BMJ Open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-006542
Article Type:	Research
Date Submitted by the Author:	13-Sep-2014
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Primary Subject Heading:	Cardiovascular medicine
Secondary Subject Heading:	Evidence based practice, Medical management, Research methods
Keywords:	Adult cardiology < CARDIOLOGY, Heart failure < CARDIOLOGY, QUALITATIVE RESEARCH

Congestive Heart Failure Adherence Redesign Trial: A Pilot Study

Short Title: CHART-P Study

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Word Count: Abstract 300; Text 2,636.

Key words: Heart Failure, Patient Education, Physician Education, Adherence to evidence based HF therapy, Multi- Level Intervention.

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ABSTRACT

Objective: Heart failure (HF) continues to be a leading cause of hospital admissions, particularly in underserved patients. We hypothesized that providing individualized self-management support to patients and feedback on use of evidence-based HF therapies (EBT) to physicians could lead to improvements in care and decrease hospitalizations. To assess the feasibility of conducting a larger trial testing the efficacy of this dual-level intervention, we conducted the Congestive Heart failure Adherence Redesign Trial Pilot (CHART-P), a proof-of-concept, quasi-experimental, feasibility pilot study.

Setting: A large tertiary care medical centre in Chicago.

Participants: Low-income patients (<$30,000/year) hospitalized for exacerbation of systolic HF (ejection fraction ≤ 50%) and their physicians. Twenty physicians and 33 patients were enrolled, 23 patients completed the study.

Interventions: Physicians received HF guidelines and periodic individualized feedback on their adherence to EBT. Patients received HF education, support and self-management training for diet and medication adherence by a trained nurse through 11 interactive sessions over a 4-month period. Evaluations were conducted pre-enrolment and 1 month post intervention completion.

Outcome measures: Feasibility was assessed by the ability to deliver intervention to patients and physicians. Exploratory outcomes included changes in medication and sodium intake for patients and adherence to EBT for physicians.

Results: Eighty seven percent and 82% of patients received >80% of interventions at 1 month and by study completion, respectively. Median sodium intake declined (3.5 vs 2.0 g; p<0.01). There was no statistically significant change in medication adherence based on electronic pill cap monitoring or Morisky Medication Adherence Scale (MMAS); however, there was a trend towards improved adherence based on MMAS. All physicians received timely intervention.

Conclusions: This pilot study demonstrated that the protocol was feasible. It provided important insights about the need for intervention and the difficulties in treating patients with a variety of psychosocial problems that undercut their effective care.

STRENGTHS AND LIMITATIONS OF THE STUDY

Strengths

- The intervention studied is multi-level, in that it targets both physicians and patients simultaneously. Such strategies are potentially more potent than those with a single focus.
- The intervention studied provided individualized feedback to patients and physicians.
- The targeted population is low income heart failure patients; who are disproportionally affected by the heart failure epidemic. Few studies have targeted this population and our pilot study helped us in gaining important insights into this challenging group of patients before conducting larger trial.

Weaknesses

- This is a pilot feasibility study performed at a single medical centre.
- The sample size is small and the duration of follow up was short.

INTRODUCTION

Heart Failure (HF) continues to increase in prevalence with enormous impact on mortality (approximately 50% at 5 years post diagnosis), hospitalizations, and cost of care ($30.7 billion in 2012)[1,2]. The prevalence of HF among those 18 years and older in the United States is projected to increase by 46% in the next 15 years resulting in more than 8 million people with HF by 2030[2]. This reality has created a significant and increasing financial burden on the health care system. Although HF therapies exist with demonstrated benefits on mortality, morbidity, and quality of life [3], these therapies are being underutilized [4, 5]. Racial minorities and socio-economically disadvantaged patients have a higher prevalence of HF and higher readmission rates [6, 7], thus contributing disproportionately to the HF epidemic.

There is a particular need to develop effective interventions targeting economically disadvantaged patients with HF [8]. Results from our previously published Heart failure Adherence and Retention Trial (HART) suggested that patients with an annual income < $30,000 might benefit from counselling to improve self-management skills as a means to lower mortality and HF hospitalization rates [9]. Since physician adherence to evidence-based therapy has been shown to be suboptimal [5], providing education to physicians could offer additional value. We hypothesized that the use of a dual-level intervention strategy, intervening simultaneously on patients and their physicians, would translate into significantly improved quality of care among low-income HF patients and improve their outcomes. To assess the feasibility of conducting a large trial to study the efficacy of this dual-level strategy, we conducted the Congestive Heart failure Adherence Redesign Trial Pilot (CHART-P) study.

METHODS

The CHART-P was a proof-of-concept, pre-post treatment group only design. The key objective was to assess the feasibility and potential impact of our dual-level intervention for low-income HF patients and their physicians. We would deem the intervention feasible if we were able to achieve 4 objectives: 1) assess patient adherence to prescribed therapies and sodium restriction, 2) deliver the intervention to patients, 3) assess physician adherence to evidence-based HF therapy, and 4) provide timely feed-back to physicians.

Recruitment

The study targeted HF patients with self-reported annual household income < $30,000, as these patients are at high risk for adverse outcomes [7, 9]. Only patients with systolic HF (ejection fraction ≤ 50% as measured by echocardiography, radionuclide ventriculography or radiographic contrast ventriculography) were included. All participants were recruited while hospitalized at Rush University Medical Center in Chicago, IL, after being identified via monitoring of hospital admission logs and echocardiography electronic databases. Exclusion criteria included being a cardiac transplant candidate, having severe aortic stenosis, uncontrolled ventricular arrhythmias, BNP <100 ng/dL, severe asthma or COPD, major psychiatric comorbidities, alcohol or drug addiction, haemodialysis treatment, debilitating neurological conditions, severe arthritis, peripheral arterial disease, or having an uncertain 12 month prognosis. Once an eligible patient was identified, it was checked whether their physician is on staff at the medical centre. If the physician was on staff, their consent for study participation was obtained. Subsequently, the patients were recruited and consented. As this was a proof-of-concept study primarily aimed at assessing feasibility, sample size calculations were not performed.

Interventions

The dual-level intervention targeted both the patients and physicians caring for their HF. Physician-level intervention provided them with evidence-based HF guidelines in the form of a brochure summarizing 2005 American College of Cardiology/American Heart Association (ACC/AHA) recommendations with updates from the 2009 guidelines, which were current at the time of our study [10, 11]. Physicians also received periodic summary reports of their patient's medication use, as obtained from medical records and patient self-report. Personal notes from our study cardiologist (JC) were included with these reports offering possible medication changes that could optimize adherence to evidence-based therapy.

Patient-level intervention provided to each enrolled patient a tailored HF self-management kit [12]. The kit included brochures featuring patient-friendly HF education material and a variety of self-management tools (scale, measuring bottle, educational materials and pill boxes). Patients were coached on use of the kit during one-on-one contacts timed to occur 3 days post hospital discharge, then once weekly for 1 month and every 2 weeks thereafter for another 3 months, totalling 11 intervention contacts. The patient contacts were performed in-person or via telephone at the patient's discretion. These contacts were conducted by a trained nurse who followed a problem-solving format in which patients were encouraged to articulate barriers to their adherence and to use a variety of self-management strategies to overcome them [13]. Simple metaphors were used to educate patients about their HF. The heart was equated to a "workhorse" carrying "load" (blood and water) throughout the body via the "road" (arteries). "Water pills" (diuretics) "lighten the load" and angiotensin converting

enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) "widen the road" making it easier for the workhorse to pump. The importance of adhering to prescribed medications, a low sodium diet, daily weighing, regular physical activity, smoking cessation, and regular follow-up with providers was emphasized. Stress reduction strategies were also discussed. Patient comprehension of these components was assessed at each contact and their knowledge reinforced whenever gaps were identified.

Outcomes, Measures, and Data Analyses

Impact of the dual-level intervention on physician adherence to evidence-based therapy focused specifically on appropriate use of an ACE-I or ARB, beta-blocker and aldosterone antagonist. Data on physician adherence were gathered by chart audit at baseline and 5 months for each patient enrolled. Only patients who remained in the study for the 5 month evaluation were included in these analyses. Physician adherence with respect to a given medication was measured using the proportion of their patients who were prescribed the medication, based upon those for whom it was appropriate according to the 2005 and 2009 ACC/AHA guidelines and as confirmed by the study cardiologist [10,11]. Pre-post change in percentage physician adherence and average physician adherence was assessed via *t*-tests or Wilcoxon tests, as appropriate.

Patient adherence to prescribed therapies was determined at baseline and 5 months, using both electronic pill-cap monitoring (using the MEMS V Trackcap; AARDEX, Zug, Switzerland) and the Morisky Medication Adherence Scale (MMAS) [14]. MMAS provides a score of 0-4, with 4 indicating highest

adherence. Each patient's pill-cap use was monitored for either an ACE-I, ARB, beta-blocker, or diuretic, in that order depending upon which of these drugs was prescribed. Patients were instructed to place a month's supply of monitored medication into their pill cap container and use it over the ensuing month. Patient adherence was then measured based on the percentage of time a patient took a pill relative to the prescribed timing. Patients were designated "adherent" if their observed adherence was ≥80% [9,13,15]. The pre-post change in percent adherence was analysed via paired *t*-tests or Wilcoxon tests, as appropriate. The pre-post change in the proportion of patients designated as "adherent" (via pill-cap or MMAS) was analysed via McNemar's exact test. Sodium intake was determined by a food frequency questionnaire specifically designed to assess sodium intake [16] and the pre-post change was analysed via paired Student's *t*-test or Wilcoxon test as appropriate.

Sensitivity analyses were conducted to account for missing data at the 5-month data collection. The analysis consisted of comparing results under 3 different data replacement approaches: 1) a "Best Case" scenario in which missing values were replaced with values indicating "adherence" (the maximum value, for the MMAS); 2) a "Worst Case" scenario in which missing values were replaced with values indicating "non-adherence" (minimum value, for the MMAS); and 3) a "Middle Case" scenario in which missing values were replaced with the last observation carried forward.

During scheduled follow up visits, patients were asked whether or not they had been recently hospitalized. Data on all reported hospitalizations were collected after obtaining proper consent. To provide a preliminary estimate of the intervention's impact on rehospitalizations, the 30-day

readmission rate among the study cohort was compared to the year 2010 30-day hospital readmission rate at the site from which they were recruited (Rush University Medical Center).

RESULTS

Between January-July 2010; 266 patients with systolic HF were screened (Figure 1); 146 met exclusion criteria; 29 were unreachable; 36 physicians and 22 patients refused participation. Thirty-three patients and their 20 physicians were enrolled; 23 patients (70%) fully completed study follow-up; 1 patient died (3%) and 5 (15%) withdrew. Four patients (12%) were lost to follow up after they had received >80% of their intervention visits. There were no clinically or statistically significant differences in the baseline characteristics of patients who completed the study versus those who did not.

Table 1 summarizes the baseline characteristics of all 33 patients enrolled. Table 2 summarizes outcome data for physicians and patients at study completion. Physician adherence with respect to any given drug class could only be evaluated in patients who have indication for that medication at both baseline and 5 months. As a result, of the 20 physicians that were enrolled, only 13 were evaluable for ACE-I/ARBs, 10 for beta-blockers, and 11 for aldosterone antagonists. At baseline, 69% and 100% of physicians were appropriately prescribing ACE-I/ARB and beta-blockers, respectively, over all of their patients enrolled in the study. At 5-months, this adherence rate increased to 77% of enrolled physicians for ACE-I/ARBs and decreased to 90% for beta-blockers. For aldosterone antagonists, physician adherence was 17% at baseline and dropped to 0% at 5-months. These changes in physician adherence rates were not statistically significant.

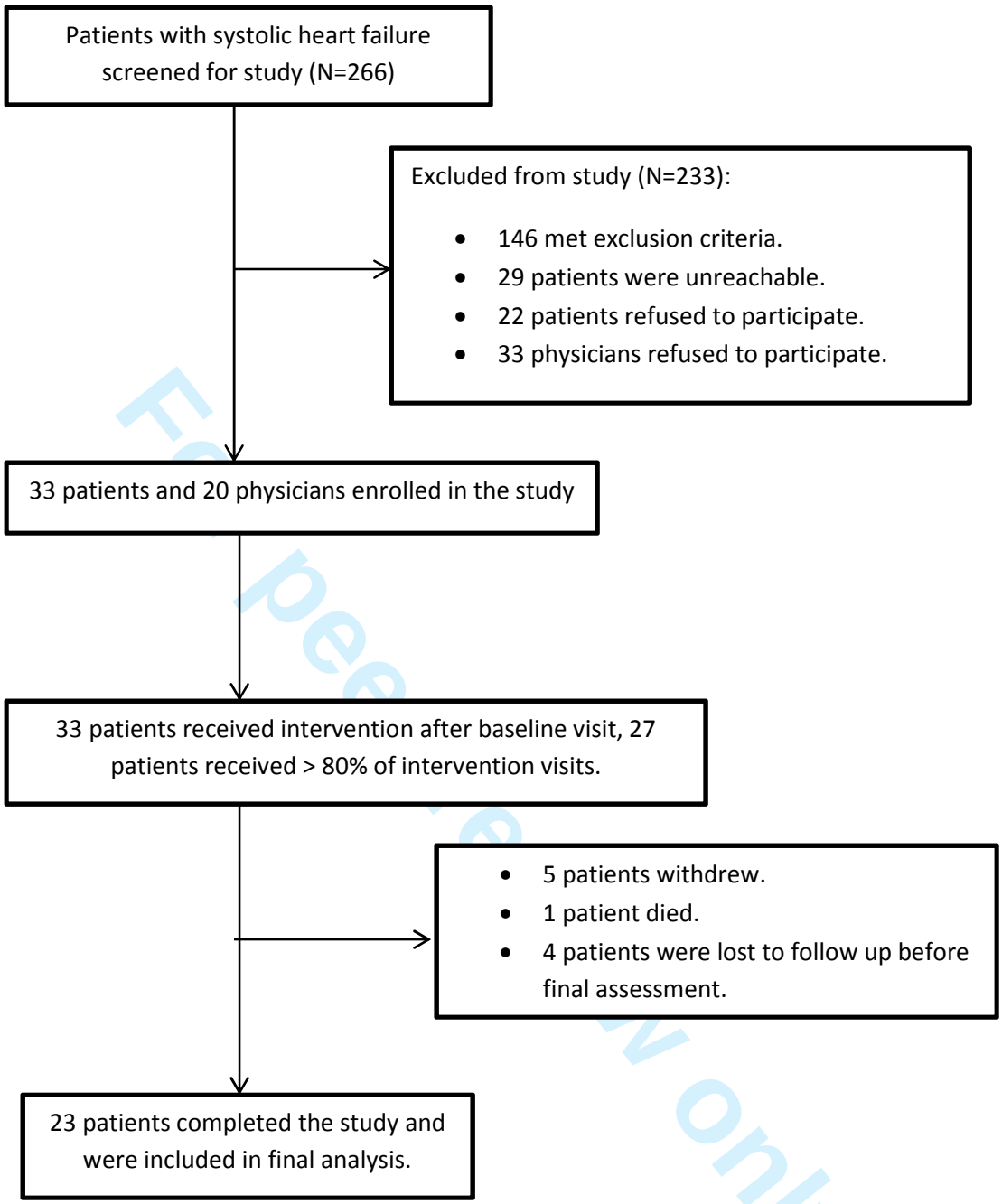

Figure 1. Flow sheet from screening to study completion.

Table 1. Baseline characteristics of enrolled patients.

Total enrolled	33
Demographics	
Age (years), mean ± SD	58 ± 13.0
Women, N (%)	21 (63.6)
Black, N (%)	29 (87.9)
Hispanic, N (%)	3 (9.1)
Age at end of education (years), N (%)	
8-11	10 (30.3)
12	13 (39.4)
13-15	9 (27.3)
17 +	1 (3.0)
Income, N (%)	
$0 - $4,999	2 (6.1)
$5000 - $9,999	9 (27.3)
$10,000 - $14,999	6 (18.2)
$15,000 - $19,999	4 (12.1)
$20,000 - $24,999	6 (18.2)
$25,000 - $29,999	6 (18.2)
Medical History, N (%)	
Current Smoker	3 (9.1)
Past Smoker	6 (18.2)
Has a pacemaker	20 (60.6)
Valvular Heart Disease	6 (18.2)
Hypertension	31 (93.9)
Coronary artery disease	19 (57.6)
Myocardial Infarction	7 (21.2)
Stroke	4 (12.1)
Diabetes Mellitus	18 (54.5)
COPD[1]	2 (6.3)
Asthma	8 (24.2)
Morisky Medication Adherence Scale score of 4; median (Q1,Q3)[#]	3(3,4)
Serum Creatinine (mg/dl), mean ± SD[1]	1.5 (0.8)
Systolic BP (mmHg), mean ± SD	116.6 (16.7)
Diastolic BP (mmHg), mean ± SD	74.1 (11.7)
BP > 130/80, N (%)	5 (15.2)
BMI (Kg/m^2), mean ± SD[1]	33.4 ± 7.7
Dietary Sodium (g), mean ± SD[1]	3.6 ± 1.5
Patient Medication Adherence	
Pill caps returned, N (%)	30 (90.9)
Medications measured, N (%)	
• ACE- Inhibitor	19 (57.6)
• Angiotensin receptor blocker	9 (27.3)
• Beta-blocker	4 (12.1)
• Diuretic	1 (3.0)

Percentage of prescribed drugs taken, median (Q1,Q3)	77.3 (55.4, 88.9)
Participants ≥ 80% adherent[2], N (%)	13 (43.3)

[1]**N=32**
[2]**N=30**
Score of 4 on Morisky Medication Adherence Scale indicates full medication adherence.
BP, Blood Pressure; **BMI,** Body Mass Index.

Table 2. Physician and patient adherence at baseline and 5 months.

	Baseline	**5 Months**
Physician Full Adherence[§]	**N=20**	**N=20**
ACE-I/ARB, N/Total (%)	9/13 (69.2)	10/13 (76.9)
Beta-blockers, N/Total (%)	10/10 (100)	9/10 (90)
Aldosterone antagonists, N/Total (%)	2/12 (16.7)	0/12 (0.0)
***Patient* Adherence**	**N= 33**	**N=23**
% of prescribed drugs taken[‡], median (Q1, Q3)	82.6 (76.0, 94.0)	71.8 (38.3, 79.8)
Participants ≥ 80% adherent[‡], N (%)	10 (43.5)	4 (17.4)
Full adherence by MMAS[†], N (%)	9 (39.1)	15 (65.2)
Sodium intake (mg), median (Q1, Q3)*	3464 (2400, 4125)	2036.5 (1800, 2384)

§ calculated only for those patients in whom the medication was indicated at both baseline and 5 months.
‡ using electronic pill caps N=23
† **MMAS**, Morisky Medication Adherence Scale (0 to 4, where 4 indicates full adherence).
*P <0.01.

For the 23 patients who completed the study, self-reported sodium intake declined by 1192 mg (p<0.01) from baseline. Their pill cap adherence decreased as only 4 out of 23 (17%) patients were adherent at study completion vs. 10 out of 23 (43%) at baseline (p = 0.02). However, the proportion of patients scoring the maximum on the MMAS improved from 9 (39.1%) at baseline to 15 (65.2%) at study completion (p=0.18).

The feasibility of the protocol for patients was assessed as adherence to patient interventions: All patients received atleast 1 intervention visit, 87% (29/33) patients completed at least 4 (80%) of the protocol-required 5 scheduled intervention visits within the first month and 82% (27/33) of participants completed at least 9 (81.8 %) of the protocol-required 11 intervention visits within the 4 month

intervention period. Among all completed visits, 66% were performed in person and the remaining by phone. All physicians received the study-supplied patient summary report within 2 weeks of the data being collected from the patient.

The 33 patients reported a total of 20 hospitalizations during study follow-up, for which medical records were reviewed. The 30-day all-cause readmission rate was 15.2% (5/33), all of which were for HF exacerbation. The 30-day all-cause readmission rate for the hospital in 2010 was 28.3% (143/505).

Sensitivity analyses with respect to missing data at the 5 month study visit revealed that the results presented in Table 2 were fairly robust given the size of the sample. Almost all changes from baseline in physician adherence continued to be non-statistically significant for all three medication classes under all three sensitivity analysis scenarios. The exception was observed under the "Worst Case" scenario, in which an even deeper decrease in adherence with respect to beta-blockers was observed that achieved statistical significance ($p< 0.01$). Sensitivity analyses with respect to patient drug adherence and sodium intake data produced results similar to those presented in Table 2, with the exception of an even greater decrease (that was statistically significant, $p<0.01$) in patient adherence as measured by pill-cap at 5 months under the "Worst Case" scenario and a statistically significant ($p=0.03$) increase in adherence as measured by Morisky score under the "Best Case" scenario.

DISCUSSION

The primary purpose of this pilot study was to assess the feasibility of a novel intervention and gain important insights into issues that may need to be addressed in a larger trial [17]. From that perspective, our pilot study had encouraging results. We were able to deliver the intervention to both physicians and patients. All physicians received appropriate patient-specific feedback in a timely manner

and more than 80% of patients completed at least 80% of their intervention visits. We were able to acquire data on hospitalizations and deaths. These findings suggest that the intervention is amenable to implementation in a larger trial. While a pilot study is not designed to provide definitive insights as to the impact of an intervention, we observed a significant decline in sodium intake and a trend towards a lower rate of HF hospitalizations in study patients compared to general hospital census. Since a high sodium diet is detrimental in HF [3], a sustained reduction in intake could translate into better clinical outcomes and reduced hospitalizations.

Our pill-cap data indicated a trend towards decreased patient adherence post-intervention while data from MMAS indicated otherwise. Although pill cap monitoring is an objective adherence measure, it relies on appropriate use by the patient. The MMAS, on the other hand, is subjective but it has been shown to correlate with cardiovascular outcomes [18]. This discordance between pill-cap and MMAS data may have been due to poor acceptability of pill caps among study participants or due to biased reporting with MMAS, as patients may have learned to provide favourable answers. Furthermore, 7 (30%) subjects who completed study follow-up did not return their electronic pill caps at study intervention, handicapping our ability to draw inferences concerning patient medication adherence and representing a large drawback to this methodology. Use of pill-caps in low income populations poses challenges. Future studies should initiate measures to ensure adequate patient education on their use and return.

Physician adherence to ACE-I/ ARB and beta-blockers was high at baseline with not much room for improvement. For aldosterone antagonists, the prescription rate was low at baseline. Aldosterone

antagonists require careful and regular monitoring of renal function and serum potassium levels. Such rigorous monitoring may be difficult in the challenging patient population that we studied, and could account for low adherence to a certain extent. In a larger trial, if we can ensure timely physician follow up, the prescription of this class of medications to appropriate patients may see a better trend.

Approximately 27% of enrolled patients withdrew or were lost to follow up. Of these, 2 patients completed their interventions but did not return for the post intervention visit; 4 patients refused additional follow up after the baseline visit. Our interactions with these participants revealed that they were experiencing a variety of social, psychological, and emotional challenges that limited their ability to effectively manage their HF. Expanding the scope of the patient-level intervention to provide stronger and more personal support may enhance their ability to self-manage their condition. This could be achieved by utilizing community health workers who are part of a patient's local community and can go directly to their homes, providing support and counselling in important psychosocial areas which undercut delivery of quality medical care. This can potentially lead to better outcomes in this challenging patient population.

CONCLUSION

Dual-level interventions appear to provide a promising strategy for improving outcomes among low-income patients with HF. Our findings indicate potential benefits but also unique challenges in treating patients from disadvantaged backgrounds. Attention to psychosocial and logistical issues that undercut effective medical care may be needed.

CONTRIBUTORSHIP STATEMENT

AM and RD helped with literature review and manuscript preparation. AM helped with data collection. EA and DR helped with data analysis and manuscript preparation. LP and JC helped with study design, conduct and manuscript preparation. JC was responsible for physician intervention and assessing physician adherence to evidence based therapy.

CONFLICTS OF INTEREST

Rami Doukky serves on the advisory board of Astellas Pharma US (Northbrook, IL) and received research funding grants from Astellas Pharma, US. Other authors have no conflicts to report.

FUNDING

Novartis (Basel, Switzerland)

DATA SHARING

No additional data is available.

ACKNOWLEDGEMENTS

Authors would like to acknowledge the efforts of Claudia Eaton for helping with data collection, patient recruitment and patient intervention, and John Kane for helping with data analysis.

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BMJ Open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-006542.R1
Article Type:	Research
Date Submitted by the Author:	24-Oct-2014
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STRENGTHS AND LIMITATIONS OF THE STUDY

Strengths

- The intervention studied is multi-level, in that it targets both physicians and patients simultaneously. Such strategies are potentially more potent than those with a single focus.
- The intervention studied provided individualized feedback to patients and physicians.
- The targeted population is low income heart failure patients; who are disproportionally affected by the heart failure epidemic. Few studies have targeted this population and our pilot study helped us in gaining important insights into this challenging group of patients before conducting larger trial.

Weaknesses

- This is a pilot feasibility study performed at a single medical centre.
- The sample size is small and the duration of follow up was short.

INTRODUCTION

Heart Failure (HF) continues to increase in prevalence with enormous impact on mortality (approximately 50% at 5 years post diagnosis), hospitalizations, and cost of care ($30.7 billion in 2012)[1,2]. The prevalence of HF among those 18 years and older in the United States is projected to increase by 46% in the next 15 years resulting in more than 8 million people with HF by 2030[2]. This reality has created a significant and increasing financial burden on the health care system. Although HF therapies exist with demonstrated benefits on mortality, morbidity, and quality of life [3], these therapies are being underutilized [4,5]. Racial minorities and socio-economically disadvantaged patients have a higher prevalence of HF and higher readmission rates [6,7], thus contributing disproportionately to the HF epidemic.

There is a particular need to develop effective interventions targeting economically disadvantaged patients with HF [8]. Results from our previously published Heart failure Adherence and Retention Trial (HART) suggested that patients with an annual income < $30,000 might benefit from counselling to improve self-management skills as a means to lower mortality and HF hospitalization rates [9]. Since physician adherence to evidence-based therapy has been shown to be suboptimal [5], providing education to physicians could offer additional value. We hypothesized that the use of a dual-level intervention strategy, intervening simultaneously on patients and their physicians, would translate into significantly improved quality of care among low-income HF patients and improve their outcomes. To assess the feasibility of conducting a large trial to study the efficacy of this dual-level strategy, we conducted the Congestive Heart failure Adherence Redesign Trial Pilot (CHART-P) study.

METHODS

The CHART-P was a proof-of-concept, pre-post treatment group only design. The key objective was to assess the feasibility and potential impact of our dual-level intervention for low-income HF patients and their physicians. We would deem the intervention feasible if we were able to achieve 4 objectives: 1) assess patient adherence to prescribed therapies and sodium restriction, 2) deliver the intervention to patients, 3) assess physician adherence to evidence-based HF therapy, and 4) provide timely feed-back to physicians.

Recruitment

The study targeted systolic HF patients with self-reported annual household income < $30,000, as these patients are at high risk for adverse outcomes [7,9]. All participants were recruited while hospitalized at Rush University Medical Center in Chicago, IL. Patients were identified via monitoring of hospital admission logs and the echocardiography laboratory database. New HF admissions with systolic dysfunction (ejection fraction ≤ 50% as measured by echocardiography, radionuclide ventriculography or radiographic contrast ventriculography) were included. Patients having HF with preserved ejection fraction were excluded as there are no set guidelines for managing these patients, deeming the proposed physician level intervention non-feasible. Eligibility of the identified candidates was then determined based on self-reported income. Exclusion criteria included being a cardiac transplant candidate, having severe aortic stenosis, uncontrolled ventricular arrhythmias, BNP <100 pg/ml, severe asthma or COPD, major psychiatric comorbidities, alcohol or drug addiction, haemodialysis treatment, debilitating neurological conditions, severe arthritis, peripheral arterial disease, or having an uncertain 12 month prognosis. Once an eligible patient was identified, it was checked whether their physician is on staff at the medical centre. If the physician was on staff, their consent for study participation was

obtained. Subsequently, the patients were recruited and consented. As this was a proof-of-concept study primarily aimed at assessing feasibility, sample size calculations were not performed.

Interventions

The dual-level intervention targeted both the patients and physicians caring for their HF (a primary care physician or a cardiologist). Physician-level intervention provided them with evidence-based HF guidelines in the form of a brochure summarizing 2005 American College of Cardiology/American Heart Association (ACC/AHA) recommendations with updates from the 2009 guidelines, which were current at the time of our study [10,11]. Physicians also received summary reports of their patient's medication use at baseline, 1 month and 4 months, as obtained from medical records and patient self-report. These reports were accompanied by standardized personal notes from our study cardiologist (JC) outlining patient specific recommendations, such as possible medication changes, that could optimize adherence to evidence-based therapy as defined by class I ACC/AHA recommendations. This being a feasibility study with short follow-up time, we addressed only evidence based medication classes but not optimal medication dosing. No feedback to the personal notes was solicited or tracked.

Patient-level intervention provided to each enrolled patient a tailored HF self-management kit [12]. The kit included brochures featuring patient-friendly HF education material and a variety of self-management tools (scale, measuring bottle, educational materials and pill boxes). Patients were coached on use of the kit during one-on-one contacts timed to occur 3 days post hospital discharge, then once weekly for 1 month and every 2 weeks thereafter for another 3 months, totalling 11 intervention contacts. The patient contacts were performed in-person or via telephone at the patient's

discretion. These contacts were conducted by a trained nurse who followed a problem-solving format in which patients were encouraged to articulate barriers to their adherence and to use a variety of self-management strategies to overcome them [13]. Simple metaphors were used to educate patients about their HF. The heart was equated to a "workhorse" carrying "load" (blood and water) throughout the body via the "road" (arteries). "Water pills" (diuretics) "lighten the load" and angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) "widen the road" making it easier for the workhorse to pump. The importance of adhering to prescribed medications, a low sodium diet, daily weighing, regular physical activity, smoking cessation, and regular follow-up with providers was emphasized. Stress reduction strategies were also discussed. Patient comprehension of these components was assessed at each contact and their knowledge reinforced whenever gaps were identified.

Outcomes, Measures, and Data Analyses

Impact of the dual-level intervention on physician adherence to evidence-based therapy focused specifically on appropriate use of an ACE-I or ARB, beta-blocker and aldosterone antagonist. Data on physician adherence were gathered by chart audit at baseline and 5 months for each patient enrolled. Only patients who remained in the study for the 5 month evaluation were included in these analyses. Physician adherence with respect to a given medication was measured using the proportion of their patients who were prescribed the medication, based upon those for whom it was appropriate according to the 2005 and 2009 ACC/AHA guidelines and as confirmed by the study cardiologist [10,11]. Pre-post change in percentage physician adherence and average physician adherence was assessed via *t*-tests or Wilcoxon tests, as appropriate.

Patient adherence to prescribed therapies was determined at baseline and 5 months, using both electronic pill-cap monitoring (using the MEMS V Trackcap; AARDEX, Zug, Switzerland) and the Morisky Medication Adherence Scale (MMAS) [14]. MMAS provides a score of 0-4, with 4 indicating highest adherence. Each patient's pill-cap use was monitored for either an ACE-I, ARB, beta-blocker, or diuretic, in that order depending upon which of these drugs was prescribed. Patients were instructed to place a month's supply of monitored medication into their pill cap container and use it over the ensuing month. Patient adherence was then measured based on the percentage of time a patient took a pill relative to the prescribed timing. Patients were designated "adherent" if their observed adherence was ≥80% [9,13,15]. The pre-post change in percent adherence was analysed via paired *t*-tests or Wilcoxon tests, as appropriate. The pre-post change in the proportion of patients designated as "adherent" (via pill-cap or MMAS) was analysed via McNemar's exact test. Sodium intake was determined by a food frequency questionnaire specifically designed to assess sodium intake [16] and the pre-post change was analysed via paired Student's *t*-test or Wilcoxon test as appropriate.

Sensitivity analyses were conducted to account for missing data at the 5-month data collection. The analysis consisted of comparing results under 3 different data replacement approaches: 1) a "Best Case" scenario in which missing values were replaced with values indicating "adherence" (the maximum value, for the MMAS); 2) a "Worst Case" scenario in which missing values were replaced with values indicating "non-adherence" (minimum value, for the MMAS); and 3) a "Middle Case" scenario in which missing values were replaced with the last observation carried forward.

During scheduled follow up visits, patients were asked whether or not they had been recently hospitalized. Data on all reported hospitalizations were collected after obtaining proper consent. To provide a preliminary estimate of the intervention's impact on rehospitalizations, the 30-day readmission rate among the study cohort was compared to the year 2010 30-day hospital readmission rate at the site from which they were recruited (Rush University Medical Center).

RESULTS

Between January and July 2010; 266 patients with systolic HF were screened (Figure 1); 146 met exclusion criteria; 29 were unreachable; 22 patients refused to enrol and the physicians for 36 patients refused to participate in the study. Data on reasons for physician refusal were not gathered. Thirty-three patients and their 20 physicians (18 cardiologists and 2 primary care physicians) were enrolled; 23 patients (70%) fully completed study follow-up; 1 patient died (3%) and 5 (15%) withdrew. Four patients (12%) were lost to follow up after they had received >80% of their intervention visits. There were no clinically or statistically significant differences in the baseline characteristics of patients who completed the study versus those who did not.

Table 1 summarizes the baseline characteristics of all 33 patients enrolled. Table 2 summarizes outcome data for physicians and patients at study completion. Physician adherence with respect to any given drug class could only be evaluated in patients who have indication for that medication at both baseline and 5 months. As a result, of the 20 physicians that were enrolled, only 13 were evaluable for ACE-I/ARBs, 10 for beta-blockers, and 11 for aldosterone antagonists. At baseline, 69% and 100% of physicians were appropriately prescribing ACE-I/ARB and beta-blockers, respectively, over all of their patients enrolled in the study. At 5-months, this adherence rate increased to 77% of enrolled physicians

for ACE-I/ARBs and decreased to 90% for beta-blockers. For aldosterone antagonists, physician adherence was 17% at baseline and dropped to 0% at 5-months. These changes in physician adherence rates were not statistically significant.

Table 1. Baseline characteristics of enrolled patients.

Total enrolled	33
Demographics	
Age (years), mean ± SD	58 ± 13.0
Women, N (%)	21 (63.6)
Black, N (%)	29 (87.9)
Hispanic, N (%)	3 (9.1)
Age at end of education (years), N (%)	
8-11	10 (30.3)
12	13 (39.4)
13-15	9 (27.3)
17 +	1 (3.0)
Income, N (%)	
$0 - $4,999	2 (6.1)
$5000 - $9,999	9 (27.3)
$10,000 - $14,999	6 (18.2)
$15,000 - $19,999	4 (12.1)
$20,000 - $24,999	6 (18.2)
$25,000 - $29,999	6 (18.2)
Medical History, N (%)	
Current Smoker	3 (9.1)
Past Smoker	6 (18.2)
Has a pacemaker	20 (60.6)
Valvular Heart Disease	6 (18.2)
Hypertension	31 (93.9)
Coronary artery disease	19 (57.6)
Myocardial Infarction	7 (21.2)
Stroke	4 (12.1)
Diabetes Mellitus	18 (54.5)
COPD[1]	2 (6.3)
Asthma	8 (24.2)
Morisky Medication Adherence Scale score of 4; median (Q1, Q3)[#]	3(3,4)
Serum Creatinine (mg/dl), mean ± SD[1]	1.5 (0.8)
Systolic BP (mmHg), mean ± SD	116.6 (16.7)
Diastolic BP (mmHg), mean ± SD	74.1 (11.7)
BP > 130/80, N (%)	5 (15.2)
BMI (Kg/m^2), mean ± SD[1]	33.4 ± 7.7

Dietary Sodium (g), mean ± SD[1]	3.6 ± 1.5
Patient Medication Adherence	
Pill caps returned, N (%)	30 (90.9)
Medications measured, N (%)	
• ACE- Inhibitor	19 (57.6)
• Angiotensin receptor blocker	9 (27.3)
• Beta-blocker	4 (12.1)
• Diuretic	1 (3.0)
Percentage of prescribed drugs taken, median (Q1,Q3)	77.3 (55.4, 88.9)
Participants ≥ 80% adherent[2], N (%)	13 (43.3)

[1]N=32

[2]N=30

Score of 4 on Morisky Medication Adherence Scale indicates full medication adherence.

BP, Blood Pressure; **BMI,** Body Mass Index.

Table 2. Physician and patient adherence at baseline and 5 months.

	Baseline	**5 Months**
***Physician Full Adherence*[§]**	**N=20**	**N=20**
ACE-I/ARB, N/Total (%)	9/13 (69.2)	10/13 (76.9)
Beta-blockers, N/Total (%)	10/10 (100)	9/10 (90)
Aldosterone antagonists, N/Total (%)	2/12 (16.7)	0/12 (0.0)
***Patient* Adherence**	**N= 33**	**N=23**
% of prescribed drugs taken[‡], median (Q1, Q3)	82.6 (76.0, 94.0)	71.8 (38.3, 79.8)
Participants ≥ 80% adherent[‡], N (%)	10 (43.5)	4 (17.4)
Full adherence by MMAS[†], N (%)	9 (39.1)	15 (65.2)
Sodium intake (mg), median (Q1, Q3)*	3464 (2400, 4125)	2036.5 (1800, 2384)

§ calculated only for those patients in whom the medication was indicated at both baseline and 5 months.

‡ using electronic pill caps N=23

† **MMAS**, Morisky Medication Adherence Scale (0 to 4, where 4 indicates full adherence).

*P <0.01.

For the 23 patients who completed the study, self-reported sodium intake declined by 1192 mg (p<0.01) from baseline. Their pill cap adherence decreased as only 4 out of 23 (17%) patients were adherent at study completion vs. 10 out of 23 (43%) at baseline (p = 0.02). However, the proportion of patients scoring the maximum on the MMAS improved from 9 (39.1%) at baseline to 15 (65.2%) at study completion (p=0.18).

The feasibility of the protocol for patients was assessed as adherence to patient interventions: All patients received atleast 1 intervention visit, 87% (29/33) patients completed at least 4 (80%) of the protocol-required 5 scheduled intervention visits within the first month and 82% (27/33) of participants completed at least 9 (81.8 %) of the protocol-required 11 intervention visits within the 4 month intervention period. Among all completed visits, 66% were performed in person and the remaining by phone. Given the small sample size, it is difficult to comment on the differences in outcomes based on whether a patient received the majority of interventions in person versus over the phone. All physicians received the study-supplied patient summary report within 2 weeks of the data being collected from the patient.

The 33 patients reported a total of 20 hospitalizations during study follow-up, for which medical records were reviewed. The 30-day all-cause readmission rate was 15.2% (5/33), all of which were for HF exacerbation. The 30-day all-cause readmission rate for the hospital in 2010 was 28.3% (143/505).

Sensitivity analyses with respect to missing data at the 5 month study visit revealed that the results presented in Table 2 were fairly robust given the size of the sample. Almost all changes from baseline in physician adherence continued to be non-statistically significant for all three medication classes under all three sensitivity analysis scenarios. The exception was observed under the “Worst Case” scenario, in which an even deeper decrease in adherence with respect to beta-blockers was observed that achieved statistical significance ($p< 0.01$). Sensitivity analyses with respect to patient drug adherence and sodium intake data produced results similar to those presented in Table 2, with the exception of an even greater decrease (that was statistically significant, $p<0.01$) in patient adherence as measured by pill-cap at 5 months under the “Worst Case” scenario and a statistically significant ($p=0.03$) increase in adherence as measured by Morisky score under the “Best Case” scenario.

DISCUSSION

The primary purpose of this pilot study was to assess the feasibility of a novel intervention and gain important insights into issues that may need to be addressed in a larger trial [17]. From that perspective, our pilot study had encouraging results. We were able to deliver the intervention to both physicians and patients. All physicians received appropriate patient-specific feedback in a timely manner and more than 80% of patients completed at least 80% of their intervention visits. We were able to acquire data on hospitalizations and deaths. These findings suggest that the intervention is amenable to implementation in a larger trial. While a pilot study is not designed to provide definitive insights as to the impact of an intervention, we observed a significant decline in sodium intake and a trend towards a lower rate of HF hospitalizations in study patients compared to general hospital census. One of the exploratory aims of our study was to assess changes in sodium intake, as sodium restriction in patients with HF was an area of potential intervention based on prevailing literature at the time [18,19]. In fact, sodium restriction in patients with HF was a class I recommendation based on 2005 and 2009 ACC/AHA guidelines [10,11]. This has been challenged more recently by studies showing adverse outcomes in HF patients with low daily sodium intake[20-22]. Current ACC/ AHA guidelines for HF still recommend sodium restriction, though as a Class IIa recommendation [3].

Our pill-cap data indicated a trend towards decreased patient adherence post-intervention while data from MMAS indicated otherwise. Although pill cap monitoring is an objective adherence measure, it relies on appropriate use by the patient. The MMAS, on the other hand, is subjective but it has been shown to correlate with cardiovascular outcomes [23]. This discordance between pill-cap and MMAS data may have been due to poor acceptability of pill caps among study participants or due to biased reporting with MMAS, as patients may have learned to provide favourable answers.

Furthermore, 7 (30%) subjects who completed study follow-up did not return their electronic pill caps at study intervention, handicapping our ability to draw inferences concerning patient medication adherence and representing a large drawback to this methodology. Use of pill-caps in low-income populations poses challenges. Future studies should initiate measures to ensure adequate patient education on their use and return.

Physician adherence to ACE-I/ ARB and beta-blockers was high at baseline with not much room for improvement. For aldosterone antagonists, the prescription rate was low at baseline. Aldosterone antagonists require careful and regular monitoring of renal function and serum potassium levels. Such rigorous monitoring may be difficult in the challenging patient population that we studied, and could account for low adherence to a certain extent. In a larger trial, if we can ensure timely physician follow up, the prescription of this class of medications to appropriate patients may see a better trend. Recruiting physicians was met with resistance, as some physicians were unwilling to participate. Our dual intervention strategy is relatively novel and with this being a pilot study, resistance from physicians is not surprizing. It is plausible that the physicians who refused to participate may represent a subset of providers who are not receptive to feedback. The impact of physicians' unwillingness to participate on patients' outcome remains unknown. Providing feedback to physicians' regarding their adherence to evidence based therapy is likely to be part of healthcare delivery going forward. These have been implemented in variety of ways such as providing reimbursement incentives, penalties and electronic medical record alerts. In this trial, we chose to provide more personalized and patient-centred feedback. The ideal mechanism and format of most effective feedback needs to be investigated.

Approximately 27% of enrolled patients withdrew or were lost to follow up. Of these, 2 patients completed their interventions but did not return for the post intervention visit; 4 patients refused additional follow up after the baseline visit. Our interactions with these participants revealed that they were experiencing a variety of social, psychological, and emotional challenges that limited their ability to effectively manage their HF. Expanding the scope of the patient-level intervention to provide stronger and more personal support may enhance their ability to self-manage their condition. This could be achieved by utilizing community health workers who are part of a patient's local community and can go directly to their homes, providing support and counselling in important psychosocial areas which undercut delivery of quality medical care. This can potentially lead to better outcomes in this challenging patient population.

Lessons Learned

Given our experiences in the CHART pilot trial we implemented the following adjustments in the large Congestive Heart Failure Adherence Redesign Trial (CHART) [NCT01698242]: 1) we decided to approach the physicians before the patients, which streamlined the recruitment process and guided appropriate resource utilization; 2) patients were screened more rigorously to avoid early dropouts; 3) we decided to provide the patient level intervention at the subjects' home, rather than at a clinic, utilizing community health workers who are members of the patients' own community and can cross cultural and logistical barriers encountered in delivering care for low-income patients; 4) we implemented reminders and incentives to enhance the return of the pill-cap bottles in order to ensure completeness of medication adherence data; 5) we enhanced the physician level intervention by providing access to online educational modules and simplifying physician feedback to include graphically presented adherence data.

CONCLUSION

Dual-level interventions appear to provide a promising strategy for improving outcomes among low-income patients with HF. Our findings indicate potential benefits but also unique challenges in treating patients from disadvantaged backgrounds. Attention to psychosocial and logistical issues that undercut effective medical care may be needed.

CONTRIBUTORSHIP STATEMENT

AM and RD contributed with literature review and manuscript preparation. AM assisted with data collection. EA and DR were responsible for data analysis and assisted with manuscript preparation. LP and JC were responsible for study design and conduct, and supervised manuscript preparation. JC was responsible for physician intervention and assessing physician adherence to evidence based therapy.

CONFLICTS OF INTEREST

Rami Doukky serves on the advisory board of Astellas Pharma US (Northbrook, IL) and received research funding grants from Astellas Pharma, US. Other authors have no conflicts to report.

FUNDING

Funding provided by Novartis (Basel, Switzerland). The sponsor had no role in the study design and execution, data analysis, or manuscript preparation.

DATA SHARING

No additional data is available.

ACKNOWLEDGEMENTS

Authors would like to acknowledge the efforts of Claudia Eaton for helping with data collection, patient recruitment and patient intervention, and John Kane for helping with data analysis.

Figure legends

Figure 1. Flow sheet from screening to study completion.

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Congestive Heart Failure Adherence Redesign Trial: A Pilot Study

Short Title: CHART-P Study

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Word Count: Abstract 300; Text 2980

Key words: Heart Failure, Patient Education, Physician Education, Adherence to evidence based HF therapy, Multi- Level Intervention.

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ABSTRACT

Objective: Heart failure (HF) continues to be a leading cause of hospital admissions, particularly in underserved patients. We hypothesized that providing individualized self-management support to patients and feedback on use of evidence-based HF therapies (EBT) to physicians could lead to improvements in care and decrease hospitalizations. To assess the feasibility of conducting a larger trial testing the efficacy of this dual-level intervention, we conducted the Congestive Heart failure Adherence Redesign Trial Pilot (CHART-P), a proof-of-concept, quasi-experimental, feasibility pilot study.

Setting: A large tertiary care medical centre in Chicago.

Participants: Low-income patients (<$30,000/year) hospitalized for exacerbation of systolic HF (ejection fraction ≤ 50%) and their physicians. Twenty physicians and 33 patients were enrolled, 23 patients completed the study.

Interventions: Physicians received HF guidelines and periodic individualized feedback on their adherence to EBT. Patients received HF education, support and self-management training for diet and medication adherence by a trained nurse through 11 interactive sessions over a 4-month period. Evaluations were conducted pre-enrolment and 1 month post intervention completion.

Outcome measures: Feasibility was assessed by the ability to deliver intervention to patients and physicians. Exploratory outcomes included changes in medication and sodium intake for patients and adherence to EBT for physicians.

Results: Eighty seven percent and 82% of patients received >80% of interventions at 1 month and by study completion, respectively. Median sodium intake declined (3.5 vs 2.0 g; p<0.01). There was no statistically significant change in medication adherence based on electronic pill cap monitoring or Morisky Medication Adherence Scale (MMAS); however, there was a trend towards improved adherence based on MMAS. All physicians received timely intervention.

Conclusions: This pilot study demonstrated that the protocol was feasible. It provided important insights about the need for intervention and the difficulties in treating patients with a variety of psychosocial problems that undercut their effective care.

STRENGTHS AND LIMITATIONS OF THE STUDY

Strengths

- The intervention studied is multi-level, in that it targets both physicians and patients simultaneously. Such strategies are potentially more potent than those with a single focus.
- The intervention studied provided individualized feedback to patients and physicians.
- The targeted population is low income heart failure patients; who are disproportionally affected by the heart failure epidemic. Few studies have targeted this population and our pilot study helped us in gaining important insights into this challenging group of patients before conducting larger trial.

Weaknesses

- This is a pilot feasibility study performed at a single medical centre.
- The sample size is small and the duration of follow up was short.

INTRODUCTION

Heart Failure (HF) continues to increase in prevalence with enormous impact on mortality (approximately 50% at 5 years post diagnosis), hospitalizations, and cost of care ($30.7 billion in 2012)[1,2]. The prevalence of HF among those 18 years and older in the United States is projected to increase by 46% in the next 15 years resulting in more than 8 million people with HF by 2030[2]. This reality has created a significant and increasing financial burden on the health care system. Although HF therapies exist with demonstrated benefits on mortality, morbidity, and quality of life [3], these therapies are being underutilized [4,5]. Racial minorities and socio-economically disadvantaged patients have a higher prevalence of HF and higher readmission rates [6,7], thus contributing disproportionately to the HF epidemic.

There is a particular need to develop effective interventions targeting economically disadvantaged patients with HF [8]. Results from our previously published Heart failure Adherence and Retention Trial (HART) suggested that patients with an annual income < $30,000 might benefit from counselling to improve self-management skills as a means to lower mortality and HF hospitalization rates [9]. Since physician adherence to evidence-based therapy has been shown to be suboptimal [5], providing education to physicians could offer additional value. We hypothesized that the use of a dual-level intervention strategy, intervening simultaneously on patients and their physicians, would translate into significantly improved quality of care among low-income HF patients and improve their outcomes. To assess the feasibility of conducting a large trial to study the efficacy of this dual-level strategy, we conducted the Congestive Heart failure Adherence Redesign Trial Pilot (CHART-P) study.

METHODS

The CHART-P was a proof-of-concept, pre-post treatment group only design. The key objective was to assess the feasibility and potential impact of our dual-level intervention for low-income HF patients and their physicians. We would deem the intervention feasible if we were able to achieve 4 objectives: 1) assess patient adherence to prescribed therapies and sodium restriction, 2) deliver the intervention to patients, 3) assess physician adherence to evidence-based HF therapy, and 4) provide timely feed-back to physicians.

Recruitment

The study targeted systolic HF patients with self-reported annual household income < $30,000, as these patients are at high risk for adverse outcomes [7,9]. All participants were recruited while hospitalized at Rush University Medical Center in Chicago, IL. Patients were identified via monitoring of hospital admission logs and the echocardiography laboratory database. New HF admissions with systolic dysfunction (ejection fraction ≤ 50% as measured by echocardiography, radionuclide ventriculography or radiographic contrast ventriculography) were included. Patients having HF with preserved ejection fraction were excluded as there are no set guidelines for managing these patients, deeming the proposed physician level intervention non-feasible. Eligibility of the identified candidates was then determined based on self-reported income. Exclusion criteria included being a cardiac transplant candidate, having severe aortic stenosis, uncontrolled ventricular arrhythmias, BNP <100 pg/ml, severe asthma or COPD, major psychiatric comorbidities, alcohol or drug addiction, haemodialysis treatment, debilitating neurological conditions, severe arthritis, peripheral arterial disease, or having an uncertain 12 month prognosis. Once an eligible patient was identified, it was checked whether their physician is on staff at the medical centre. If the physician was on staff, their consent for study participation was

obtained. Subsequently, the patients were recruited and consented. As this was a proof-of-concept study primarily aimed at assessing feasibility, sample size calculations were not performed.

Interventions

The dual-level intervention targeted both the patients and physicians caring for their HF (a primary care physician or a cardiologist). Physician-level intervention provided them with evidence-based HF guidelines in the form of a brochure summarizing 2005 American College of Cardiology/American Heart Association (ACC/AHA) recommendations with updates from the 2009 guidelines, which were current at the time of our study [10,11]. Physicians also received summary reports of their patient's medication use at baseline, 1 month and 4 months, as obtained from medical records and patient self-report. These reports were accompanied by standardized personal notes from our study cardiologist (JC) outlining patient specific recommendations, such as possible medication changes, that could optimize adherence to evidence-based therapy as defined by class I ACC/AHA recommendations. This being a feasibility study with short follow-up time, we addressed only evidence based medication classes but not optimal medication dosing. No feedback to the personal notes was solicited or tracked.

Patient-level intervention provided to each enrolled patient a tailored HF self-management kit [12]. The kit included brochures featuring patient-friendly HF education material and a variety of self-management tools (scale, measuring bottle, educational materials and pill boxes). Patients were coached on use of the kit during one-on-one contacts timed to occur 3 days post hospital discharge, then once weekly for 1 month and every 2 weeks thereafter for another 3 months, totalling 11 intervention contacts. The patient contacts were performed in-person or via telephone at the patient's

discretion. These contacts were conducted by a trained nurse who followed a problem-solving format in which patients were encouraged to articulate barriers to their adherence and to use a variety of self-management strategies to overcome them [13]. Simple metaphors were used to educate patients about their HF. The heart was equated to a "workhorse" carrying "load" (blood and water) throughout the body via the "road" (arteries). "Water pills" (diuretics) "lighten the load" and angiotensin converting enzyme inhibitor (ACE-I) or angiotensin receptor blocker (ARB) "widen the road" making it easier for the workhorse to pump. The importance of adhering to prescribed medications, a low sodium diet, daily weighing, regular physical activity, smoking cessation, and regular follow-up with providers was emphasized. Stress reduction strategies were also discussed. Patient comprehension of these components was assessed at each contact and their knowledge reinforced whenever gaps were identified.

Outcomes, Measures, and Data Analyses

Impact of the dual-level intervention on physician adherence to evidence-based therapy focused specifically on appropriate use of an ACE-I or ARB, beta-blocker and aldosterone antagonist. Data on physician adherence were gathered by chart audit at baseline and 5 months for each patient enrolled. Only patients who remained in the study for the 5 month evaluation were included in these analyses. Physician adherence with respect to a given medication was measured using the proportion of their patients who were prescribed the medication, based upon those for whom it was appropriate according to the 2005 and 2009 ACC/AHA guidelines and as confirmed by the study cardiologist [10,11]. Pre-post change in percentage physician adherence and average physician adherence was assessed via *t*-tests or Wilcoxon tests, as appropriate.

Patient adherence to prescribed therapies was determined at baseline and 5 months, using both electronic pill-cap monitoring (using the MEMS V Trackcap; AARDEX, Zug, Switzerland) and the Morisky Medication Adherence Scale (MMAS) [14]. MMAS provides a score of 0-4, with 4 indicating highest adherence. Each patient's pill-cap use was monitored for either an ACE-I, ARB, beta-blocker, or diuretic, in that order depending upon which of these drugs was prescribed. Patients were instructed to place a month's supply of monitored medication into their pill cap container and use it over the ensuing month. Patient adherence was then measured based on the percentage of time a patient took a pill relative to the prescribed timing. Patients were designated "adherent" if their observed adherence was ≥80% [9,13,15]. The pre-post change in percent adherence was analysed via paired *t*-tests or Wilcoxon tests, as appropriate. The pre-post change in the proportion of patients designated as "adherent" (via pill-cap or MMAS) was analysed via McNemar's exact test. Sodium intake was determined by a food frequency questionnaire specifically designed to assess sodium intake [16] and the pre-post change was analysed via paired Student's *t*-test or Wilcoxon test as appropriate.

Sensitivity analyses were conducted to account for missing data at the 5-month data collection. The analysis consisted of comparing results under 3 different data replacement approaches: 1) a "Best Case" scenario in which missing values were replaced with values indicating "adherence" (the maximum value, for the MMAS); 2) a "Worst Case" scenario in which missing values were replaced with values indicating "non-adherence" (minimum value, for the MMAS); and 3) a "Middle Case" scenario in which missing values were replaced with the last observation carried forward.

During scheduled follow up visits, patients were asked whether or not they had been recently hospitalized. Data on all reported hospitalizations were collected after obtaining proper consent. To provide a preliminary estimate of the intervention's impact on rehospitalizations, the 30-day readmission rate among the study cohort was compared to the year 2010 30-day hospital readmission rate at the site from which they were recruited (Rush University Medical Center).

RESULTS

Between January and July 2010; 266 patients with systolic HF were screened (Figure 1); 146 met exclusion criteria; 29 were unreachable; 22 patients refused to enrol and the physicians for 36 patients refused to participate in the study. Data on reasons for physician refusal were not gathered. Thirty-three patients and their 20 physicians (18 cardiologists and 2 primary care physicians) were enrolled; 23 patients (70%) fully completed study follow-up; 1 patient died (3%) and 5 (15%) withdrew. Four patients (12%) were lost to follow up after they had received >80% of their intervention visits. There were no clinically or statistically significant differences in the baseline characteristics of patients who completed the study versus those who did not.

Table 1 summarizes the baseline characteristics of all 33 patients enrolled. Table 2 summarizes outcome data for physicians and patients at study completion. Physician adherence with respect to any given drug class could only be evaluated in patients who have indication for that medication at both baseline and 5 months. As a result, of the 20 physicians that were enrolled, only 13 were evaluable for ACE-I/ARBs, 10 for beta-blockers, and 11 for aldosterone antagonists. At baseline, 69% and 100% of physicians were appropriately prescribing ACE-I/ARB and beta-blockers, respectively, over all of their patients enrolled in the study. At 5-months, this adherence rate increased to 77% of enrolled physicians

for ACE-I/ARBs and decreased to 90% for beta-blockers. For aldosterone antagonists, physician adherence was 17% at baseline and dropped to 0% at 5-months. These changes in physician adherence rates were not statistically significant.

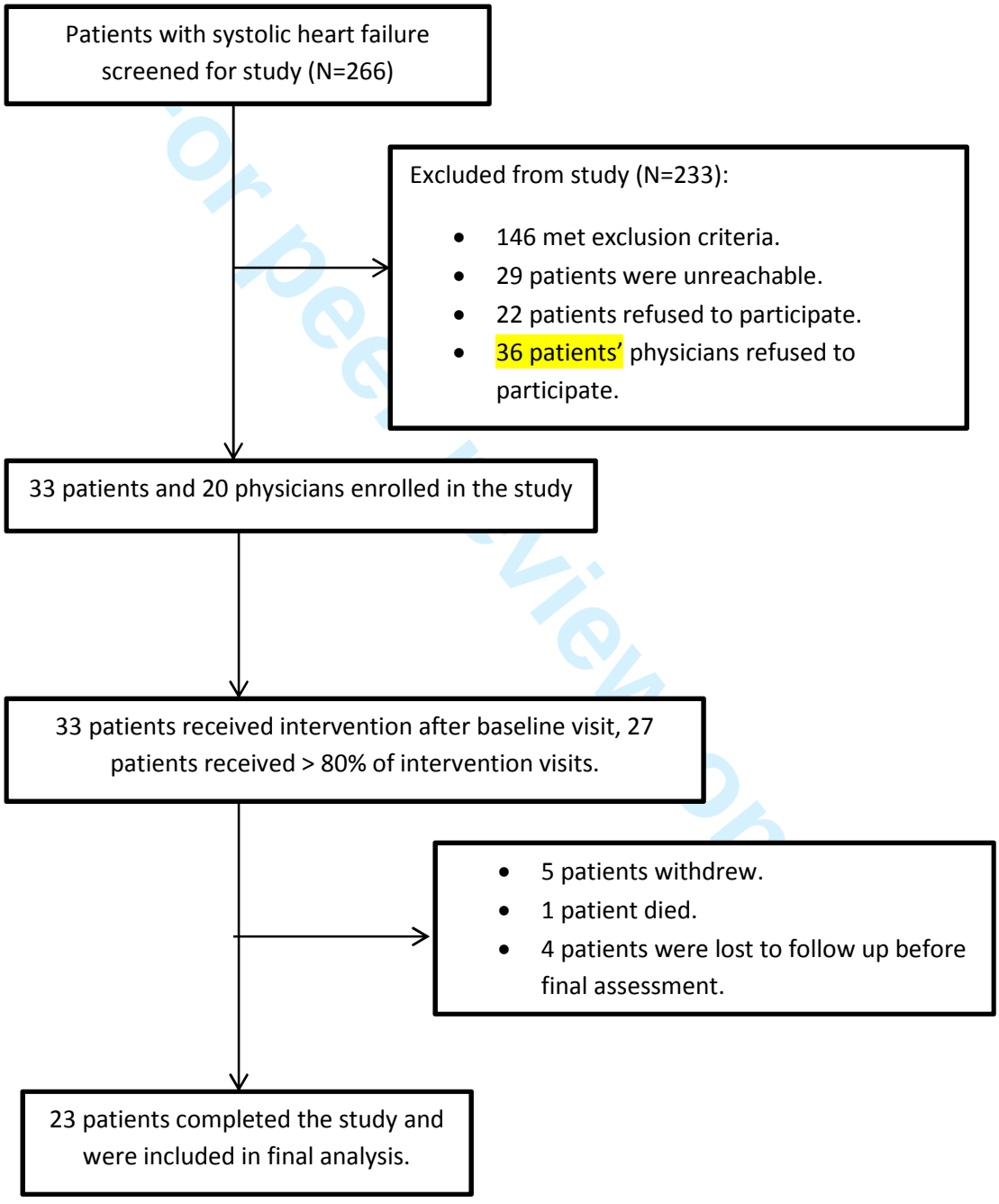

Figure 1. Flow sheet from screening to study completion.

Table 1. Baseline characteristics of enrolled patients.

Total enrolled	33
Demographics	
Age (years), mean ± SD	58 ± 13.0
Women, N (%)	21 (63.6)
Black, N (%)	29 (87.9)
Hispanic, N (%)	3 (9.1)
Age at end of education (years), N (%)	
8-11	10 (30.3)
12	13 (39.4)
13-15	9 (27.3)
17 +	1 (3.0)
Income, N (%)	
$0 - $4,999	2 (6.1)
$5000 - $9,999	9 (27.3)
$10,000 - $14,999	6 (18.2)
$15,000 - $19,999	4 (12.1)
$20,000 - $24,999	6 (18.2)
$25,000 - $29,999	6 (18.2)
Medical History, N (%)	
Current Smoker	3 (9.1)
Past Smoker	6 (18.2)
Has a pacemaker	20 (60.6)
Valvular Heart Disease	6 (18.2)
Hypertension	31 (93.9)
Coronary artery disease	19 (57.6)
Myocardial Infarction	7 (21.2)
Stroke	4 (12.1)
Diabetes Mellitus	18 (54.5)
COPD[1]	2 (6.3)
Asthma	8 (24.2)
Morisky Medication Adherence Scale score of 4; median (Q1, Q3)[#]	3(3,4)
Serum Creatinine (mg/dl), mean ± SD[1]	1.5 (0.8)
Systolic BP (mmHg), mean ± SD	116.6 (16.7)
Diastolic BP (mmHg), mean ± SD	74.1 (11.7)
BP > 130/80, N (%)	5 (15.2)
BMI (Kg/m^2), mean ± SD[1]	33.4 ± 7.7
Dietary Sodium (g), mean ± SD[1]	3.6 ± 1.5
Patient Medication Adherence	
Pill caps returned, N (%)	30 (90.9)
Medications measured, N (%)	
• ACE- Inhibitor	19 (57.6)
• Angiotensin receptor blocker	9 (27.3)
• Beta-blocker	4 (12.1)
• Diuretic	1 (3.0)

Percentage of prescribed drugs taken, median (Q1,Q3)	77.3 (55.4, 88.9)
Participants ≥ 80% adherent[2], N (%)	13 (43.3)

[1]**N=32**
[2]**N=30**
Score of 4 on Morisky Medication Adherence Scale indicates full medication adherence.
BP, Blood Pressure; **BMI,** Body Mass Index.

Table 2. Physician and patient adherence at baseline and 5 months.

	Baseline	**5 Months**
Physician Full Adherence[§]	**N=20**	**N=20**
ACE-I/ARB, N/Total (%)	9/13 (69.2)	10/13 (76.9)
Beta-blockers, N/Total (%)	10/10 (100)	9/10 (90)
Aldosterone antagonists, N/Total (%)	2/12 (16.7)	0/12 (0.0)
***Patient* Adherence**	**N= 33**	**N=23**
% of prescribed drugs taken[‡], median (Q1, Q3)	82.6 (76.0, 94.0)	71.8 (38.3, 79.8)
Participants ≥ 80% adherent[‡], N (%)	10 (43.5)	4 (17.4)
Full adherence by MMAS[†], N (%)	9 (39.1)	15 (65.2)
Sodium intake (mg), median (Q1, Q3)*	3464 (2400, 4125)	2036.5 (1800, 2384)

§ calculated only for those patients in whom the medication was indicated at both baseline and 5 months.
‡ using electronic pill caps N=23
† **MMAS**, Morisky Medication Adherence Scale (0 to 4, where 4 indicates full adherence).
*P <0.01.

For the 23 patients who completed the study, self-reported sodium intake declined by 1192 mg (p<0.01) from baseline. Their pill cap adherence decreased as only 4 out of 23 (17%) patients were adherent at study completion vs. 10 out of 23 (43%) at baseline (p = 0.02). However, the proportion of patients scoring the maximum on the MMAS improved from 9 (39.1%) at baseline to 15 (65.2%) at study completion (p=0.18).

The feasibility of the protocol for patients was assessed as adherence to patient interventions: All patients received atleast 1 intervention visit, 87% (29/33) patients completed at least 4 (80%) of the protocol-required 5 scheduled intervention visits within the first month and 82% (27/33) of participants completed at least 9 (81.8 %) of the protocol-required 11 intervention visits within the 4 month

intervention period. Among all completed visits, 66% were performed in person and the remaining by phone. Given the small sample size, it is difficult to comment on the differences in outcomes based on whether a patient received the majority of interventions in person versus over the phone. All physicians received the study-supplied patient summary report within 2 weeks of the data being collected from the patient.

The 33 patients reported a total of 20 hospitalizations during study follow-up, for which medical records were reviewed. The 30-day all-cause readmission rate was 15.2% (5/33), all of which were for HF exacerbation. The 30-day all-cause readmission rate for the hospital in 2010 was 28.3% (143/505).

Sensitivity analyses with respect to missing data at the 5 month study visit revealed that the results presented in Table 2 were fairly robust given the size of the sample. Almost all changes from baseline in physician adherence continued to be non-statistically significant for all three medication classes under all three sensitivity analysis scenarios. The exception was observed under the "Worst Case" scenario, in which an even deeper decrease in adherence with respect to beta-blockers was observed that achieved statistical significance ($p< 0.01$). Sensitivity analyses with respect to patient drug adherence and sodium intake data produced results similar to those presented in Table 2, with the exception of an even greater decrease (that was statistically significant, $p<0.01$) in patient adherence as measured by pill-cap at 5 months under the "Worst Case" scenario and a statistically significant ($p=0.03$) increase in adherence as measured by Morisky score under the "Best Case" scenario.

DISCUSSION

The primary purpose of this pilot study was to assess the feasibility of a novel intervention and gain important insights into issues that may need to be addressed in a larger trial [17]. From that perspective, our pilot study had encouraging results. We were able to deliver the intervention to both

physicians and patients. All physicians received appropriate patient-specific feedback in a timely manner and more than 80% of patients completed at least 80% of their intervention visits. We were able to acquire data on hospitalizations and deaths. These findings suggest that the intervention is amenable to implementation in a larger trial. While a pilot study is not designed to provide definitive insights as to the impact of an intervention, we observed a significant decline in sodium intake and a trend towards a lower rate of HF hospitalizations in study patients compared to general hospital census. One of the exploratory aims of our study was to assess changes in sodium intake, as sodium restriction in patients with HF was an area of potential intervention based on prevailing literature at the time [18,19]. In fact, sodium restriction in patients with HF was a class I recommendation based on 2005 and 2009 ACC/AHA guidelines [10,11]. This has been challenged more recently by studies showing adverse outcomes in HF patients with low daily sodium intake[20-22]. Current ACC/ AHA guidelines for HF still recommend sodium restriction, though as a Class IIa recommendation [3].

Our pill-cap data indicated a trend towards decreased patient adherence post-intervention while data from MMAS indicated otherwise. Although pill cap monitoring is an objective adherence measure, it relies on appropriate use by the patient. The MMAS, on the other hand, is subjective but it has been shown to correlate with cardiovascular outcomes [23]. This discordance between pill-cap and MMAS data may have been due to poor acceptability of pill caps among study participants or due to biased reporting with MMAS, as patients may have learned to provide favourable answers. Furthermore, 7 (30%) subjects who completed study follow-up did not return their electronic pill caps at study intervention, handicapping our ability to draw inferences concerning patient medication adherence and representing a large drawback to this methodology. Use of pill-caps in low-income

populations poses challenges. Future studies should initiate measures to ensure adequate patient education on their use and return.

Physician adherence to ACE-I/ ARB and beta-blockers was high at baseline with not much room for improvement. For aldosterone antagonists, the prescription rate was low at baseline. Aldosterone antagonists require careful and regular monitoring of renal function and serum potassium levels. Such rigorous monitoring may be difficult in the challenging patient population that we studied, and could account for low adherence to a certain extent. In a larger trial, if we can ensure timely physician follow up, the prescription of this class of medications to appropriate patients may see a better trend. Recruiting physicians was met with resistance, as some physicians were unwilling to participate. Our dual intervention strategy is relatively novel and with this being a pilot study, resistance from physicians is not surprizing. It is plausible that the physicians who refused to participate may represent a subset of providers who are not receptive to feedback. The impact of physicians' unwillingness to participate on patients' outcome remains unknown. Providing feedback to physicians' regarding their adherence to evidence based therapy is likely to be part of healthcare delivery going forward. These have been implemented in variety of ways such as providing reimbursement incentives, penalties and electronic medical record alerts. In this trial, we chose to provide more personalized and patient-centred feedback. The ideal mechanism and format of most effective feedback needs to be investigated.

Approximately 27% of enrolled patients withdrew or were lost to follow up. Of these, 2 patients completed their interventions but did not return for the post intervention visit; 4 patients refused additional follow up after the baseline visit. Our interactions with these participants revealed that they

were experiencing a variety of social, psychological, and emotional challenges that limited their ability to effectively manage their HF. Expanding the scope of the patient-level intervention to provide stronger and more personal support may enhance their ability to self-manage their condition. This could be achieved by utilizing community health workers who are part of a patient's local community and can go directly to their homes, providing support and counselling in important psychosocial areas which undercut delivery of quality medical care. This can potentially lead to better outcomes in this challenging patient population.

Lessons Learned

Given our experiences in the CHART pilot trial we implemented the following adjustments in the large Congestive Heart Failure Adherence Redesign Trial (CHART) [NCT01698242]: 1) we decided to approach the physicians before the patients, which streamlined the recruitment process and guided appropriate resource utilization; 2) patients were screened more rigorously to avoid early dropouts; 3) we decided to provide the patient level intervention at the subjects' home, rather than at a clinic, utilizing community health workers who are members of the patients' own community and can cross cultural and logistical barriers encountered in delivering care for low-income patients; 4) we implemented reminders and incentives to enhance the return of the pill-cap bottles in order to ensure completeness of medication adherence data; 5) we enhanced the physician level intervention by providing access to online educational modules and simplifying physician feedback to include graphically presented adherence data.

CONCLUSION

Dual-level interventions appear to provide a promising strategy for improving outcomes among low-income patients with HF. Our findings indicate potential benefits but also unique challenges in treating patients from disadvantaged backgrounds. Attention to psychosocial and logistical issues that undercut effective medical care may be needed.

CONTRIBUTORSHIP STATEMENT

AM and RD contributed with literature review and manuscript preparation. AM assisted with data collection. EA and DR were responsible for data analysis and assisted with manuscript preparation. LP and JC were responsible for study design and conduct, and supervised manuscript preparation. JC was responsible for physician intervention and assessing physician adherence to evidence based therapy.

CONFLICTS OF INTEREST

Rami Doukky serves on the advisory board of Astellas Pharma US (Northbrook, IL) and received research funding grants from Astellas Pharma, US. Other authors have no conflicts to report.

FUNDING

Funding provided by Novartis (Basel, Switzerland). The sponsor had no role in the study design and execution, data analysis, or manuscript preparation.

DATA SHARING

No additional data is available.

ACKNOWLEDGEMENTS

Authors would like to acknowledge the efforts of Claudia Eaton for helping with data collection, patient recruitment and patient intervention, and John Kane for helping with data analysis.

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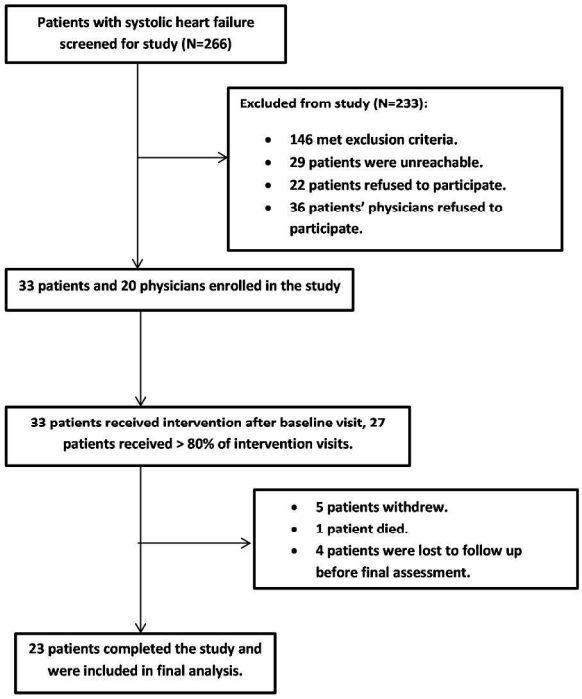

Figure 1. Flow sheet from screening to study completion.
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