# Rapid Response:

## Contradictory results in randomised clinical trials concerning to pharmacists-led intervention: looking for one possible explanation

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Dear Editor:

The recently published HeartMed (1) trial showed that isolated interventions by community pharmacists, in patients with heart failure (HF), do not yield a significant decrease neither in hospital readmissions nor in mortality, over six months after discharge from hospital. We have read with great interest the possible explanations for these unexpected results, suggested by the authors and rapid responses, which are mainly concerned with the following issues: sample size, main outcome measures, health professionals who carry out the interventions, and design of the intervention. We agree with the reasons provided, however we consider that an intervention focused on patients results is the key element of success, of any program intended to improve outcomes for patients with heart failure.

Several earlier trials, namely the Homer (2) and the Medman (3) study support the findings by Holland et al, while, on the contrary, a number of randomized clinical trials (4-6) have demonstrated positive effects on admissions, mortality, quality of life, and length of hospitalization, concluding that pharmacist-led intervention can significantly improve patients' outcomes. As it can be seen in the appendix below, the contradictory results across studies are seemingly connected with

substantial differences in the interventions; process vs. results and process together.

Based on this, we propose a pharmacist intervention consisting of a series of key elements. To begin with, pharmacist's intervention must not only focus on the process (degree of compliance of HF patients), but on the outcomes of pharmacotherapy (parameters of effectiveness and safety, i.e., exertional dyspnea, exertional fatigue, weight, heart rate, blood pressure (BP), and potassium and sodium levels). Therefore, pharmacist's interventions should be based on the follow up of the effectiveness and safety of drug therapy through a patient outcomes assessment, within the framework of a multidisciplinary team. This will allow feedback from GPs to make appropriate changes in the pharmacotherapeutic management of patients. In order to assess pharmacist intervention it would be also useful to know whether the reasons for admissions are due to effectiveness or safety problems.

Furthermore, since patients with HF are at high risk for re-hospitalisation, we consider very important to discuss the predictive factors for readmission (7), such as: age, atrial fibrillation, BP, serum sodium and potassium levels, diabetes mellitus, polipharmacy, absence of patient motivation, depression, dependent in self-care, functional capacity, New York Heart Association (NYHA) classification, previous hospitalisation and not having a specific follow-up plan, thus implementing different types of interventions based on evidence-based factors in readmissions in this group of patients. As for the design of a tailored intervention, it is important that the pharmacist sets the goals and draws up a plan of action to achieve them.

REFERENCES

1. Holland R, Brooksby I, Lenaghan E, Ashton K, Hay L, Smith R, et al. Effectiveness of visits from community pharmacists for patients with heart failure: HeartMed randomised controlled trial. BMJ 2007;334:1098.

2. Holland R, Lenaghan E, Harvey I, Smith R, Shepstone L, Lipp A, et al. Does home based medication review keep older people out of hospital? The HOMER randomised controlled trial. BMJ 2005;330:293.

3. The Community Pharmacy Medicines Management Project Evaluation Team. The MEDMAN study: a randomized controlled trial of community pharmacy-led medicines management for patients with coronary heart disease. Fam Pract 2007;24:189-200.

4. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure

Assessment Recommendation and Monitoring (PHARM) Study. Arch Intern Med 1999;159;160:1939-45.

5. Tsuyuki RT, Johnson JA, Teo KK, Simpson SH, Ackman ML, Biggs RS et al. A randomized trial of the effect of community pharmacist intervention on cholesterol risk management: the Study of Cardiovascular Risk Intervention by Pharmacists (SCRIP). Arch Intern Med 2002;162:1149-55.

6. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. JAMA 2006;296:2563 -71.

7. Anderson MA, Levsen J, Dusio ME, Bryant PJ, Brown SM, Burr CM, et al. Evidenced-based factors in readmission of patients with heart failure. J Nurs Care Qual 2006;21:160-7.

Appendix. Some characteristics of study with contradictory results concerning to pharmacists-led intervention

Study with “negative” results

Study: HeartMed trial (1)

• Intervention focused to process (P): Two home visits consisting of: Patient education (P), encourage completion of sign and symptom, monitoring diary cards (P), remove discontinued drugs (P), and fed-Back recommendations to the GP and local pharmacist (P)

• Results/Conclusions: Community pharmacist intervention did not lead to reductions in hospital admissions nor in mortality and no statistically significant difference in quality of life

Study: HOMER trial (2)

• Intervention focused to process (P): Two home visits consisting of: Patient education (P), remove out of date drugs (P), inform local pharmacist if a compliance aid is needed (P), and inform GP of drug reactions or interactions (P)

• Results/Conclusions: Significantly higher rate of hospital admissions, and not significantly improve quality of life or reduce deaths

Study: MEDMAN trial (3)

• Intervention focused to process (P): One or more consultations (according to pharmacist determined patient need) consisting of:

Assessments of therapy, medication compliance, lifestyle (P) and fed-Back recommendations to the GP (P)

• Results/Conclusions: No statistically significant differences in lifestyle factors nor in the global score for appropriateness of treatment, few differences in quality of life, the total National Health Service cost increased, significant improvements in satisfaction score, and no differences in self reported compliance

Study characteristics with "positive" results

Study: The PHARM trial (4)

• Intervention focused to process (P) and results of the pharmacotherapy (R): Clinical Pharmacist evaluation that included : Medication evaluation (P), therapeutic recommendations to the physician (P), patient education (P), and telephone follow-up at week 2, 12 and 24 to identify drug-related problems, and the occurrence of clinical events (R)

• Results/Conclusions: Outcomes in Heart Failure can be improved with a clinical pharmacist as a member of the multidisciplinary heart failure team

Study: SCRIP trial (5)

• Intervention focused to process (P) and results of the pharmacotherapy (R): Regular follow up, consisting of: Interview by the pharmacist (P), point of care cholesterol measurement (R), patient education (P), and referral to the doctor according to cholesterol measurement (R)

• Results/Conclusions: Community pharmacist intervention improved cholesterol management for patients at high risk for cardiovascular disease

Study: FAME trial (6)

• Intervention focused to process (P) and results of the pharmacotherapy (R): Regular follow up, consisting of: Interview by the pharmacist (P), measurement of adherence (P) BP (R) and LDL-C (R), individualized patient education (P), medication dispensed using adherence aid (P), regular follow up with clinical pharmacist every 2 months (R)

• Results/Conclusions: A pharmacy care program lets to increases in medication adherence and persistence, reduction in BP, and discontinuation of the program decrease medication adherence and persistence

Competing interests:
None declared

**Competing interests:** No competing interests