Pharmacy-based interdisciplinary intervention for patients with chronic heart failure: results of the PHARM-CHF randomized controlled trial

Martin Schulz

on behalf of the Co-PI Ulrich Laufs, MD, and the PHARM-CHF Steering Committee and Investigators

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Declaration of Interest

• PHARM-CHF was funded by ABDA – Federal Union of German Associations of Pharmacists; Pharmacists’ Foundation Westphalia-Lippe; Chamber of Pharmacists North Rhine; Lesmueller Foundation; Foundation Pharmaceutical Care (all Germany).

• The study design, funding, and governance are independent from commercial sponsorship of any kind.
Background and Rationale

• Medication non-adherence affects 30–50% of patients with chronic heart failure (CHF) and
• is associated with worse quality of life, morbidity, and mortality.
• Pharmacotherapy for CHF and various co-morbidities leads to polypharmacy and subsequent drug-related problems.
• However, randomized evidence on interventions addressing these problems is scarce and
• a pharmacy-based RCT aiming to improve medication adherence and quality of life in elderly CHF patients is absent.

Trial Objectives

PHARM-CHF was designed to investigate whether a continuous pharmacy-based interdisciplinary intervention
• improves medication adherence and
• quality of life
in elderly patients with chronic heart failure and whether
• it affects hospitalizations and mortality.

Study Design

Prospective, multicentre, randomized controlled trial with a median follow-up of 2.0 years

**Physician: all patients**
Baseline visit, phone contacts at 6 and 18 months, visits at 12 and 24 months, final visit.

**Usual Care (n=127)**

**Pharmacy Care (n=110)**
Initial medication review in the pharmacy, followed by (bi-)weekly pharmacy visits including
- individual counselling
- measurement of blood pressure/pulse rate
- drug-related problems/change in vital signs? → physician
- medication dispensed in weekly dosing aids (pillboxes)
Patient Profile

Inclusion Criteria

• Diagnosis of heart failure (HF)
• ≥ 60 years
• Stable HF medication (no relevant change within past 4 weeks) including a diuretic
• Hospitalization for decompensated HF within past 12 months or
  BNP ≥ 350 pg/mL or
  NT-proBNP ≥ 1400 pg/mL
• Written informed consent

Exclusion Criteria

• Regular/assisted use of a weekly dosing aid (pillbox)
• Unwillingness or inability to visit a participating pharmacy (bi-)weekly
• Planned cardiac surgery
• Life-expectancy < 6 months
• Unwillingness or inability to comply with the study protocol
• Participation in other studies (currently or in the last 4 weeks)
Primary Endpoints

Efficacy

• Medication adherence as mean Proportion of Days Covered (PDC) within 365 days for three heart failure medication classes:
  – beta-blockers
  – angiotensin-converting enzyme inhibitors (ACEi) or angiotensin receptor blockers (ARB)
  – mineralocorticoid receptor antagonists (MRA)

• Source: pharmacy claims data

Safety

• Days lost due to unplanned cardiovascular hospitalizations (blindly adjudicated) or all-cause death during 365 days follow-up.

$PDC = \frac{\text{Number of Days in Period "covered"}}{\text{Number of Days in Period}}$
Main Secondary Outcomes

Efficacy

• Percentage of patients with a mean PDC ≥80%, classified as adherent
• Quality of Life (MLHFQ)
• PDC for each heart failure (HF) medication class
• Percentage of patients with a PDC ≥80% for each HF medication class

Safety

• Percentage days lost due to unplanned cardiovascular (CV) hospitalizations or all-cause death
• All-cause mortality or unplanned CV hospitalizations as recurrent event
• Unplanned CV hospitalizations
• Unplanned hospitalizations for heart failure (HF)
### Main Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Pharmacy Care</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>($n=110$)</td>
<td>($n=127$)</td>
</tr>
<tr>
<td><strong>Age</strong>, mean ± SD (range)</td>
<td>74.1 ± 6.8 (60–86)</td>
<td>74.1 ± 7.2 (60–88)</td>
</tr>
<tr>
<td><strong>Men</strong></td>
<td>62%</td>
<td>61%</td>
</tr>
<tr>
<td><strong>BMI</strong>, kg/m$^2$</td>
<td>29.0 ± 5.2</td>
<td>29.2 ± 4.9</td>
</tr>
<tr>
<td><strong>NYHA class</strong>, I/II vs. III/IV</td>
<td>41% vs. 59%</td>
<td>41% vs. 59%</td>
</tr>
<tr>
<td><strong>LVEF &lt;40%</strong></td>
<td>25%</td>
<td>24%</td>
</tr>
<tr>
<td><strong>SBP / DBP</strong>, mean</td>
<td>127.1 / 76.0 mmHg</td>
<td>129.4 / 77.3 mmHg</td>
</tr>
<tr>
<td><strong>Heart rate</strong>, mean ± SD</td>
<td>73.5 ± 13.2 min$^{-1}$</td>
<td>75.8 ± 13.8 min$^{-1}$</td>
</tr>
<tr>
<td><strong>Co-morbidities</strong>, mean ± SD</td>
<td>7.4 ± 2.5</td>
<td>6.9 ± 2.2</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>97%</td>
<td>98%</td>
</tr>
<tr>
<td><strong>CAD</strong></td>
<td>73%</td>
<td>67%</td>
</tr>
<tr>
<td><strong>Depression</strong> (PHQ-9 ≥10)</td>
<td>23%</td>
<td>28%</td>
</tr>
<tr>
<td><strong>Quality of Life</strong> (MLHFQ 0-105)</td>
<td>39.9 ± 19.9</td>
<td>42.5 ± 22.3</td>
</tr>
</tbody>
</table>
## Baseline Therapy & Adherence

<table>
<thead>
<tr>
<th></th>
<th>Pharmacy Care</th>
<th>Usual Care</th>
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</thead>
<tbody>
<tr>
<td><strong>No. drugs</strong>, mean ± SD (range)</td>
<td>8.8 ± 3.0 (4–16)</td>
<td>8.9 ± 3.2 (4–18)</td>
</tr>
<tr>
<td><strong>No. single doses per day</strong>, mean ± SD (range)</td>
<td>10.7 ± 3.8 (4–23)</td>
<td>11.0 ± 4.3 (2–23)</td>
</tr>
<tr>
<td><strong>Beta-blocker</strong></td>
<td>91%</td>
<td>95%</td>
</tr>
<tr>
<td><strong>ACEi or ARB</strong></td>
<td>78%</td>
<td>83%</td>
</tr>
<tr>
<td><strong>MRA</strong></td>
<td>45%</td>
<td>41%</td>
</tr>
<tr>
<td><strong>Mean adherence (PDC) -183 days</strong>, mean ± SD, %</td>
<td>68.1 ± 29.7</td>
<td>68.5 ± 27.6</td>
</tr>
<tr>
<td><strong>Mean PDC ≥80% (adherent)</strong></td>
<td>44%</td>
<td>42%</td>
</tr>
<tr>
<td><strong>Loop diuretic</strong></td>
<td>79%</td>
<td>83%</td>
</tr>
<tr>
<td><strong>Cardiac glycoside</strong></td>
<td>15%</td>
<td>13%</td>
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</tbody>
</table>
Adherence to Three HF Medication Classes
Proportion of Adherent Patients

<table>
<thead>
<tr>
<th>OR</th>
<th>Δ%</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.9</td>
<td>18</td>
</tr>
<tr>
<td>2.7</td>
<td>17</td>
</tr>
<tr>
<td>2.2</td>
<td>14</td>
</tr>
<tr>
<td>2.9</td>
<td>12</td>
</tr>
</tbody>
</table>

% Patients with PDC ≥80%

- **P<0.05
- **P<0.01

Pharmacy Care vs Usual Care

Heart Failure 2019

#HeartFailure2019
Hospitalizations and Mortality

<table>
<thead>
<tr>
<th>365 day follow-up</th>
<th>Pharmacy Care</th>
<th>Usual Care</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause deaths, n (%)</td>
<td>8 (7%)</td>
<td>8 (6%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Unplanned cardiovascular (CV) hospitalizations, n</td>
<td>47</td>
<td>48</td>
<td>-</td>
</tr>
<tr>
<td>Days lost due to unplanned CV hospitalizations or death, mean (95% CI)</td>
<td>24.8 (10.6–38.9)</td>
<td>16.5 (6.1–26.8)</td>
<td>0.70</td>
</tr>
<tr>
<td>% days lost due to unplanned CV hospitalizations or death, mean (95% CI)</td>
<td>6.78 (2.91–10.66)</td>
<td>4.51 (1.67–7.35)</td>
<td>0.70</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>End of study follow-up</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause deaths, n (%)</td>
<td>20 (18%)</td>
<td>27 (21%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Unplanned CV hospitalizations, n</td>
<td>91</td>
<td>93</td>
<td>-</td>
</tr>
<tr>
<td>All events (hospitalizations of any cause and deaths), n</td>
<td>253</td>
<td>266</td>
<td>-</td>
</tr>
</tbody>
</table>
Quality of Life (MLHFQ global score)

-1.9 (-7.6 to 3.8), $P=0.51$

-7.8 (-14.5 to -1.1), $P=0.02$

365 Days
- Pharmacy Care: -3.9
- Usual Care: -2.0

730 Days
- Pharmacy Care: -4.2
- Usual Care: 3.6

#HeartFailure2019
PHARM-CHF Conclusions

A pharmacy-based interdisciplinary intervention safely
• improved mean adherence to three heart failure medication classes and
• the proportion of adherent patients, and
• led to clinically important improvements in quality of life.
Thank You

- Community pharmacists, general practitioners, internal medicine specialists, and cardiologists
- Steering Committee: Stefan D. Anker, Michael Boehm, Nina-Griese-Mammen, Charlotte Kloft, Friedrich Koehler, and Dietmar Trenk
- Clinical Event Committee: Stephan von Haehling (Chair), Heinrich Bechtold, Sabine Genth-Zotz, Markus Haass, and Rolf Wachter
- Sponsors
- PHARM-CHF co-ordinators

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Pharmacy-based interdisciplinary intervention for patients with chronic heart failure: results of the PHARM-CHF randomized controlled trial

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