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EFFECT OF PATIENT-CENTERED TRANSITIONAL CARE SERVICES ON PATIENT-REPORTED OUTCOMES: SEX SPECIFIC ANALYSIS OF THE PACT-HF RANDOMIZED CONTROLLED TRIAL

Vanessa Blumer, MD¹; Anastasia Gayowsky²; Feng Xie, PhD^{3,4}; Stephen J Greene MD^{1,5}; Michelle M Graham MD^{6,7}; Justin A. Ezekowitz MBBCh MSc⁶; Richard Perez²; Dennis T Ko, MD, MSc^{2,8}; Lehana Thabane^{3,9}; Faiez Zannad PhD¹⁰; Harriette GC Van Spall, MD, MPH^{2,3,9,11}

¹ Division of Cardiology, Duke University School of Medicine, Durham, NC

² ICES (formerly the Institute for Clinical Evaluative Sciences), Ontario, Canada

³ Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Ontario, Canada

⁴ Centre for Health Economics and Policy Analysis, McMaster University, Hamilton, Ontario, Canada

⁵ Duke Clinical Research Institute, Durham, North Carolina.

⁶ Division of Cardiology, University of Alberta, Edmonton, Alberta, Canada.

⁷ Mazankowski Heart Centre, University of Alberta, Edmonton, Alberta, Canada.

⁸ Sunnybrook Heart Centre, Toronto, Ontario, Canada

⁹ Population Health Research Institute, Hamilton, Ontario, Canada

¹⁰ Université de Lorraine, INSERM CIC-P 1433, and INSERM U1116 CHRU Nancy Brabois F-CRIN INICRCT, Nancy France.

¹¹ Department of Medicine, McMaster University, Hamilton, Ontario, Canada

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Corresponding Author:

Harriette GC Van Spall MD MPH

20 Copeland Avenue

David Braley Research Institute Bldg, Suite C3-117

Hamilton ON L8L 2X2

Phone: (905) 521-2100 X40601

Email: harriette.vanspall@phri.ca

ABSTRACT

Aims: We assessed the effect of transitional care on patient reported outcomes (PROs) in women and men hospitalized for heart failure (HF).

Methods: In this sex-specific analysis of a cluster randomized trial in Canada, the effect of a patient-centered transitional care model was tested on prespecified PROs of discharge preparedness (B-PREPARED score, range 0-22), quality of transition (Care Transitions Measure-3 [CTM-3] score, 0-100), and health-related quality of life (HRQOL) (EQ-5D-5L, 0-1).

Results: Among 986 patients (47.4% women), B-PREPARED at 6 weeks was greater with intervention than usual care (mean difference [MD], 4.01 [95% confidence interval (CI), 2.90-5.12]; $P < 0.001$) with no sex differences (P sex interaction=0.24). CTM-3 at 6 weeks was greater with intervention than usual care (MD, 10.52 [95% CI, 6.00-15.04]; $P < 0.001$), with no sex differences (P sex-interaction=0.69). EQ-5D-5L was greater with intervention than usual care at discharge (MD, 0.17 [95% CI, 0.12-0.22]; $P < 0.001$), 6 weeks (MD, 0.06 [95% CI, 0.01-0.12]; $P = 0.02$), and 6 months (MD, 0.05 [95% CI, -0.01-0.12]; $P = 0.09$), although the 6-month difference was not statistically significant. At discharge, women reported lower EQ-5D-5L but experienced significantly greater treatment benefit than men (P sex-interaction=0.02). Treatment effect on EQ-5D-5L was numerically greater in women than men at 6 weeks and 6 months, but there were no significant sex differences (P sex-interaction 0.18 and 0.19, respectively).

Conclusion: A patient-centered transitional care model improved discharge preparedness, transition quality, and HRQOL in the weeks following HF hospitalization, with effects largely consistent in women and men. However, women reported lower HRQOL and experienced greater treatment benefit than men at hospital discharge.

Trial registration [Clinicaltrials.gov, NCT02112227](https://clinicaltrials.gov/ct2/show/study/NCT02112227)

Keywords: heart failure, women, quality of life, transitional care

ABBREVIATIONS

CTM-3= Care Transitions Measure

HRQOL= health related quality of life

HF= heart failure

PACT-HF= Patient-Centered Care Transitions in HF

PRO= patient-reported outcome

QALY= quality-adjusted life years

INTRODUCTION

The incidence of heart failure (HF) continues to increase globally, and more than half of those affected are women¹⁻³. While women and men are known to have differences across multiple aspects of HF care and outcomes, most trials under-enroll women relative to disease prevalence and do not have adequate statistical power to test for sex-specific differences in treatment effect^{4,5}. Furthermore, while most surgical, device, drug, and health service trials have focused on clinical endpoints in HF, less is known regarding the effect of interventions on patient-reported outcome (PROs)^{6,7}. PROs are recommended as quality-of-care measures as they provide invaluable insight into health status and perceptions of care across the spectrum of well-being from the patient's perspective^{8,9}, but when they are reported, sex differences are rarely taken into account¹⁰⁻¹⁵.

In the Patient-Centered Care Transitions in HF (PACT-HF) stepped-wedge cluster randomized trial, in Ontario, Canada a patient-centered transitional care model did not improve clinical endpoints among adults hospitalized for HF, but there was significant effect modification by sex; relative to usual care, women who received the intervention had greater improvement in clinical outcomes than men 6 months following hospital discharge^{16,17}. While the transitional care model improved the PROs of discharge preparedness, quality of care transition, and quality of life following hospitalization for HF, interceding clinical outcomes among those providing PRO data were not considered, and sex-specific differences in PROs were not assessed. Previous studies have shown that women with HF have worse baseline health-related quality of life (HRQOL) than men^{18,19} across the spectrum of ejection fraction in chronic stable HF²⁰. However, it is less clear whether women have poorer HRQOL than men during hospitalization for decompensated HF, and whether transitional care services have the

potential to improve this.

In this analysis of the PACT-HF trial, we examined the overall and sex-specific effect of a patient-centered²¹ transitional care model on the prespecified outcomes of discharge preparedness, quality of transition, and HRQOL among adults hospitalized for HF in Ontario, Canada. In addition, we estimated the overall and sex-specific treatment effect on quality adjusted life years (QALY). Recognizing that baseline characteristics and clinical outcomes following hospitalization can influence PROs, we adjusted all analyses for differences in baseline characteristics and interceding clinical outcomes following hospital discharge.

METHODS

Study Design and Population

The study design and primary results of the PACT-HF trial, a stepped-wedge cluster randomized controlled trial in 10 hospitals in Ontario, Canada, have been previously reported^{17,22} (Supplement 1). Patients were enrolled from February 1, 2015, to March 30, 2016. Eligible patients had a primary admission diagnosis of HF, identified daily from hospital electronic medical records. We excluded patients who did not have HF, did not consent to inclusion, died during hospitalization, were transferred to another hospital, or were discharged with a primary diagnosis other than HF. During the intervention phase, Boston criteria and/or serum thresholds of brain natriuretic peptide (BNP) or N-terminal pro-b-type natriuretic peptide (NT-pro-BNP) were used to exclude a diagnosis of HF.

Randomization

The unit of recruitment and randomization was the hospital, and the unit of analysis was the patient. The randomization sequence was determined by a number generator. Hospitals

crossed over from usual care to intervention at monthly intervals following stepped wedge cluster randomized design.

Intervention

In hospitals undergoing the intervention, a hospital nurse navigator provided the following at the time of discharge: HF self-care education to the patient and informal caregiver; a structured patient centered discharge summary with a symptom-driven action plan to the patient and the family physician; family physician follow-up arrangements within 1 week of discharge; and referrals to post discharge nurse-led home visits and heart function clinics care for high-risk patients. The nurse-led visits included weekly, structured, face-to-face and telephone assessments lasting 4 to 6 weeks until patients were seen in the heart function clinics. In the event of deterioration, the home-care nurse helped the patient follow the discharge action plan and contacted the heart function clinics for expedited care. HF guidelines were distributed, but management was left to clinicians' discretion.

In the usual care group, transitional care occurred at the discretion of clinicians. None of the eight hospitals participating in this sub-study provided nurse-led in-hospital education to patients with HF as part of usual care. Most hospitals had access to regional Heart Function clinics; referrals to these clinics after hospitalization were at the discretion of providers.

Blinding

Clinicians were unblinded to treatment allocation and patients were considered unblinded. Personnel who collected patient-reported outcomes were blinded. Clinical outcomes were adjudicated independent of this trial. To avoid contamination, we concealed the randomization sequence and crossover date from each institution until 3 months before crossover, designed month-long steps to shorten the trial length and minimize changes in usual care, and withheld

intervention details, training, and toolkits until the month before crossover.

Outcomes

To reduce the risk of Type I error, data on PROs were collected from a nested sample of 8 hospitals. To identify clinical outcomes²², we used the Canadian Institute for Health Information's (CIHI) discharge abstract database (DAD) at ICES (formerly the Institute for Clinical Evaluative Sciences) (ICES). ICES is an independent, non-profit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health system evaluation and improvement. These datasets were linked using unique encoded identifiers and analyzed at ICES. All patients in PACT-HF provided verbal informed consent for study participation. Because services were evidence-informed and considered quality improvement, the study was approved by all institutional Research Ethics Boards with oral consent and waiver of written consent^{21,23}.

The PRO measures were selected based on input from patients during a preceding one-center pilot phase²². A majority of patients selected the measures used in the study over other validated disease-specific health-related quality of life questionnaires, which they deemed challenging to respond to over the telephone. All outcomes were measured relative to the discharge date of the index HF hospitalization, defined as the first unplanned hospitalization for HF in a participating hospital during the study period²⁴. The outcomes in this sub-study were all prespecified as secondary outcomes for the PACT-HF trial^{17,22}:

1. Patient discharge preparedness, measured by the validated 11-item B-PREPARED telephone survey instrument. Based on a 3-point Likert Scale, it assesses domains of self-care information, services, and confidence, with scores ranging from 0 to 22; higher

scores correlate with patient satisfaction and predict freedom from ED usage²⁵. The BPREPARED was administered 6 weeks after the patient's discharge.

2. Care Transitions Measure (CTM-3), a 3-item measure of coordination at hospital discharge care. This score reflects the overall quality of the care transition, ranging from 0 to 100, with higher score indicating a higher quality of care²⁴. The CTM-3 was administered 6 weeks after the patient's discharge.
3. EQ-5D-5L, a preference-based generic HRQOL instrument, which measures health status in 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression²⁶. Each dimension has 5 response levels: no problem (Level 1), slight problems (Level 2), moderate problems (Level 3), severe problems (Level 4), and extreme problem (Level 5). Health utilities for the EQ-5D-5L anchored at 0 (dead) to 1 (full health) are calculated using a scoring algorithm based on general public's preferences²⁷. Respondents were also asked to rate their global health status on a 0-100 visual analog scale (EQ-VAS), ranging from 0 ("worst imaginable health state") to 100 ("best imaginable health state"). The EQ-5D-5L was administered during the index admission and via telephone 6 weeks and 6 months after the patient's hospital discharge.

We estimated Quality-adjusted life year (QALY), a metric that combines the effects of health interventions on mortality and morbidity. In this study, QALY ranged from 0 (dead) to 0.5 (full health at 6 months). We used the area-under-the-curve approach with the EQ-5D-5L utilities and corresponding time duration to calculate QALY^{27,28}.

Statistical analysis

Patients, the unit of analysis, were analyzed according to treatment allocation (intention-to-treat). Data were summarized using mean with standard deviation (SD) or median with

interquartile range (IQR) for continuous variables and counts with percentages for categorical variables. A two-sided $p < 0.05$ significance threshold was used for all analyses. Regression models for outcomes were adjusted for the stepped-wedge design, with the intervention and steps (time) as fixed-effects and hospitals as random-effects²⁹.

We measured the effect of the intervention on B-PREPARED, CTM-3, and EQ-5D-5L using generalized linear mixed models, reporting mean scores, mean differences (MDs), and 95% CIs. We used multiple imputation, imputing missing data for living patients using age, sex, and LACE score; we used the Markov Chain Monte Carlo method and assumed that all the variables followed a joint multivariate normal distribution. We imputed missing EQ-5D-5L scores at either 6 weeks or 6 months if baseline and one of two follow-up measures were collected. Overall, less than 25% of data was imputed for each of the PRO measures with missing data (1.1%-24.8%). We calculated QALY using the area-under-the-curve approach with EQ-5D-5L-derived utilities and corresponding survival duration^{27,28}. We analyzed the intervention's effect on QALY using mixed linear regression, adjusting for discharge EQ-5D-5L.

In addition to estimating the treatment effect in the overall population, we performed an exploratory sex-specific analysis, comparing the treatment effect in men and women. Within each sex group, we adjusted for imbalance in baseline characteristics including age; comorbidities with statistically significant difference (standardized difference [SD] ≥ 0.1) between intervention groups (chosen from a list including hypertension, diabetes, atrial fibrillation, chronic kidney disease, myocardial infarction (MI), chronic obstructive pulmonary disorder (COPD), peripheral vascular disease (PVD), cerebrovascular disease, dementia, GI bleed, liver disease); interceding hospitalizations at 6 weeks and 6 months; and interceding ED visits that did not result in hospitalizations at 6 weeks and 6 months. Comorbidities with small

cells (<6) were excluded from adjustment in the models.

We explored effect modification by sex. We calculated p-values for the sex-intervention interaction for Least-Squares Mean in these adjusted models. Consistent with this exploratory analysis, results were not adjusted for multiple testing. A detailed analysis of the statistical analysis plan of PACT-HF is included in the **Supplement 2**. All analyses were conducted using SAS Version 9.4 for UNIX (SAS Institute Inc., Cary, North Carolina).

RESULTS

Patient Characteristics

According to the prespecified protocol, PROs were collected from 8 of the 10 enrolled hospitals, and 986 patients (47.4% women) were represented in the dataset (**Figure 1**).

Baseline characteristics among the 986 patients who provided PROs were similar to the 2494 trial patients from whom primary outcomes were collected, although this cohort of patients was slightly younger and with a lower prevalence of dementia (**Supplemental Table 1**).

Within each sex group, there were some imbalances in baseline characteristics between treatment and usual care groups (**Table 1**); this diverged from the balanced characteristics between treatment groups in the primary trial¹⁷. When compared to the intervention group, men in the usual care group had a greater prevalence of complicated diabetes (57.4% vs 51.2%), COPD (23.6% vs 18.5%), and cerebrovascular disease (13.3% vs 6.2%) (all SD >0.10). Women in the usual care group had greater prevalence of chronic kidney disease (19.5% vs 15.6%), COPD (27.0% vs 20.9%), and dementia (7.6% vs 5.0%), and a lower prevalence of gastrointestinal bleeding (5.9% vs 11.0%) than in the intervention group (all SD >0.10) (**Table 1**). These differences were adjusted for in the analysis.

Health care utilization based on mean resource intensity weights³⁰ during the index hospitalization was similar for both men and women when comparing the intervention and usual care group (SD \leq 0.10).

Sex-Specific Patient-Reported Endpoints

All PROs described below represent adjusted analysis. PRO metrics adjusted for the clinical events are summarized in **Supplemental Table 2**.

B-PREPARED

The B-PREPARED score at 6 weeks was significantly greater in the intervention versus usual care group (mean 17.01 vs. 13.00; MD, 4.01 [95% CI, 2.90-5.12]; $P < 0.001$); this was noted in men (mean 16.90 vs. 12.92; MD, 3.98 [95% CI, 2.40-5.57]; $P < 0.001$) as well as women (mean 17.04 vs. 13.05; MD, 3.99 [95% CI, 2.40-5.57]; $P < 0.001$) (**Figure 2A, Table 2**).

There was no significant sex-treatment interaction (P for sex interaction=0.24).

CTM-3

The CTM-3 score at 6 weeks was significantly greater in the intervention versus usual care group (mean 77.47 vs. 66.95; MD, 10.52 [95% CI, 6.00-15.04]; $P < 0.001$); this was observed in both men (mean 78.94 vs. 69.03; MD, 9.92 [95% CI, 3.44-16.39]; $P = 0.003$) and women (mean 72.71 vs. 63.58; MD, 9.14 [95% CI, 2.67-15.61]; $P = 0.006$) (Figure 2B, Table 2).

There was no significant sex-treatment interaction (P for sex interaction=0.69).

EQ-5D-5L and QALY

At hospital discharge, the EQ-5D-5L score was greater with intervention than usual care overall (0.71 vs. 0.53; MD, 0.17 [95% CI, 0.12-0.22]; $P < 0.001$). Among those receiving usual care, women had substantially lower EQ-5D-5L scores than men (0.37 [95% CI, 0.30-0.44] versus 0.62 [95% CI, 0.57-0.67]). There was a larger difference between the intervention and

usual care group in women (0.59 vs. 0.37; MD, 0.22 [95% CI, 0.2-0.3]; $P < 0.0001$) than in men (0.73 vs. 0.62; MD, 0.11 [95% CI, 0.04-0.20]; $P = 0.002$), with a significant sex-treatment interaction (P for sex interaction = 0.02 at discharge) (**Figure 3, Table 2**).

At 6 weeks, the EQ-5D-5L score was greater in the intervention versus usual care group overall (0.69 vs. 0.63; MD, 0.06 [95% CI, 0.01-0.12]; $P = 0.02$). EQ-5D-5L was significantly greater with intervention than usual care in women (0.64 vs. 0.56; MD, 0.08 [95% CI, 0.01-0.20]; $P = 0.03$), but not men (0.71 vs 0.68; MD 0.03 [95% CI -0.05-0.11]; $P = 0.42$). A numeric difference was seen in both sexes, however, and there was no significant sex-treatment interaction (P for sex interaction = 0.18 at 6 weeks) (**Figure 3, Table 2**).

At 6 months, the EQ-5D-5L score was numerically greater in the intervention versus usual care group (0.68 vs. 0.63; MD, 0.05 [95% CI, -0.01-0.12]; $P = 0.09$). EQ-5D-5L was numerically greater with treatment versus usual care in men (0.72 vs. 0.68; MD, 0.04 [95% CI, -0.04-0.12; $P = 0.35$) and women (0.60 vs. 0.53; MD, 0.07 [95% CI, -0.03-0.16; $P = 0.35$), with no statistically significant differences and no sex-treatment interaction (P for sex interaction = 0.19) (**Figure 3, Table 2**).

At 6 months, there was no difference in QALY in the intervention versus usual care group (0.34 vs. 0.34; MD, -0.001 [95% CI, -0.02-0.02]; $P = 0.94$), with similar findings in men (0.36 vs. 0.36; MD, -0.001 [95% CI, -0.03-0.03]; $P = 0.96$) and women (0.32 vs. 0.32; MD, -0.002 [95% CI, -0.003-0.03]; $P = 0.90$). There was no sex-treatment interaction (P for sex interaction = 0.39) (**Table 2**).

Results pertaining to adjusted analyses for all PROs were consistent with unadjusted analyses (**Supplemental Table 3**).

DISCUSSION

In this sex-specific analysis of prespecified secondary outcomes of the PACT-HF trial, we found that a patient-centered transitional care model improved discharge preparedness and care transition quality following hospitalization for HF. There were sex-differences in treatment effect on these self-reported outcomes, which were obtained 6 weeks following discharge. The intervention improved HRQOL at discharge, 6 weeks, and 6 months, although the treatment effect at 6 months did not reach statistical significance. At discharge, among those receiving usual care, women reported substantially lower HRQOL, but experienced significantly greater benefit from the intervention than men. There was no sex-specific effect modification on HRQOL at 6 weeks or 6 months. The intervention had no effect on QALY at 6 months and there was no sex-treatment interaction for this outcome (**Graphical Abstract**).

To our knowledge, we present the first sex-specific analysis on the effect of a transitional care model on patient-reported outcomes in HF. This was a robustly designed pragmatic trial that tested the effect of the intervention among patients hospitalized for HF. The PRO instruments were selected in partnership with patients. Because the sex-disaggregated analysis was exploratory, there were some baseline differences between the intervention and usual care groups in each sex. Analysis accounted for these baseline differences and also for the interceding clinical endpoints that could have potentially influenced PROs; for example, we adjusted for hospitalizations and ED visits during the follow up period to account for the influence that these events may have had on self-reported discharge preparedness, care quality, or HRQOL.

The PROs selected for this study were guided by patients and represent measures that were deemed both relevant and patient-centered. To decrease trial burden on patients, the

PROs were collected via the telephone rather than face to face visits. While scales such as the Kansas City Cardiomyopathy Questionnaire (KCCQ) and Minnesota Living with Heart Failure Questionnaire (MLWHF) are more commonly than EQ-5D-5L^{10,11,13} in HF, patients engaged in the planning of this trial preferred the user friendliness and brevity of the EQ-5D-5L scale, particularly for telephone collection. The EQ-5D-5L can measure small changes in the health state, especially in patients with mild health conditions³⁷. EQ-5D-5L has previously been used in HF populations^{12,38} and has been mapped onto the MLWHFQ - validated for use in HF⁹ with good predictive accuracy³⁹.

The patient-centered transitional care model with hospital and post-discharge components improved discharge preparedness and quality of care transition in both men and women, with no evidence of effect modification by sex. B-PREPARED and the CTM-3 have been previously used as a measure of discharge preparedness and readmission risk^{25,40-44}, but sex-specific differences in the preparedness for hospital discharge have not been evaluated. In our primary analysis, the transitional care model increased discharge preparedness and quality of care transition overall, but results were not disaggregated by sex.²⁰ Our findings are clinically relevant as transition of care from hospital to home is known to represent a vulnerable period for patients, and discharge preparedness can improve self care, self-efficacy, and clinical outcomes⁴⁵. The magnitude of improvement in these scores - approximately 18% and 10% B-PREPARED and CTM-3 scores, respectively - is well above differences considered minimally important in PROs. In an observational cohort of adult patients recently hospitalized for acute coronary syndrome and/or acute HF, the B-PREPARED score was more strongly associated with readmission or death than the CTM-3⁴⁰. The CTM-3 appears to be influenced by

patient characteristics, demonstrates a ceiling effect, and may not reflect fluctuating aspects of care transitions^{40,46,47}.

We found that at hospital discharge, women had significantly lower HRQOL than men and derived a greater benefit from the transitional care model than men; women also experienced a significant benefit from the intervention at 6 weeks. The transitional care model improved HRQOL in the trial population overall at 6 weeks, but missed statistical significance at 6 months, possibly related to inadequate statistical power. Women hospitalized with HF in clinical settings are older than men, which was the case in this pragmatic trial too; they may have been predeceased by their partners and lived with less caregiver support, factors that can influence HRQOL.⁴⁸ Even though women with HF survive longer than men³⁴, their additional years of life are of poorer quality, with greater self-reported psychological and physical disability^{20,34}. In addition, prior work has suggested women are less likely to receive guideline recommended therapies for HF with reduced ejection fraction⁴³. In the context of proven benefits of guideline-directed medical therapy on patient health status and quality of life, lower utilization of evidence-based therapies among women may contribute to the observed greater impairment in HRQOL.

Prior reports on sex-differences in HRQOL in HF have mostly focused on chronic outpatient populations³¹⁻³³. Our current analysis, extends the analysis of PROs to the transitional care period following hospitalization, a high-risk period for adverse events and during which system modifications could improve outcomes³⁵. The burden of symptoms and QOL are known to disproportionately affect women^{15,20,34,36}, yet tailored interventions that can improve PROs in women are lacking. Identifying strategies that address this unmet need among women, such as the intervention explored in PACT-HF, may be one means of bridging this disparity. While the

PACT-HF intervention had a neutral overall effect on the primary composite outcome of death, hospital readmission or ED visit¹⁷, there were sex-specific differences noted, with improved clinical outcomes in women relative to men¹⁶. Thus, while the patient-centered transitional care model offered early benefits in discharge preparedness, quality of care transition and HRQOL in the entire trial population, it may be particularly effective in women, who experience benefits in HRQOL as well as clinical outcomes¹⁶.

Despite improvements in HRQOL, the transitional care model did not improve QALY in either men or women. QALY has been used as a summary measure of health outcome for economic evaluation and has established itself as the leading metric to perform cost effective analysis in evaluating new interventions, as it incorporates the impact of both quantity and quality of life^{28,48,49}. Although the lack of improvement in QALY in the intervention group regardless of sex might suggest the need of better evidence to support funding for a transitional care model, this must be weighed against the patient's perception of discharge preparedness, quality of care transitions, and HRQOL.

Limitations

This study is not without limitations. While the outcomes were prespecified secondary outcomes, the sex-specific comparisons of PROs were exploratory and the trial was not adequately powered to test for sex differences. Second, these data reflect results from patients consenting to provide PROs in a randomized clinical trial and the extent to which findings reflect patients in routine clinical practice is unclear. Third, there was evidence of referral bias in the sample; fewer and sicker patients in the usual care group provided PRO data, although we accounted for the imbalance in our regression models. Fourth, of the PRO metrics used,

only EQ-5D-5L has been specifically validated in HF populations⁵¹. Lastly, the analysis was exploratory and results were not adjusted for multiple comparisons.

CONCLUSIONS

Among patients hospitalized for HF in a nested sample of 8 hospitals in Ontario, Canada, the implementation of a patient-centered transitional care model was associated with improved perception of discharged preparedness and care transition quality in both men and women. The model was associated with improved HRQOL at discharge, 6 weeks, and 6 months, although the treatment effect at 6 months missed statistical significance. Women receiving usual care reported poorer HRQOL than men at hospital discharge, but the transitional care model was associated with better HRQOL in women than men at hospital discharge, with no sex-treatment interaction at 6 weeks and 6 months. The overall benefit in PROs with the intervention provides justification for the delivery of transition care services to men and women hospitalized for HF. Further research on tailored strategies that can mitigate sex-disparities in PROs is warranted.

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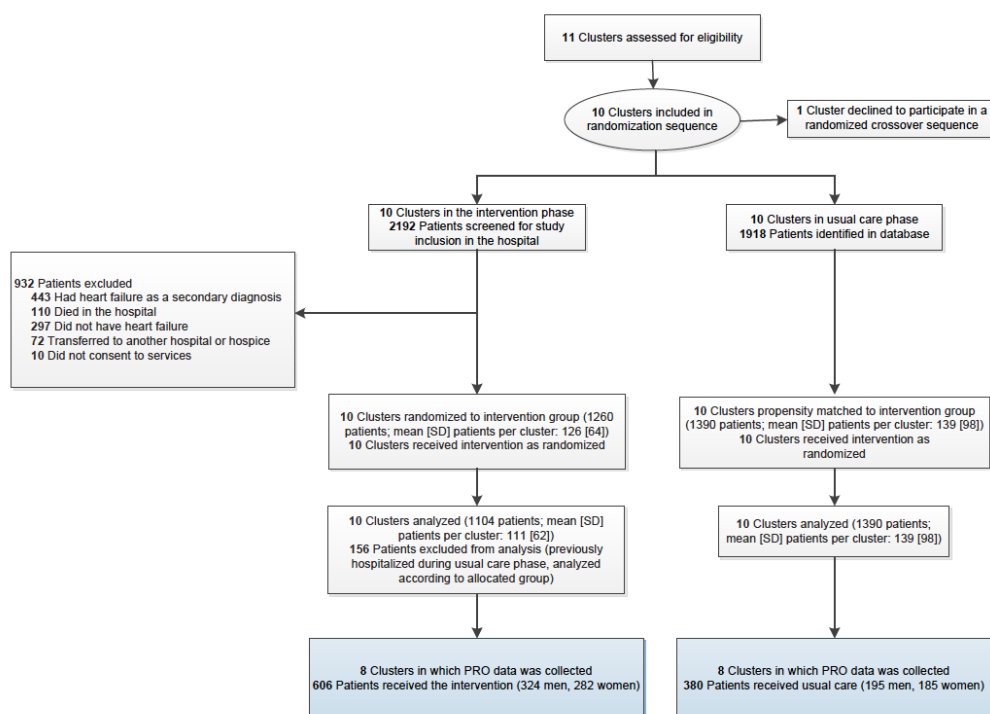
FIGURE LEGENDS

Figure 1. Flow Diagram for the Patient-Centered Care Transitions in HF Pragmatic Stepped-Wedge Cluster Randomized Trial. Ten hospitals crossed over unidirectionally from usual care to the intervention in a randomized sequence. PRO data was obtained from a nested sample of 8 hospitals.

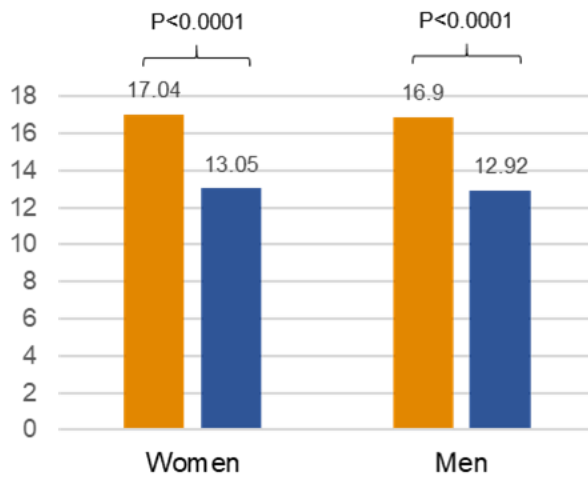
Figure 2. Sex differences in the effect of the Transitional Care Model on Discharged Preparedness and Care Transitions Quality (A) B-PREPARED at 6 weeks, and (B) CTM-3 at 6 weeks. Data reflect Least-Squares mean values with p-values for mean differences between PACT-HF and Usual Care groups. Models were adjusted for stepped wedge design, baseline imbalance in characteristics, and interceding clinical outcomes. Women and men experienced a significant benefit in both outcomes with the intervention, with no evidence of treatment modification by sex. CTM-3, 3-Item Care Transitions Measure.

Figure 3. Sex differences in the effect of the Transitional Care Model on Health-Related Quality of Life in Women and Men. EQ-5D-5L at discharge, 6 weeks, and 6 months. Data in figure reflect Least-Squares adjusted mean differences between PACTHF and Usual Care groups, along with 95% confidence intervals. Adjusted mean values of each group are presented under the figure. Models were adjusted for stepped wedge design, baseline imbalance in characteristics, and interceding clinical outcomes. Women had lower scores than men at discharge, with effect modification by sex. There was no sex-treatment interaction at 6 weeks and 6 months. EQ-5D-5L, 5-level EQ-5D version.

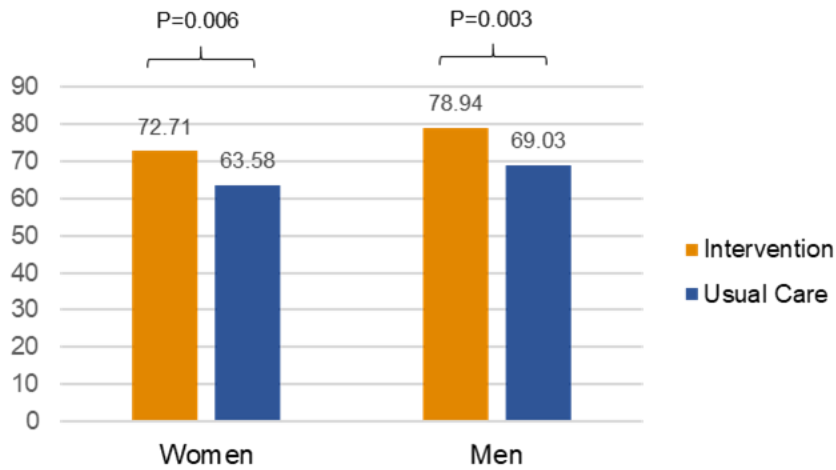
Graphical abstract. In this sex-specific analysis of a stepped wedge cluster randomized trial in Canada, a patient-centered transitional care model improved patient-reported outcomes (PROs) of discharge preparedness (B-PREPARED score), quality of transition [Care Transitions Measure-3 (CTM-3)], and health-related quality of life (HRQOL) (EQ-5D-5L) in the weeks following heart failure hospitalization, with effects largely consistent in women and men. However, women reported lower HRQOL than men at hospital discharge and experienced greater improvement in HRQOL with the intervention than did men.

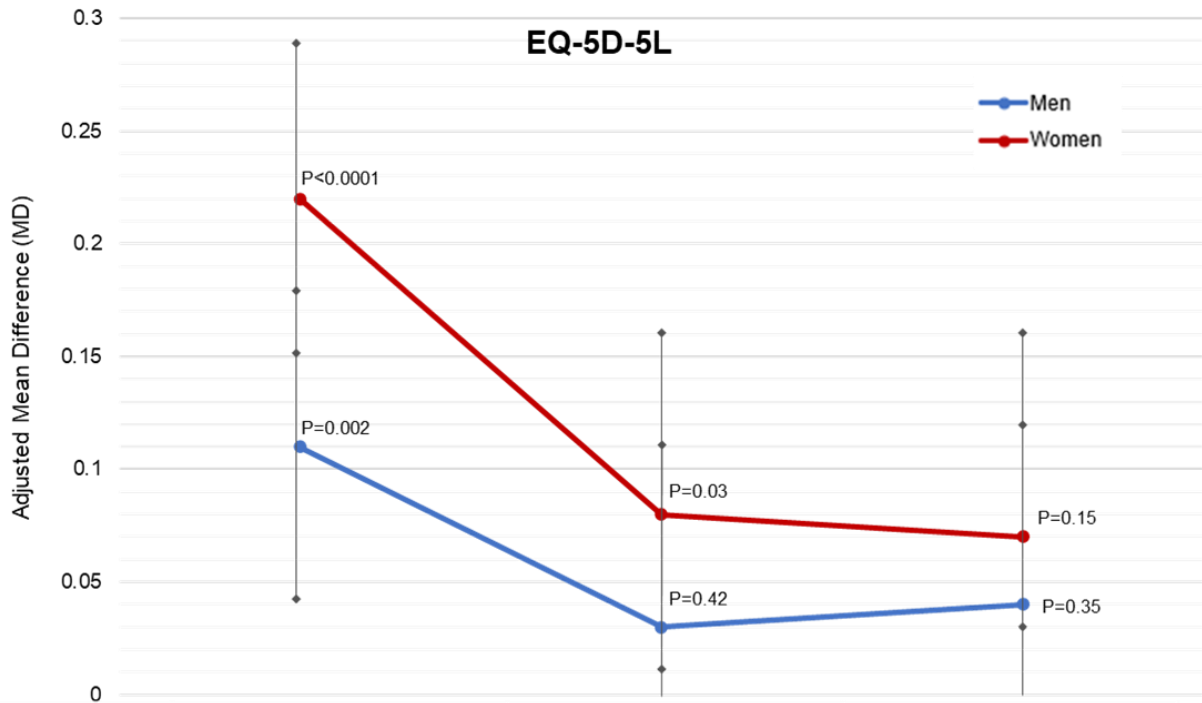


(A) B-PREPARED
6 weeks



(B) CTM-3
6 weeks





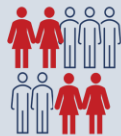
Men	0.11 (95% CI, 0.04-0.18)	0.03 (95% CI, -0.05-0.11)	0.04 (95% CI, -0.04-0.12)
Women	0.22 (95% CI, 0.15-0.29)	0.08 (95% CI, 0.01-0.16)	0.07 (95% CI, -0.03-0.16)

Effect of Patient-Centered Transitional Care Services on Patient-Reported Outcomes in Heart Failure: Sex-Specific Analysis of the PACT-HF RCT

BACKGROUND

Transitional care services can improve patient-reported outcomes (PROs) among those hospitalized for heart failure (HF).

The role of sex / gender in response to transitional care has not previously been explored.



AIM

To assess sex differences in the effect of a patient-centered transitional care program on PROs in patients hospitalized for HF

METHODS

Patients admitted for HF in 8 of the hospitals enrolled in the Patient Centered Care Transitions in HF (PACT-HF) stepped-wedge cluster randomized controlled trial



Intervention
In-hospital and post-discharge transitional care services versus usual care

Prespecified PROs



Discharge Preparedness (B-PREPARED) + Quality of care transition (CTM-3) + HRQOL (EQ-5Q-5L)

RESULTS

986 patients (47.4% women)



- Discharge preparedness improved** with the intervention at 6 weeks, no sex differences
- Quality of care transition improved** with the intervention at 6 weeks, no sex differences
- HRQOL improved** with the intervention at discharge, 6 weeks, and 6 months. Women had lower baseline HRQOL scores but experienced greater benefit with the intervention than men at discharge. There were no sex differences at 6 weeks + 6 months.

Table 1. Characteristics of patients (N=986) from whom PRO data was collected in the PACT-HF trial, stratified by sex

	Men (N=519)			Women (N=467)		
	PACT-HF (N=324)	Usual Care (N=195)	Standardized Difference	PACT-HF (N=282)	Usual Care (N=185)	Standardized Difference
Baseline Demographics and Quality of Life						
Age, mean years (SD)	74.15±13.64	75.34±12.26	0.09	78.82±11.21	78.49±10.64	0.03
Resides in long-term care, n (%)	31 (9.6)	16 (8.2)	0.05	47 (16.7)	30 (16.2)	0.01
Baseline Comorbidities†						
Hypertension‡, n (%)	230 (71.0)	144 (73.8)	0.06	201 (71.3)	127 (68.6)	0.06
Atrial Fibrillation, n (%)	157 (48.5)	98 (50.3)	0.04	146 (51.8)	95 (51.4)	0.01
Diabetes‡, n (%)	166 (51.2)	112 (57.4)	0.12	142 (50.4)	99 (53.5)	0.06
Chronic Kidney Disease, n (%)	75 (23.1)	47 (24.1)	0.02	44 (15.6)	36 (19.5)	0.10
Myocardial Infarction, n (%)	77 (23.8)	45 (23.1)	0.02	65 (23.0)	37 (20.0)	0.07
Chronic Pulmonary disease, n (%)	60 (18.5)	46 (23.6)	0.12	59 (20.9)	50 (27.0)	0.14
Peripheral Vascular Disease, n (%)	37 (11.4)	23 (11.8)	0.01	23 (8.2)	18 (9.7)	0.06
Cerebrovascular Disease, n (%)	20 (6.2)	26 (13.3)	0.24	17 (6.0)	13 (7.0)	0.04
Gastrointestinal Bleeding, n (%)	22 (6.8)	13 (6.7)	0.00	31 (11.0)	11 (5.9)	0.18
Resource utilization and risk profile						
ED visits in prior 6 months, median (IQR)	2 (1-3)	2 (1-3)	0.05	2 (1-2)	2 (1-3)	0.14
Acute length of hospital stay, median (IQR)	6 (3-9)	6 (4-9)	0.19	7 (4-10)	6 (4-10)	0.03
Resource Intensity Weight§, mean (SD)	1.49±1.26	1.42±0.79	0.06	1.38±1.16	1.47±0.94	0.09
LACE index , mean (SD)	11.69±2.62	12.19±2.19	0.21	11.70±2.39	12.11±2.36	0.17
Charlson comorbidity index#, mean (SD)	3.94±2.39	4.35±2.38	0.18	3.53±2.15	3.85±2.15	0.15

Abbreviations: ED, emergency department; IQR, interquartile range; SD, standard deviation.

* EQ-Visual Acuity score, measured by the EuroQOL visual scale, is a self-reported quality of life or health status measure ranging from 0-100, with higher scores reflecting better health status. This was measured on hospital admission.

†Baseline comorbidities were obtained using a 5-y retrospective review of databases.

‡Combined variable (hypertension = hypertension uncomplicated and complicated; diabetes = diabetes with and without chronic complication; liver disease = mild, moderate, or severe liver disease)

§Resource intensity weights (RIW)³⁰ provide an estimate of the cost of resources used in the care of a patient relative to the average hospitalized patient. The higher the RIW, the higher the resource utilization relative to the average inpatient.

||LACE₅₀ index is derived from length of stay, acuity of presentation, comorbidities, and ED visits in the preceding 6 months. Range: 1 to 19, with higher scores associated with a higher risk of readmission or death following hospitalization.

#Charlson comorbidity index⁵¹ is a method of predicting mortality and assessing disease burden based on comorbidities. The severity of comorbidity is categorized into 3 grades: mild (scores of 1-2); moderate (scores of 3-4); and severe (scores 5).

**Small cells (<6) suppressed for privacy.

Table 2. Patient-reported outcomes for the intervention and usual care groups following hospitalization for heart failure

		Fully Adjusted Least-Squares ^a Mean (95% CI)				
		PACT-HF (n=606)	Usual Care (n=380)	Adjusted* Difference	P-value for mean difference	P-value for sex interaction †
B-PREPARED[‡]						
6-week score						
Total		17.01 (15.95, 18.07)	13.00 (12.03, 13.98)	4.01 (2.90, 5.12)	<0.001	
Men		16.90 (15.46-18.33)	12.92 (11.58-14.25)	3.98 (2.36-5.59)	<0.001	0.24
Women		17.04 (15.01-19.07)	13.05 (11.12-14.99)	3.99 (2.40-5.57)	<0.001	
CTM-3[§]						
6-week score						
Total		77.47 (73.18, 81.76)	66.95 (63.03, 70.88)	10.52 (6.00, 15.04)	<0.001	
Men		78.94 (73.14-84.74)	69.03 (63.63-74.42)	9.92 (3.44-16.39)	0.003	0.69
Women		72.71 (64.62-80.80)	63.58 (55.86-71.29)	9.14 (2.67-15.61)	0.006	
EQ-5D-5L score						
Discharge						
Total		0.71 (0.66, 0.75)	0.53 (0.50, 0.57)	0.17 (0.12, 0.22)	<0.001	
Men		0.73 (0.67-0.79)	0.62 (0.57-0.67)	0.11 (0.04-0.18)	0.002	0.02
Women		0.59 (0.51-0.66)	0.37 (0.30-0.44)	0.22 (0.15-0.29)	<0.001	
6-week						
Total		0.69 (0.64, 0.74)	0.63 (0.58, 0.67)	0.06 (0.01, 0.12)	0.02	
Men		0.71 (0.64-0.78)	0.68 (0.61-0.74)	0.03 (-0.05-0.11)	0.42	0.18
Women		0.64 (0.53-0.75)	0.56 (0.45-0.66)	0.08 (0.01-0.16)	0.03	
6-month						
Total		0.68 (0.62, 0.74)	0.63 (0.58, 0.68)	0.05 (-0.01, 0.12)	0.09	
Men		0.72 (0.65-0.79)	0.68 (0.61-0.75)	0.04 (-0.04-0.12)	0.35	0.19
Women		0.60 (0.50-0.70)	0.53 (0.42-0.64)	0.07 (-0.03-0.16)	0.15	
QALY[#]						
6-month						
Total		0.34 (0.32, 0.36)	0.34 (0.33, 0.36)	-0.001 (-0.02-0.02)	0.94	
Men		0.36 (0.34-0.39)	0.36 (0.34-0.39)	-0.001 (-0.03-0.03)	0.96	0.39
Women		0.32 (0.28-0.35)	0.32 (0.28-0.36)	-0.002 (-0.03-0.03)	0.90	

*Adjusted among men for diabetes, COPD, cerebrovascular disease; adjusted among women for chronic kidney disease, COPD, dementia, and gastrointestinal bleeding. Adjusted for interceding hospitalizations and interceding ED visits that did not result in hospitalizations in both men and women.

†Adjusted for interceding hospitalizations and interceding ED visits that did not result in hospitalizations within the respective timeframes, age, COPD, and cerebrovascular disease.

‡B-PREPARED score²⁵ is a measure of discharge preparedness, ranging from 0 (worst) to 22 (best)

§Care Transitions Measure (CTM-3)²⁴ is a measure for quality of care transition, ranging from 0 (worst) to 100 (best),

||EQ-5D-5²⁶ is a measure of quality of life based on domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The scale is ranges from 0 (dead) to 1 (best quality of life).

#Quality Adjusted Life Year(s) (QALY)²⁸, a measure of both quantity and quality of life, is obtained by multiplying the utility value associated with a given state of health by the years lived in that state. QALY of 1 implies perfect health for 1 year; QALY was measured over 6 months, so it is anchored at 0 (dead) and 0.5 (best health at 6 months).

SUPPLEMENTAL MATERIALS

SEX-SPECIFIC DIFFERENCE IN PATIENT-REPORTED OUTCOMES OF THE PATIENT-CENTERED CARE TRANSITIONS IN HEART FAILURE (PACT-HF) RANDOMIZED TRIAL

Corresponding Author:

Harriette GC Van Spall MD MPH

20 Copeland Avenue

David Braley Research Institute Bldg, Suite C3-117

Hamilton ON L8L 2X2

Phone: (905) 521-2100 X40601

Email: harriette.vanspall@phri

Supplemental Table 1. Baseline characteristics of patients in whom PRO data was collected (986 patients, 8 hospitals)

Variable	PRO Sub-study (N = 986)		
	PACT-HF (N=606)	Usual Care (N=380)	Standardized Difference
Age	76.32 ± 12.77	76.88 ± 11.59	0.05
Baseline comorbidities			
Hypertension**	431 (71.1%)	271 (71.3%)	0.00
Atrial fibrillation	303 (50.0%)	193 (50.8%)	0.02
Diabetes**	308 (50.8%)	211 (55.5%)	0.09
Chronic kidney disease	119 (19.6%)	83 (21.8%)	0.05
Myocardial Infarction	142 (23.4%)	82 (21.6%)	0.04
Chronic obstructive pulmonary disease	119 (19.6%)	96 (25.3%)	0.14
Peripheral vascular disease	60 (9.9%)	41 (10.8%)	0.03
Cerebrovascular disease	37 (6.1%)	39 (10.3%)	0.15
Dementia	31 (5.1%)	19 (5.0%)	0.01
Gastrointestinal bleeding	53 (8.7%)	24 (6.3%)	0.09

Supplemental Table 2. Table of Outcomes

Variable	Men (N=519)				Women (N=467)			
	PACT-HF N=324	Usual Care N=195	Standardized Difference	P-Value	PACT-HF N=282	Usual Care N=185	Standardized Difference	P-Value
Hospitalization in the 6 weeks following discharge	91 (28.1%)	59 (30.3%)	0.05	0.597	73 (25.9%)	52 (28.1%)	0.05	0.596
Hospitalization in the 6 months following discharge	179 (55.2%)	122 (62.6%)	0.15	0.102	155 (55.0%)	102 (55.1%)	0.00	0.971
Emergency department visit in the 6 weeks following discharge	53 (16.4%)	22 (11.3%)	0.15	0.111	36 (12.8%)	30 (16.2%)	0.10	0.295
Emergency department visit in the 6 months following discharge	125 (38.6%)	49 (25.1%)	0.29	0.002	82 (29.1%)	61 (33.0%)	0.08	0.372

Supplemental Table 3. Patient-reported outcomes following hospitalization for heart failure, by sex. All models are adjusted from the stepped wedge cluster randomized

	Unimputed Least-Squares Mean (95% CI)				Imputed Crude Mean (SD)		Imputed Least-Squares Mean (95% CI)			
	PACT-HF (n=606)	Usual Care (n=380)	Difference	P-value for mean difference	P-value for sex interaction	PACT-HF (n=606)	Usual Care (n=380)	PACT-HF (n=606)	Usual Care (n=380)	Difference
B-PREPARED[†]										
6-week score										
Men	16.82 (15.67-17.98)	12.94 (11.85-14.04)	3.88 (2.26-5.50)	<0.0001		15.49 (4.84)	14.03 (5.15)	16.79 (15.65-17.92)	12.94 (11.5-14.03)	3.85 (2.26-5.50)
Women	16.97 (15.74-18.19)	13.02 (11.88-14.17)	3.94 (2.35-5.53)	<0.0001	0.24	15.67 (4.56)	13.23 (5.45)	16.94 (15.74-18.15)	12.98 (11.84-14.11)	3.96 (2.35-5.53)
CTM-3[‡]										
6-week score										
Men	78.86 (73.85-83.87)	67.45 (62.47-72.43)	11.41 (4.41-18.41)	0.002		75.59 (20.59)	69.75 (17.00)	78.12 (73.53-82.71)	67.95 (63.54-72.37)	10.17 (4.41-18.41)
Women	74.74 (69.39-80.09)	64.22 (59.20-69.23)	10.52 (3.56-17.48)	0.003	0.97	75.02 (19.78)	67.75 (18.73)	73.67 (68.78-78.56)	64.37 (59.69-69.05)	9.30 (3.56-17.48)
EQ-5D-5L[§] score										
Discharge										
Men	0.75 (0.71-0.80)	0.64 (0.59-0.68)	0.12 (0.05-0.19)	0.001		0.74 (0.23)	0.64 (0.25)	0.75 (0.71-0.80)	0.64 (0.59-0.68)	0.12 (0.05-0.19)
Women	0.68 (0.64-0.73)	0.46 (0.42-0.50)	0.22 (0.15-0.29)	<0.0001	0.02	0.66 (0.24)	0.48 (0.28)	0.68 (0.65-0.72)	0.46 (0.43-0.50)	0.22 (0.15-0.29)
6-week										
Men	0.75 (0.69-0.80)	0.70 (0.64-0.75)	0.05 (-0.03-0.13)	0.21		0.73 (0.24)	0.73 (0.23)	0.74 (0.68-0.79)	0.69 (0.64-0.75)	0.04 (-0.03-0.13)
Women	0.71 (0.65-0.77)	0.61 (0.56-0.67)	0.10 (0.02-0.17)	0.02	0.25	0.68 (0.25)	0.63 (0.25)	0.69 (0.63-0.76)	0.60 (0.55-0.66)	0.09 (0.02-0.17)
6-month										
Men	0.74 (0.69-0.80)	0.70 (0.65-0.75)	0.04 (-0.04-0.13)	0.33		0.73 (0.24)	0.72 (0.26)	0.75 (0.69-0.80)	0.70 (0.65-0.75)	0.05 (-0.04-0.13)
Women	0.67 (0.61-0.73)	0.61 (0.55-0.67)	0.06 (-0.03-0.15)	0.20	0.28	0.66 (0.26)	0.59 (0.29)	0.65 (0.59-0.72)	0.59 (0.52-0.65)	0.07 (-0.03-0.15)
QALYs										
First 6 months										
Men	0.37 (0.35-0.39)	0.37 (0.36-0.39)	-0.01 (-0.04-0.02)	0.60		0.37 (0.10)	0.36 (0.10)	0.37 (0.35-0.39)	0.37 (0.35-0.39)	0.00 (-0.04-0.02)
Women	0.33 (0.31-0.35)	0.33 (0.31-0.35)	-0.002 (-0.03-0.03)	0.91	0.43	0.34 (0.10)	0.30 (0.11)	0.32 (0.30-0.34)	0.33 (0.31-0.34)	-0.002 (-0.03-0.03)

Abbreviations: CTM-3, 3-Item Care Transitions Measure; EQ-5D-5L, 5-level EQ-5D version; QALY, quality-adjusted life-year.

*Least Square Mean models are all adjusted for the stepped wedge design and include unimputed dataset as well as imputed dataset fully adjusted for imbalance in baseline characteristics between sex-specific treatment groups and interceding clinical outcomes. The 6-week and 6-month EQ5D5L scores and Quality Adjusted Life Years are adjusted for discharge EQ-5D-5L scores.

[†]B-PREPARED score is a measure of discharge preparedness, ranging from 0 (worst) to 22 (best)

[‡]Care Transitions Measure (CTM-3) is a measure for quality of care transition, ranging from 0 (worst) to 100 (best),

[§]EQ-5D-5L is a measure of quality of life based on domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, The scale is ranges from 0 (dead) to 1 (best quality of life).

^{||}Quality Adjusted Life Year(s) (QALY), a measure of both quantity and quality of life, is obtained by multiplying the utility value associated with a given state of health by the years lived in that state. QALY of 1 implies perfect health for 1 year; QALY was measured over 6 months, so it is anchored at 0 (dead) and 0.5 (best health at 6 months).