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Predictors of refill non-adherence in patients with heart failure

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What is already known about this subject

- Non-adherence to recommended treatment is common in patients with heart failure and is associated with poor outcomes.
- Personal beliefs as well as experiences with medications and illness could influence medication use.

What this study adds

- Perception regarding barrier to medication use was a stronger predictor of non-adherence than demographic or clinical variables.
- Patients who were non-adherent to nonpharmacological management of heart failure were more likely to be non-adherent to their medications.
- Regimen complexity should not be considered in isolation when strategies for addressing adherence issues are designed.

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Aim
To identify the health beliefs and patient characteristics associated with medication non-adherence in patients attending a heart failure outpatient clinic.

Methods
A survey was administered to 350 consenting clinic patients. Questions focused on relevant demographic and clinical characteristics, the Health Belief Model, the Beliefs About Medicines Questionnaire and the Multidimensional Health Locus of Control. Multivariate logistic regression was used to identify independent predictors of refill non-adherence (<90%).

Results
Refill non-adherence was found in 77 (22%) participants. Being a smoker [odds ratio (OR) 2.4, 95% confidence interval (CI) 1.0, 5.8, $P = 0.045$], two or fewer medication administration times (OR 2.4, 95% CI 1.2, 4.6, $P = 0.01$), and positive response to 'Have you changed your daily routine to accommodate your heart failure medication schedule' (OR 2.4, 95% CI 1.2, 4.5, $P = 0.01$) were the independent predictors of refill non-adherence.

Conclusion
Perceptions regarding barriers to medication taking and fewer administration times could result in medication non-adherence in congestive heart failure patients. Medication regimens should be designed after accounting for patients' existing routines.

Introduction

Management of congestive heart failure (CHF) has been revolutionized by advances in therapy; however, the full societal benefit of these developments has not been realized due to clinician non-adherence to evidence-based strategies [1] and patient non-adherence to treatment recommendations [2]. Non-adherence to recommended treatment is common in patients with CHF, leading to

reduced quality of life, increased hospitalizations and increased morbidity [3–8]. Researchers have used various direct and indirect methods for evaluating medication adherence [9]. Medication refill data offer a convenient, accessible and reliable measure of patient adherence [10, 11]. Morisky's scale [12], a self-reported measure of adherence, has also demonstrated satisfactory reliability in various patient populations [13–15].

Whether patients follow treatment recommendations is likely to be influenced by their personal beliefs as well as experiences with medications and illness [16–18]. The role of health beliefs in treatment adherence has been recognized as a priority for adherence research [19–21]. There is little information evaluating how health beliefs influence medication-taking behaviour in CHF patients. This study attempted to identify the association between non-adherence to CHF medications and health beliefs, in conjunction with demographic and clinical characteristics.

Methods

Patients attending either a heart failure clinic or the preheart transplant clinic at St Paul's Hospital in Vancouver, British Columbia were sent an invitation to participate in the study if their clinic records indicated use of any CHF medication. A consent form was sent to patients who indicated their willingness to participate and who confirmed they had taken any CHF medication for at least 3 months. A minimum of 3 months of medication consumption was required to determine past adherence through medication refill records (maximum 100-day supply dispensed according to provincial regulations). Once signed consent was obtained, a prepiloted survey was administered in person or by telephone by a trained research technician. The survey queried general health and prescription and nonprescription medication use (11 open/closed questions), socio-demographic information (nine open/closed questions) and included questionnaires such as the Heath Belief Model (HBM) scale (14 items on a five-point Likert-type scale) [22], the Multidimensional Health Locus of Control (MHLC) scale (18 items on a six-point Likert-type scale) [23], the Beliefs About Medicines (BAM) questionnaire (10 items on a five-point Likert-type scale) [24], perceived stress scale (four items on a five-point Likert-type scale) [25] and the Morisky scale (four items with a binary response option, yes or no; a score of 1 for each 'yes' and 0 for each 'no') [12]. In addition, relevant data (concurrent disease states, severity of heart failure, number of clinic visits during the past year, duration of attendance at the clinic and year of heart failure onset) were also recorded from clinic records, where available.

The questionnaire relating to the HBM explored the five fundamental concepts of the HBM: perceived susceptibility; perceived severity; perceived benefits; perceived barriers; and perceived quality of medical care. The question 'Have you changed your daily routine to accommodate your heart failure medication schedule' was added to this section of the survey based on the clinical experience of one author (S.J.S.). Although this question relates to a potential barrier to taking medications, responses to this question were not included in the statistical analysis of the HBM scale scores since it deviates from the specific principles outlined in the original HBM studies. The MHLC assesses a patient's belief regarding how health outcomes are controlled and has three domains: internal locus of control; powerful others locus of control; and chance locus of control. The BAM addresses people's beliefs about the necessity of their medicines *vs.* the concerns about taking them.

Refill adherence data were obtained by manual review of patient profiles in the British Columbia prescription claims database called PharmaNet [26]. PharmaNet retains the past 14 months of prescription dispensation data for all patients regardless of medication insurance coverage (excluding HIV medications). Adherence was calculated for each individual CHF medication using the following formula:

$$\%\ \text{adherence} = (\text{no. of days supply}/\text{actual no. of days to refill}) \times 100$$

Due to the relatively high rate of adherence observed in previous studies of patients with CHF [3, 27, 28], non-adherence was defined as <90% mean refill adherence with CHF medications.

Data were analysed using SPSS (version 13.0; SPSS Inc., Chicago, IL, USA). Internal consistencies of the various scales used in the study were assessed using Cronbach's α. Univariate analyses (χ^2 test for dichotomous variables, Mann–Whitney *U*-test for ordinal data and Student's *t*-test for continuous variables) were performed to compare the data from subjects who were categorized as adherent and non-adherent (<90% mean refill adherence to CHF medications). Significant variables ($P < 0.10$) were entered into a logistic regression model (forward conditional method and verified using backward conditional method) to identify the independent predictors of non-adherence. This study was approved by the St Paul's Hospital Research Ethics Board; written informed consent was obtained from all participants.

Results

Of the 819 patients identified, 469 were excluded for the following reasons: unable to contact ($n = 202$), not interested ($n = 158$), not available for interview ($n = 35$), unable to communicate effectively in English ($n = 31$), signed consent form never received ($n = 28$), and PharmaNet data not available or did not meet inclusion criteria ($n = 15$). The mean age of the clinic attendees was 61.7 ± 14.4 years and 72.2% were male. Data were obtained from 350 patients, whose baseline characteristics are given in Table 1.

Refill non-adherence was found in 78 (22.3%) participants. One hundred and thirty-four (38.3%) patients self-reported non-adherence (Morisky score >0), 38 of whom also demonstrated refill non-adherence. Morisky score >0 had a sensitivity of 0.49 and a specificity of 0.69 in detecting <90% refill adherence. Internal consistencies of the various scales and subscales used in the study were: HBM scale (0.46); Internal Locus of Control scale (0.58); External Locus of Control – Powerful Others subscale (0.68); and External Locus of Control – Chance subscale (0.72); BAM – Necessity subscale (0.81); BAM – Concerns subscale (0.67); Perceived stress scale (0.78); and Morisky's scale (0.18). Univariate analysis of the scales/subscales used in the questionnaire against refill non-adherence is given in Table 2. Other variables significantly ($P < 0.10$) associated with refill non-adherence were: patient self-reported adherence in per cent ($P < 0.01$); being a smoker ($P = 0.01$); use of medications twice daily or less frequently ($P = 0.02$); use of adherence aids ($P = 0.06$); born in North America ($P = 0.06$); and use of antidepressants ($P = 0.08$).

When significant variables from univariate analysis were further analysed in a logistic regression model (Table 3), answering positively to the HBM scale item 'Have you changed your daily routine to accommodate your heart failure medication schedule?' became the best independent predictor of refill non-adherence, followed by use of medications twice daily or less frequently and being a smoker.

Table 1
Characteristics of the study cohort ($n = 350$)

Characteristic	Number (%)/ Mean ± SD
Male	243 (69.4)
Age (years)	61.2 ± 12.6
New York Heart Association class	
Class I	158 (45.1)
Class II	135 (38.6)
Class III	45 (12.9)
Class IV	1 (0.3)
Unknown	11 (3.1)
Time since diagnosis of heart failure (years)	7.3 ± 8.3
Number of concurrent disease states	2.5 ± 0.9
Number of clinic visits in the last 12 months	2.6 ± 1.5
Number of heart failure medications used	4.0 ± 1.3
Use of specific heart failure medications	
β-Blockers	302 (86.3)
Angiotensin converting enzyme inhibitors	246 (70.3)
Furosemide	222 (63.4)
Digoxin	211 (60.3)
Spironolactone	199 (56.9)
Angiotensin receptor blockers	69 (19.7)
Hydralazine/nitrate	20 (5.7)
Number of total regular medications used	8.0 ± 3.1
Frequency of daily medication use	2.5 ± 0.94
Refill adherence of all medications (%)	98.5 ± 6.5
Refill adherence of heart failure medications (%)	93.4 ± 8.6
Use of adherence aids	186 (53.1)
Use of over-the-counter medications	302 (86.3)
Use of complementary medicine products	119 (34)
Use of antidepressants	70 (20)
Highest level of education	
Elementary school	16 (4.6)
Some high school	68 (19.4)
High school graduate	78 (22.3)
Some university/college training	66 (18.9)
University/college undergraduate degree	71 (20.3)
Graduate degree (Masters, PhD, etc.)	18 (5.1)
No response	33 (9.4)
Born in North America	230 (69.9)
Current smoker	23 (6.6)
Lives alone ± visiting caregiver	57 (18.4)

Discussion

Perceived need to make major changes in the daily routine in an attempt to accommodate the recommended medication schedule, continuing smoking and fewer medication administration times were found to be associated with non-adherence in CHF patients. The only health belief-related item independently associated with non-adherence was the one regarding overcoming a barrier in the HBM scale. However, this item was a stronger predictor of non-adherence than most other commonly studied demographic or clinical variables.

Most studies evaluating the association between health beliefs and adherence have limited evaluation of adherence to self-reported measures [17, 29–31]. An inverse relationship between perceived difficulty with treatments (including medications) and self-reported adherence has been previously demonstrated in heart failure patients [8]. Few studies have evaluated associations between health beliefs and objectively measured

Table 2
Univariate comparison of health beliefs in adherent and non-adherent patients ($n = 350$)

Item	Refill adherence <90% ($n = 78$)	Refill adherence ≥90% ($n = 272$)
Health Belief Model scale		
Perceived susceptibility score	6.8 ± 2.0	6.8 ± 1.9
Perceived severity score	7.2 ± 2.0	7.3 ± 1.7
Perceived benefits score	4.0 ± 1.8**	3.6 ± 1.4
Perceived barriers score	7.8 ± 2.5	7.6 ± 2.4
Perceived quality of medical care score	2.9 ± 1.5	2.8 ± 1.3
Health Locus of Control scale		
Internal locus of control score	26.4 ± 5.4	26.8 ± 4.9
Powerful others locus of control score	25.2 ± 5.5	25.6 ± 5.9
Chance locus of control score	18.0 ± 6.8	17.5 ± 6.4
Beliefs About Medicine Questionnaire		
Necessity score	19.7 ± 4.1	20.5 ± 3.2
Concerns score	12.3 ± 3.9	12.2 ± 3.8
Perceived Stress scale score	8.0 ± 3.6	7.7 ± 3.2
Morisky scale score >0	49.4**	35.2
†Have you changed your daily routine to accommodate your medication schedule?	66.2*	76.2

*Data presented as mean ± SD or %. Two-sided Student's t-test used for comparison of means and χ^2 test used for comparison of proportions. †Results are listed as the proportion answering 'yes' to the question. *P = 0.10; **P = 0.05.*

Table 3
Logistic regression predicting refill adherence <90% ($n = 309$)

Variable	Odds ratio (95% CI)	*P*-value
Use of medications twice daily or less frequently	2.35 (1.20, 4.60)	0.01
Changed daily routine to accommodate medication schedule	2.35 (1.23, 4.52)	0.01
Smoker	2.42 (1.02, 5.75)	0.045
Morisky score >0	1.69 (0.93, 3.07)	0.09
Born in North America	1.52 (0.79, 2.91)	0.21
Health Belief Model – Perceived benefits score	1.14 (0.94, 1.38)	0.18
Use of antidepressants	0.99 (0.48, 2.05)	0.98
Patient self-reported adherence (%)	0.98 (0.95, 1.02)	0.36
Use of adherence aids	0.74 (0.41, 1.36)	0.34

Hosmer and Lemeshow goodness-of-fit P-value = 0.51.

adherence. Perceived barriers, based on the HBM, were a significant predictor of both refill non-adherence and self-reported non-adherence in a study of low-income patients attending an outpatient anticoagulation clinic [32].

The association between increased number of medications or administration times and higher adherence has been reported earlier [27, 32, 33]. It is possible that, for certain patients, taking a larger number of medications may necessitate a higher level of attention to medication-taking routine and thus improve adherence. It appears that the CHF clinic patients evaluated in the current study fit this description. Having a highly structured daily routine is known to be a strong independent predictor of adherence [34]. For the patients in the current study, it appears that needing to disrupt this daily routine in an attempt to accommodate the prescribed medication schedule leads to non-adherence. Failure to abstain from smoking by itself could be considered as a deviation from recommended disease management in CHF and has been identified by others as a predictor of medication non-adherence [35, 36]. It suggests that patients who are non-adherent to nonpharmacological

management are more likely to be non-adherent to their recommended therapy.

According to DiMatteo *et al.* [37], patients with depression are three times more likely to become non-adherent than nondepressed patients. In the present study, though use of antidepressants was associated with non-adherence in univariate analysis, it was not an independent predictor of non-adherence. Similarly, Morisky score and self-reported adherence (%) also failed to be significant independent predictors of non-adherence. Poor internal consistency of Morisky scale has been reported earlier [28]. In the present study, Morisky score >0 had moderate sensitivity and specificity when verified against refill adherence. These suggest that self-reporting offers a simple and useful tool for preliminary adherence screening rather than for quantification of adherence in research studies. Self-reported adherence using Morisky scale is also qualitatively informative and might be useful in identifying the reason for non-adherence along with its detection in routine clinical practice.

Our study has a few limitations. First, non-adherent subjects may have been less likely to participate in the survey and grant access to their confidential prescription records, resulting in a selection bias. However, the study participants were representative of the clinic attendees with regard to their mean age and gender distribution. Moreover, demographics and adherence patterns of our patients were similar to those of another large CHF cohort [35], confirming the significance of our findings in other CHF populations. Nevertheless, it is possible that the health beliefs of the nonparticipants, especially those who declined to participate, were different from those who participated. In a review of adherence in patients with CHF (age range 51–81 years), younger patients (mean age 54 years) and patients >85 years old were found to demonstrate better adherence [38]. We found no association between age and adherence in the present study. However, the participants in our study were younger and extrapolation of our findings to older CHF patient cohorts should be done with caution. The number of non-adherent patients in this cohort was relatively small, limiting the power to detect potential predictors. Using prescription claims does not capture all aspects of medication adherence as not all prescriptions filled might have been taken as recommended. However, the moderate concordance between self-reported adherence and prescription refill data observed in the present study and reported elsewhere [39] supports the validity of the refill data. Lastly, the internal consistencies of the health belief scales and subscales employed were moderate. Nevertheless, when tabulated health belief scores were replaced by individual health belief survey questions, the same predictors of non-adherence were identified.

Perceived difficulty in overcoming a barrier to medication use was the main predictor of non-adherence in this cohort of CHF patients. Our results highlight the need for closer monitoring of pharmacotherapy in patients who are non-adherent to nonpharmacological management. Simple measures such as self-reporting could be used for routine screening of adherence in CHF patients during clinic visits. Regimen complexity should not be considered in isolation when strategies for addressing adherence issues are designed. Medication regimens should be designed after accounting for existing routines to ensure that the new regimen has least disruption on the daily routines of patients and their families.

Competing interests: None declared.

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