

# Influence of self-management on patient-reported outcomes for individuals with chronic heart failure: a multilevel model approach from a longitudinal study

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## Research article

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# Abstract

**Purpose:** Self-management is highly heterogeneous in quality of life in individuals with chronic heart failure. The distributions, the extents of self-management strategies and changes over time of these may play a role in this uncertainty. The aim of this study was to identify clinically meaningful strategies that improve quality of life reflected by patient-reported outcomes in those with chronic heart failure.

**Methods:** A multicenter, prospective cohort study of 555 patients with heart failure were enrolled from May 2017 to May 2019. Self-management advice was provided in written form at discharge to all patients. Information regarding chronic heart failure in patient-reported outcomes and self-management were collected during follow-up. Multilevel models were applied to dynamically evaluate the effects of self-management strategies for patient-reported outcome of chronic heart failure (CHF-PRO) scores, as well as its physical and psychological domains. Minimal clinically important difference was introduced to further evaluate clinical significance.

**Results:** Scores for CHF-PRO improved significantly after discharge. A regular schedule, avoidance of over-eating, and a low-sodium diet increased scores on patient-reported outcomes, including overall scores and physical and psychological scores. In addition, exercise improved patient-reported outcomes and its physical domain. The use of angiotensin-converting enzyme inhibitors also increased physical scores. Among these variables, a regular daily schedule and avoidance of over-eating almost every day reached clinical significance for CHF-PRO scores, as well as its physical and psychological domains.

**Conclusions:** Self-management, especially the avoidance of over-eating and maintenance of a regular schedule will improve patient-reported outcomes in those with chronic heart failure.

**Trial registration:** 2018LL128, January 2, 2018.

## Background

Chronic heart failure (CHF) is the terminal and most severe stage of heart disease, which affects 1.5% to 2% of the adult population in developed countries [1], and 0.9% of the population aged 35 to 74 years in China [2]. Patients with CHF suffer from poor quality of life (QoL) and prognosis. The 12-month mortality and re-hospitalization rates of CHF reach 17% and 44%, respectively [3]. Improving outcomes in patients with CHF is an important social problem that requires urgent attention. Self-management is very important to CHF. The 2019 American College of Cardiology Expert Consensus highlighted that self-management strategies can improve outcomes in patients with heart failure (HF) and that the implementation of such strategies is encouraged [4]. Self-management has been proven to be effective in decreasing hospitalization and death rates in patients with CHF [5]. However, in terms of QoL, self-management is highly heterogeneous [6,7].

Self-management involves all aspects of a patient's activities of daily living, including medication adherence, a reasonable diet, limiting alcohol consumption, staying physically active, avoiding tobacco

use, and maintenance of a regular daily routine, among others [3]. Self-management strategies have attracted significant attention from investigators. However, the most useful of all proposed strategies, and the extent that results in meaningful clinical changes, have not been identified in previous studies. Moreover, changes in strategies and patient conditions over time should not be ignored. All of these may play a role in the uncertainty of the effect of self-management on QoL [6,7]. Multilevel models could solve time-dependent data and discover potential relationship between multiple dependent variables. They are suitable for our cohort study which focused on roles of dynamic changes in self-management strategies to changes in QoL. Patient-reported outcome of chronic heart failure (CHF-PRO) was applied to evaluate QoL of patients with CHF in this study [8, 9]. Therefore, this study focused on self-management after discharge and applied multilevel models in an attempt to determine effective self-management strategies to improve CHF-PRO scores. Moreover, minimal clinically important difference (MCID) was applied to identify clinically meaningful strategies in this study [10].

## Methods

### Participants

Patients from three medical centers in the Shanxi province of China were enrolled according to predefined inclusion and exclusion criteria. The inclusion criteria were: age  $\geq 18$  years; diagnosed with HF according to current guidelines [3]; New York Heart Association (NYHA) functional class II-IV; and receipt of HF therapy in the past month. Patients who experienced acute cardiovascular events in the past 2 months, had a life expectancy of  $< 1$  year, could not understand or complete the questionnaire due to language barriers or intellectual disabilities, and those who refused to participate in this project were excluded.

### Procedure and data collection

The present investigation was a multicenter, prospective cohort study performed from May 2017 to May 2019. Self-management advice, which included medication use, regular schedule, keeping warm, dietary instructions, health education, smoking cessation, temperance, and exercise, was provided in written form to the all of the participants at discharge. Therefore, this was an observation study rather than an intervention study. Dietary instructions included a low-sodium diet (LSD), low-fat diet, and the avoidance of over-eating. Among these strategies, a regular schedule was defined as maintaining relatively fixed sleep and wake times, and LSD intake  $< 5$  g of salt per day.

Information regarding baseline data, self-administered questionnaire, and CHF-PRO scores were collected during hospitalization. All participants were followed-up at 1, 3, and 6 months after discharge in face-to-face consultations or telephone follow-up to obtain information regarding the self-administered questionnaire and CHF-PRO scores [9]. To ensure quality, all questionnaires were administered by professionally trained individuals.

Baseline information included patient age, sex, height, weight, marital status, education, annual income, family history of cardiovascular disease, NYHA functional class, blood pressure, and complications. The

Charlson comorbidity index was applied to assess complications.

The self-administered questionnaire was developed to assess self-management. The questionnaire contained all strategies provided at discharge as mentioned above, with responses scored on a 5-point Likert, as follows: 0 (never happens); 1 (happens occasionally); 2 (happens half of the time); 3 (happens often); and 4 (happens every day).

The CHF-PRO was developed by the authors' research group and adopted in this study. This questionnaire contains 57 items, 12 subdomains, and 4 domains, which consisted of physical, psychological, social, and therapeutic domains [9]. Patients responded to each item on a 5-point Likert scale to reflect how often they had experienced each issue.

## Statistical analysis

Continuous variables are expressed as mean  $\pm$  standard deviation (SD) or median (interquartile range). Univariate analysis of variables and calculation of MCID were performed using SPSS version 25.0 (IBM Corporation, Armonk, NY, USA). The backward method was used for statistically significant variables ( $P < 0.1$ ). Further multilevel model assumptions were confirmed through analysis of residuals generated by MLwiN version 3.0 software (Centre for Multilevel Modelling, University of Bristol, Bristol, United Kingdom).

## Multilevel model

(see Supplementary Files for Multilevel model)

# Results

## Sample characteristics

Baseline characteristics of the patients are shown in Table 1. A total of 555 patients with CHF, with a mean  $\pm$  SD age of  $67.86 \pm 14.58$  years, was enrolled. Of these patients, 44.14% were female. Most participants were married (80.72%) and had a low level of education (below secondary high school [72.61%]), and 49.19% and 47.75% had a low and medium annual income, respectively.

## CHF-PRO scores

The mean CHF-PRO scores for OS, PSYS, and PHYS were  $222.84 \pm 23.18$ ,  $59.40 \pm 10.84$ , and  $89.60 \pm 12.90$ , respectively. The scores were lowest during hospitalization, and improved significantly after discharge. Scores peaked at 3 months after discharge and declined at 6 months. The results are shown in Table 2.

## Multilevel model of self-management on CHF-PRO

Three model levels were applied to assess self-management strategies on OS of CHF-PRO; the results are summarized in Table 3. Model 1 demonstrated that the variance of level 2 (individual level) was statistically significant. It indicated that the data had aggregation and hierarchical structure at the individual level. Model 3 demonstrated that a regular schedule, an LSD, avoidance of over-eating, and exercise improved OS in PRO. Advanced age, female sex, and increased NYHA functional class were negatively correlated. A -2log likelihood was applied as the goodness fit evaluation index. The -2log likelihood of model 2 was smaller than model 1 (14697.680 versus [vs.] 14972.598); more specifically, the goodness fit of model 2 was better than model 1. For the same reason, model 3 had better goodness fit than model 2 (14300.712 vs. 14697.680). The residual distribution diagram is close to a straight line. Therefore, it indicated that the assumption of normal distribution of each level residuals was reasonable (Fig. 1).

A two-variable, three-level model was applied to analyze the roles of self-management strategies to PHYS and PSYS, the results are presented in Table 4. Model 1 demonstrated that the variance of level 3 (individual level) was statistically significant. It indicated that the data had aggregation and hierarchical structure at the individual level. According to the model, a regular schedule, an LSD, and avoidance of over-eating increased PHYS and PSYS. In addition, taking angiotensin-converting enzyme inhibitors and exercise also improved the PHYS of patients with CHF. Advanced age, female sex, and increased NYHA functional class were negatively correlated with PHYS and PSYS. A -2log likelihood demonstrated that the goodness fit of model 2 was better than model 1 (237,96.849 vs. 24,339.047), and model 3 was better than model 2 (18,669.687 vs. 24,339.047). The residual distribution diagram is close to a straight line. Therefore, it indicated that the assumption of normal distribution of each level residuals was reasonable (Fig. 2).

## MCID and its interpretation to the multilevel model

As shown in Fig 3, the MCIDs for OS, PHYS, and PSYS were 10.71, 4.14, and 5.35, respectively. Compared with MCID, the avoidance of over-eating of grade 5 and regular schedule of grade 4 and 5 reached clinical significance for OS. Avoidance of over-eating of grade 5 and regular schedule of grade 5 reached clinically significance for PHY. Regarding the PSY, avoidance of over-eating of grade 4 and 5 and regular schedule of grade 5 also demonstrated the clinical significance.

## Discussion

The present study assessed the impact of several types of self-management strategies on CHF-PRO scores. Here, we confirmed that maintenance of a regular schedule, exercise, an LSD, and avoidance of

over-eating could improve CHF-PRO scores in patients with CHF. Among these, however, only a regular schedule and avoidance of over-eating reached clinical significance. Compared to previous studies, various strategies were considered and changes in these over time were assessed. Moreover, based on statistical significance, clinical significance was emphasized by virtue of the MCID. The characteristics of patients with CHF have an impact on PRO. In our study, a high NYHA functional class, female sex, and advanced age decreased the OS in CHF-PRO, as well as PHYS and PSYS. These factors have already been shown to influence factors of PRO in patients with CHF in previous studies [13-15]. We used multivariate statistical methods to avoid the influence of these covariates on the results; thus, we were able to obtain self-management strategies that improved CHF-PRO more accurately.

Results of our study demonstrated that maintaining a regular schedule improved CHF-PRO. The same result was obtained in previous studies using other PRO scales of HF. Broström et al found that sleep disturbances affected virtually all dimensions of the Short-form 36 and Kansas City Cardiomyopathy Questionnaire (KCCQ) for patients with CHF, while daytime sleepiness decreased total Minnesota Living with Heart Failure (MLWHF) scores, as well as scores on physical and emotional subscales [16]. Liu et al reported that poor sleepers had significantly lower scores in physical, psychological, and social domains of the World Health Organization Quality of Life-BREF (WHOQOL-BREF) scale [17]. Sleep disorders in patients with CHF are caused by sleep-disordered breathing, depression, and HF symptoms such as dyspnea and dysrhythmias [18]. These investigations were cross-sectional studies, and dynamic changes in sleeping habits and PRO were not observed. Our study applied a multilevel model to introduce time as a variable. A prospective cohort study using one-way repeated measures analysis reported that exercise and cognitive behavioral therapy may improve sleep quality and QoL in patients with CHF [19]. In our study, patients were informed that they should maintain a regular routine, regardless of the strategy they used. The results of our study emphasize the importance of a regular schedule in patients with CHF. Moreover, only patients who maintained a regular schedule virtually every day achieved MCID, reflecting that it is necessary for patients to be compliant with physician recommendations.

Over-eating often relies on patient perception and lacks objective indicators for evaluation. As such, few studies have extensively investigated this factor. Our study unexpectedly found that avoidance of over-eating dramatically decreased OS, as well as PHYS and PSYS in CHF-PRO. Research presented at the American Heart Association meeting in 2000 found that a single large meal led to a fourfold increase in heart attacks within 2 h of the meal [20]. A rich diet burdens the heart due to diversion of the circulation to the gastrointestinal tract following a meal. Such a diversion increases cardiac blood and causes further stress on the heart. Moreover, acute fluctuations in blood pressure and heart rate occur after a rich meal and lead to further damage to the heart [21]. If an individual with CHF consumed a large, high-salt meal, acute decompensation could even occur [22]. The avoidance of over-eating may improve CHF-PRO by decreasing the incidence of these types of adverse events. This result provides new evidence supporting the management of CHF and direction for future studies.

An LSD was recommended by the 2016 European Society of Cardiology Guidelines for CHF [3]. In the present study, we confirmed that an LSD increased OS, PHYS, and PSYS of CHF-PRO. Previous studies

and the ongoing Geriatric Out-of-Hospital Randomized Meal Trial in Heart Failure (GOURMET-HF) study applied the KCCQ summary score as an indicator of QoL outcome and drew the same conclusion as that in our study [23-25]. Regarding PHYS, the reason for the increase may be that an LSD improved symptoms and signs of CHF [26, 27] and promoted exercise tolerance in patients [27]. However, few studies have focused on the relationship between LSD and psychological states. More studies are needed to confirm this and the mechanism also remains to be further elucidated. Adherence to an LSD has also been noted by researchers. Chung et al confirmed that patients who adhered to an LSD perceived more benefits than those who were non-adherent [28]. All of the research above focused exclusively on statistical significance and ignored clinical significance. When MCID was introduced, it did not reach clinical significance, regardless of a patient's adherence to an LSD in this study. This also may be because some patients did not accurately calculate the amount of salt they ate at home. More stringent studies and investigations examining clinical significance are needed in the future.

Regular aerobic exercise is encouraged in patients with HF to improve functional capacity and symptoms, as per guideline recommendations [3]. Studies have shown that exercise can reduce all-cause mortality and readmission for patients with CHF; however, the effects of exercise on QoL remain uncertain [29]. A recent meta-analysis confirmed that exercise improved both exercise capacity and QoL compared with the no-exercise control group at the 12-month follow-up, but with weaker evidence for a treatment effect at the 6-month follow-up [30]. Our study demonstrated that exercise improved PRO, especially physical condition. This is consistent with previous studies and provides the new evidence for the effect at the 6-month follow-up. However, this strategy did not reach MCID. It may be because we only defined the frequency and time of exercise, but not the intensity.

The findings of this study should be interpreted in light of its limitations. First, all advice adopted in this study was beneficial to strategies for patients with CHF. Based on ethical considerations, we provided all participants with advice when they were discharged; as such, there was no control group. It revealed that the causal effect was not as strong as that from a randomized controlled trial. We will use randomized controlled trial design in future research to assess one of the meaningful strategies in this study. Second, although this was a multicenter study, all patients were from the Shanxi Province of China and, as such, the findings may be regionally biased. Larger-scale studies are needed in the future to confirm the findings in this regard. Finally, some of the self-management strategies used in this study were not precisely defined. For example, a regular schedule did not limit the sleep time per day or apply related scales to measure sleep quality, which may have led to some imprecision. In future studies, we will further quantify the strategies addressed in this study to obtain more effective self-management strategies for patients with CHF.

## Conclusions

In summary, the present study analyzed the effect of various self-management strategies on the dynamics of PRO using multi-level models and further evaluated clinical significance with MCID. Our data suggested that self-management, especially the avoidance of over-eating and maintenance of a regular

schedule improved patient-reported outcomes in those with chronic heart failure. Patients could pay more attention to effective self-management strategies and the compliance to improve PRO.

## List Of Abbreviations

CHF: Chronic heart failure; CHF-PRO: patient-reported outcome of chronic heart failure; HF: heart failure; KCCQ: Kansas City Cardiomyopathy Questionnaire; LSD: low-sodium diet; MCID: minimal clinically important difference; NYHA: New York Heart Association; OS: overall summary; PHYS: physical scores; PRO: Patient-reported outcome; PSYS: psychological scores; QoL: quality of life; SD: standard deviation.

## Declarations

### Ethics approval and consent to participate

This study was reviewed and approved by the Institutional Review Board of Shanxi Medical University and the trial registration number was 2018LL128. All procedures performed were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Patients were informed verbally and in writing about the study and gave written informed consent.

### Consent for publication

All authors have approved the manuscript for publication.

### Availability of data and material

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

### Competing interests

The authors declare that they have no competing interests.

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### Authors' contributions

All authors participated in the study design. JT was responsible for collecting the data and drafting the article. QZ, JR and LH participated in the data collection and modified the article. JZ and JL participated

in the data analysis and modified the article. QH and YZ proposed the original concept for this study, supervised the data analysis, and revised the paper. All authors read and approved the final manuscript.

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## References

1. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE, Colvin MM, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure—a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation*. 2017; 136(6): 137-161.
2. Hu S, Gao R, Liu L, Zhu M, Wang W, Wang Y, et al. et al. Summary of the 2018 Report on Cardiovascular Diseases in China. *Chinese Circulation Journal*. 2019; 34(3): 209-220.
3. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. *Eur. Heart J*. 2016; 37(27): 2129–2200.
4. Seferovic PM, Ponikowski P, Anker SD, Bauersachs J, Chioncel O, Cleland JGF, et al. Clinical practice update on heart failure 2019: pharmacotherapy, procedures, devices and patient management. An expert consensus meeting report of the Heart Failure Association of the European Society of Cardiology. *Eur. J. Heart Fail*. 2019; 21(10): 1-17.
5. Van Spall HGC, Rahman T, Mytton O, Ramasundarahettige C, Ibrahim Q, Kabali C, et al. Comparative effectiveness of transitional care services in patients discharged from the hospital with heart failure: a systematic review and network meta-analysis. *Eur J Heart Fail*. 2017; 19: 1427-1443.
6. Jonkman NH, Westland H, Groenwold RH, Agren S, Atienza F, Blue L, et al. Do Self-Management Interventions Work in Patients With Heart Failure? An Individual Patient Data Meta-Analysis. *Circulation*. 2016; 133(12): 1189–1198.
7. Riegel B, Lee CS, Dickson VV, Medscape. Self care in patients with chronic heart failure. *Nat Rev Cardiol*. 2011; 8(11): 644–654.
8. U.S. Department of Health and Human Services FDA Center for drug evaluation and research, U.S. Department of Health and Human Services FDA Center for biologics evaluation and research, U.S. Department of Health and Human Services FDA Center for devices and radiological health. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes*. 2006; 4(79): e1-e20.
9. Tian J, Xue J, Hu X, Han Q, Zhang Y. CHF-PROM: validation of a patient-reported outcome measure for patients with chronic heart failure. *Health Qual Life Outcomes*. 2018; 16(1): e1-e14.

10. Sedaghat AR. Understanding the Minimal Clinically Important Difference (MCID) of Patient-Reported Outcome Measures. *Otolaryngol Head Neck Surg.* 2019; 161(4): 1-10.
11. Goldstein H. *Multilevel statistical models.* 3rd ed. Arnold. London. 2003.
12. Wright A, Hannon J, Hegedus EJ, Kavchak AE. Clinimetrics corner: a closer look at the minimal clinically important difference (MCID). *J Man Manip Ther.* 2012; 20 (3): 160-166.
13. Carson P, Tam SW, Ghali JK, Archambault WT, Taylor A, Cohn JN, et al. Relationship of quality of life scores with baseline characteristics and outcomes in the African-American heart failure trial. *J. Card. Fail.* 2009; 15(10): 835-842.
14. Lewis EF, Kim HY, Claggett B, Spertus J, Heitner JF, Assmann SF, et al. Impact of Spironolactone on Longitudinal Changes in Health-Related Quality of Life in the Treatment of Preserved Cardiac Function Heart Failure With an Aldosterone Antagonist Trial. *Circ Heart Fail.* 2016; 9(3): e1-9.
15. Napier R, McNulty SE, Eton DT, Redfield MM, AbouEzzeddine O, Dunlay SM. Comparing Measures to Assess Health-Related Quality of Life in Heart Failure With Preserved Ejection Fraction. *JACC Heart Fail.* 2018; 6(7): 552-560.
16. Broström A, Strömberg A, Dahlström U, Fridlund B. Sleep difficulties, daytime sleepiness, and health-related quality of life in patients with chronic heart failure. *J Cardiovasc Nurs.* 2004; 19(4): 234-242.
17. Liu JC, Hung HL, Shyu YK, Tsai PS. The impact of sleep quality and daytime sleepiness on global quality of life in community-dwelling patients with heart failure. *J Cardiovasc Nurs.* 2011; 26(2): 99-105.
18. F Johansson P, Dahlström U, Broström A. Factors and interventions influencing health-related quality of life in patients with heart failure: a review of the literature. *Eur J Cardiovasc Nurs.* 2006; 5(1): 5-15.
19. Chang YL, Chiou AF, Cheng SM, Lin KC. Tailored educational supportive care programme on sleep quality and psychological distress in patients with heart failure: A randomised controlled trial. *Int J Nurs Stud,* 2016; 7(2): 219-229.
20. American Heart Association (2000) 'Heavy Meals May Trigger Heart Attacks.' *Science Daily.*
21. Cox HS, Kaye DM, Thompson JM, Turner AG, Jennings GL, Itsiopoulos C, et al. Regional sympathetic nervous activation after a large meal in humans. *Clin Sci (Lond).* 1995; 89(2): 145-154.
22. Bibbins-Domingo K, Chertow GM, Coxson PG, Moran A, Lightwood JM, Pletcher MJ, et al. Projected effect of dietary salt reductions on future cardiovascular disease. *N. Engl. J. Med.* 2010; 362(7): 590-599.
23. Chen YW, Wang CY, Lai YH, Liao YC, Wen YK, Chang ST, et al. Home-based cardiac rehabilitation improves quality of life, aerobic capacity, and readmission rates in patients with chronic heart failure. *Medicine (Baltimore).* 2018; 97(4): 1-5.
24. Colin-Ramirez E, McAlister FA, Zheng Y, Sharma S, Armstrong PW, Ezekowitz JA. The long-term effects of dietary sodium restriction on clinical outcomes in patients with heart failure. The SODIUM-HF (Study of Dietary Intervention Under 100 mmol in Heart Failure): a pilot study. *Am. Heart J.* 2015; 169(2): 274-281.

25. Hummel SL, Karmally W, Gillespie BW, Helmke S, Teruya S, Wells J, et al. Home-Delivered Meals Postdischarge From Heart Failure Hospitalization. *Circ Heart Fail.* 2018; 11(8): 1-10.
26. Philipson H, Ekman I, Forslund HB, Swedberg K, Schaufelberger M. Salt and fluid restriction is effective in patients with chronic heart failure. *Eur. J. Heart Fail.* 2013; 15(11): 1304-1310.
27. Welsh D, Lennie TA, Marcinek R, Biddle MJ, Abshire D, Bentley B, et al. Low-sodium diet self-management intervention in heart failure: pilot study results. *Eur J Cardiovasc Nurs.* 2013; 12(1): 87-95.
28. Chung ML, Park L, Frazier SK, Lennie TA. Long-Term Adherence to Low-Sodium Diet in Patients With Heart Failure. *West J Nurs Res.* 2017; 39(4): 1-15.
29. Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of exercise-based cardiac rehabilitation in patients with heart failure (ExTraMATCH II) on mortality and hospitalisation: an individual patient data meta-analysis of randomised trials. *Eur J Heart Fail.* 2018; 20(12): 1735-1743.
30. Taylor RS, Walker S, Smart NA, Piepoli MF, Warren FC, Ciani O, et al. Impact of Exercise Rehabilitation on Exercise Capacity and Quality-of-Life in Heart Failure: Individual Participant Meta-Analysis. *J. Am. Coll. Cardiol.* 2019; 73(12): 1430-1443. doi: 10.1016/j.jacc.2018.12.072.

## Tables

Table 1. Baseline characteristics of patients with CHF

Variables	n=555
Age	67.86±14.58
Female	245 (44.14%)
Marital state	
Married	448 (80.72%)
Single	10 (1.80%)
Divorced/separated	9 (1.62%)
Widowed	88 (15.86%)
Education	
Illiteracy	63 (11.35%)
Low level	403 (72.61%)
Secondary school and high level	89 (16.04%)
Income	
Low	273 (49.19%)
Medium	265 (47.75%)
High	17 (3.06%)
Nonmanual workers	259 (46.67%)
Weight (kg)	66.67±20.77
Height (cm)	165.27±8.40
Systolic pressure (mmHg)	123.17±19.61
Diastolic pressure (mmHg)	74.37±13.00
Charlson score	2.47±1.30
Family history	115 (20.72%)
History of smoking	435 (78.38%)
History of drinking	468 (84.32%)
NYHA	
II	245 (44.15%)
III	211 (38.02%)
IV	99 (17.84%)
Drugs	
Nitrates	208 (37.48%)
Beta-blocker	378 (68.11%)
ACEI or ARB	250 (45.05%)
Aldosterone antagonist	359 (64.68%)

Diuretic	390 (70.27%)
Digoxin	113 (20.36%)

ACEI, angiotensin converting enzyme inhibitors; ARB, Angiotensin receptor antagonist, NYHA, New York Heart Association functional class.

Table 2. OS, PHYS and PSYS of CHF-PRO in different times

	Number	OS	PHY	PSY
Baseline	555	222.84±23.18	59.40±10.84	89.60±12.90
One month	555	243.83±14.84	69.88±7.79	98.55±6.14
Three months	405	243.61±15.43	69.92±7.57	98.96±6.34
Six months	166	238.76±19.19	68.84±8.55	96.12±10.08

OS, overall scores; PHYS, physical scores; PSYS, psychological scores; CHF-PRO, chronic heart failure - patient reported outcome.

Table 3. Three-level models for OS of CHF-PRO for patients with CHF

Parameters	Model 1	Model 2	Model 3
Fixed effects			
Intercept	236.25±0.55	220.64±1.34	223.75±3.74
Time		7.60±0.54*	3.29±0.57*
Age			-0.19±0.03*
Female			-2.95±0.93*
NYHA			-8.16±0.61*
Low-sodium diet			1.96±0.51*
Avoid over-eating			3.40±0.64*
Regular schedule			4.01±0.54*
Exercises			1.49±0.36*
Random effects			
Level 2 (subjects)			
(Intercept)	33.73±11.22	480.63±63.81*	486.43±56.27*
(Time)		57.05±9.72*	60.12±8.47*
Level 1 (Time point)			
(Intercept)	401.27±16.75	263.77±13.60*	209.25±10.73*
-2 Log likelihood	14972.598	14697.680	14300.712

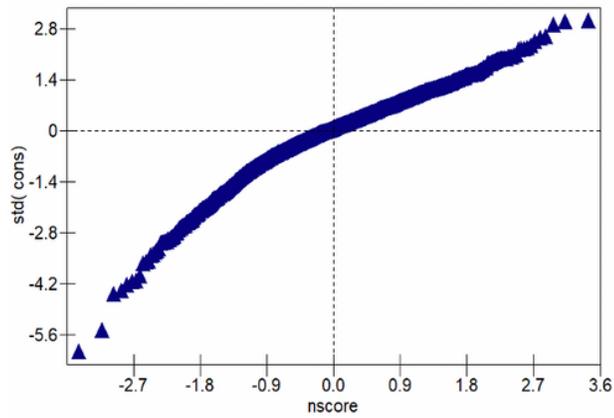
OS, overall scores; CHF-PRO, chronic heart failure - patient reported outcome. NYHA, New York Heart Association functional class.

Table 4. Multilevel multivariate models for PHYS and PSYS of CHF-PRO

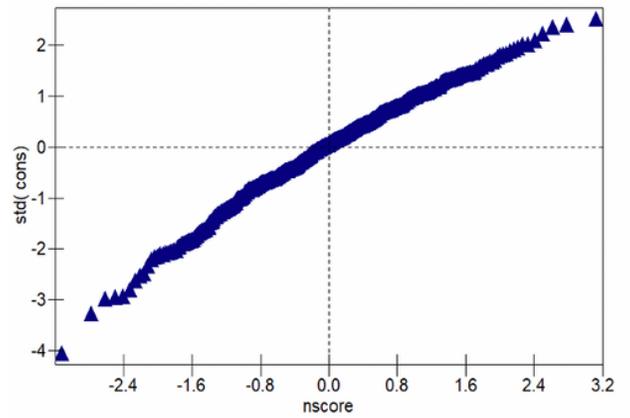
Parameters	Model 1		Model 2		Model 3	
	PHY	PSY	PHY	PSY	PHY	PSY
Fixed effects						
Intercept	66.27±0.28	95.45±0.27	57.79±0.63	88.49±0.72	69.23±2.02	84.43±2.27
Time			4.14±0.25*	3.39±0.28*	2.37±0.26*	1.53±0.30*
Age					-0.10±0.02*	-0.03±0.02
Female					-1.46±0.42*	-1.85±0.47*
NYHA					-5.00±0.28*	-2.14±0.31*
Charlson score					-0.38±0.16*	0.26±0.18
ACEI or ARB					1.33±0.42*	0.19±0.47
Regular schedule					1.18±0.25*	1.59±0.28*
Avoid over-eating					1.14±0.29*	1.91±0.33*
Low sodium diet					0.83±0.23*	0.89±0.26*
Exercises					0.92±0.17*	0.18±0.19
Random effects						
Level 3 (Subjects)						
(Intercept)		11.36±2.78*		105.71±14.03*		102.35±11.83*
□Intercept□		-1.84±2.14		66.61±12.73		69.16±11.23*
(Intercept)		7.11±2.66*		173.59±17.83*		170.75±16.61*
(Time)				11.39±2.07*		12.02±1.74*
(Time)				21.28±2.65*		20.93±2.43*
Level 2 (Time point)						
(Intercept)		92.04±3.84*		57.82±2.98*		44.23±2.26*
(Intercept)		62.52±3.43*		34.41±2.45*		25.52±1.94*
(Intercept)		92.27±4.06*		57.00±2.95*		49.58±2.55*
-2 Log likelihood		24339.047		23796.849		23177.694

ACEI, angiotensin converting enzyme inhibitors; ARB, Angiotensin receptor antagonist; CHF-PRO, chronic heart failure - patient reported outcome; NYHA, New York Heart Association functional class; PHYS, physical scores; PSYS, psychological scores.

## Figures



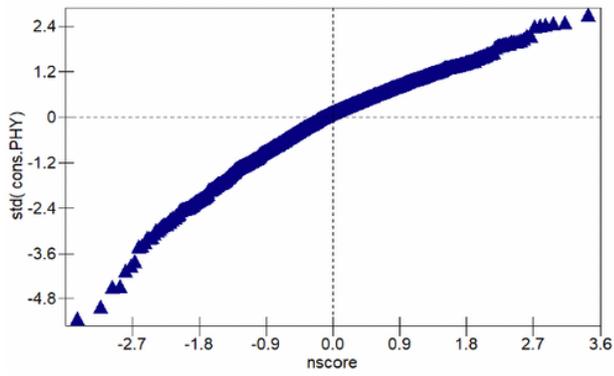
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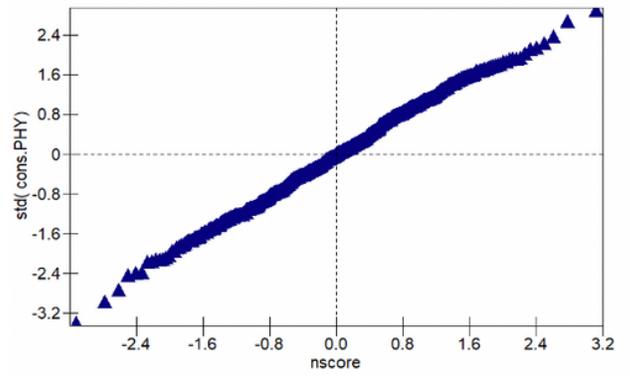
b

### Figure 1

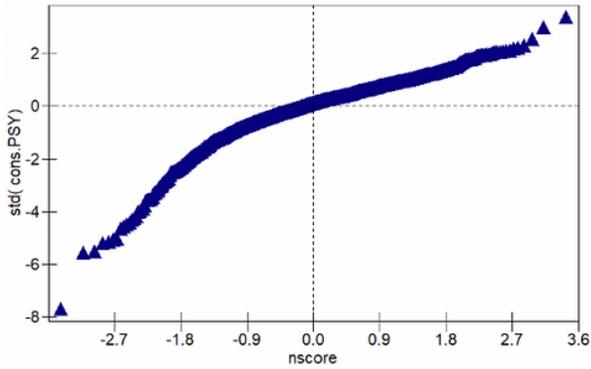
Residual normality test diagram of OS. Figure (a) and figure (b) are the residual normality test graphs of OS at the different time points level and the individual level, respectively. The ordinates of the diagrams represent the standardized residuals of each level, and the abscissas are their normal fractions. The curve of each figure represents the residual normality test of each level. The residual is normally distributed when the curve performs as a straight line.



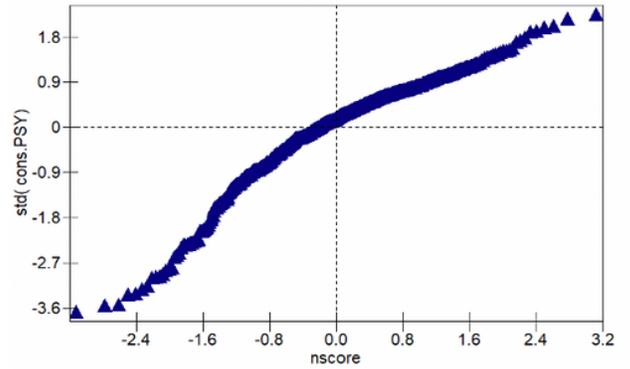
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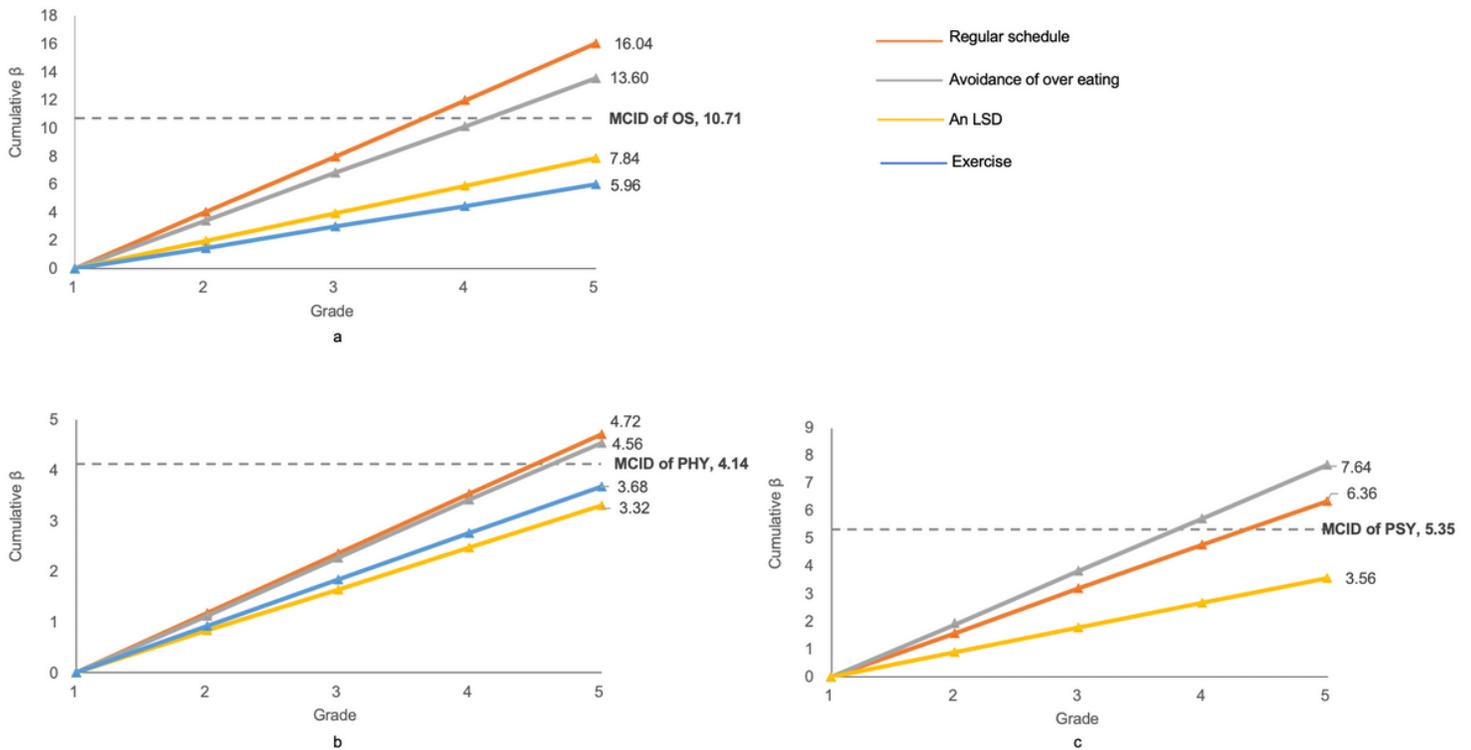
c



d

## Figure 2

Residual normality test diagram of PHYS and PSYS. Figure (a) and figure (b) represent the residual normality tests of PHY at the timepoint level and the individual level, respectively. Figure (c) and figure (d) represent the residual normality test of PSY at the time-point level and the individual level, respectively.



**Figure 3**

Comparison of MCID to the cumulative  $\beta$  for variables. Each point represents the value that the correspond  $\beta$  of strategy multiplied by (grade-1). MCID is shown as a dotted black line. The strategy is of the clinical significance when the its value is larger than MCID. Figure (a) represents the influence of management strategies on OS. Figure (b) and (c) represent the influence of management strategies on PHY and PSY, respectively.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Multilevelmodel.pdf](#)