



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

ClinicalTrials.gov Identifier: NCT01692119

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.

Laufs U et al. Eur Heart J. 2011;32:264-8; Molloy GJ et al. Circ Heart Fail. 2012;5:126-33; Nieuwlaat R et al. Cochrane Database Syst Rev. 2014;11:CD000011; Krueger K et al. Int J Cardiol. 2015;184:728-35; Schulz M et al. Int J Cardiol. 2016;220:556-76. Krueger K et al. Heart Fail Rev. 2018;23:63-71. Ihle P et al. Clin Pharmacol Ther. 2019, March 12.

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.

Laufs U et al. Eur J Heart Fail. 2018;20:1350–9.

Study Design

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

Screening &
Randomization by
Physician

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 $\geq 80\%$, classified as *adherent***
- **Quality of Life (MLHFQ)**
- PDC for each heart failure (HF) medication class
- Percentage of patients with a PDC $\geq 80\%$ 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)

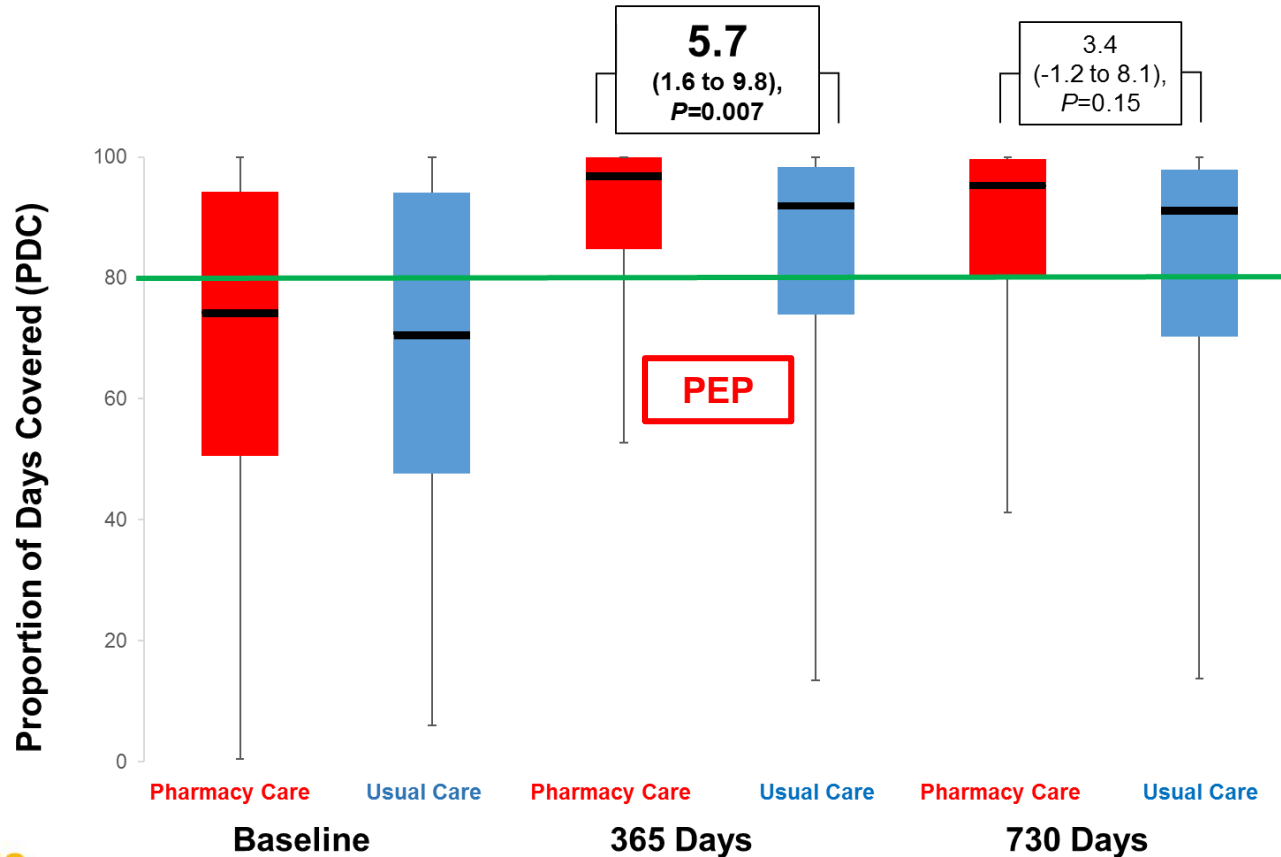
Main Baseline Characteristics

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

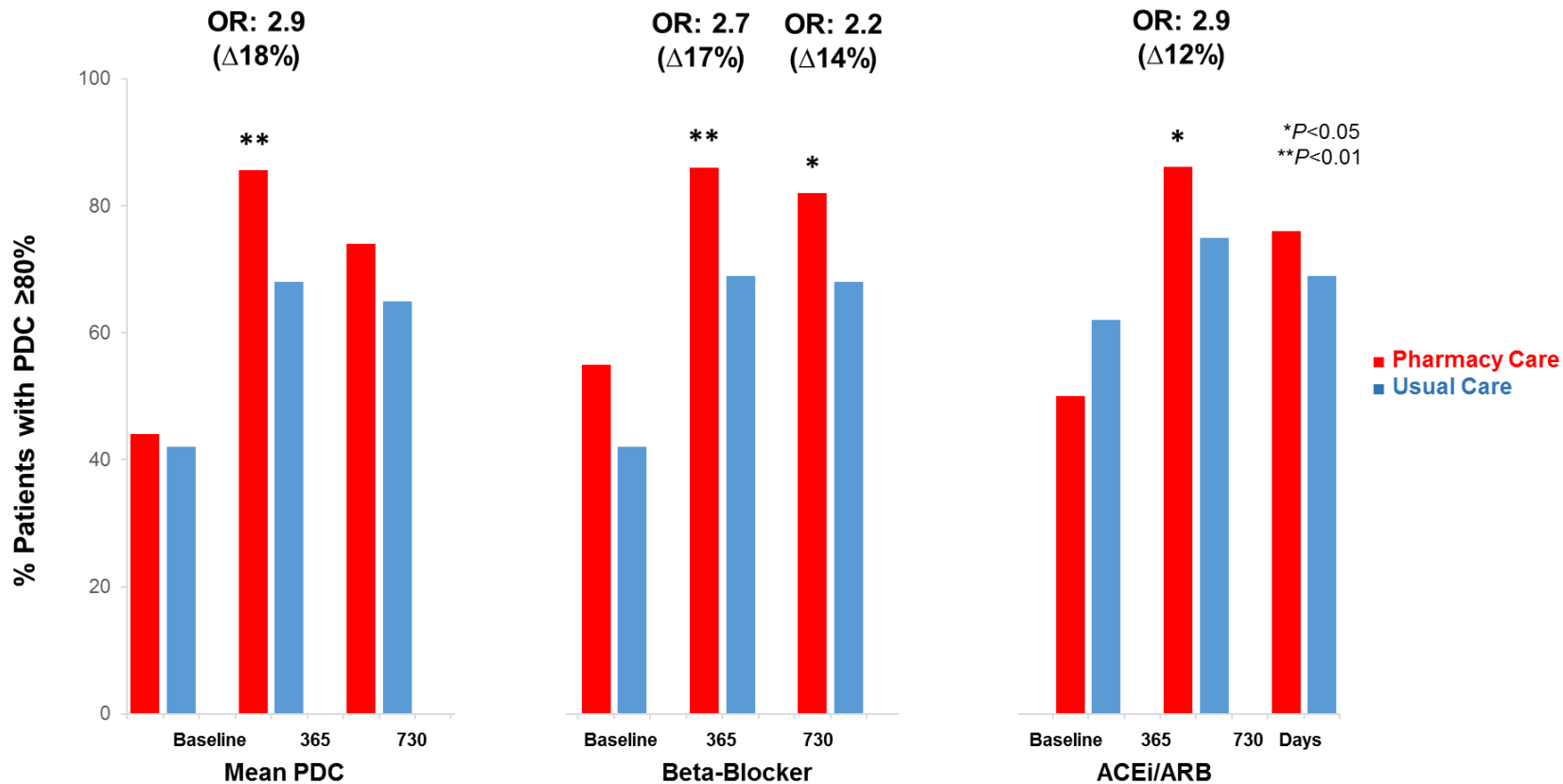
Baseline Therapy & Adherence

	Pharmacy Care	Usual Care
No. drugs , mean \pm SD (range)	8.8 \pm 3.0 (4–16)	8.9 \pm 3.2 (4–18)
No. single doses per day , mean \pm SD (range)	10.7 \pm 3.8 (4–23)	11.0 \pm 4.3 (2–23)
Beta-blocker	91%	95%
ACEi or ARB	78%	83%
MRA	45%	41%
Mean adherence (PDC) -183 days mean \pm SD, %	68.1 \pm 29.7	68.5 \pm 27.6
Mean PDC \geq80% (<i>adherent</i>)	44%	42%
Loop diuretic	79%	83%
Cardiac glycoside	15%	13%

Adherence to Three HF Medication Classes



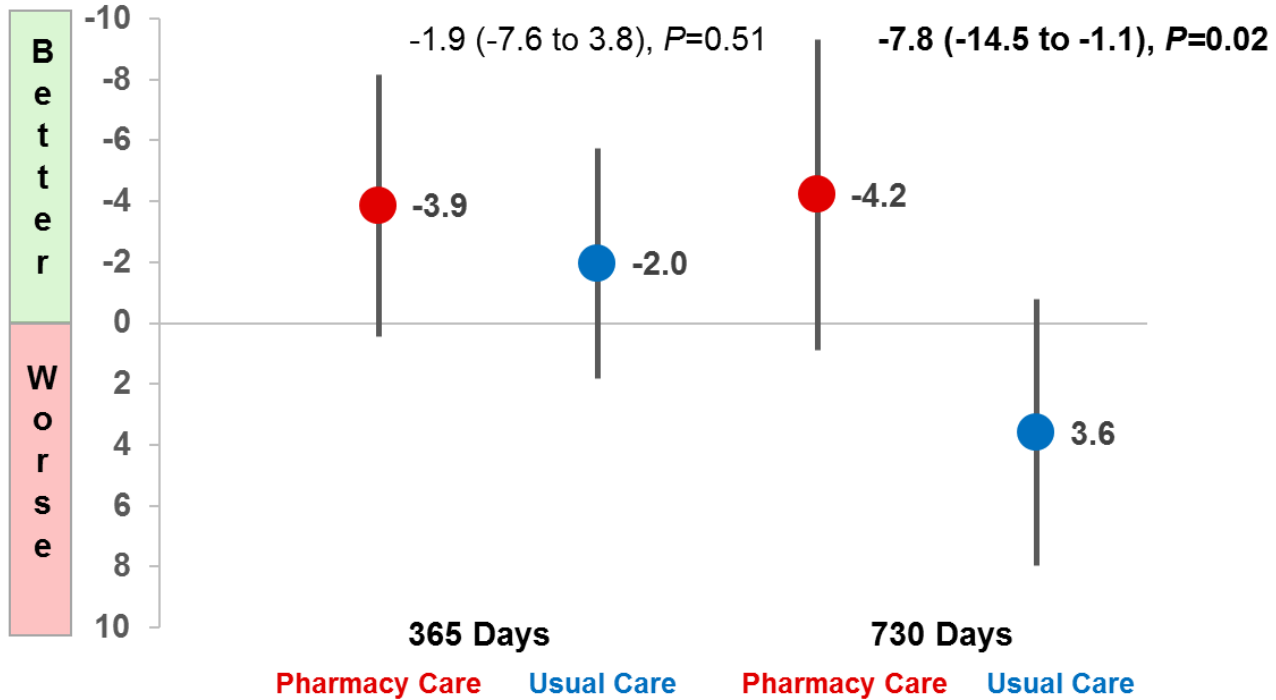
Proportion of Adherent Patients



Hospitalizations and Mortality

365 day follow-up	Pharmacy Care	Usual Care	P-value
All-cause deaths, <i>n</i> (%)	8 (7%)	8 (6%)	0.77
Unplanned cardiovascular (CV) hospitalizations, <i>n</i>	47	48	-
Days lost due to unplanned CV hospitalizations or death, mean (95% CI)	24.8 (10.6–38.9)	16.5 (6.1–26.8)	0.70
% days lost due to unplanned CV hospitalizations or death, mean (95% CI)	6.78 (2.91–10.66)	4.51 (1.67–7.35)	0.70
End of study follow-up			
All-cause deaths, <i>n</i> (%)	20 (18%)	27 (21%)	0.55
Unplanned CV hospitalizations, <i>n</i>	91	93	-
All events (hospitalizations of any cause and deaths), <i>n</i>	253	266	-

Quality of Life (MLHFQ global score)



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

Prof. Dr. Martin Schulz, FFIP, FESCP

Department of Medicine, ABDA, and
Institute of Pharmacy, Freie Universität Berlin

m.schulz@fu-berlin.de
www.pharm-chf.de

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Martin Schulz^{1,2,3*}, Nina Griese-Mammen¹, Stefan D. Anker⁴, Friedrich Koehler⁵, Peter Ihle⁶, Christian Ruckes⁷, Pia M. Schumacher¹, Dietmar Trenk⁸, Michael Böhm⁹, and Ulrich Laufs¹⁰, for the PHARM-CHF Investigators[†]