Journal of Clinical Epidemiology 83 (2017) 48–56

Journal of Clinical Epidemiology

# Complex self-management interventions in chronic disease unravelled: a review of lessons learned from an individual patient data meta-analysis

Nini H. Jonkman[a,b,*], Rolf H.H. Groenwold[a], Jaap C.A. Trappenburg[a], Arno W. Hoes[a], Marieke J. Schuurmans[a]

[a]*Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, HP STR 6.131, P.O. Box 85500, Utrecht 3508 GA, The Netherlands*
[b]*Faculty of Behavioural and Movement Sciences, VU University Amsterdam, Van der Boechorststraat 7, MF A-613, Amsterdam 1081 BT, The Netherlands*

Accepted 16 January 2017; Published online 23 January 2017

## Abstract

**Objectives:** Meta-analyses using individual patient data (IPD) rather than aggregated data are increasingly applied to analyze sources of heterogeneity between trials and have only recently been applied to unravel multicomponent, complex interventions. This study reflects on methodological challenges encountered in two IPD meta-analyses on self-management interventions in patients with heart failure or chronic obstructive pulmonary disease.

**Study Design and Setting:** Critical reflection on prior IPD meta-analyses and discussion of literature.

**Results:** Experience from two IPD meta-analyses illustrates methodological challenges. Despite close collaboration with principal investigators, assessing the effect of characteristics of complex interventions on the outcomes of trials is compromised by lack of sufficient details on intervention characteristics and limited data on fidelity and adherence. Furthermore, trials collected baseline variables in a highly diverse way, limiting the possibilities to study subgroups of patients in a consistent manner. Possible solutions are proposed based on lessons learnt from the methodological challenges.

**Conclusion:** Future researchers of complex interventions should pay considerable attention to the causal mechanism underlying the intervention and conducting process evaluations. Future researchers on IPD meta-analyses of complex interventions should carefully consider their own causal assumptions and availability of required data in eligible trials before undertaking such resource-intensive IPD meta-analysis. 

*Keywords:* Chronic disease; Complex interventions; Individual patient data meta-analysis; Randomized trials; Self-care; Self-management; Subgroup analysis

## 1. Introduction

Interventions to support the self-management of patients with a chronic condition have received increasing attention over the past years [1]. Like other behavioral interventions, self-management interventions contain multiple interacting components and can be considered ‘‘complex interventions’’ [2]. In such interventions, patients are taught new complex skills, such as monitoring signs and symptoms to detect deterioration, adherence to drug treatment, or lifestyle change, and they are expected to apply those skills in their daily lives [3,4]. The potential of self-management interventions lies in providing health benefits for patients as well as reducing the burden on health care utilization [1].

Pooled evidence from early randomized trials seemed to favor self-management interventions in patients with various chronic conditions for a range of outcomes [5–8], but several more recently conducted large randomized trials have shown no effects [9–13], or even negative effects [14,15]. This inconsistency has tempered the initial enthusiasm for self-management interventions and raised questions regarding large-scale implementation. These heterogeneous findings can partly be attributed to the complex nature of self-management interventions: evaluated interventions varied considerably regarding intensity, duration, mode, and content. Additionally, variations between included study populations might play a role, as certain

Conflicts of interest: None.

Funding: This work was supported by the Dutch Ministry of Health, Welfare and Sports, ZonMw grant number 520001002. The funding source had no involvement in the design and conduct of the study; in collection, management, analysis, and interpretation of the data; in the writing of the report; and in the decision to submit the article for publication.

* Corresponding author. Tel.: +31-20-59-88533.
*E-mail address*: n.h.jonkman@vu.nl (N.H. Jonkman).

http://dx.doi.org/10.1016/j.jclinepi.2017.01.004
0895-4356/

**What is new?**

**Key findings**

- Assessing the effect of intervention characteristics with use of individual patient data (IPD) meta-analysis is compromised by few details on intervention characteristics and limited data on fidelity and adherence.
- Baseline variables are collected in a highly diverse way, limiting the possibilities to study subgroups of patients in a consistent manner across trials.

**What this adds to what was known?**

- Trials on multicomponent self-management interventions have shown heterogeneous results, yielding new questions regarding the effectiveness of such interventions, for which IPD meta-analyses are increasingly applied.
- Methodological challenges encountered in two IPD meta-analyses on self-management interventions may help researchers to carefully prepare the resource-intensive IPD meta-analyses.

**What is the implication and what should change now?**

- Future researchers of multicomponent interventions should pay considerable attention to the causal mechanism underlying the intervention and conducting process evaluations.
- Researchers who are planning to undertake IPD meta-analyses of complex interventions are advised to carefully consider their own causal assumptions and availability of required data in eligible trials before undertaking the resource-intensive IPD meta-analysis.

patients may respond better to the self-management intervention than others.

Meta-analysis or meta-regression techniques can be used to explore the heterogeneity in outcomes across trials and assess which program-specific characteristics are associated with better outcomes [16]. Identifying subgroups of patients who benefit most from an intervention in a ''classical'' aggregated data meta-analysis is often subject to ecological bias [17]. For example, trials including patients with on average more severe symptoms might yield a larger effect than trials including patients with on average less severe symptoms. This does not necessarily mean that the intervention will have a large effect in an individual patient with more severe symptoms. Furthermore, individual trials often lack power for subgroup analyses [18,19]. Meta-analyses using individual patient data (IPD) may overcome these issues [18,19]. IPD meta-analysis allows for checking the data uncertainties with principal investigators, enables a uniform statistical analysis [18], and provides better power for subgroups analyses [20]. This approach has been mainly executed to study pharmacological treatments for cancer and cardiovascular disease [18] and has only recently been applied to evaluate complex interventions [21].

Based on our experience with two IPD meta-analyses of self-management interventions in patients with chronic heart failure (CHF) and in patients with chronic obstructive pulmonary disease (COPD), we provide a critical reflection on the value of this study design to unravel multicomponent interventions. This may provide valuable insights for other researchers and clinicians in the field of complex interventions in chronic disease. We will first briefly address the findings of our project to provide a background context. Subsequently, we will critically reflect on methodological challenges encountered and how the IPD meta-analyses contributed to the initial objectives.

## 2. Findings from the IPD meta-analyses

The two IPD meta-analyses included 20 trials on patients with CHF ($n$ = 5,624) and 14 trials on patients with COPD ($n$ = 3,282), respectively. The major findings have been presented elsewhere [22–25] and are summarized in Table 1. The duration of self-management interventions for patients with CHF ranged from 0.5 to 18 months, and the majority was delivered to individual patients by a specialized nurse. Two interventions used a group approach, and two interventions consisted of case management by telephone. The interventions for patients with COPD ranged from 1 day to 24 months with the majority including an action plan and consisting of individual sessions with a nurse. Overall, self-management interventions showed beneficial effects on health-related quality of life at 12 months and reduced disease-specific hospitalization both in patients with CHF and in patients with COPD. The main aim of both IPD meta-analyses was to identify (program or patient specific) determinants of the success of self-management interventions. Effects in subgroups of patients were analyzed in a one-stage approach, in which all observations were analyzed simultaneously while accounting for clustering within studies [17]. A two-stage approach was applied for the analysis of program characteristics, by estimating the intervention effect within one study and subsequently pooling the effects across studies, as a one-stage approach was not possible for reasons explained in the following. The effects of specific program characteristics and patient subgroups benefiting from the self-management intervention were only observed for a selection of outcomes, whereas any characteristic modifying the treatment effect can be expected to do so across multiple health outcomes. The diffuse pattern of differential