterogeneity: Tau² = 0.08; Chi² = 3.41, df = 1 (P = 0.06); I² = 71%							
Test for overall effect: Z = 1.36 (P = 0.17)							
1.21.2 No CM/HP meetings							
Rich 1993	-0.136	0.332	63	35	6.2%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	8.3%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	12.0%	0.76 [0.60, 0.96]	1999
Riegel 2000	0.054	0.164	140	140	10.7%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	84	81	8.2%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228	9.0%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.201	0.219	131	125	9.0%	0.82 [0.53, 1.26]	2003
Thompson 2005	-1.288	0.298	58	48	7.0%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	8.4%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	11.1%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	10.0%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1405**	**1440**	**100.0%**	**0.75 [0.60, 0.93]**	
Heterogeneity: Tau² = 0.09; Chi² = 32.20, df = 10 (P = 0.0004); I² = 69%							
Test for overall effect: Z = 2.59 (P = 0.010)							



Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0%

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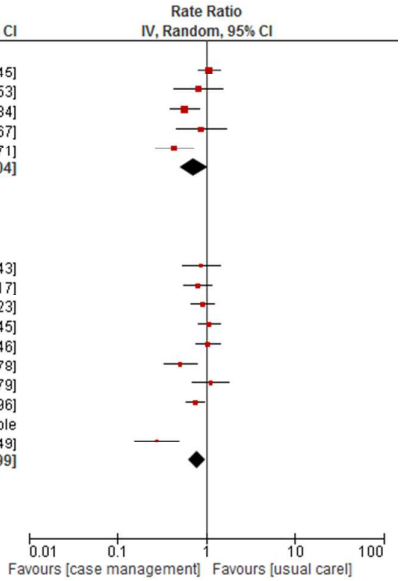
g) Patient-directed access

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI
1.22.1 Patient directed access						
Jaarsma 2008	0.076	0.151	344	339	25.4%	1.08 [0.80, 1.45]
Laramee 2003	-0.201	0.321	131	125	16.1%	0.82 [0.44, 1.53]
Naylor 2004	-0.563	0.197	118	121	22.8%	0.57 [0.39, 0.84]
Rich 1993	-0.136	0.332	63	35	15.6%	0.87 [0.46, 1.67]
Rich 1995	-0.825	0.245	100	100	20.1%	0.44 [0.27, 0.71]
Subtotal (95% CI)			**756**	**720**	**100.0%**	**0.72 [0.50, 1.04]**
Heterogeneity: Tau² = 0.12; Chi² = 12.80, df = 4 (P = 0.01); I² = 69%						
Test for overall effect: Z = 1.75 (P = 0.08)						
1.22.2 No patient-directed access						
Blue 2001	-0.129	0.248	84	81	9.2%	0.88 [0.54, 1.43]
Brotons 2009	-0.211	0.188	144	139	11.4%	0.81 [0.56, 1.17]
DeBusk 2004	-0.098	0.157	228	234	12.6%	0.91 [0.67, 1.23]
Jaarsma 2008	0.076	0.151	344	339	12.9%	1.08 [0.80, 1.45]
Riegel 2000	0.054	0.164	140	140	12.4%	1.06 [0.77, 1.46]
Riegel 2002	-0.675	0.219	130	228	10.3%	0.51 [0.33, 0.78]
Riegel 2006	0.112	0.24	69	65	9.5%	1.12 [0.70, 1.79]
Stewart 1999	-0.279	0.122	100	100	14.0%	0.76 [0.60, 0.96]
Stewart 2012	0.018	0.071	143	137		Not estimable
Thompson 2005	-1.288	0.298	58	48	7.7%	0.28 [0.15, 0.49]
Subtotal (95% CI)			**1297**	**1374**	**100.0%**	**0.80 [0.64, 0.99]**
Heterogeneity: Tau² = 0.08; Chi² = 26.32, df = 8 (P = 0.0009); I² = 70%						
Test for overall effect: Z = 2.03 (P = 0.04)						



Test for subgroup differences: Chi² = 0.21, df = 1 (P = 0.65), I² = 0%

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix one
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6-7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 & Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-11 plus figures 3 & 4 and appendix 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9-11 plus figures 3 & 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-11 plus figures 3 & 4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15

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PRISMA 2009 Checklist

FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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BMJ Open

Does case management for patients with heart failure based in the community reduce unplanned hospital admissions? A systematic review and meta-analysis

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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	General practice / Family practice, Emergency medicine
Keywords:	systematic review, meta-analysis, Heart failure < CARDIOLOGY, case management, hospital admission
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Figure_2a.tiff	

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Version 21st March 2016

Does case management for patients with heart failure based in the community reduce unplanned hospital admissions? A systematic review and meta-analysis

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Key words: systematic review, meta-analysis, heart failure, case management, hospital admission

Word count: 3887

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ABSTRACT

Objectives

The aim of this systematic review of randomised controlled trials (RCTs) and controlled trials (NRCTs) is to investigate the effectiveness and related costs of case management (CM) for patients with heart failure (HF) predominantly based in the community in reducing unplanned readmissions and length of stay (LOS).

Setting

CM initiated either whilst as an inpatient, or on discharge from acute care hospitals, or in the community and then continuing on in the community.

Participants

Adults with a diagnosis of HF and resident in Organisation for Economic Co-operation and Development countries.

Intervention

CM based on nurse co-ordinated multi-component care which is applicable to the primary care based health systems.

Primary and secondary outcomes

Primary outcomes of interest were unplanned (re)admissions, LOS and any related cost data. Secondary outcomes were primary health care resources.

Results

Twenty-two studies were included: 17 RCTs and five NRCTs. Seventeen studies described hospital-initiated CM (n=4794) and five described community-initiated CM of HF (n=3832). Hospital-initiated CM reduced readmissions (rate ratio 0.74 [95%CI 0.60, 0.92] p=0.008) and LOS (mean difference -1.28 days [95%CI -2.04,-0.52] p=0.001) in favour of CM compared to usual care. Nine trials described cost data of which six reported no difference between CM and usual care. There were four studies of community-initiated CM versus usual care (2RCTs and 2NRCTs) with only the 2 NRCTs showing a reduction in admissions.

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Conclusions

Hospital-initiated CM can be successful in reducing unplanned hospital readmissions for HF and length of hospital stay for people with HF. Nine trials described cost data; no clear difference emerged between CM and usual care. There was limited evidence for community-initiated CM which suggested it does not reduce admission.

Protocol registration

No

Strengths of review

- High quality systematic review
- Interventions examine nurse-led multicomponent care of heart failure patients
- Focus on use of resources specific to heart failure

Limitations of review

- Community-initiated case management trials were limited in quantity and were mostly of low quality.
- Lack of cost data in most trials

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INTRODUCTION

Applying current prevalence figures to population estimates suggests that more than 550,000 individuals (more than 308,000 men and slightly fewer than 250,000 women) in the UK are living with heart failure (HF).[1] Quality and Outcome Framework (QOF) data supports this: in 2012/13 just over 480,000 patients were recorded as having heart failure.[2] The average age of HF patients in general practice in the UK is 77 years.[3]

Prior to 1990, 60–70% of patients died within 5 years of diagnosis, and admission to hospital with worsening symptoms was a regular and recurrent event.[4-6] Effective treatment has improved care, with a relative reduction in hospitalization in recent years of 30–50%, and smaller but significant decreases in mortality.[4-6]

More than £6.8 billion was spent on treating all cardiovascular disease within the NHS in England in 2012/13 with 63% of these costs coming from within secondary care and 21% within primary care. Within secondary care, non-elective inpatient admittance for cardiovascular disease, i.e. emergency admissions, had the greatest expenditure with £1,925 million.[1]

Case management (CM) is the process of planning, coordinating and reviewing the care of an individual. We used the definition cited by the King's Fund in the UK 'A collaborative process of assessment, planning, facilitation, care coordination, evaluation, and advocacy for options and services to meet an individual's and family's comprehensive health needs through communication and available resources to promote quality cost-effective outcomes.'[7] The NHS has used less-intensive approaches than the traditional US model, for example, through the use of nurses to support older people and those with long-term conditions at home.[8] In this review we have focused on CM based on nurse co-ordinated multi-component care of patients which is applicable to the primary care based health systems such as that in the UK.

A previous systematic review and meta-analysis shows that CM is not effective in reducing unplanned hospital admissions for the general older/elderly population.[9] However limited data suggests that CM for patients with HF is promising.[10] This current review aimed to a) identify the evidence of the effectiveness and related costs of CM interventions for HF patients predominantly based in the community and b) to better understand the potential success of CM by examining the components of tested interventions.

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METHODS

Search

Databases and registries

A search strategy was developed using keywords for the electronic databases according to their specific subject headings or searching structure. The search strategy was run from 1985 – 2012 in the OVID databases - Medline®, Excerpta Medica Database (Embase), Cumulative Index to Nursing and Allied Health Literature (CINAHL®), PsycINFO® on the 2nd July 2014. (Appendix one) The search strategy was modified to search internet sites such as the Agency for Healthcare Research and Quality (AHRQ) and the King's Fund. A pragmatic update of these searches was conducted on the 20/11/15 using the full search strategy and run in Medline and Medline in process only.

Other sources

Once the included papers were determined, both backwards (reference list of paper) and forwards citation searching (via google scholar) was performed to identify any other potentially relevant studies. All authors of included studies in the field were contacted with data queries and to identify additional relevant studies.

Eligibility criteria:

Randomised controlled trials (RCTs), and other controlled studies (NRCTs) (controlled trials, controlled before and after studies, analytic cohorts, comparative studies) were included as determined by our eligibility criteria. We were aware from our previous work that not all community-based studies were randomised and felt it was important to be more inclusive in order to understand why CM may work for HF. CM interventions needed to be initiated either whilst as an inpatient or on discharge from acute care hospitals including the emergency department (ED), or in the community, and then continue on in the community. Only studies including adults with HF in Organisation for Economic Co-operation and Development (OECD) countries were included as the outcomes were more likely to be comparable for synthesis, and relevant to the UK situation.[11] Studies were included as long as one of the outcomes of interest was unplanned hospital (re)admissions, ED attendance, length of hospital stay (LOS) as well as related costs of the interventions. Other outcomes of interest were primary health care resources e.g. GP visits, visits to other primary care health professionals or

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services and prescriptions. Studies written in any language were considered if there was an English abstract available.

Reference management and study selection

EndNote and Excel were used to manage the references. Duplicates were removed from the Endnote file. References underwent a two stage process of screening using the inclusion and exclusion criteria by two reviewers independently (AH, AK, RJ). Firstly, a screen of titles and abstracts (if abstract available) and secondly screening of the full paper was conducted. Where there was continued disagreement between reviewers about including or excluding a paper, a third reviewer made the final decision (SP or RJ).

In addition to the included quantitative intervention papers, we identified relevant reviews from the search. Any potentially relevant conference proceedings were followed up, firstly by searching in Medline to see if the study had been published. If the study was not published, the authors were contacted where possible to check if the studies were likely to be published within the work frame of this review.

Data extraction and assessment of risk of bias

Data were extracted into a custom-designed table which included description of trial type, participants, intervention, controls, outcome measures and results. Based on the Kings Fund definition of case management we devised taxonomy of intervention components.[8] (table 1) As part of this data extraction process, the intervention and control treatments were also described by their component parts e.g. monitoring signs and symptoms using the framework of the CM definition.

Quantitative data concerning the outcomes of interest were extracted into the Cochrane Revman software. The Cochrane risk of bias tool was used to record trial bias for RCTs and the EPOC Risk of bias tool was used for non-randomised controlled trials (NRCTs).[12] These processes were performed by one author and checked by a second. (AH, AK) Any disagreements were resolved by discussion and if necessary with a third author. (RJ, SP)

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Data analysis

Trials were divided as previously described by Huntley *et al* 2013 into hospital-initiated CM and community-initiated CM.[9] Where there were data from three or more studies, effect sizes were calculated and presented in forest plots as rate ratios ((re)admissions) or mean differences (LOS) using Revman software. If the heterogeneity of the combined data was greater than 50%, a random effects model was used for analysis.

We conducted pre-specified sensitivity analysis in response to the risk of bias assessment of studies, removing high risk of bias studies as appropriate; the results of both analyses are presented.[13] We conducted pre-specified subgroup-analysis to explore the effects of CM duration (3,6 and 12 months plus) on hospital admission and LOS. There was insufficient detail in trials to perform sub-analysis by severity of HF or intensity of intervention.

Data were assessed narratively in respect of the components of interventions using the CM definition cited above as guidance.[8] (table 1) In addition, where possible post-hoc subgroup-analysis was conducted in Revman in which interventions with components of interest were compared with those that did not have these components.

RESULTS

The systematic review yielded 22 studies with data published over 32 papers of which 17 were RCTs and five were NRCTs all published in the English language. [14-45] (Figure one) No relevant studies were identified in a pragmatic update using the full search strategy run in Medline and Medline in process only in November 2015. Seventeen of these studies described hospital-initiated CM (n=4794)[14,15,17,18,20-24,26-28,31,32,] and five described community-initiated CM of HF (n=3832).[38,42-45] The PRISMA checklist was used to ensure the quality of our systematic review manuscript.

Profile of patients (table 2)

The range of female participants in the trials was 1-58%, but the majority of trials had relatively even gender divide. Co and multi-morbidity were common. Eight of the 22 trials gave no detail on ethnicity of participants; in four studies the trialists used white/non-white and English speaking/non-English speaking categories. In the remaining 10 studies, a fuller profile was described. Twelve of the 22 trials

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were conducted in the USA and the ethnicity profile reflected that including Spanish speaking/Hispanic, American Indian, Black, African American, Asian and White participants.

The majority of trials described the severity of HF using New York Heart Association (NYHA) classification. Twelve of the trials gave a breakdown of numbers or percentages in the I-IV classes with some trials only giving numbers of participants for the III and IV class. In these trials the percentage range of III and IV class patients was 6-98%. Four trials gave mean and median values of NYHA status, one trial used the APR-DRG severity of illness scale, and five trials did not describe disease severity.

Profile of interventions (table 2)

The majority of studies (n=15) described the intervention being delivered by a case manager/ specialist nurse with no specific mention of other health professionals, and the remaining seven studies described a case manager/speciality nurse working as part of a multi-disciplinary team.
All but two studies compared CM with usual care although the control group was not always described. The two remaining studies were comparative: one RCT comparing CM with specialist clinics and one RCT comparing CM with telemedicine plus CM. [32,42,]
The duration of the CM interventions in the studies was 1-24 months with the majority having a 3 or 6 month duration. The majority of studies were conducted face to face or a combination of in-person and by phone. Four interventions were conducted purely by phone.[21,22,26, 42] Outcomes were measured to match the total duration of intervention in the majority of studies. For many of the studies the intensity of interventions was not stated explicitly. When intensity was described it was always a tapered approach after an initial intensive period.
Risk of bias (Figure 2a&b)

The degree of risk of bias was starkly different between the RCTs and NRCTs. All five of the NRCTs were rated at high risk or unknown risk for most domains.[35,36,37, 44,45]

The majority of the RCTs were rated at low risk for most domains with the exception of the domain of blinding of the participants and personnel which is not applicable to this type of intervention. Three RCTs were assessed as at high risk for at least one domain: both Hancock and Wade gave no description of the randomisation process or allocation concealment, Riegel 2002 was randomised at physician level and patients were chosen by physician preference.[21, 42,43] Four of the five community-

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initiated trials (2 RCTs and 2 NRCTs) were assessed to be at high risk of bias, and in some studies did not present usable data. [35-37,42]

All the intervention studies reported unplanned hospital (re)admissions [14-45] and 17 reported length of time in hospital.[14, 15, 17, 18, 20-22, 24, 26-28, 35, 38, 42-45] There were few data on A and E attendance and primary care resource use. However, only some of the data could be used in meta-analysis with the main reasons being that data were presented in different formats where neither confidence intervals, standard errors nor raw data were given. Due to heterogeneity of data all analysis was conducted using a random effects model.

Unplanned HF (re)admissions data (figure 3)

Hospital-initiated CM

Thirteen of the hospital-initiated CM trials had data that could be used in a meta-analysis of which 12 were RCTs. The pooled data from the RCTs showed a rate ratio of readmissions was 0.74 [95% CI 0.60, 0.92] p=0.008 I^2 =69% in favour of hospital- initiated CM. (figure 3a) A sensitivity analysis was conducted, removing Riegel 2002 (RCT with high risk of bias for randomisation domain); this had a minimal effect on the rate ratio and heterogeneity 0.77 [0.61, 0.96] p=0.02 I^2 =68%.[21,35] Sub-analysis looking at 3, 6 and 12-18 month data did not produce a clear time-related effect which is most likely due to heterogeneity within and between studies.(figure 3b,c,d). There was one hospital-initiated CM trial which compared CM with specialist clinics which reported no differences in hospital readmissions between the two groups.[32]

Community initiated CM

Of the four community initiated trials (2 RCTs and 2 NRCTs) comparing admissions between CM with usual care, two reported no significant differences[38,43] and two reported statistically significant reductions in favour of CM.[44,45] One further trial compared CM, with telehealth and CM and reported no differences in admissions but data were not presented.[42]

Length of hospital stay (LOS) (figure 4)

Hospital-initiated CM

Nine of the hospital-initiated CM trials had data that could be used in a meta-analysis of which 8 were RCTs. The pooled data from the RCTs showed that mean LOS was reduced in the CM group

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compared to usual care mean difference (MD) -1.28 days [-2.04,-0.52] p=0.001 I^2 =63%. (figure 4a) A sensitivity analysis was conducted removing Riegel 2002 which had an important effect on the rate ratio and heterogeneity MD -1.76 [-2.29,-1.23] p<0.00001 I^2 = 14%. [21,35] Sub-analysis looking at 3, 6 and 12-18 month data suggests this effect is short-term (first 3 months) but a longer time-related effect was difficult to assess due to lack of data.(figure 4b,c,d).

The one study comparing CM with specialist clinic care, reported that CM patients accumulated 592 and clinic patients 547 *all-cause* hospitalizations (p = 0.087) associated with 3067 versus 4410 days of hospital stay (p < 0.01 for rate and duration of hospital stay).[32]

Community initiated CM

Of the 4 community initiated trials comparing CM with usual care, two did not report LOS [38, 43] one reported median values in favour of CM[44] and the remaining one reported a mean reduction in LOS. [45] (table 2). The one comparative trial between community-initiated CM, and telehealth and CM did not report any useful data.[42]

Intervention components (table 1 and appendix 2)

Fourteen intervention components were identified and grouped as per the CM definition in methods and prevalence determined for both hospital and community –initiated CM studies with a usual care control group (table 2). [7]

Hospital-initiated CM (appendix 2)

Data from individual studies which contained components of family involvement showed an overall reduction in hospital readmissions in comparison with usual care and a reduction in hospital readmissions observationally in comparison with interventions which did not contain these components (rate ratio of 0.56 [0.34, 0.92] p=0.003). However, post-hoc analysis comparing these studies in which the component was present with those studies in which the component was absent did not yield any statistically significant differences (p=0.15). (appendix 2a) The same calculations for medication review, referral to other services, and assessment of home environment, CM meetings and patient-directed access did not indicate any specific effect of these components of hospital-initiated CM on rates of admission. (appendix 2 b-g) The majority of the interventions included

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education/self-management and there were insufficient data from studies without this component to allow comparison.

Community initiated CM

There were insufficient data to conduct any subgroup-analysis on any of the remaining components of hospital-initiated CM, community initiated studies or the LOS data.

Outpatient health care resources

Only six of the included studies measured outpatient resource use. In some studies, outpatient resource data were all-cause and not HF-specific. In some studies primary and secondary use was combined.[23,24,35,38,42, 45] Two of these studies also reported ED attendance.[23, 42] All but one of these studies reported no difference between intervention and control group for these measures with the exception of Lowery which showed a statistically significant greater use of outpatient resources in the usual care group (optional primary care visits 1yr 16.75(13.62),10.43(9.6) p<0.001 , 2yr 14.27(11.98),9.35(9.97) p<0.001).[45]

Costs (table 3)

Nine of the seventeen hospital initiated trials described cost data. Of these, six reported no statistically significant difference between CM (3 or 6 month duration) and usual care.[17,18,22,24, 26 35,] and three reported costs in favour of CM although data from Stauffer was brief.[15,32,37] One of these was 12-18 months[32] and two were 3 months in duration. It was difficult from the intervention descriptions to determine their intensity. There were no cost data reported from the community-initiated trials.

DISCUSSION

This systematic review confirms that hospital-initiated CM can be successful in reducing unplanned hospital readmissions, and reducing LOS in hospital in the short term for people with HF. There were only five community-initiated CM studies (3RCTs and 2NRCTs) of which four were at high risk of bias. This limited evidence suggests no effect of community-initiated CM on hospital admissions. A

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minority of trials report cost comparisons with usual care and most of those show no difference. There were limited data on the effect of CM on other health care resources.

Many factors are likely to modify the effect of CM on use of emergency care seen in these studies. It is generally accepted that CM is more appropriate for people with severe HF and poorer general health. However it was difficult to compare the health status of the study participants in both hospital-initiated and community-initiated trials as in some studies there was little detail, others gave median and mean figures for NYHA status, and the presentation format and detail of co-morbidities varied. All the included studies have been conducted within the past 12 years so it is important to put these results in the context of overall improved treatment and reduction in hospital admissions since the early 1990's.[4-6]

Seventeen studies described hospital-initiated CM and five described community initiated CM of heart failure although often the participants were identified via hospital clinic records. Overall the meta-analysis showed that CM reduced readmissions and hospital LOS. This may be explained by the fact that in most of the trials the participants were identified via hospital contact and therefore were likely to have had a recent exacerbation of their HF and to be at increased risk of re-admission in the post-discharge period. In addition, it is likely that interventions are acting at a time of highest risk as reflected by HF mortality in first year of diagnosis.[4] Therefore once they were assessed and given extra support they were stable for a period of time. Previous work by Roland *et al* 2005 suggests that admission rates in people aged 65 with two or more emergency admissions in 12 months fall in subsequent years without any intervention and account for fewer than 10% of admissions in the following year and thus effectiveness of admission avoidance schemes cannot be judged by tracking admission rates without careful comparison with a control group.[46] The data from trials of community-initiated CM was lacking both in the number of studies , and the fact there were limited useable data that showed no effect on unplanned hospital admissions. It is likely that these patients were likely to be in more stable health.[41]

A meta-review of a wide range of HF disease management programs by Savard 2011 reports that nine previous systematic reviews (2001-2009) identified significant reductions in HF admissions with reductions in risk ranging from 30-56%.[47] However the authors caution that these reviews are limited by inadequate reporting in the population, setting, intervention and comparator components. They

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report that reviewers have not taken into account statistical, clinical and methodological heterogeneity in interventions.[47] Our review focussed specifically on CM avoiding some of these limitations and indicates a reduction in HF readmissions with hospital-initiated CM in the range of 10-30%.

Wakefield *et al* in 2013 looked at common components of a range of HF care programs focusing mainly on disease management and education investigated in RCTs, and 10/35 of the discussed studies were included in our review.[48] They described patient education, symptom management by health professionals and by patients, and medication adherence strategies as the most commonly occurring elements of care. A literature review by Jaarsma 2012 looked at 70 'home care' controlled studies (mostly RCTs) which encompassed 9 of our included CM studies covering a wide range of approaches such as telemedicine, hospital at home and health buddies for patients with HF.[49] They identified a multi-disciplinary team, continuity of care, care plans, optimising titration of medication, education/counselling of patients and caregivers and increased access as important. Unfortunately we had insufficient data to perform sub-analysis on the component of education/self-management. Previous systematic reviews have investigated the role of the lay caregiver in HF patient management.[50-52] These suggest that better relationship quality and communication were related to reduced mortality, increased health status and less distress and improved patient self-care outcomes. Our review adds to this evidence base by suggesting that more family involvement in CM may also reduce unscheduled readmissions.

Education about HF and about its pharmacological and non-pharmaceutical treatment has been well-reviewed both as an individual approach and as part of complex interventions, and is considered to be essential for improving many patient outcomes. [49, 53,54]A recent mixed method study, suggests asking patients with HF to write down their learning needs before the education increases their chances of receiving education based on their individual needs.[55] Qualitative interviews with health professionals caring for HF patients suggest that communication with, and education by specialist nurses facilitated by continuity of care is essential to good care of HF patients. The authors also highlight the role of the specialist nurse in multi-disciplinary team communication and functioning; essentially describing the role of the specialist nurse as a case manager.[56]

Our review of CM suggests that the evidence for its cost-effectiveness is lacking with most studies that have performed cost comparisons with usual care show no advantage. Previous work by de Bruin

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et al 2001 looked at cost effectiveness of disease management for a range of chronic conditions and concluded that the data is most positive for HF with 5 out of the 8 included studies showing cost-effectiveness.[57]

Strengths and limitations

The contribution of our high quality systematic review to the above is that we have focused on CM which is based on nurse co-ordinated multi-component care of patients which is applicable to the primary care based health systems such as that in the UK. We have focused on HF (re)admissions and LOS as opposed to all-cause data which many of the previous reviews have used.

By examining the components of CM we have a profile of the components most likely to lead to the success of CM of patients with heart failure in terms of reducing (re)admissions and hospital LOS. Our review has high-lighted the potential importance of family involvement albeit in post-hoc analysis.

The limitations of this review are that majority of the community-initiated CM studies were of low quality with the exception of one low risk of bias RCT, and provided limited evidence. Whilst funnel plot analysis was not appropriate with our data we acknowledge that there may be publication bias on this topic.[58] This was counteracted by the fact that the hospital-initiated studies comprised of predominantly community-based case management. There is a lack of cost data and analysis in the included papers. This point needs to be emphasised for future trials. It is possible that cost effectiveness will be more likely with intervention for patients with more severe HF.

CONCLUSIONS

Hospital-initiated CM reduces unplanned hospital admissions, and length of stay for people with HF in the short term. Cost data is limited. There was limited evidence for community-initiated CM which suggested it does not reduce hospital admission. Further research is needed to determine the individual components of CM that contribute to reduced admissions.

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Contributorship statement

Alyson Huntley. Main systematic reviewer, worked across all stages of the review from inception to completed draft.

Rachel Johnson. Cardiology and primary care expertise. Worked on screening, selection of studies, commenting on analysis, and development and checking of final document content.

Anna King. Second reviewer, involved in screening, selection, data checking and commenting on developing and final document content.

Richard Morris. Statistical expertise, advising on data analysis and commenting on the developing and final document content.

Sarah Purdy. Primary care and admission avoidance expertise. Advised throughout project, third reviewer for screening process and commenting on the developing and final document content.

Competing interests

None declared

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Data sharing statement

Full data extraction tables and data analysis files are available on request

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Table 1: Components of CM interventions

Definition & total prevalence of Components of CM interventions	Number of hospital-initiated CM vs. usual care with component present (total studies=16)	Number of community-initiated CM vs. usual care with component present (total studies=4)
Assessment /Evaluation		
Monitoring signs & symptoms (n=18) Encompasses general care of CHF patients which is likely to include establishing a relationship with patient over visits, physical and cardiac status checking, lifestyle assessment, general medication check and screening tests e.g. depression, dementia	14	4
Medication review (n=8) Review and adjustment of medication by experienced case manager (nurse), pharmacist, GP or consultant often using a combination of these health professionals.	6	2
Assessment of home environment (n=4) Assessment carried out by case manager to identify any issues or potential issues with home environment e.g. stairs	4	0
Planning		
CM meetings/feedback to other HPs (n=5) Group meetings of health professionals involved in CHF patients care with the aim of reporting on and planning for patients care.	3	2
Appointment organisation (n=2) Case manager checking medical appointments, ensuring ability to go etc.	2	0
Advance care planning (n=1)	1	
Facilitation		
Education/self-management (n=18) Educating CHF patients about their condition, treatment and what to expect. The aim of this is to assist self-management (care with assistance of health professionals) and self-care (patient engaging in activities to promote their health and well-being).	15	3
Patient–directed access (n=6) The ability of CHF patients to initiate care from the case manager or case management service.	6	0
Care co-ordination		
Referral to …. (n=14) When the case manager refers the patient to other health or social care professionals, this can be GP hospital consultant, social care or tests.	11	3
Advocacy for options & services		
Equipment (n=4) Provision of items to assist patient's health care such as pill counters, weighing scales and measured water bottles.	3	1
Physical therapy (n=1) CHF patient receiving physical therapy/rehabilitation	1	0
Support group (n=1) CHF attending or being offered the opportunity of a support group.	1	0
Other		
Family involvement (n=9) When the case manager involves the patient's family in terms of information, education or involvement e.g. goal setting in patients' care or active monitoring	8	1
Emotional support (n=1) Case manager providing emotional support to CHF patient.	0	1

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Table 2: study characteristics of intervention studies

Study n=randomised Recruitment/setting	Baseline characteristics of participants: CM vs. usual care	Intervention	Control	Main results Intervention vs. control
Hospital Initiated CM - RCTs				
Rich[14] **1993** USA n=98 randomised Patients ≥70 yrs admitted to medical wards of Jewish Hospital at Washington University Medical Centre were screened for congestive HF.	**Age** 80(6.3),77.3(6.1) yrs p=0.04 **% Female:** 60.3, 47.1% **Ethnicity:** White 46,57.1% **Disease Status:** Mean NYHA status 2.7(1.1),3.0(1.0)	**Non-pharmacological comprehensive multidisciplinary treatment strategy** NPCM (n=63) ***Components of intervention at home:*** Monitoring signs& symptoms Medication review (nurse) Education /Self-management support Assessment of home environment Patient directed access to study personnel	**Usual care UC** (n=35) **Components of intervention:** Visits by home nurse	**No. of readmissions (%)** **21**[CI 21.7, 44.9](33.3%), **16** [29.2,62.2] (45.7%) **Total hospital days** 272, 200 **Mean no of days** 4.3(SD1.1),5.7(SD2.0)
Rich [15] **1995** USA n=285 randomised As above for Rich 1993 .	**Age:** 80.1(5.9),78.4(6.1) yrs p=0.02 **% Female:**68,59% **Ethnicity:** Non-white race 52,59% **Disease Status:** Mean NYHA class 2.4(1.0),2.4(1.1)	**Nurse-directed multidisciplinary intervention** (n=142) As above for Rich 1993	**Usual care** (n=140) As above for Rich 1993	**No. of readmissions** 24,54 p=0.04 **Total hospital days** 556,865 **Mean no. of days** 3.9(10), 6.2(11.4) P=0.04
Stewart [17] **1998** Australia n=97 randomised Patients were recruited whilst admitted to a large tertiary hospital	**Age:** 76 (11), 74(10) yrs **% Female:**55,48% **Ethnicity:** Non-English speaking 20.4,18.75% **Disease Status:** NYHA II 49,50% III 47,42% III 4,4%	**Home-based intervention** (n=49) **Components of intervention at home:** Monitoring signs& symptoms Education (pharmacist)/self-management support Medication review (pharmacist) Referral to GP Family involvement Equipment	**Usual care** (n=48) **Components of intervention:** Disease management	**No. of readmissions** 36,63 (p=0.03) **No. of patients experiencing a readmission** 24,31 (p=0.12) **LOS in days** 261,452 (p=0.05)
Stewart [18,19] **1999** Australia n=200 randomised Patients admitted to a tertiary referral hospital	**Age:** 75.2(7.1),76.1(9.3) **% Female:** 35,41% **Ethnicity:** Primary language not English 32,32 **Disease Status:** NYHA II 42,48 III 46,43 IV 12,9	**Multidisciplinary home base intervention (n=100)** **Components of intervention at home:** Monitoring signs& symptoms Referral to other health & social care Appointment organisation Assessment of home environment Family involvement Education/self-management support Medication review (nurse/GP/cardiologist)	**Usual care (n=100)** **Components of intervention:** Contact with other health and social professionals Appointment with GP or cardiac clinic or both	6mths **No. of readmissions** 68,188 (event rates give p=0.02) **Rate of readmissions** 0.14(0.1,018), 0.34 (0.19,0.49) p=0·031 **LOS in days** 460,1174 0.9 (0.6,1.2) 2.9(1.9,3.9) p=0.004 18mths **No. of readmissions** 64,125 p=0.02 **Mean number of hospital days** 10.5 (14.4), 21.1(24.1) days per patient p=0.004
Blue[20] **2001** UK n=165 randomised Patients admitted as an emergency to the acute medical ward of the hospital	**Age:** (SD)74.4(8.6),75.6(7.9)yrs **% Female:** 36,49% **Ethnicity:** Not reported **Disease Status:** NYHA II 19(23), 16(20) III 28(34), 33 (42) IV 36 (43), 30(38) **Co or Multi-morbidity:** Angina 40(49), 38(45) Past MI 41 (51), 46(55) Diabetes 15(19), 15(18) Chronic lung disease 18(22),23(27) Hypertension 42(52), 36(43) AF 42(52), 29(35) Valve disease 12(15),15(18)	**Specialist nurse intervention** (n=82) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Referral to other health & social care Appointment organisation Medication review (nurse, cardiologist)	**Usual care** (n=75) **Components of intervention:** GP care	**No.(%) of readmissions** 12(14), 26(32) Hazard ratio 0.38 (0.19,0.76) p=0.0044 **LOS in days** 3.43 (12.2), 7.46(16.6) CI 0.6 (0.41, 0.88) p=0.0051)
Riegel[21] **2002** USA n=281 physicians randomised Patients admitted at 2 Southern California hospitals.	**Age:** 72.52(13.05), 74.63(12) **% Female:**46.2,53.9 **Ethnicity:**(Primary language) English 91(70), 168(73.7) Spanish 35 (26.9), 58(25.4) **Disease Status:** NYHA II 2.3,3.6 III 35.9, 38.4 IV 61.7,58.0	**Telephonic case management** (n=130) **Components of intervention at home:** Monitoring signs& symptoms Self-management support Referral to other HPs (includ.GP) & social care Family involvement	**Usual care** (n=228) **Components of intervention:** Not known	**Readmission rates** 3mths 14.6, 22.8 p=0.06 [calculation 19 people vs. 52 exp 1 or more ad] 6mths 17.7, 27.6 p=0.06 [calculation 23 people vs. 63 people exp 1 or more ad] **LOS in days** 3mths 0.85(2.3), 1.6(3.9) p=0.56 6mths 1.1 (3.1), 2.1(4.6) p=0.05

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Laramee[22] **2003** USA n=287 randomised Patients admitted to hospital for CHF were screened.	**Age:** 70.6(11.4), 70.8(12.2) yrs. **% female:** 42,50% **Ethnicity:** Not reported **Disease Status (SD):** NYHA I 10(7),35(26) II 76(55),47(36) III 50(36),46(35) IV 3(2),4(3) Note P<0.001	**Case management** (n=131 data available) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement Equipment Patient–directed access to CM	**Usual care** (n=125 data available) **Components of intervention:** Not known	**No. of readmissions** 3mth period 18(14) vs.21(17) ns **LOS in days** in hospital for those patients with ≥1 readmission 6.9(6.5), 9.5(9.8) ns
De Busk[23] **2004** USA n=462 randomised Patients who were admitted with a provisional diagnosis of HF from Kaiser Permanente medical centres in California	**Age:** <60yrs 15,14%, 6-70yrs 22,24%,70-80yrs 40,37%, >80yrs 21,26% **% Female:**52,45% **Ethnicity:** American Indian 0,1% Asian 4,8% Black 2,2% White 5,6% Hispanic 3,3% **Disease Status:** NHYA I-II 50,50% III-IV 50,50%	**Case management** (n=228) **Components of intervention at home:** Monitoring signs& symptoms Education /Self-management support CM meetings/feedback to other health providers	**Usual care** (n=234) **Components of interventions:** not known	**Total no. of readmissions** in one year 76,86 no stats available
Naylor [24,25] **2004** USA n=239 patients randomised Patients aged 65yrs+ admitted to 6 study hospitals from home with a diagnosis of HF were screened for participation.	**Age:** 76.4(6.9),75.6(6.5) **% Female:**60, 56% **Ethnicity:** African American 34,38%, White 66, 62% **Disease Status:** Functional Status (Moinpur C 1992) Personal 17.1(5.8),16.9(5.8) Social 8.4(2.6),8.6(2.6) Total 25.5(8),25.4(7.8)	**Transitional care intervention with advanced practice nurses (APNs)** (n=118) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement CM meetings/feedback to other health providers Patient–directed access to CM	**Usual care** (n=121) **Components of intervention:** Care from standard home care services Patient–directed access to home care services	**No. of readmissions** *40 vs. 72* ns *$175,840,$498,110* **Total hospital days (all cause)** 588, 970 Per patient, mean ±SD 5.0 ± 7.3 8.0 ±2.3 ns Per hospitalized patient, mean± SD 11.1±7.2 14.5±13.4 ns
Riegel[26] **2006** San Diego USA n=135 randomised Self-identified Hispanics were identified at 2 community hospitals close to US-Mexico border	**Age:** 71.6910.8),72.7(11.2) **% Female:**58,49.2% **Ethnicity:** Hispanic patients Speak/read only Spanish 60.9,65.1% **Disease Status:** NYHA II 17.4,20% III 44.9,47.7% IV 37.7,32.3%	**Telephonic case management** (n=69) **Components of intervention at home:** Monitoring signs& symptoms self-management support Referral to other HPs (includ.GP) & social care Family involvement	**Usual care** (n=65) **Components of intervention:** Disease management Information	**Readmission rates** (%) (no. of people) all ns 1mth 8.7,13.8% [Calculation 6.003,8.97] 3mth 21.7,26.2% [calculation 14.49,17.03] 6mth 31.9,33.8% [calculation 22.011,21.97] **LOS in days** (mean) all ns 1mth 0.59(2.3),1.41(5.5) 3mth 2.19(5.4),2.4(6.2) 6mth 3.65(7.8),3.4(7.1)
Thompson[27] **2005** UK Randomisation was at GP practice level Patients recruited from 2 North of England general hospitals following an admission	**Age:** 73(14),72(12) **% Female:**38,27% **Ethnicity:**No details **Disease Status:** NYHA III &IV 76,73%	**Clinic & home based intervention** (n=58) **Components of intervention at home:** Monitoring signs& symptoms Education/self-management support Family involvement *In outpatient clinic* Monitoring signs& symptoms Education/self-management support Family involvement Referral to other health and social care	**Usual care** (n=48) **Components of intervention at home:** unknown	**No. of patients experiencing one or more readmissions** 13,21 **Total no. of readmissions** 15,45 **Total no of hospital days** 108,459 P<0.01 for all at 6 mths
Jaarsma [28,29] **2008** The Netherlands n=1049 randomised All patients had been admitted to hospital with symptoms of HF	**Age:** 71(11),70(12),72(11) **% Female:**34,39,40% **Ethnicity:** No detail **Disease Status:** NYHA II 51,48,54% III 47,48,42% IV3,4,4%	**Basic nurse support (BNS)** (n=340) **Components of intervention:** *Outpatients* Education /Self-management support Patient directed access to HF nurse **Intensive nurse support (INS)** (n=344) **Components of intervention at home:** Patient directed access to HF nurse Referral to other health & social care Education/Self-management support Equipment	**Usual care group (n=339)** **Components of intervention:** Disease management	**No. of readmissions** 121,134,120 ns **LOS in days** (medians) 8.0(4,14),9.5(5,17),12(5,19.5) P<0.01 between BNS grp & control but ns between INS grp & control
Brotons[31] **2009** Spain n=283 randomised Patients were recruited by well-trained nurses at 2 university hospitals	**Age:** 76.6(7.5),76(8.9)yrs. **% Female:**54.2,56.1% **Ethnicity:** Not reported **Disease Status:** NHYA I 42.4,55.4% II 52.1,37.4% III 4.9,5.8% IV 0.7,1.4%	**Home based intervention** (n=144) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Medication review (nurse, physician, cardiologist) Referral to physician or cardiologist as necessary	**Usual care** (n=139) **Components of intervention:** not known	**No. of readmissions** 52, 62 ns **Mean no. of readmissions** 1.01,1.3 ns

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Stewart [32] **2012** WHICH trial Australia n=280 randomised Patients admitted to participating hospitals were screened for study eligibility	**Home vs. Clinic** **Age:** 70 (15), 73(13) yrs **% Female:**27,28% **Ethnicity:** No details **Disease Status:** NYHA II or III 83,88% Months since CHF diagnosis 34.6(55.3),44.8(71.0)	**Home based intervention** (n=143) **Components of intervention at home:** Monitoring signs& symptoms Family involvement CM meetings/feedback to other health providers Referral to other health or social care Assessment of home environment Medication review (nurse, pharmacist, physician, cardiologist)	**Clinic-based intervention** (n=137) **Components of intervention:** *In clinic* Disease management Assessment of home environment Family involvement? Referral to other health or social care CM meetings/feedback to other health providers	**Rates of readmissions/100 days/patient** 0.52±0.76,0.53±1.02 ns **Mean days of hospitalisation** 4.96±8.57,3.62±6.36 ns At 12-18mths
Hospital Initiated CM - NRCTs				
Riegel[35] **2000** USA n=240 were randomised Patients were recruited from 5 hospitals following a hospitalisation for HF.	**Age:** 74.44 yrs. (10.65), 70.77 (11.77) **% female:**55, 55% **Ethnicity:** No details **Disease Status:** NYHA I 19.2,24.2% II 26.7,18.3% III 43.3,44.2% IV 10.8,13.3%	**Multidisciplinary disease management (DM)** (n=120) **Components of intervention at home:** Monitoring signs& symptoms Support group Referral to specialist RN visits	**Usual Care** (n=120) **Components of intervention at home:** Disease management	**Readmission rates** 3mths 0.22 (0.52),0.13 (.45) (ns) 6mths 0.32(0.58),0.23(0.53) (ns) **LOS in days** 3mths 0.89 (3.34), 0.48(1.64) (ns) 6mths 1.31(3.77), 1.08(3.46) (ns)
Russell[36] **2011** USA n=447 Patients were referred from a single large not-for-profit general medical and surgical hospital	**Age:**79.4(10.7),79.9(10.7) **% Female:**55.6,57.6 (numbers) **Ethnicity:** White non-Hispanic 56.9,58.4 African-American 17.0,16.5 Hispanic 14.8,14. Asian/other 11.2,10.7 **Disease Status:** Patients with a primary or secondary diagnosis of CHF	**Transitional care service** (n=223) **Components of intervention at home:** Self-management support Referral to other health & social care Assessment of home environment CM meetings/feedback to other health providers Advance care planning Physical therapy	**Usual home care services** (n=224) **Components of intervention at home:** Nurse visits Physical therapy (44.6) Home health aide service (27.7)	**Readmissions** Unadjusted odds ratio 30 days 0.58 (0.38,0.88) p<0.01 Adjusted odds ratio 30 days 0.57 (0.38,0.87) p<0.01
Stauffer[37] **2011** USA n=140 Patients were screened for eligibility within 48 hours of hospital admission	**Age:** 78.9(8.3), 81.4(8.3) **% Female:**58.1, 54.8% **Ethnicity:** Hispanic ethnicity 7.1,3.6% **Disease Status:** APR-DRG severity of illness 1 5.4,1.2% 2 44.6,31% 3 37.5,57.1% 4 12.5,10.7%	**Nurse-led transitional care intervention** (n=56) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Family involvement Referral (Assessing availability of social care) Patient directed access to study personnel	**Control group** (n=84) **Components of interventions:** unknown	**Readmission rate at 30 days** 12.6 (7.4,17.8) difference -12.6, % change -48%; 16.4(14,18.7) difference -1.6 % change 11%
Community-initiated CM-RCTs				
Peters-Klimm [39] **2010** Germany n=199 at randomisation Recruitment was via general practice by mail.	**Baseline characteristics of participants: CM,UC** **Age:** 70.4yrs (10.0), 68.9 (9.7) **% Female**:29, 26% **Ethnicity:** No details **Disease Status:** NYHA I 1(1.0), 5 (5) II 63 (64.9),67 (67) III 33 (34),27 (27) IV 0, 1(1.0) Mean yrs. with CHD 6.2(4.6) (n=79),6.8(6.3)(n=74	**Case management** (n=97) **Components of intervention at home:** Monitoring signs& symptoms Education/Self-management support Medication review (CM/GP) Referral to GP	**Usual care** (n=100) **Components of control intervention:** Disease management Education	**No. of admissions** (baseline 36 vs. 35) 18 vs. 9 at 12 mths (ns) No. of patients experiencing one or more CHF admissions 11 vs. 7 at 12 mths (ns)
Wade[42] **2011** USA n=2,200 were randomised Aetna Medicare Advantage members with medical & pharmacy benefits were identified through analysis of claims	**Age:** 75.8, 77.7 yrs. **% female:** No detail **Ethnicity:** Black/African American 24,20.4% **Disease Status (SD):** No detail	**Case management** (n=152) **Components of intervention at home:** Referral to other health & social care Equipment	**Tele health with case management (THCM) (n=164)** **Components of intervention:** Disease management Education Referral to other health & social care	No data available for primary outcome but described as ns The participant population overall had 42% fewer inpatient days during the intervention period compared with the previous year. No data
Hancock [43] **2012** UK n=28 randomised Residents from 33 of 35 long-term residential & nursing homes	**Age:** 85.1 (6.7), 81.8 (7.1)yrs **% Female:**56%, 58% **Ethnicity:**100% white British **Disease Status:** I:II:III:IV 10:1:4:1, 5:4:1:1	**Case management** (n=16) **Components of interventions at home:** Monitoring signs and symptoms Education CM meetings/feedback to other health providers Medication review (CM/GP/cardiologist)	**Routine GP-led care** (n=12) **Components of intervention:** Disease management	**No. of admissions** at 6 & 12 months 0, 0 at 6mths 0,0 at 12 mths
Community –initiated CM -NRCTs				
Bonarek- Hessamfar [44] **2008** France n=362 Compared patients included prospectively from Jan 1st 2004- Dec 31st 2005 from GP list	**Age:** Median 78, 80 yrs. **% Female:** No details **Ethnicity:** No details **Disease Status:** NHYA Median of III, IV	**Co-ordinated care via multidisciplinary network** (n=129) **Components of intervention at home:** Monitoring signs& symptoms Education (diet) Physical therapy CM meetings/feedback to other health provider.	**Usual care** (n=233) **Components of intervention:** not known	**No. of patients experiencing at least one admission** 26,58 **Total no. of admissions** 35,96 **Median LOS** 9.2,11.7 days In the 2yr period

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Lowery[45] **2012** USA n=1043 Intervention implemented in 4 Midwest VA medical centres from the same region & one affiliated outpatient clinic and 2 VA medical centres served as control.	**Age:** 65.4(0.51),67.4(0.45) yrs. **% female:**1, 1% **Ethnicity:** White 71.2,79.9% Black 24,16.1% Other 4.8,4.0% **Disease Status:** No details	**Nurse-practitioner-led disease management model** (n=457) **Components of intervention at home:** Location was lead tertiary centre, other medical centres (some primary care) or one affiliated outpatient clinic. Monitoring signs& symptoms Education /Self-management support Referral to other health & social care Family involvement	**Usual care** (n=510) **Components of intervention:** not known	**Mean no. of readmissions** 1yr 0.7(0.32) , 0.23(0.65) p<0.001 (417,428) 2yr 0.15 (0.58), 0.13(0.42) ns (384,382) **Mean no. of days in hospital** 1yr 0.37(2.25),0.97(3.15) p=0.0014 2yr 0.86 (3.98),0.66(2.74) ns

Key : AF atrial fibrillation, CHF Chronic heart failure, COPD chronic obstructive pulmonary disease, CM case management or case manager, HOCM/RCM Hypertrophic Obstructive/Restrictive Cardiomyopathy, GP general practitioner, UC usual care, NYHA, LV left ventricular SNF skilled nursing facility, PAD peripheral arterial disease.

Table 3: Available cost data from studies (n=9)

Study	**Cost data** Intervention vs. control (ns= not statistically significant)
Rich 1995	**3 month data** Study intervention cost US$216 per person Hospital readmissions $2178 vs. 3,236 p=0.03
Stewart 1998	**6 month data** Cost of study intervention Aus$190 per person Mean cost of hospital based care $3200 (1800-4600), 5400 (3200-6800) ns Cost of community based care $620(460,740), 680(550,800) ns
Stewart 1999	**6 and 18 month data** 6 months Total hospital based care Aus$490,300 vs. 922,600 ns 18 month data Total hospital based care $ 5100 (6800) vs.10,600(13000) ns
Laramee 2003	**3 month data** Total care costs Mean(US$) 23,054 vs.25,536 ns
Naylor 2004	**12 month data** CHF readmissions US $175,840 vs. 498,110? Physician's office (outpatients)$4,549, 5,169 ns ER visits $1780, vs. 5650 ns Home visits (all cause) Visiting nurse $11021, 64,531 p<0.001 APN $104,019 vs. 0 Physical therapist $7,120 vs. 10,918 ns Social worker $178,vs. 534 ns Home health aides $9,167 vs. 11,081 ns Total home visits $138,649 vs. 97.883 p<0.001 Total costs $725,903, 1,163,810 ns
Stewart 2012	**12-18 month data** Costs per patient Au$1813(220) vs. 1829(174) ns Total costs Au $3.93 million vs. 5.53 million p=0.03 for median costs per day
Riegel 2000	**3 & 6 month data** Total costs 3mths US$ 632 (2,378) vs. 317 (1,188) ns 6mths $1,024(3,017) vs. 686(2,225) ns
Riegel 2006	**1, 3 & 6 month data** HF inpatient costs all ns 1mth US$1012(4022) vs. 2830 (13,896) 3mth $3045(7784) vs. 4130 (14,468) 6mth $5567(13,137) vs. 6151 (16,650)
Stauffer 2011	**1 month data** 'under the current payment system, the intervention reduced the hospital financial contribution on average by US$227for each Medicare patient with HF'

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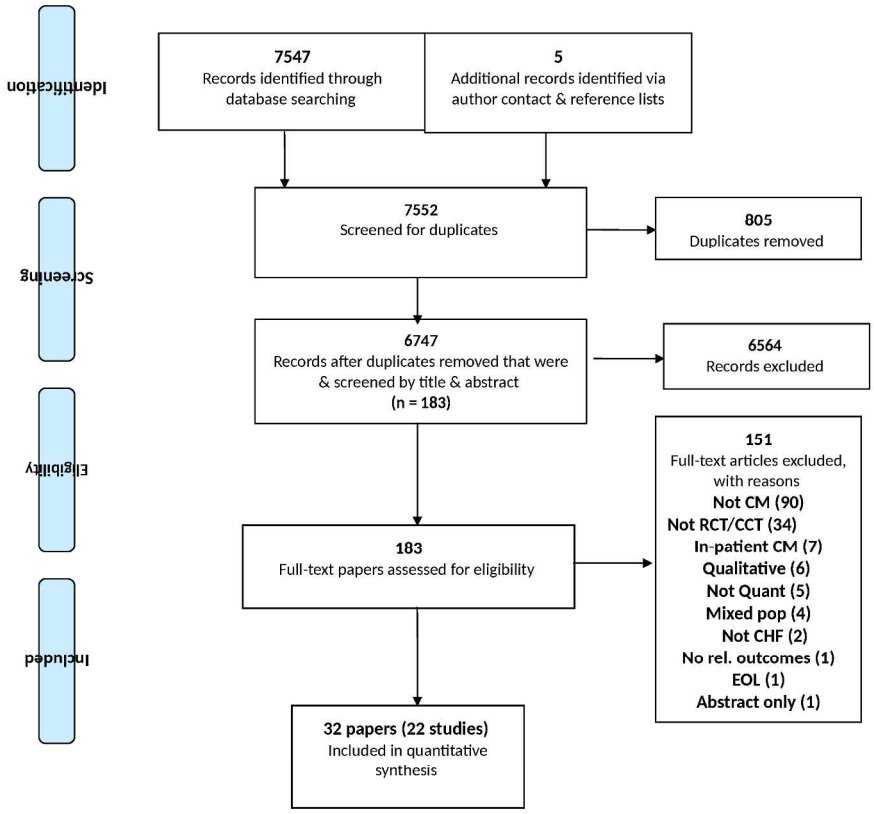
Figure 1: PRISMA Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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Figure 2b EPOC Risk of bias for Non-randomised controlled trials (NRCTs)

Study name	Allocation sequence adequately generated	Allocation adequately concealed	Baseline outcome measurements similar	Baseline characteristics similar	Incomplete outcome data	Knowledge of the allocated interventions	Protected against contamination	Selective outcome reporting	Other risks of bias
Bonarek-Hessamfar 2008	High risk	High risk	Unclear risk	High risk	Unclear risk	Low risk	Unclear risk	High risk	High risk
Lowery 2012	High risk	High risk	Unclear risk	Low risk	High risk	Low risk	Unclear risk	Low risk	High risk
Riegel 2000	High risk	High risk	Unclear risk	Unclear Risk/High risk	Unclear risk	Low risk	Unclear risk	Low risk	High risk
Russell 2011	High risk	High risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	High risk
Stauffer 2011	High risk	High risk	Unclear risk	Low risk	Unclear risk	Low risk	Unclear risk	Low risk	Low risk

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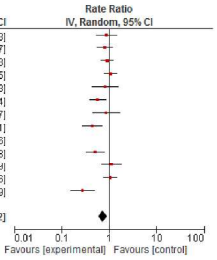
Figure 3: CHF admissions data

a) Overall for hospital –initiated CM

Study or Subgroup	log[Rate Ratio]	SE	CM Total	Usual Care Total	Weight	Rate Ratio IV, Random, 95% CI
Blue 2001	-0.129	0.248	84	81	7.9%	0.88 [0.54, 1.43]
Brotons 2009	-0.211	0.188	144	139	9.3%	0.81 [0.56, 1.17]
DeBusk 2004	-0.098	0.157	228	234	10.1%	0.91 [0.67, 1.23]
Jaarsma 2008	0.076	0.151	344	339	10.3%	1.08 [0.80, 1.45]
Laramee 2003	-0.201	0.321	131	125	6.2%	0.82 [0.44, 1.53]
Naylor 2004	-0.563	0.197	118	121	9.1%	0.57 [0.39, 0.84]
Rich 1993	-0.136	0.332	63	35	6.0%	0.87 [0.46, 1.67]
Rich 1995	-0.825	0.245	142	140	7.9%	0.44 [0.27, 0.71]
Riegel 2000	0.054	0.164	140	140	0.0%	1.06 [0.77, 1.46]
Riegel 2002	-0.675	0.219	130	228	8.5%	0.51 [0.33, 0.78]
Riegel 2006	0.112	0.24	69	65	8.0%	1.12 [0.70, 1.79]
Stewart 1999	0.054	0.164	140	140	10.0%	1.06 [0.77, 1.46]
Thompson 2005	-1.288	0.298	59	49	6.7%	0.28 [0.15, 0.49]
Total (95% CI)			**1651**	**1695**	**100.0%**	**0.74 [0.60, 0.92]**

Heterogeneity: Tau² = 0.10; Chi² = 35.59, df = 11 (P = 0.0002); I² = 69%
Test for overall effect: Z = 2.66 (P = 0.008)

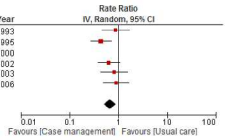


Sensitivity analysis: (Riegel 2002 removed) I^2 = 68% RR 0.77 [0.61, 0.96] p=0.02

b) 3 month data for hospital –initiated CM

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
Rich 1993	-0.136	0.332	63	35	16.1%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	26.2%	0.44 [0.27, 0.71]	1995
Riegel 2000	0.486	0.318	120	120		Not estimable	2000
Riegel 2002	-0.445	0.268	130	228	22.9%	0.64 [0.38, 1.08]	2002
Laramee 2003	-0.201	0.321	131	125	17.0%	0.82 [0.44, 1.53]	2003
Riegel 2006	-0.109	0.313	69	65	17.8%	0.90 [0.49, 1.66]	2006
Total (95% CI)			**535**	**593**	**100.0%**	**0.67 [0.51, 0.90]**	

Heterogeneity: Tau² = 0.02; Chi² = 4.92, df = 4 (P = 0.30); I² = 19%
Test for overall effect: Z = 2.73 (P = 0.006)

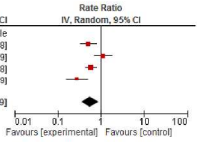


Sensitivity analysis: (Riegel 2002 removed) I^2 = 39% RR 0.70 [0.48, 1.01] p=0.06

c) 6 month data for hospital –initiated CM

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual Care Total	Weight	Rate Ratio IV, Random, 95% CI
Riegel 2000	0.054	0.164	140	140		Not estimable
Riegel 2002	-0.675	0.219	130	228	25.5%	0.51 [0.33, 0.78]
Riegel 2006	0.112	0.24	69	65	24.4%	1.12 [0.70, 1.79]
Stewart 1999	-0.551	0.152	100	100	28.6%	0.58 [0.43, 0.78]
Thompson 2005	-1.200	0.290	59	49	21.5%	0.30 [0.15, 0.49]
Total (95% CI)			**357**	**441**	**100.0%**	**0.56 [0.35, 0.89]**

Heterogeneity: Tau² = 0.17; Chi² = 14.06, df = 3 (P = 0.003); I² = 79%
Test for overall effect: Z = 2.43 (P = 0.01)



Sensitivity analysis: (Riegel 2002 removed) I^2 = 85% RR 0.57 [0.30, 1.21] p=0.1

d) 12-18 months for hospital –initiated CM

Study or Subgroup	log[Rate Ratio]	SE	CM Total	Usual Care Total	Weight	Rate Ratio IV, Random, 95% CI
Blue 2001	0.129	0.248	84	81	9.5%	0.88 [0.54, 1.43]
Brotons 2009	-0.211	0.188	144	139	14.5%	0.81 [0.56, 1.17]
DeBusk 2004	-0.098	0.157	228	234	18.5%	0.91 [0.67, 1.23]
Jaarsma 2008	0.076	0.151	344	339	19.4%	1.08 [0.80, 1.45]
Naylor 2004	-0.563	0.197	118	121	13.6%	0.57 [0.39, 0.84]
Stewart 1999	-0.279	0.122	100	100	24.5%	0.76 [0.60, 0.96]
Total (95% CI)			**1018**	**1014**	**100.0%**	**0.83 [0.70, 0.98]**

Heterogeneity: Tau² = 0.01; Chi² = 7.64, df = 5 (P = 0.18); I² = 35%
Test for overall effect: Z = 2.24 (P = 0.03)

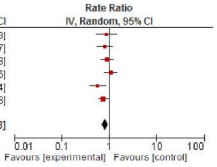


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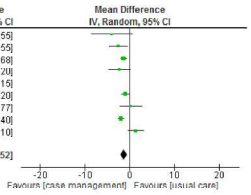
Figure 4: CHF length of stay

a) Overall for hospital –initiated CM

Study or Subgroup	Case management Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Blue 2001	3.42	12.2	82	7.46	16.6	75	2.5%	-4.04 [-8.63, 0.55]
Laramee 2003	6.9	6.5	131	9.5	9.8	125	9.1%	-2.60 [-4.65, -0.55]
Rich 1993	4.3	1.1	63	5.7	2	35	21.2%	-1.40 [-2.12, -0.68]
Rich 1995	3.9	10	142	6.2	11.4	140	6.8%	-2.30 [-4.80, 0.20]
Riegel 2000	1.31	3.77	120	1.08	3.46	120	0.0%	0.23 [-0.69, 1.15]
Riegel 2002	1.1	3.1	130	2.1	4.6	228	20.3%	-1.00 [-1.80, -0.20]
Riegel 2006	3.65	7.8	69	3.4	7.1	65	6.8%	0.25 [-2.27, 2.77]
Stewart 1999	0.9	0.9	100	2.9	2.9	100	22.5%	-2.00 [-2.60, -1.40]
Stewart 2012	4.96	8.57	143	3.62	6.36	137	10.9%	1.34 [-0.42, 3.10]
Total (95% CI)			**860**			**905**	**100.0%**	**-1.28 [-2.04, -0.52]**

Heterogeneity: Tau² = 0.58; Chi² = 18.75, df = 7 (P = 0.009); I² = 63%
Test for overall effect: Z = 3.29 (P = 0.001)

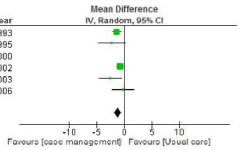


Sensitivity analysis: (Riegel 2002 removed) I^2 = 14% MD -1.76[-2.29,-1.23] p<0.00001

b) 3 month data for hospital –initiated CM

Study or Subgroup	Case management Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Year
Rich 1993	4.3	1.1	63	5.7	2	35	37.0%	-1.40 [-2.12, -0.68]	1993
Rich 1995	3.9	10	142	6.2	11.4	140	5.5%	-2.30 [-4.80, 0.20]	1995
Riegel 2000	0.89	3.34	120	0.48	1.64	120		Not estimable	2000
Riegel 2002	0.85	2.3	130	1.6	3.9	228	41.0%	-0.75 [-1.39, -0.11]	2002
Laramee 2003	6.9	6.5	131	9.5	9.8	125	8.0%	-2.60 [-4.65, -0.55]	2003
Riegel 2006	2.19	5.4	69	2.4	6.2	65	9.5%	-0.21 [-2.18, 1.76]	2006
Total (95% CI)			**535**			**593**	**100.0%**	**-1.18 [-1.79, -0.57]**	

Heterogeneity: Tau² = 0.13; Chi² = 5.54, df = 4 (P = 0.24); I² = 28%
Test for overall effect: Z = 3.77 (P = 0.0002)

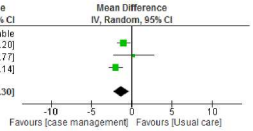


Sensitivity analysis: (Riegel 2002 removed) I^2 = 6% MD -1.46 [-2.15,-0.77] p<0.0001

c) 6 month data for hospital –initiated CM

Study or Subgroup	Case management Mean	SD	Total	Usual care Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Riegel 2000	1.31	3.77	120	1.08	3.46	120		Not estimable
Riegel 2002	1.1	3.1	130	2.1	4.6	228	44.9%	-1.00 [-1.80, -0.20]
Riegel 2006	3.65	7.8	69	3.4	7.1	65	12.1%	0.25 [-2.27, 2.77]
Stewart 1999	0.9	0.9	49	2.9	2.9	48	43.0%	-2.00 [-2.86, -1.14]
Total (95% CI)			**248**			**341**	**100.0%**	**-1.28 [-2.25, -0.30]**

Heterogeneity: Tau² = 0.38; Chi² = 4.47, df = 2 (P = 0.11); I² = 55%
Test for overall effect: Z = 2.57 (P = 0.01)



Sensitivity analysis: (Riegel 2002 removed so n=2) I^2 = 63% MD -1.20 [-3.31,0.91] p=0.26

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Appendix 1:

Database: Medline In-process - Current week, Medline 1950 to present

Search Strategy:

---

1 randomized controlled trial.pt. (376608)
2 random$.tw. (717987)
3 control$.tw. (2630023)
4 intervention$.tw. (556397)
5 evaluat$.tw. (2214967)
6 or/1-5 (5041451)
7 Qualitative Research/ (20094)
8 semi-structured questionnaire.mp. (1162)
9 observation methods.mp. (152)
10 Observation/mt [Methods] (635)
11 Nvivo.mp. (639)
12 interview/ (25018)
13 Personal Narratives/ (877)
14 Focus Groups/ (16824)
15 patient experience*.mp. (8525)
16 or/7-15 (70071)
17 exp Heart Failure/ (87270)
18 exp Heart Failure, Diastolic/ (496)
19 exp heart failure, systolic/ (789)
20 exp Ventricular Dysfunction/ (26332)
21 chronic heart failure.mp. (11341)
22 congestive heart failure.mp. (33082)
23 cardiac failure.mp. (10151)
24 LV dysfunction.mp. (2827)
25 left ventricular dysfunction.mp. (9373)
26 left ventricular impairment.mp. (188)
27 diastolic impairment.mp. (121)
28 systolic impairment.mp. (93)
29 or/17-28 (135885)
30 exp Case Management/ (8326)
31 exp Patient Care Planning/ (52319)
32 organisation of care.mp. (367)
33 community matron.mp. (44)

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34 "Continuity of Patient Care"/ (14497)
35 Community Health Nursing/ (18371)
36 transit* care.mp. (580)
37 Interdisciplinary Communication/ (10602)
38 Patient Discharge/ (18977)
39 discharge plan.mp. (176)
40 exp Patient Care Management/ (535496)
41 Comprehensive Health Care/ (6078)
42 exp Managed Care Programs/ (38918)
43 Primary Health Care/ (54234)
44 Community Health Services/ (26923)
45 General Practitioners/ (1943)
46 Family Practice/ (60223)
47 Physicians, Family/ (14745)
48 multidisciplinary.mp. (44988)
49 or/30-48 (674050)
50 6 or 16 (5094326)
51 29 and 50 (47009)
52 49 and 51 (2590)
53 52 not (case report/ or case study/ or letter/ or editorial/ or expert opinion.mp.) (2489)
54 53 not (Algeria$ or Egypt$ or Liby$ or Morocc$ or Tunisia$ or Western Sahara$ or Angola$ or Benin or Botswana$ or Burkina Faso or Burundi or Cameroon or Cape Verde or Central African Republic or Chad or Comoros or Congo or Djibouti or Eritrea or Ethiopia$ or Gabon or Gambia$ or Ghana or Guinea or Keny$ or Lesotho or Liberia or Madagasca$ or Malawi or Mali or Mauritania or Mauritius or Mayotte or Mozambiq$ or Namibia$ or Niger or Nigeria$ or Reunion or Rwand$ or Saint Helena or Senegal or Seychelles or Sierra Leone or Somalia or South Africa$ or Sudan or Swaziland or Tanzania or Togo or Ugand$ or Zambia$ or Zimbabw$ or China or Chinese or Hong Kong or Macao or Mongolia$ or Taiwan$ or Belarus or Moldov$ or Russia$ or Ukraine or Afghanistan or Armenia$ or Azerbaijan or Bahrain or Cyprus or Cypriot or Georgia$ or Iran$ or Iraq$ or Israel$ or Jordan$ or Kazakhstan or Kuwait or Kyrgyzstan or Leban$ or Oman or Pakistan$ or Palestin$ or Qatar or Saudi Arabia or Syria$ or Tajikistan or Turkmenistan or United Arab Emirates or Uzbekistan or Yemen or Bangladesh$ or Bhutan or British Indian Ocean Territory or Brunei Darussalam or Cambodia$ or India$ or Indonesia$ or Lao or People's Democratic Republic or Malaysia$ or Maldives or Myanmar or Nepal or Philippin$ or Singapore or Sri Lanka or Thai$ or Timor Leste or Vietnam or Albania$ or Andorra or Bosnia$ or Herzegovina$ or Bulgaria$ or Croatia$ or Estonia or Faroe Islands or Greenland or Liechtenstein or Lithuani$ or Macedonia or Malta or maltese or Romania or Serbia$ or Montenegro or Slovenia or Svalbard or

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Argentina$ or Belize or Bolivia$ or Brazil$ or chile or Chilean or Colombia$ or Costa Rica$ or Cuba or Ecuador or El Salvador or French Guiana or Guatemala$ or Guyana or Haiti or Honduras or Jamaica$ or Nicaragua$ or Panama or Paraguay or Peru or Puerto Rico or Suriname or Uruguay or Venezuela or developing countr$ or south America$).ti,sh. (2413)

55 54 not animal/ (2393)

56 remove duplicates from 55 (2335)

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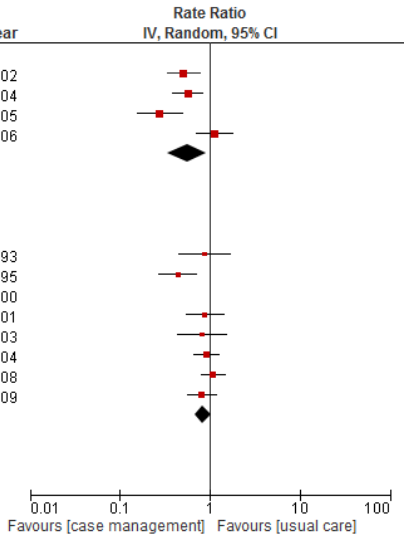
Appendix 2: Subgroup-analysis of unplanned readmission data by intervention component- hospital initiated studies

a) Family involvement

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.12.1 CM & FI							
Riegel 2002	-0.675	0.219	130	228	25.9%	0.51 [0.33, 0.78]	2002
Naylor 2004	-0.563	0.197	118	121	26.9%	0.57 [0.39, 0.84]	2004
Thompson 2005	-1.288	0.298	58	48	22.3%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	24.9%	1.12 [0.70, 1.79]	2006
Subtotal (95% CI)			**375**	**462**	**100.0%**	**0.56 [0.34, 0.92]**	
Heterogeneity: Tau² = 0.20; Chi² = 14.07, df = 3 (P = 0.003); I² = 79%							
Test for overall effect: Z = 2.30 (P = 0.02)							
1.12.2 CM minus FI							
Rich 1993	-0.136	0.332	63	35	8.0%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	12.5%	0.44 [0.27, 0.71]	1995
Riegel 2000	0.054	0.164	140	140	0.0%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	82	75	12.3%	0.88 [0.54, 1.43]	2001
Laramee 2003	-0.201	0.321	131	125	8.5%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	20.5%	0.91 [0.67, 1.23]	2004
Jaarsma 2008	0.076	0.151	344	339	21.2%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	17.1%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1134**	**1087**	**100.0%**	**0.83 [0.67, 1.02]**	
Heterogeneity: Tau² = 0.03; Chi² = 10.07, df = 6 (P = 0.12); I² = 40%							
Test for overall effect: Z = 1.76 (P = 0.08)							

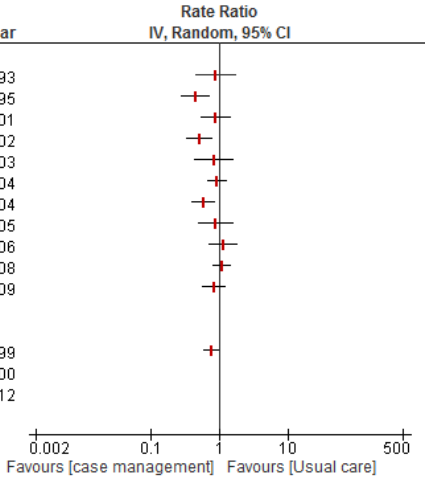


Test for subgroup differences: Chi² = 2.09, df = 1 (P = 0.15), I² = 52.1%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.98 df=1 (p=0.32) I^2-0%

b) education & self-management

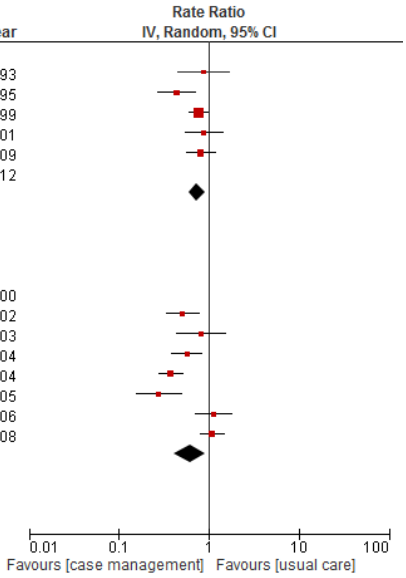
Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Rate Ratio IV, Random, 95% CI	Year
1.20.1 Education and self-management						
Rich 1993	-0.136	0.332	63	35	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	0.44 [0.27, 0.71]	1995
Blue 2001	-0.129	0.248	84	81	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.201	0.321	131	125	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	0.57 [0.39, 0.84]	2004
Thompson 2005	-0.1288	0.298	58	48	0.88 [0.49, 1.58]	2005
Riegel 2006	0.112	0.24	69	65	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	0.81 [0.56, 1.17]	2009
1.20.2 No education and self-management						
Stewart 1999	-0.279	0.122	100	100	0.76 [0.60, 0.96]	1999
Riegel 2000	0.054	0.164	140	140	1.06 [0.77, 1.46]	2000
Stewart 2012	0.018	0.071	143	137	Not estimable	2012



There were inadequate data in the no education/self-management group to perform a comparison.

c) medication review

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.19.1 Medication review							
Rich 1993	-0.136	0.332	63	35	9.3%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	15.4%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	37.5%	0.76 [0.60, 0.96]	1999
Blue 2001	-0.129	0.248	84	81	15.1%	0.88 [0.54, 1.43]	2001
Brotons 2009	-0.211	0.188	144	139	22.7%	0.81 [0.56, 1.17]	2009
Stewart 2012	0.018	0.071	143	137		Not estimable	2012
Subtotal (95% CI)			**533**	**495**	**100.0%**	**0.73 [0.59, 0.91]**	
Heterogeneity: Tau² = 0.02; Chi² = 5.56, df = 4 (P = 0.23); I² = 28%							
Test for overall effect: Z = 2.87 (P = 0.004)							
1.19.2 No medication review							
Riegel 2000	0.054	0.164	140	140	0.0%	1.06 [0.77, 1.46]	2000
Riegel 2002	-0.675	0.219	130	228	14.5%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.201	0.321	131	125	12.1%	0.82 [0.44, 1.53]	2003
Naylor 2004	-0.563	0.197	118	121	15.0%	0.57 [0.39, 0.84]	2004
DeBusk 2004	-0.98	0.157	228	234	15.8%	0.38 [0.28, 0.51]	2004
Thompson 2005	-1.288	0.298	58	48	12.7%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	14.0%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	15.9%	1.08 [0.80, 1.45]	2008
Subtotal (95% CI)			**1078**	**1160**	**100.0%**	**0.61 [0.41, 0.91]**	
Heterogeneity: Tau² = 0.24; Chi² = 38.84, df = 6 (P < 0.00001); I² = 85%							
Test for overall effect: Z = 2.45 (P = 0.01)							

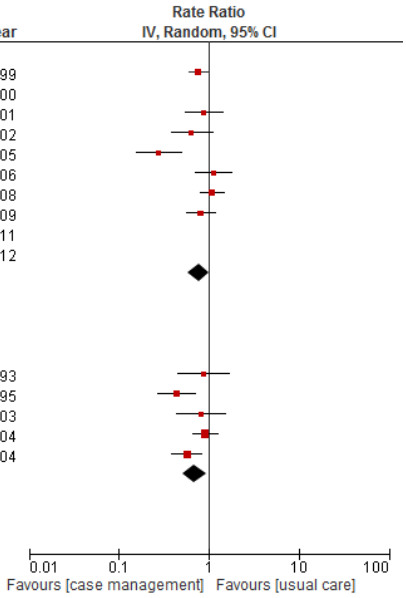


Test for subgroup differences: Chi² = 0.65, df = 1 (P = 0.42), I² = 0%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.36 df=1 (p=0.55) I^2-0%

d) Referral to other services

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.16.1 Referral to others							
Stewart 1999	-0.279	0.122	100	100	18.6%	0.76 [0.60, 0.96]	1999
Riegel 2000	0.486	0.318	120	120	0.0%	1.63 [0.87, 3.03]	2000
Blue 2001	-0.129	0.248	84	81	12.8%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.445	0.268	120	120	11.9%	0.64 [0.38, 1.08]	2002
Thompson 2005	-1.288	0.298	58	48	10.8%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	13.1%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	17.3%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	0	15.5%	0.81 [0.56, 1.17]	2009
Russell 2011	0	0	0	0		Not estimable	2011
Stewart 2012	0.018	0.071	143	137		Not estimable	2012
Subtotal (95% CI)			**919**	**753**	**100.0%**	**0.77 [0.59, 1.00]**	
Heterogeneity: Tau² = 0.09; Chi² = 19.67, df = 6 (P = 0.003); I² = 69%							
Test for overall effect: Z = 1.93 (P = 0.05)							
1.16.2 No referral							
Rich 1993	-0.136	0.332	63	35	13.7%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	19.6%	0.44 [0.27, 0.71]	1995
Laramee 2003	-0.201	0.321	131	125	14.3%	0.82 [0.44, 1.53]	2003
DeBusk 2004	-0.098	0.157	228	234	28.3%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	24.1%	0.57 [0.39, 0.84]	2004
Subtotal (95% CI)			**682**	**655**	**100.0%**	**0.69 [0.51, 0.93]**	
Heterogeneity: Tau² = 0.06; Chi² = 8.13, df = 4 (P = 0.09); I² = 51%							
Test for overall effect: Z = 2.47 (P = 0.01)							

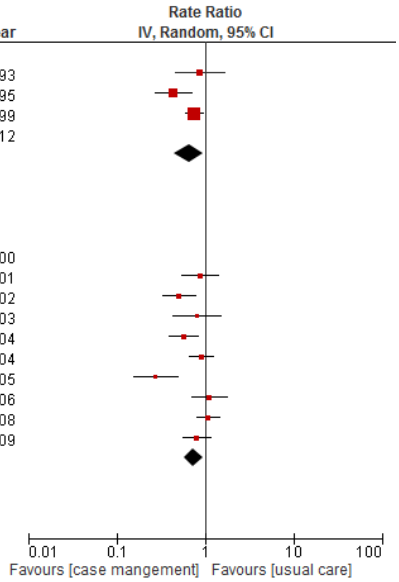


Test for subgroup differences: Chi² = 0.28, df = 1 (P = 0.60), I² = 0%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.36 df=1 (p=0.55) I^2=0%

e) Assessment of home environment

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.18.1 Home assessment							
Rich 1993	-0.136	0.332	63	35	21.5%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	30.3%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	48.2%	0.76 [0.60, 0.96]	1999
Stewart 2012	0.018	0.071	143	137		Not estimable	2012
Subtotal (95% CI)			**305**	**275**	**100.0%**	**0.66 [0.45, 0.96]**	
Heterogeneity: Tau² = 0.06; Chi² = 4.50, df = 2 (P = 0.11); I² = 56%							
Test for overall effect: Z = 2.15 (P = 0.03)							
1.18.2 No home assessment							
Riegel 2000	0.054	0.164	140	140	0.0%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	84	81	10.3%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228	11.2%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.21	0.321	131	125	8.2%	0.81 [0.43, 1.52]	2003
Naylor 2004	-0.563	0.197	118	121	11.9%	0.57 [0.39, 0.84]	2004
DeBusk 2004	-0.098	0.157	228	234	13.3%	0.91 [0.67, 1.23]	2004
Thompson 2005	-1.288	0.298	58	48	8.8%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	10.5%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	13.5%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	12.3%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1306**	**1380**	**100.0%**	**0.74 [0.57, 0.95]**	
Heterogeneity: Tau² = 0.10; Chi² = 26.58, df = 8 (P = 0.0008); I² = 70%							
Test for overall effect: Z = 2.35 (P = 0.02)							

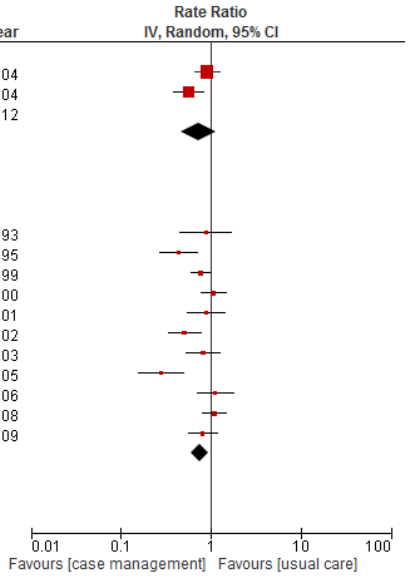


Test for subgroup differences: Chi² = 0.23, df = 1 (P = 0.63), I² = 0%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.46 df=1 (p=0.50) I^2=0%

f) Case management/health professional meetings

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI	Year
1.21.1 CM/HP meeting							
DeBusk 2004	-0.098	0.157	228	234	53.3%	0.91 [0.67, 1.23]	2004
Naylor 2004	-0.563	0.197	118	121	46.7%	0.57 [0.39, 0.84]	2004
Stewart 2012	0.018	0.071	143	137	0.0%	1.02 [0.89, 1.17]	2012
Subtotal (95% CI)			**346**	**355**	**100.0%**	**0.73 [0.46, 1.15]**	
Heterogeneity: Tau² = 0.08; Chi² = 3.41, df = 1 (P = 0.06); I² = 71%							
Test for overall effect: Z = 1.36 (P = 0.17)							
1.21.2 No CM/HP meetings							
Rich 1993	-0.136	0.332	63	35	6.2%	0.87 [0.46, 1.67]	1993
Rich 1995	-0.825	0.245	142	140	8.3%	0.44 [0.27, 0.71]	1995
Stewart 1999	-0.279	0.122	100	100	12.0%	0.76 [0.60, 0.96]	1999
Riegel 2000	0.054	0.164	140	140	10.7%	1.06 [0.77, 1.46]	2000
Blue 2001	-0.129	0.248	84	81	8.2%	0.88 [0.54, 1.43]	2001
Riegel 2002	-0.675	0.219	130	228	9.0%	0.51 [0.33, 0.78]	2002
Laramee 2003	-0.201	0.219	131	125	9.0%	0.82 [0.53, 1.26]	2003
Thompson 2005	-1.288	0.298	58	48	7.0%	0.28 [0.15, 0.49]	2005
Riegel 2006	0.112	0.24	69	65	8.4%	1.12 [0.70, 1.79]	2006
Jaarsma 2008	0.076	0.151	344	339	11.1%	1.08 [0.80, 1.45]	2008
Brotons 2009	-0.211	0.188	144	139	10.0%	0.81 [0.56, 1.17]	2009
Subtotal (95% CI)			**1405**	**1440**	**100.0%**	**0.75 [0.60, 0.93]**	
Heterogeneity: Tau² = 0.09; Chi² = 32.20, df = 10 (P = 0.0004); I² = 69%							
Test for overall effect: Z = 2.59 (P = 0.010)							

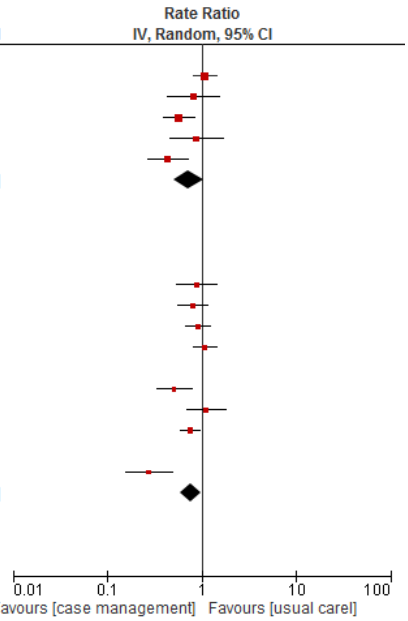


Test for subgroup differences: Chi² = 0.01, df = 1 (P = 0.91), I² = 0%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.07 df=1 (p=0.07) I^2=0%

g) Patient-directed access

Study or Subgroup	log[Rate Ratio]	SE	Case management Total	Usual care Total	Weight	Rate Ratio IV, Random, 95% CI
1.22.1 Patient directed access						
Jaarsma 2008	0.076	0.151	344	339	25.4%	1.08 [0.80, 1.45]
Laramee 2003	-0.201	0.321	131	125	16.1%	0.82 [0.44, 1.53]
Naylor 2004	-0.563	0.197	118	121	22.8%	0.57 [0.39, 0.84]
Rich 1993	-0.136	0.332	63	35	15.6%	0.87 [0.46, 1.67]
Rich 1995	-0.825	0.245	100	100	20.1%	0.44 [0.27, 0.71]
Subtotal (95% CI)			**756**	**720**	**100.0%**	**0.72 [0.50, 1.04]**
Heterogeneity: Tau² = 0.12; Chi² = 12.80, df = 4 (P = 0.01); I² = 69%						
Test for overall effect: Z = 1.75 (P = 0.08)						
1.22.2 No patient-directed access						
Blue 2001	-0.129	0.248	84	81	10.7%	0.88 [0.54, 1.43]
Brotons 2009	-0.211	0.188	144	139	13.0%	0.81 [0.56, 1.17]
DeBusk 2004	-0.098	0.157	228	234	14.3%	0.91 [0.67, 1.23]
Jaarsma 2008	0.076	0.151	344	339	14.6%	1.08 [0.80, 1.45]
Riegel 2000	0.054	0.164	140	140	0.0%	1.06 [0.77, 1.46]
Riegel 2002	-0.675	0.219	130	228	11.8%	0.51 [0.33, 0.78]
Riegel 2006	0.112	0.24	69	65	11.0%	1.12 [0.70, 1.79]
Stewart 1999	-0.279	0.122	100	100	15.8%	0.76 [0.60, 0.96]
Stewart 2012	0.018	0.071	143	137		Not estimable
Thompson 2005	-1.288	0.298	58	48	9.0%	0.28 [0.15, 0.49]
Subtotal (95% CI)			**1157**	**1234**	**100.0%**	**0.76 [0.60, 0.97]**
Heterogeneity: Tau² = 0.08; Chi² = 23.89, df = 7 (P = 0.001); I² = 71%						
Test for overall effect: Z = 2.19 (P = 0.03)						



Test for subgroup differences: Chi² = 0.07, df = 1 (P = 0.80), I² = 0%

Sensitivity analysis (removing Riegel 2002) Test for subgroup differences Chi^2 0.25 df=1 (p=0.61) I^2=0%

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4-5
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix one
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	6
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6-7
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6-7
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6-7

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PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7 & Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7-8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	9
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	9-11
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	9-11 plus figures 3 & 4 and appendix 2
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	9-11 plus figures 3 & 4
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	9-11 plus figures 3 & 4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12,14-15
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	15

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FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	21

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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