Pharmacist intervention to prevent hospitalization and death in patients with heart failure: A prospective cluster randomized controlled trial

R Lowrie, FS Mair, N Greenlaw, P Forsyth, PS Jhund, A McConnachie, B Rae, JJV McMurray

On behalf of the Heart failure Optimal Outcomes from Pharmacy Study (HOOPS) investigators

NHS Greater Glasgow and Clyde

University of Glasgow

Background and Introduction

- **Disease-modifying drugs (e.g. ACE inhibitors and β-blockers) are under-used and under-dosed in patients with heart failure in primary care.**
- **“Collaborative medication review” - pharmacists evaluate patients’ medications and suggest changes which are enacted with the agreement of the patient and the family doctor.**
- **We hypothesised that pharmacist intervention to optimize medical treatment in patients with left ventricular systolic dysfunction would improve clinical outcomes.**
- **Comparative-effectiveness, cluster randomized, trial in primary care**

Patients: Inclusion and Exclusion Criteria

- **Inclusion:** **Left ventricular systolic dysfunction (confirmed by cardiac imaging). Patients did not have to have symptoms or signs of heart failure.**
- **Exclusions:**
  - **Registration with heart failure-nurse service - provided to patients recently hospitalized with heart failure (excluded higher risk patients with more severe symptoms).**
  - **Concurrent disease (other than heart failure) likely to reduce life-expectancy; severe cognitive impairment or psychiatric illness; dialysis, or a resident in a long-term care facility.**

Pharmacist Intervention

- **27 pharmacists**
- **30 minute, face-to-face consultation**
- **If changes were made (e.g. treatment initiation or dose modification), 3-4 additional consultations were arranged**
- **All study pharmacists attended a training day which covered signs and symptoms and evidence based medical treatment of left ventricular systolic dysfunction**

Primary and Secondary Outcomes

- **Primary:** **Death from any cause or hospital admission for worsening heart failure**
- **Secondary:**
  - **Death from any cause or hospital admission for pre-specified cardiovascular causes**
  - **Death from any cause or hospital admission for any cause**
  - **Total number of admissions (and patients admitted) for heart failure, cardiovascular causes and any cause**
  - **Days alive out of hospital**
  - **ER visits, hospital out-patient clinics, primary care visits,**
  - **Prescribing of disease modifying medicines**

Statistical Assumptions

- **Rate of primary endpoint in the usual care group 10% per year**
- **Relative risk reduction in the primary outcome of 26% with pharmacist intervention**
- **2.6 years recruitment plus 2 further years of follow-up**
- **Needed 673 patients to experience primary outcome for 80% power to detect a difference between treatments.**
- **Sample size inflated by a factor of 1.55 to account for cluster-randomization design - needed 87 practices/1044 patients per group.**
- **Due to longer than anticipated recruitment >750 patients expected to experience primary outcome providing 80% power to detect a 19% relative risk reduction.**

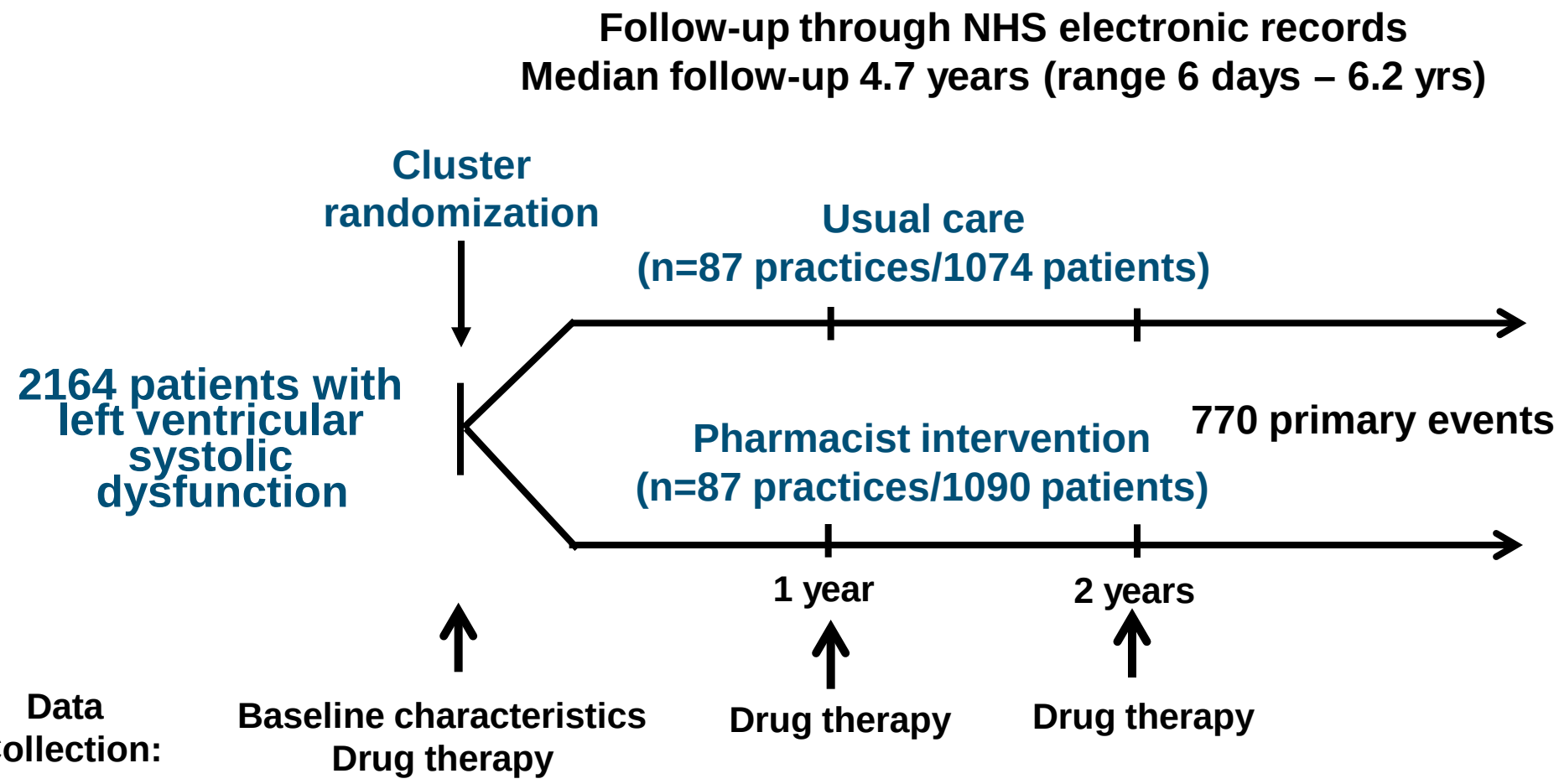
Statistical analysis

- **The primary analysis compared the main outcomes between the treatment groups using a Cox proportional hazards frailty model.**
- **Treatment effect adjusted for:**
  - the stratification variables - level of socioeconomic deprivation (affluent, intermediate, deprived) and practice type (single-handed or group-practice)
  - and age, creatinine, grade of left ventricular systolic dysfunction, atrial fibrillation, respiratory disease, total number of medications and diuretic use.

Setting and Patients

- **The UK National Health Service – Greater Glasgow & Clyde Health Board. 1.2 million people ~25% of Scottish population.**
- **Whole population registered with one of 220 family medical centers (practices); all centers invited to participate.**
- **174 of 220 centers consented (6620 patients with left ventricular systolic dysfunction).**
- **4451 patients declined/did not reply; 2169 (33%) patients consented and enrolled between Oct 2004 and Sept 2007.**
- **Randomization by center (cluster-randomization design) to avoid “contamination”.**

Study Outline



Results

- **Baseline characteristics and treatment**
- **Effect of pharmacist intervention on prescribing**
- **Effect of pharmacist intervention on clinical outcomes**

Baseline Characteristics (1)

Characteristic	Pharmacist intervention (n=1092)	Usual care (n=1077)
Age (years)	71	71
Age ≥ 70 years (%)	55	55
Female (%)	29	31
Systolic/diastolic BP (mmHg)	127/72	128/72
Degree of left ventricular systolic function (%)		
Mild	43	39
Moderate	41	44
Severe	17	17
Principal cause of left ventricular systolic function (%)		
Ischemic	80	76
Non ischemic/unknown	18/2	21/3

Baseline Characteristics (2)

Characteristic	Pharmacist intervention (n=1092)	Usual care (n=1077)
Medical history (%)		
Admission for heart failure in past yr.	2	2
Hypertension	50	46
Myocardial infarction	66	62
Atrial fibrillation or flutter	27	28
Diabetes mellitus	22	20
Stroke	14	15
Respiratory disease	30	30
Asthma	*7*	*8*
Smoker	24	25

Baseline Cardiovascular Medication

Patients taking drug (%)	Pharmacist intervention (n=1092)	Usual care (n=1077)
ACE inhibitor or/and ARB	**87**	**85**
ACE inhibitor	**75**	**71**
*≥100% recommended dose**	*60*	*62*
ARB	**14**	**17**
*≥100% recommended dose**	*23*	*19*
Beta-blocker	**62**	**62**
*≥100% recommended dose**	*22*	*20*
Aldosterone antagonist	**5**	**5**
Digitalis glycoside	**14**	**11**
Diuretic	**61**	**61**
Antithrombotic	**91**	**90**
Lipid lowering agent	**79**	**78**

**Of patients taking drug*

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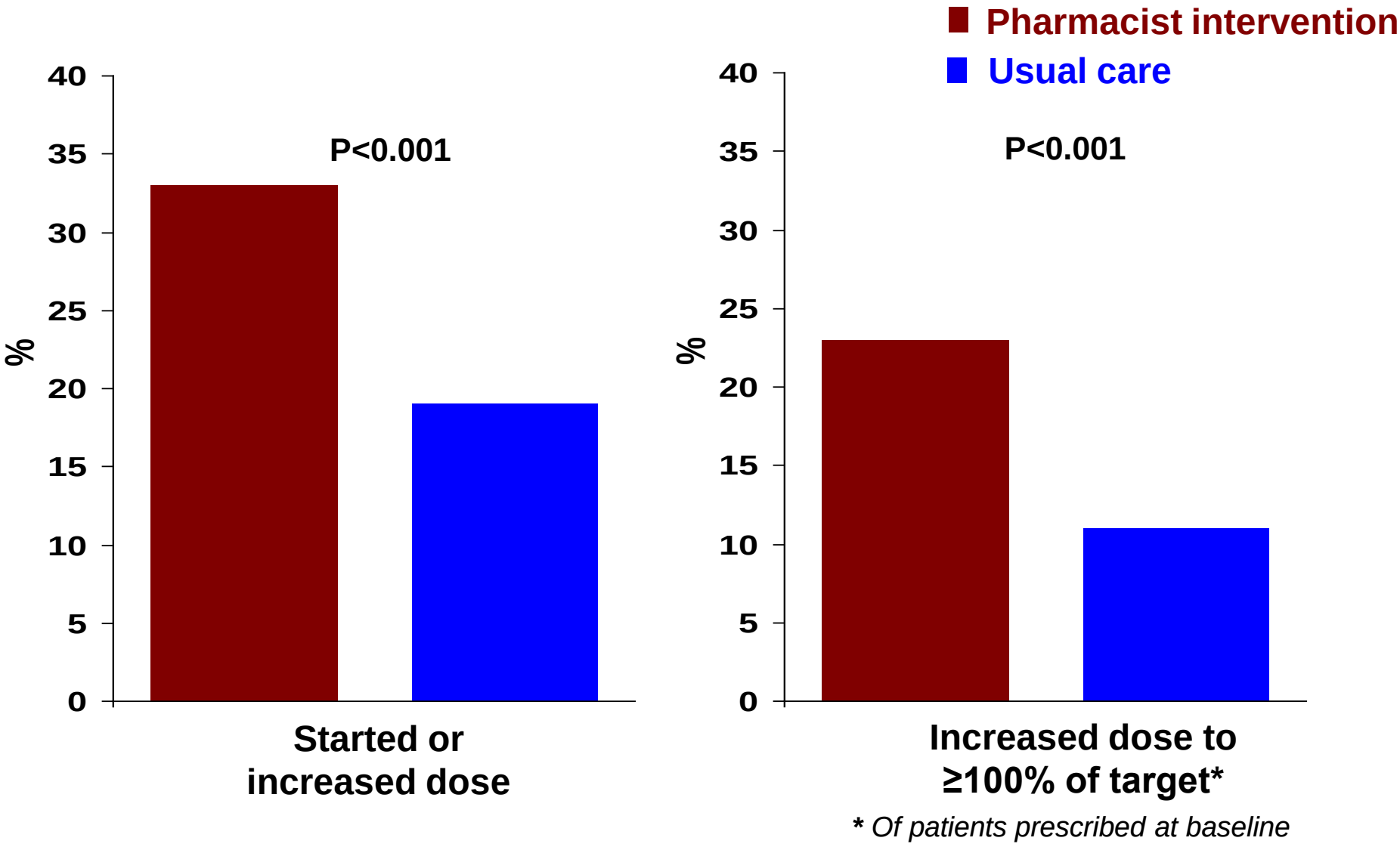
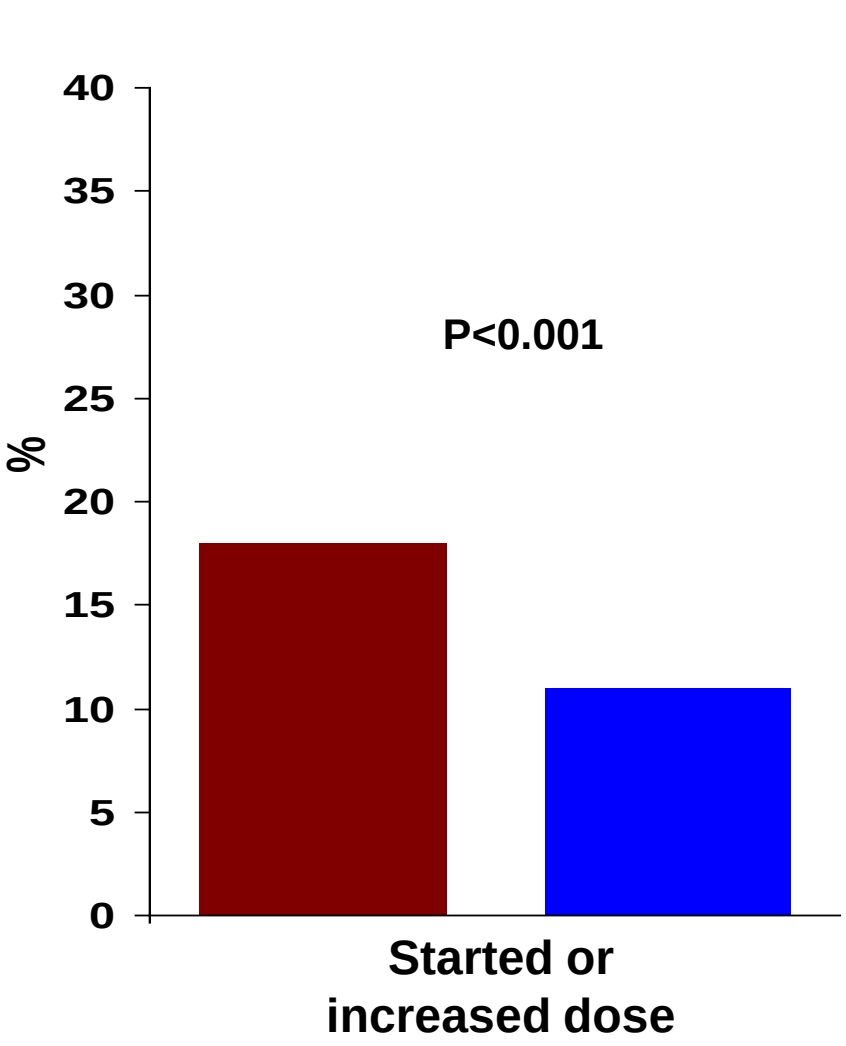
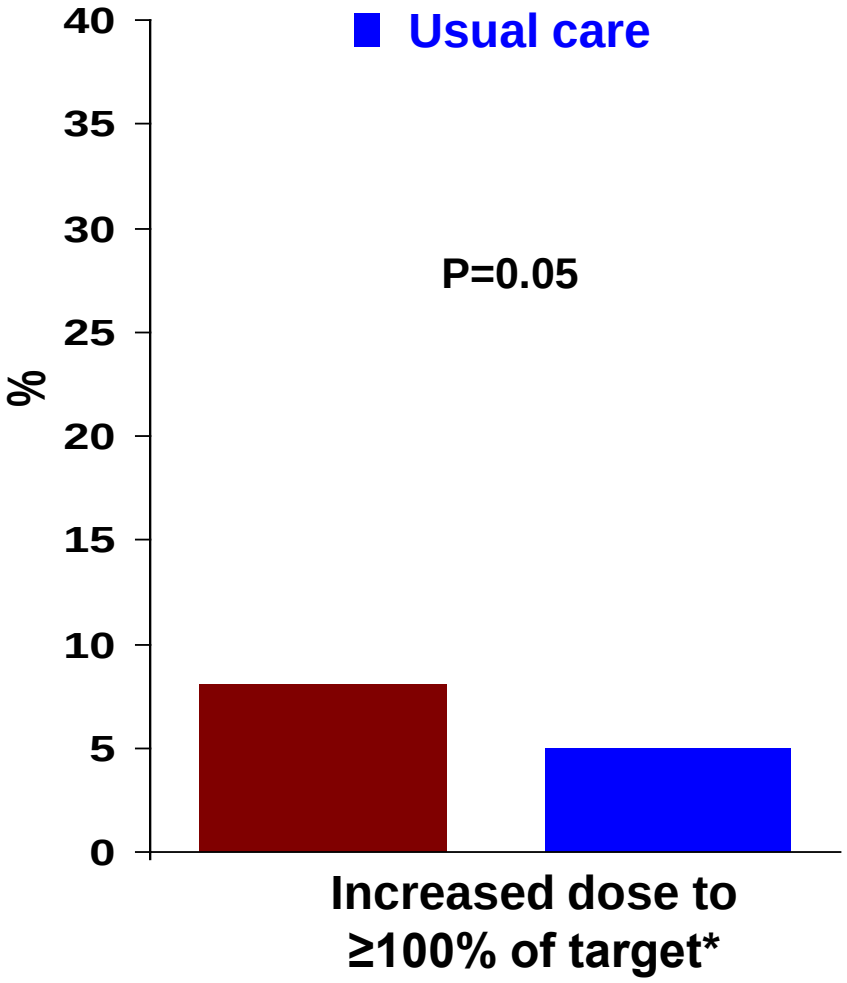
Changes in ACE inhibitor or ARB Prescribing (end of first year follow up)



** Of patients prescribed at baseline*

Changes in Beta-blocker Prescribing (end of first year of follow up)





** Of patients prescribed at baseline*

Results

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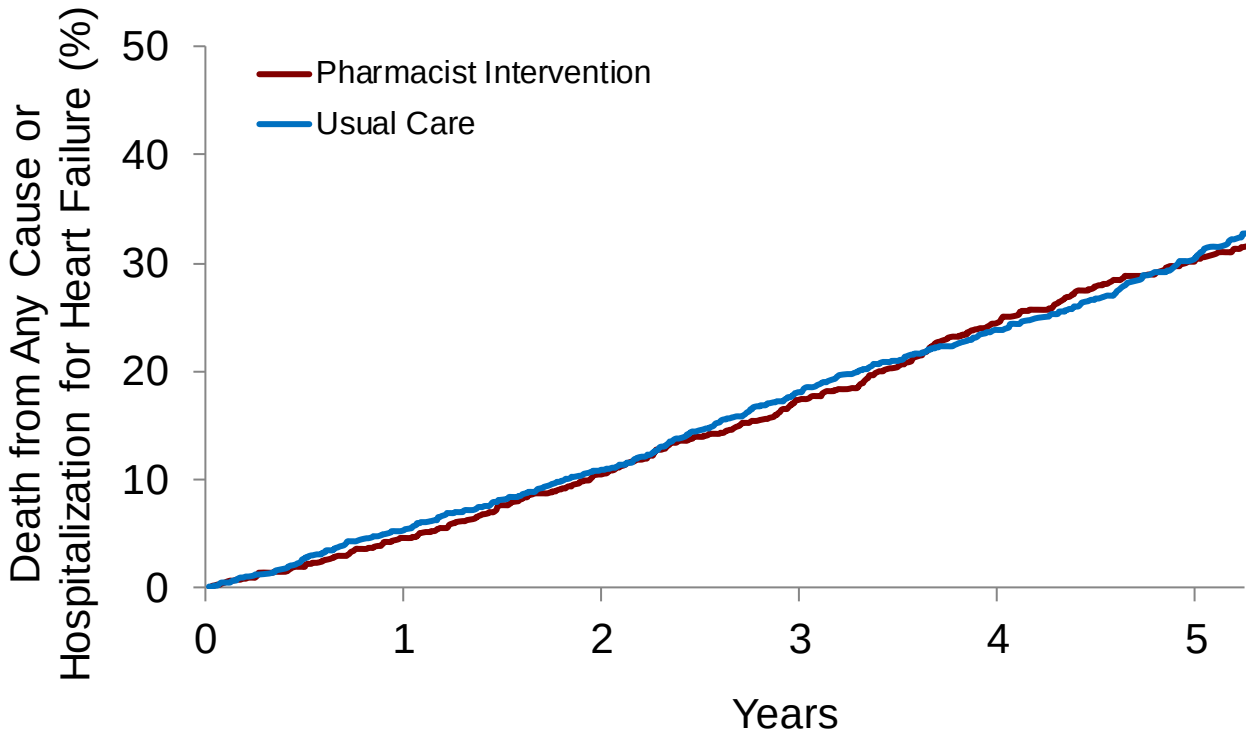
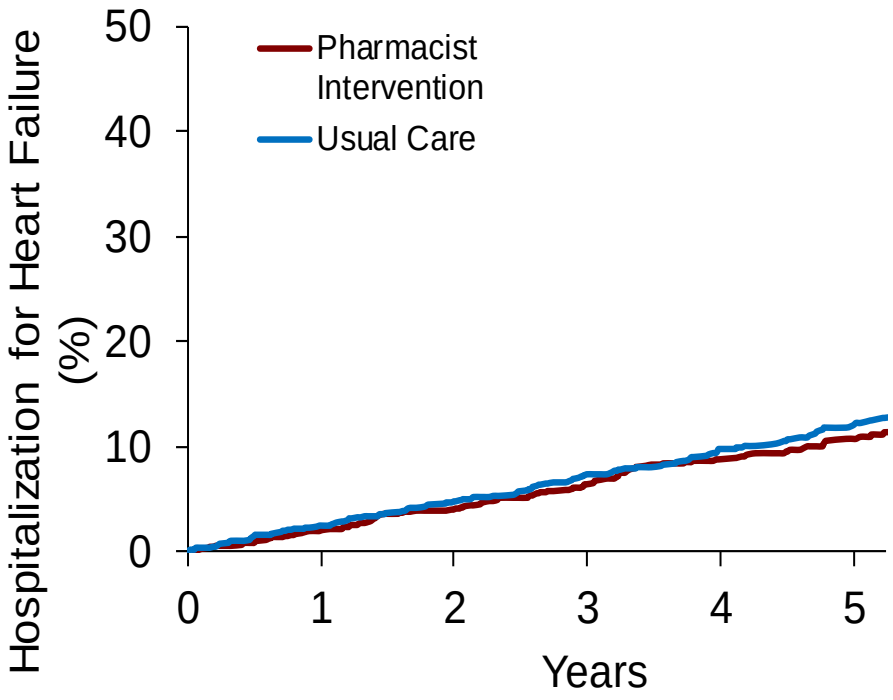
Death or Hospitalization for Heart Failure



Number at risk:						
Pharmacist Intervention	1092	1026	950	860	673	470
Usual Care	1077	996	922	835	692	393

Components of the Primary Composite Outcome

Heart Failure Hospitalization



Number at risk:

Pharmacist Intervention	1092	1026	950	860	673	470
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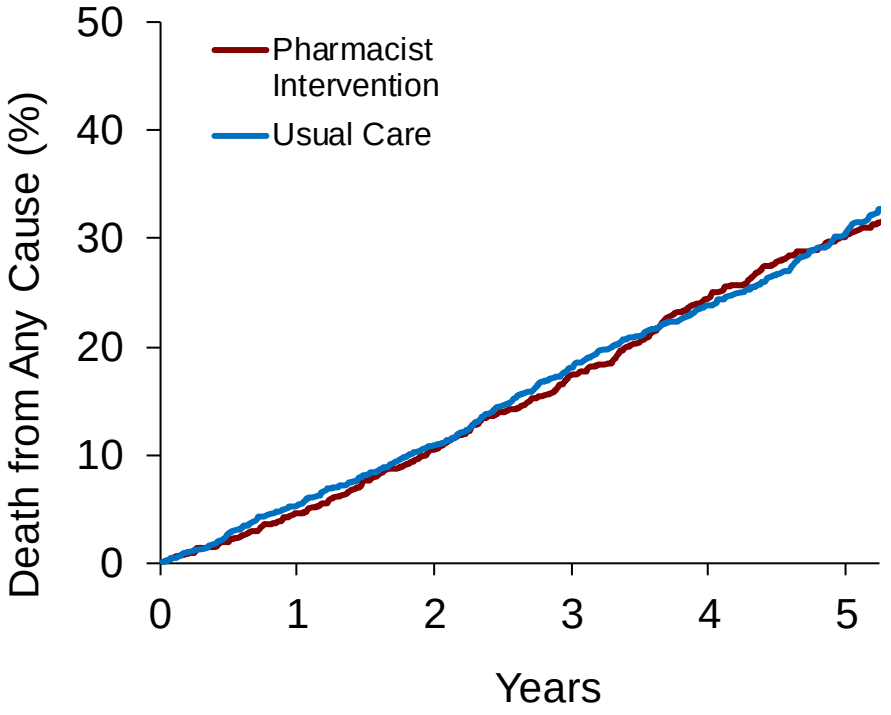
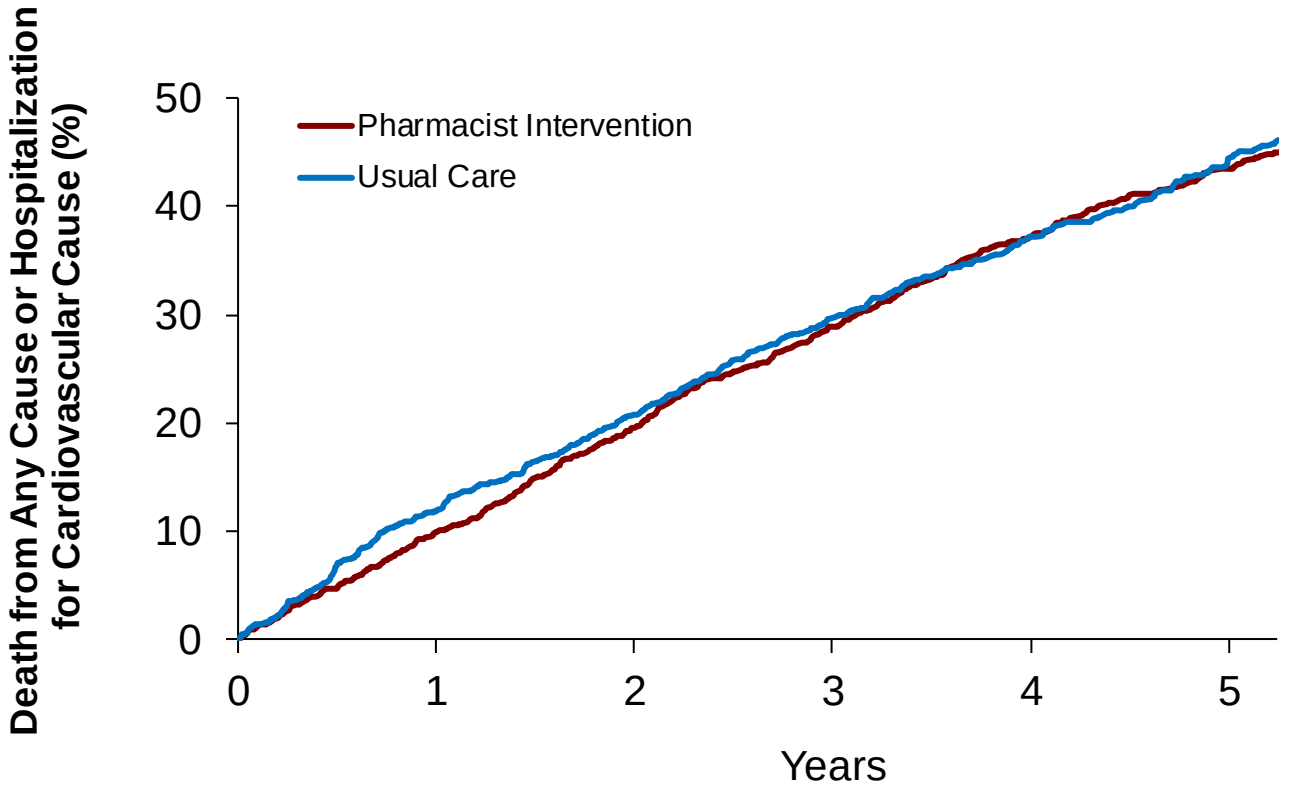
All-cause Mortality



Number at risk:

Pharmacist Intervention	1092	1040	976	901	716	505
Usual Care	1077	1018	957	880	737	423

All-cause Death or Cardiovascular Hospitalization



Number at risk:						
Pharmacist Intervention	1092	982	877	775	602	411
Usual Care	1077	947	851	755	606	339

Summary and Conclusion

- **A low-intensity, pharmacist-led, collaborative intervention in primary care resulted in:**
  - modest improvements in prescribing of disease-modifying medications
  - but did not improve clinical outcomes in a population that was relatively well treated at baseline.

Discussion

- **High baseline use of ACE inhibitors/ARBs a surprise – UK Government "pay for performance" scheme for family physicians?**
- **Consequently, less scope to initiate or increase doses of ACE inhibitors/ARBs.**
- **More scope to improve β-blocker prescribing but pharmacists failed to initiate these drugs (and limited success in increasing dose). Why?**
- **Low frequency of heart failure hospitalization and high proportion of non-cardiovascular deaths reduced likelihood of showing treatment effect.**