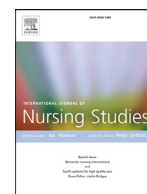




Contents lists available at ScienceDirect

International Journal of Nursing Studies

journal homepage: www.elsevier.com/ijns

Patient and caregiver contributions to self-care in multiple chronic conditions: A multilevel modelling analysis

Paolo Iovino^{a,b}, Karen S. Lyons^c, Maddalena De Maria^{a,*}, Ercole Vellone^a, Davide Ausili^d, Christopher S. Lee^c, Barbara Riegel^e, Maria Matarese^f

^a University of Rome "Tor Vergata", Rome, Italy

^b Australian Catholic University, Melbourne, Australia

^c Boston College, MA, United States

^d University of Milan-Bicocca, Monza, Italy

^e University of Pennsylvania, Philadelphia, United States

^f Campus Bio-Medico University of Rome, Rome, Italy

ARTICLE INFO

Article history:

Received 23 September 2019

Received in revised form 22 February 2020

Accepted 7 March 2020

Available online xxx

Keywords:

Determinants

Dyads

Multiple chronic conditions

Older people

Self-care

Caregivers

ABSTRACT

Background: Multiple chronic conditions (MCC) are highly prevalent worldwide, especially among older populations. Patient self-care and care partner (or caregiver) contributions to self-care are recommended to reduce the impact of MCC and improve patients' outcomes.

Objectives: To describe patient self-care and care partner contributions to self-care and to identify determinants of patient self-care and care partner contributions to self-care at the patient and care partner level.

Design: Multicentre cross-sectional study.

Setting: Outpatient and community settings in Italy.

Participants: A sample of 340 patients with MCC and care partner dyads was recruited between 2017 and 2018.

Methods: We measured patient's self-care and care partner contributions to self-care in dyads using the Self-care of Chronic Illness Inventory and the Caregiver Contribution to Self-care of Chronic Illness Inventory. To control for dyadic interdependence, we performed a multilevel modelling analysis.

Results: Patients' and care partners' mean ages were 76.65 (\pm 7.27) and 54.32 (\pm 15.25), respectively. Most care partners were female and adult children or grandchildren. The most prevalent chronic conditions in patients were diabetes (74%) and heart failure (34%). Patients and care partners reported higher levels of self-care monitoring than self-care maintenance and management behaviours. Important patient clinical determinants of self-care included cognitive status, number of medications and type of chronic condition. Care partner determinants of self-care contributions included age, gender, education, perceived income, care partner burden, caregiving hours per week and the presence of a secondary care partner.

Conclusions: Our findings support the importance of taking a dyadic approach when focusing on patients with MCC and their care partners. More dyadic longitudinal research is recommended to reveal the modifiable determinants of self-care and the complex relationships between patients and care partners in the context of MCC.

© 2020 Published by Elsevier Ltd.

What is already known about the topic?

- Multiple chronic conditions are increasing worldwide, due to the ageing of the population and the rise in life expectancy.
- Self-care of chronic conditions has been shown to improve symptoms and quality of life and to reduce mortality, hospital readmissions and healthcare costs.

* Corresponding author.

E-mail addresses: paolo.iovino@uniroma2.it (P. Iovino), karen.lyons@bc.edu (K.S. Lyons), maddalena.demaria@outlook.it (M. De Maria), ercole.vellone@uniroma2.it (E. Vellone), davide.ausili@unimib.it (D. Ausili), leeddo@bc.edu (C.S. Lee), briegel@nursing.upenn.edu (B. Riegel), m.matarese@unicampus.it (M. Matarese).

<https://doi.org/10.1016/j.ijnurstu.2020.103574>

0020-7489/© 2020 Published by Elsevier Ltd.

Please cite this article as: P. Iovino, K.S. Lyons and M. De Maria et al., Patient self-care and caregiver contributions to self-care in multiple chronic conditions: A multilevel modeling analysis, Int. J. Nurs. Stud., <https://doi.org/10.1016/j.ijnurstu.2020.103574>

- Care partner contributions to self-care can facilitate patients' self-care behaviours.

What this paper adds

- Patients with multiple chronic conditions and their care partners showed adequate engagement in self-care monitoring but lower engagement in self-care maintenance and management behaviours when controlling for interdependence.
- Sociodemographic characteristics influence self-care and contributions to self-care both in patients with multiple chronic conditions and their care partners.
- Clinical characteristics of patients with multiple chronic conditions influence their engagement in self-care behaviours, whereas caregiving characteristics influence care partner contributions.

1. Introduction

Multiple chronic conditions (MCC), defined as the co-occurrence of two or more chronic conditions (Smith and O'Dowd, 2007), have increased worldwide (Orueta et al., 2012; Raghupathi and Raghupathi, 2018), especially in older populations (Hajat and Stein, 2018; Marengoni et al., 2011). In the United States, over two thirds of individuals aged 65 years or older have two or more chronic conditions (Lochner et al., 2013), whereas in Europe, the prevalence ranges from 24.7% to 51% (Palladino et al., 2016). Compared to people affected by a single illness, individuals with MCC have more impairment in physical functioning, worse quality of life, and higher hospitalization and mortality rates (Gijsen et al., 2001).

To reduce the impact of chronic conditions and manage symptoms, patients with MCC perform self-care on a daily basis (Kennedy et al., 2007). Self-care, according to the middle-range theory of self-care of chronic illness (Riegel et al., 2012) includes three distinct but related dimensions: (i) self-care maintenance, consisting of those practices directed at improving well-being and maintaining physical and emotional stability; (ii) self-care monitoring, defined as tracking behaviour and observing oneself for changes in signs and symptoms; and (iii) self-care management, entailing the behaviours necessary to respond to signs and symptoms when they occur.

Research has shown that self-care in chronic illnesses can improve health-related quality of life (Cannon et al., 2016) and reduce mortality (He et al., 2017; Ruppert et al., 2016), hospital admissions (Hamar et al., 2015; Zwerink et al., 2014) and costs (Wheeler et al., 2003). Despite these benefits, chronically ill patients often engage in insufficient levels of self-care (Ausili et al., 2018; Cocchieri et al., 2015; Restrepo et al., 2008). In these contexts, the contributions of care partners to patients' self-care – that is, the process of engage in self-care or performing recommending that patients engage in self-care or performing self-care duties on their behalf – are critical. Contributions to self-care, typically provided by family members or other unpaid persons (Vellone et al., 2019), can improve patients' medication adherence (Aggarwal et al., 2013; Trivedi et al., 2012) promote healthy lifestyle behaviours (Trivedi et al., 2012) and reduce emergency service utilization (Wakabayashi et al., 2011).

Several factors are known to influence self-care behaviours in individuals with chronic illness, including sociodemographic factors (such as age, gender, socioeconomic status, and education level), patient clinical characteristics (e.g., number of chronic conditions, prescribed medications) and care partner burden (De Maria et al., 2019a). However, most of the literature has investigated these self-care determinants solely at the patient (Ausili

et al., 2018; Cocchieri et al., 2015; Dickens et al., 2019) or care partner level (Sevinc and Samancioglu, 2017; Watson et al., 1998). Very few studies have considered illness management as a dyadic phenomenon and investigated self-care determinants at a dyadic level. In addition, those that have considered illness management as a dyadic phenomenon have exclusively addressed self-care of individuals with specific chronic diseases (Bidwell et al., 2015; Lyons et al., 2015). This study aimed to fill this gap in the literature.

1.1. Aims

The aims of this study were to: (i) describe MCC patient self-care and care partner contributions to self-care in dyads, and (ii) identify determinants of patient self-care and care partner contribution to self-care at the dyadic level.

2. Methods

2.1. Design

We analysed baseline data of an ongoing longitudinal study, 'SODALITY', which described patient self-care and care partner contributions to self-care in MCC. A detailed description of the study protocol has been published elsewhere (De Maria et al., 2019a).

2.2. Participants

Patients aged 65 years and older with a diagnosis of diabetes mellitus (DM), chronic obstructive pulmonary disease (COPD) or heart failure (HF) with at least one additional chronic condition were enrolled in the study. Individuals were excluded if they had cancer or dementia or were unable to provide informed consent. Care partners were enrolled if they were at least 18 years old, identified by the patients as the main unpaid person providing most of the informal care and able to provide informed consent.

2.3. Data collection

Data were collected from outpatient and community settings in Southern and Central Italy between April 2017 and December 2018. Older MCC patients and their care partners were enrolled by trained research assistants, all of whom were registered nurses. Research assistants met with potential participants to explain the study, answer questions, and obtain informed consent. Only complete dyads were enrolled; if one member of the dyad chose not to participate, the other member was not enrolled.

2.4. Instruments

The Self-Care of Chronic Illness Inventory (SC-CII) (Riegel et al., 2018) was used to measure self-care. The SC-CII is a self-reported instrument with three separate scales measuring self-care maintenance (7 items), self-care monitoring (5 items) and self-care management (7 items). According to the theory underpinning the instrument (Riegel et al., 2012), the self-care maintenance scale measures health-promoting (e.g., physical activity) and illness-related (e.g., treatment adherence) behaviours; the self-care monitoring scale measures behaviour tracking and the ability to recognize signs and symptoms (e.g., symptoms of hypoglycaemia); and the self-care management scale measures the ability to recognize signs and symptoms and implement a treatment as needed (e.g., take a pill to relieve pain). Each scale uses a standardized score ranging from 0 to 100, with higher scores reflecting better self-care. A cut-point of 70 is used to reflect adequate self-care (Riegel et al., 2009). The SC-CII demonstrated construct validity in confirmatory factor

analysis (CFA) (Confirmatory Fit Index [CFI] 0.93 to 1.0; Root Mean Square Error of Approximation [RMSEA] 0.06 to 0.00 across the three scales) and supportive reliability measured using the global reliability index (ranging from 0.67 to 0.81 across the three scales) (Riegel et al., 2018). Construct validity has been confirmed in Italian population (De Maria et al., 2019b).

The Caregiver Contribution to Self-care of Chronic Illness Inventory (CC-SC-CII) is the care partner version of the SC-CII and measures the contributions of the care partner to self-care maintenance, monitoring and management of patients. While the SC-CII asks patients to report how often they have performed specific self-care behaviours, the CC-SC-CII asks care partners to report how often they recommend or perform the self-care behaviours for patients. The SC-CII and the CC-SC-CII are mirror images of one another and ask about the same behaviours. The CC-SC-CII also uses a standardized score from 0 to 100, with higher scores reflecting greater care partner contributions to self-care, with 70 used as the cut-point for adequacy. The psychometric properties of the CC-SC-CII support construct validity in CFA (CFI ranging from 0.97 to 0.99 and RMSEA ranging from 0.05 to 0.06 across the three scales) and support reliability (Cronbach's alpha ranging from 0.76 and 0.93; Lorini et al., 2019).

The Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005) was used to measure cognitive functioning in patients. The MoCA is a 30-item instrument that measures cognitive status across eight dimensions (visuospatial abilities, executive functions, short term memory recall, attention, concentration, working memory, language and orientation to time and space). Scores range from 0 to 30, with higher scores indicating better cognitive functioning. The MoCA is a valid and reliable tool (Nasreddine et al., 2005) that has been widely used to measure cognitive functioning in chronic conditions (Crisan et al., 2014; Hawkins et al., 2014; Mori et al., 2015).

Caregiver burden was measured in care partners using the Caregiver Burden Inventory (CBI; Novak and Guest, 1989). The CBI is a 24-item instrument that assesses the burden experienced by care partners across five dimensions (time-dependence, developmental, physical, social and emotional burden). CBI scores are standardized from 0 to 100, with higher scores indicating greater care partner burden. The CBI has been tested in various care partner groups, including Italian samples, demonstrating satisfactory validity and reliability (Greco et al., 2017; Marvardi et al., 2005).

We also collected the sociodemographic characteristics of patients and care partners, including age, gender, marital status (married or unmarried), education level (low: less than middle school or high: middle school or above) and perceived income adequacy (low: less than needed or high: enough for a living or more than needed). Patients reported their living condition (living alone or with the care partner) and whether they lived with others affected by a chronic condition. The medical records of the patients were also reviewed for clinical characteristics, including the number of chronic conditions, number of medications and documentation of DM, COPD and HF. Care partners were asked to report the years of caregiving and caregiving hours per week, the presence of another care partner who contributed to the care of the patient (secondary care partner) and the type of relationship with the patient (spouse or other).

2.5. Ethical considerations

The study was conducted following the ethical norms and standards reported in the Declaration of Helsinki (World Medical Association, 2013). Ethical approval for the study was obtained by the Institutional Review Board of a regional healthcare system (Protocol number: ComET ASReM 2017/138). All participants were fully informed about the study, reassured that their data would be kept

confidential and advised they could leave the study at any time without penalty.

2.6. Data analysis

Descriptive statistics such as mean, standard deviation (SD), frequencies and percentages were used to characterize the sample. Paired sample t-tests, McNemar and Bowker tests were used to examine differences between patient and care partner sociodemographic and clinical characteristics.

Multilevel modelling was used to analyse data at the level of the patient-care partner dyad to control for data non-independence (Lyons and Sayer, 2005; Sayer and Klute, 2005) and to identify actor effects (e.g., patient characteristics associated with patient self-care maintenance, monitoring and management) and partner effects (e.g., patient characteristics associated with care partner contributions to self-care maintenance, monitoring and management). Three separate models (one for each self-care dimension) were tested. First, three unadjusted within-dyad models were run. Each model represented a latent self-care score for each member of the patient-care partner dyad and a residual score that represented measurement error. These unadjusted within-dyad models provided estimates of the population averages of self-care maintenance, monitoring and management within dyads, the interdependence of self-care behaviours within-dyads (represented by tau correlation), and the variability in self-care behaviours across dyads (tested with a chi-square).

Second, adjusted between-dyad models were run, consisting of simultaneous regression equations for patients and care partners with latent self-care scores from the unadjusted models serving as dependent variables. These adjusted models included patient and care partner demographic and clinical characteristics as determinants of dyadic self-care behaviours. Unstandardized regression coefficients (B) and their standard errors (SE) were used to describe the actor and partner effects in the models. Determinants with a *p* value of < 0.05 (two-tailed) were considered statistically significant.

SPSS version 21.0 (IBM® SPSS® Statistics, USA) was used to analyse the sociodemographic and clinical characteristics. Hierarchical Linear and Nonlinear Modelling (HLM) v7 (Raudenbush et al., 2011) was used to perform the multilevel modelling analysis.

3. Results

3.1. Characteristics of the sample

Of the 386 eligible patient-care partner dyads, 340 (88%) agreed to participate. The 46 (12%) who declined participation reported lack of time or interest or reluctance to sign the informed consent form. The sociodemographic and clinical characteristics of the final sample are shown in Tables 1 and 2. Patients were mostly female and, on average, more than 15 years older than the care partners. The education level was higher in care partners than in patients, and most of them were unemployed (56%) and non-spouses/partners (69%). DM was the most prevalent chronic condition in patients (74%).

3.2. Self-care maintenance behaviors

In the unadjusted model, patients and care partners, on average, scored below the adequate levels of engagement in self-care maintenance behaviours (67.69 vs. 64.10, respectively). There was significant heterogeneity (*p* < 0.001) in the level of engagement in self-care maintenance behaviours across dyads, indicating that some dyads engaged in low levels and some dyads en-

Table 1
Patients and care partners' sociodemographic characteristics (N = 340 dyads).

Variables	Patient	Care partner
	n (%)	n (%)
<i>Gender</i>		
Male	156 (45.88)	95 (27.94)***
Female	184 (54.12)	245 (72.06)
<i>Education</i>		
< middle school	194 (57.06)	38 (11.18)***
≥ middle school	146 (42.94)	302 (88.82)
<i>Marital Status</i>		
Married/Partnered	216 (63.53)	—
Single/Divorced/Widowed	124 (36.47)	—
<i>Employment status</i>		
Employed	—	151 (44.40)
Unemployed/Retired	340 (100)	189 (55.60)
<i>Perceived income adequacy</i>		
More than needed	38 (11.18)	51 (15)
Enough for living	283 (83.24)	273 (80.29)
Less than needed	19 (5.59)	16 (4.71)
<i>Living with the care partner</i>		
Yes	186 (54.71)	—
No	154 (45.29)	—
<i>Living with others with a chronic condition</i>		
Yes	230 (67.65)	—
No	110 (32.35)	—
<i>Relationship patient–care partner</i>		
Spouse	—	104 (30.59)
Non-spouse	—	236 (69.41)
Children/grandchildren		201 (59.00)
Others		35 (10.41)
<i>Presence of a secondary care partner</i>		
Yes		199 (58.53)
No		141 (41.47)
	<i>M ± SD (range)</i>	<i>M ± SD (range)</i>
Age (years)	76.65 ± 7.27 (65–99)	54.32 ± 15.25 (19–86)***
Years of caregiving	—	8.94 ± 6.72 (0.25–40)
Caregiving hours per week	—	24.11 ± 34.17 (1–168)

Note. M = Mean; SD = Standard Deviation; *** = $p < 0.001$.

Table 2
Patients and care partners' clinical characteristics (N = 340 dyads).

Variables	Patient	Care partner
	n (%)	
<i>Primary chronic disease</i>		
Diabetes mellitus	252 (74.12)	—
Heart failure	116 (34.12)	—
Chronic obstructive pulmonary disease	48 (14.12)	—
	<i>M ± SD (range)</i>	<i>M ± SD (range)</i>
Number of medications	6.40 ± 3.06 (1–15)	—
Number of chronic conditions	3.23 ± 1.31 (2–9)	—
Cognitive status (MoCa)	23.02 ± 4.58 (10–30)	—
Caregiver burden (CBI)	—	10.59 ± 13.18 (0–64)
<i>Self-care of chronic illness inventory</i>		
Self-care maintenance score	67.69 ± 14.80	64.10 ± 23.50**
Self-care monitoring score	74.70 ± 20.40	75.20 ± 23.50
Self-care management score	63.80 ± 17.80	69.40 ± 18.30***

Note. CBI = Caregiver Burden Inventory; M = Mean; MoCA = Montreal Cognitive Assessment; SD = Standard Deviation; ** = $p < 0.01$; *** = $p < 0.001$.

gaged in high levels of self-care maintenance. The tau correlation between patient self-care maintenance and care partner contributions to self-care maintenance was 0.32, indicating moderate interdependence of maintenance behaviours within dyads. In the adjusted models (Table 3, Model 1), patients were significantly more engaged in self-care maintenance behaviours when they were older and reported higher perceived income adequacy, were cared for by a woman and cared for by someone reporting low care partner burden. Care partners were significantly more engaged in self-care maintenance behaviours if they were women, no secondary care partner was identified,

they reported higher care partner burden and more caregiving hours per week and the patients they cared for were less educated.

3.3. Self-care monitoring behaviours

In the unadjusted model, patients and care partners reported, on average, adequate levels of engagement in self-care monitoring behaviours (74.70 vs. 75.20, respectively). There was significant heterogeneity ($p < 0.001$) in levels of engagement in mon-

Table 3Multilevel models predicting dyadic self-care behaviours ($N = 340$ dyads).

	Model 1 Self-care maintenance		Model 2 Self-care monitoring		Model 3 Self-care management	
	Effect on patient	Effect on care partner contribution	Effect on patient	Effect on care partner contribution	Effect on patient	Effect on care partner contribution
	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)	B (SE)
<i>Patient variables</i>						
Age	0.35 (0.13)**	0.22 (0.20)	0.18 (0.18)	0.14 (0.19)	-4.24 (2.47)	0.18 (0.18)
Gender (women)	-0.99 (1.82)	-2.33 (2.79)	4.95 (2.44)*	-2.46 (2.66)	1.94 (2.47)	-2.26 (2.40)
Married/partnered	0.43 (1.93)	-0.27 (2.96)	-0.28 (2.59)	0.60 (2.82)	2.49 (2.53)	-3.66 (2.48)
Education (>middle school)	2.13 (1.85)	-7.37 (2.84)**	1.10 (2.48)	-5.93 (2.71)*	2.56 (2.57)	-4.24 (2.47)
Perceived income adequacy ^a	-4.18 (2.07)*	3.38 (3.18)	-10.39 (2.78)**	0.07 (3.03)	-7.73 (2.71)**	2.14 (2.66)
Living with care partner	0.38 (1.99)	3.92 (3.07)	3.57 (2.68)	-4.05 (2.92)	4.24 (2.59)	-2.78 (2.52)
Living with others with chronic conditions	-1.65 (1.71)	0.65 (2.62)	-1.85 (2.29)	-4.99 (2.50)*	-2.90 (2.31)	0.23 (2.28)
Number of comorbidities	0.29 (0.73)	0.06 (1.12)	-0.22 (0.97)	1.15 (1/06)	-0.85 (1.07)	0.34 (1.05)
Number of medications	0.30 (0.31)	0.19 (0.47)	1.85 (0.41)**	0.18 (0.45)	0.26 (0.43)	-0.30 (0.42)
Diagnosis of HF	-2.36 (2.26)	-1.95 (3.46)	-2.95 (3.02)	-3.38 (3.30)	-4.58 (2.99)	0.59 (2.92)
Diagnosis of COPD	-3.58 (2.54)	-1.06 (3.90)	-4.22 (3.40)	-4.37 (3.71)	-1.86 (3.33)	-5.85 (3.29)
Diagnosis of DM	0.51 (2.42)	3.18 (3.72)	-7.89 (3.25)*	-2.27 (3.54)	-0.32 (3.14)	1.03 (3.10)
Cognitive status (MoCa) ^b	0.33 (0.21)	0.19 (0.32)	0.90 (0.28)**	-0.26 (0.31)	0.16 (0.27)	-0.19 (0.27)
<i>Care partner variables</i>						
Gender (women)	3.72 (1.76)*	-6.89 (2.70)*	3.48 (2.36)	9.34 (2.57)**	-1.22 (2.35)	8.07(2.37)**
Education (>middle school)	-4.29 (2.91)	0.64 (4.46)	-2.93 (3.89)	2.60 (4.25)	-3.86 (4.05)	0.69 (4.04)
Employed	0.93 (1.78)	0.87 (2.73)	-3.50 (2.38)	1.33 (2.60)	2.74 (2.33)	0.51 (2.28)
Perceived income adequacy ^a	3.82 (1.96)	2.09 (3.01)	6.38 (2.63)*	0.62 (2.87)	5.33 (2.61)*	-2.01 (2.53)
Relationship with patient (spouse)	3.51 (2.87)	3.91 (4.41)	3.35 (3.84)	-3.92 (4.19)	2.37 (3.89)	-1.93 (3.82)
Caregiving years	0.03 (0.12)	-0.21 (0.19)	-0.06 (0.17)	-0.08 (0.18)	0.09 (0.16)	0.18 (0.16)
Caregiving hours per week	0.04 (0.03)	0.10 (0.04)*	-0.02 (0.03)	0.12 (0.04)**	-0.01 (0.03)	0.08 (0.03)*
Caregiver burden (CBI)	-0.22 (0.07)**	0.34 (0.10)**	-0.13 (0.09)	0.40 (0.10)**	-0.08 (0.09)	0.09 (0.09)
Presence of secondary care partner	-0.99 (1.67)	-6.26 (2.57)*	0.20 (2.24)	-5.92 (2.44)*	-1.46 (2.22)	-2.94 (2.19)

Note. B = Unstandardized coefficient; SE = Standard Error; CBI = Caregiver Burden Inventory; COPD = Chronic Obstructive Pulmonary Disease; DM = Diabetes Mellitus; HF = Heart Failure; MoCa= Montreal Cognitive Assessment;

^a = Higher scores of perceived income adequacy indicate less income than needed;

^b = Higher scores on cognitive status indicate less impairment.

* = $p < 0.05$;

** = $p < 0.01$;

*** = $p < 0.001$.

itoring behaviours across dyads, indicating that some dyads engaged in low levels and some dyads engaged in high levels of self-care monitoring. The tau correlation between patient self-care monitoring and care partner contributions to self-care monitoring was 0.06, indicating very little interdependence within dyads. In the adjusted models (Table 3, Model 2), patients were significantly more likely to engage in self-care monitoring if they were women, did not have DM, were less cognitively impaired, reported higher perceived income adequacy, were taking a higher number of medications and had a care partner who perceived lower income adequacy. Care partners were significantly more likely to contribute to self-care monitoring behaviours if they were women, there was no secondary care partner identified, they reported higher care partner burden and spent more hours caregiving per week, the patient did not live with anyone else with a chronic condition and the patient reported less formal education.

3.4. Self-care management behaviours

In the unadjusted model, patients and care partners reported scores below the adequate level of engagement in self-care management behaviours (63.80 vs. 69.40, respectively) on average. There was significant heterogeneity ($p < 0.001$) in levels of engagement in self-care management behaviours across dyads, indicating that some dyads engaged in low levels and some dyads engaged in high levels of self-care management. The tau correlation between patient and care partner self-care management behaviours was 0.34, which indicates moderate interdependence of management behaviours within dyads. In the adjusted models (Table 3, Model 3), patients were significantly more likely to engage in self-

care management behaviours when they reported higher perceived income adequacy and when their care partners reported lower perceived income adequacy. Care partners were significantly more likely to contribute to self-care management if they were women and reported providing more hours of care per week.

4. Discussion

To our knowledge, this is the first study describing MCC patient self-care and care partner contributions to self-care and determinants of self-care while controlling for interdependence within the dyads. Our findings confirm the need to adopt a dyadic perspective when assessing self-care and its determinants, since we found that the characteristics of a member of the dyad can influence the self-care behaviours of the other. Routine assessment of such determinants could facilitate the early detection of MCC dyads at risk of engaging in poor self-care.

Consistent with other studies conducted on single chronic conditions (Bidwell et al., 2015; Cocchieri et al., 2015; Mei et al., 2019), we found that MCC patients had self-care maintenance scores below the cut-point for adequacy. Riegel et al. (2016) claimed that patients with chronic conditions frequently delay self-care maintenance behaviours until they become symptomatic or have an exacerbation. Nearly half of our patients were not symptomatic at the time of data collection, which could also explain the insufficient care partner contributions to maintenance behaviours. The importance of prompting healthy behaviours may have been underestimated as a result of relative illness stability of the care recipients.

In our study, patients and care partners performed better in self-care monitoring than self-care maintenance or management.

Previous studies have demonstrated that patients with a single chronic condition performed self-care monitoring practices; however, these studies did not examine the other self-care behaviours of maintenance and management (Huygens et al., 2017; Mirel et al., 2011). Greater self-care monitoring behaviours in MCC could be facilitated by the increasing use of health monitoring devices, which in turn can improve motivation and patient-provider collaboration (Lancaster et al., 2018). Moreover, healthcare providers themselves might encourage these behaviours in order to have clinical data available. In our study, care partners contributed adequately to self-care monitoring. The existence of more than one chronic condition may have increased their awareness of and attention to signs and symptoms. We also found low interdependence between patient self-care and care partner contributions to self-care monitoring, suggesting that one member's engagement in self-care monitoring did not increase the other member's engagement.

In self-care management, we also found that patients scored below the level of adequacy, as found in previous studies (Cocchieri et al., 2015; Vellone et al., 2013). Self-care management can be particularly complex in MCC patients; symptoms and clinical manifestations may overlap and require skilled decision-making and problem-solving (Riegel et al., 2012). The care partners likely experienced the same difficulty, although they performed better than the patients in our study.

4.1. Determinants of patient self-care

We identified several patient determinants associated with patient self-care (actor effects) and with care partner contributions to self-care (partner effects), as well as care partner determinants associated with their contribution to self-care (actor effects) and with patient self-care (partner effects).

4.1.1. Actor effects

We found that patient older age was associated with better self-care maintenance, in contrast with previous studies wherein this variable predicted worse self-care (Bell et al., 2010; Cocchieri et al., 2015; Smith et al., 2017). It may be that our patients were in better physical and clinical condition, as they were recruited from community settings. We also found that patients were more likely to engage in all self-care behaviours when they perceived higher income adequacy, confirming income as a powerful variable influencing health-related behaviours at all ages (Braveman and Gottlieb, 2014).

Female patients were more likely to monitor their diseases compared to males, as reported in other studies in patients with DM and stroke (Chiu and Wray, 2011; Focht et al., 2014). Patients taking more medications were also better at self-care monitoring. It is possible that the number of medications may induce patients to perceive themselves as seriously ill, thus increasing their motivation to monitor themselves or that the increased risk of side effects related to more medications may stimulate such behaviours.

We also found that patients who were less cognitively impaired were more likely to engage in self-care monitoring behaviours compared to the other self-care behaviours. Some studies have suggested that all the self-care dimensions could be affected by cognitive functioning (Cocchieri et al., 2015; Tomlin and Sinclair, 2016; Uchmanowicz et al., 2017), while others have found evidence of an influence only on specific self-care behaviours (Cameron et al., 2010). However, self-care monitoring entails systematic and constant surveillance of the body (Riegel et al., 2012), which requires the integrity of memory and attention more than do other self-care behaviours. The possibility that patients might also acquire self-care skills over time should not be excluded, especially for repetitive, easier-to-perform monitoring tasks, which could compensate for impaired cognition.

Self-care monitoring was also influenced by the type of chronic disease. Patients with DM were less likely to perform adequate self-care monitoring than those without DM. This is a surprising finding because self-care monitoring is indispensable in maintaining metabolic control and preventing or slowing disease-related complications (Ausili et al., 2018).

4.1.2. Partner effects

One determinant of better patient self-care maintenance was having a female care partner. Others have observed that women are more emotionally and physically involved in caregiving than men (Polenick et al., 2020; Swinkles et al., 2019). We also found that patients were more likely to engage in self-care monitoring and management behaviours when care partners reported lower perceived income adequacy. Research has shown that having a family member affected by a chronic condition can drain financial resources (Lai, 2012). However, in women, lower income has also been associated with more caregiving engagement (Lee et al., 2015), which could explain the better self-care behaviours of their care recipients.

Lower care partner burden was another determinant of better patient self-care maintenance. Perhaps when patients performed adequate self-care, care partners did not need to be involved and thus experienced less burden. However, the cross-sectional nature of our study does not allow us to establish the directionality of this association.

4.2. Determinants of care partner contributions to self-care

4.2.1. Actor effects

Female care partners were more likely to contribute in all self-care dimensions compared to men, corroborating prior evidence that women are socialized to be caregivers (Polenick et al., 2020; Swinkles et al., 2019). Caregiving for more hours per week and contributing specifically to self-care maintenance and monitoring were associated with burden. Another contributor to caregiving load was sole caregiving or not having a secondary care partner available. Together, these factors may reflect the intensity of the care partner's commitment to caregiving. These results highlight the need to support care partners who dedicate a considerable amount of time to caring, those without support of another caregiver and those exhibiting higher burden levels.

4.2.2. Partner effects

Care partner contributions to self-care maintenance and monitoring were higher when caring for less educated patients. In this situation, perhaps care partners needed to intensify their contributions to compensate for the patients' poor knowledge or understanding of self-care practices. No previous study has analysed the influence of education on self-care in dyads, although other studies of specific patient populations have identified worse self-care in less educated patients (Alguwaihes and Shah, 2009; Geboers et al., 2016).

4.3. Implications for practice and research

In clinical settings, healthcare professionals should consider the dyad as the 'unit of care', especially in the context of MCC, since self-care for patients and care partners is more challenging due to the possibility of contradictory requirements of the various diseases. Regular assessments of patients and care partners and their self-care behaviours are needed. Support and resources should be offered, especially for dyads with the risk factors we identified (gender, income, education, and availability of a second care partner). Respite care and homecare services should be offered when possible.

Additional dyadic studies with longitudinal design are needed in MCC to confirm our results and identify the causal-effect direction. Moreover, intervention studies are needed to modify the risk factors identified.

4.4. Strengths and limitations

The limitations of the study include the cross-sectional nature of the data, which limits interpretation of causal relationships. Second, participants were recruited mainly from community settings, which may have resulted in a sample with different characteristics from the general MCC population. We tried, however, to counterbalance the convenience sample by recruiting participants from different regions in Southern and Central Italy. Third, self-care and related variables are sensitive to sociocultural influences, so caution is needed when generalizing our findings to other countries. Finally, we considered only a limited number of self-care determinants; research on other possible influencing factors is needed. In particular, self-efficacy and psychological distress should be considered in future studies.

Strengths of the study include the use of theoretically grounded instruments, multicentre enrolment, robust sample size, and the enrolment of dyads similar to those described in different contexts.

5. Conclusion

Our study shows the reciprocal influence of sociodemographic and clinical characteristics of patients with MCC and their care partner on self-care behaviours in both members of the dyad. Our results advocate for the importance of taking a dyadic approach when analysing the determinants of self-care in patients and the contribution to self-care in care partners.

Declaration of Competing Interest

No conflict of interest has been declared by the authors.

CRediT authorship contribution statement

Paolo Iovino: Writing - original draft, Visualization. **Karen S. Lyons:** Conceptualization, Formal analysis. **Maddalena De Maria:** Data curation, Investigation. **Ercole Vellone:** Conceptualization, Methodology. **Davide Ausili:** Conceptualization, Methodology. **Christopher S. Lee:** Conceptualization, Formal analysis. **Barbara Riegel:** Writing - review & editing, Visualization. **Maria Matarese:** Conceptualization, Methodology, Project administration, Supervision.

Funding

This study was funded by a grant (n. 2.16.9) from the Centre of Excellence for Nursing Scholarship (CECRI), Rome, Italy.

References

- Aggarwal, B., Liao, M., Mosca, L., 2013. Medication adherence is associated with having a caregiver among cardiac patients. *Ann. Behav. Med.* 46 (2), 237–242.
- Alguwaihes, A., Shah, B.R., 2009. Educational attainment is associated with health care utilization and self-care behavior by individuals with diabetes. *Open Diabetes J.* 2, 24–28.
- Ausili, D., Rossi, E., Rebora, P., Luciani, M., Tonoli, L., Ballerini, E., Androni, S., Vellone, E., Riegel, B., Di Mauro, S., 2018. Socio-demographic and clinical determinants of self-care in adults with type 2 diabetes: a multicentre observational study. *Acta Diabetol.* 55 (7), 691–702.
- Bell, R.A., Andrews, J.S., Arcury, T.A., Snively, B.M., Golden, S.L., Quandt, S.A., 2010. Depressive symptoms and diabetes self-management among rural older adults. *Am. J. Health Behav.* 34 (1), 36–44.
- Bidwell, J.T., Vellone, E., Lyons, K.S., D'Agostino, F., Riegel, B., Juarez-Vela, R., Hiatt, S.O., Alvaro, R., Lee, C.S., 2015. Determinants of heart failure self-care maintenance and management in patients and caregivers: a dyadic analysis. *Res. Nurs. Health* 38 (5), 392–402.
- Braveman, P., Gottlieb, L., 2014. The social determinants of health: it's time to consider the causes. *Public Health Rep.* 129 (2), 19–31.
- Cameron, J., Worrall-Carter, L., Page, K., Riegel, B., Lo, S.K., Stewart, S., 2010. Does cognitive impairment predict poor self-care in patients with heart failure? *Eur. J. Heart Fail.* 12 (5), 508–515.
- Cannon, D., Buys, N., Sriram, K.B., Sharma, S., Morris, N., Sun, J., 2016. The effects of chronic obstructive pulmonary disease self-management interventions on improvement of quality of life in COPD patients: a meta-analysis. *Respir. Med.* 121, 81–90.
- Chiu, C.J., Wray, L.A., 2011. Gender differences in functional limitations in adults living with type 2 diabetes: biobehavioral and psychosocial mediators. *Ann. Behav. Med.* 41 (1), 71–82.
- Cocchieri, A., Riegel, B., D'Agostino, F., Rocco, G., Fida, R., Alvaro, R., Vellone, E., 2015. Describing self-care in Italian adults with heart failure and identifying determinants of poor self-care. *Eur. J. Cardiovasc. Nurs.* 14 (2), 126–136.
- Crisan, A.F., Oancea, C., Timar, B., Fira-Mladinescu, O., Crisan, A., Tudorache, V., 2014. Cognitive impairment in chronic obstructive pulmonary disease. *PLoS ONE* 9 (7), e102468.
- De Maria, M., Matarese, M., Strömberg, A., Ausili, D., Vellone, E., Jaarsma, T., Osokpo, O.H., Daus, M. M., Riegel, B., Barbaranelli, C., 2019b. Cross-cultural assessment of the Self-Care of Chronic Illness Inventory: A psychometric evaluation. *Inter. J. Nurs. Stud.* doi:10.1016/j.ijnurstu.2019.103422, In press.
- De Maria, M., Vellone, E., Ausili, D., Alvaro, R., Di Mauro, S., Piredda, M., De Marinis, M., Matarese, M., 2019a. Self-care of patient and caregiver DyAds in multiple chronic conditions: a Longitudinal study (SODALITY) protocol. *J. Adv. Nurs.* 75 (2), 461–471.
- Dickens, C., Dickson, V.V., Piano, M.R., 2019. Perceived stress among patients with heart failure who have low socioeconomic status: a mixed-methods study. *J. Cardiovasc. Nurs.* 34 (3), E1–E8.
- Focht, K.L., Gogue, A.M., Whote, B.M., Ellis, C., 2014. Gender differences in stroke recognition among stroke survivors. *J. Neurosci. Nurs.* 46 (1), E11–E12.
- Geboers, B., de Winter, A.F., Spoorenberg, S.L., Wynia, K., Reijneveld, S.A., 2016. The association between health literacy and self-management abilities in adults aged 75 and older, and its moderators. *Qual. Life Res.* 25 (11), 2869–2877.
- Gijsen, R., Hoeymans, N., Schellevis, F.G., Ruwaard, D., Satariano, W.A., van den Bos, G.A., 2001. Causes and consequences of comorbidity: a review. *J. Clin. Epidemiol.* 54 (7), 661–674.
- Greco, A., Pancani, L., Sala, M., Annoni, A.M., Steca, P., Paturzo, M., D'Agostino, F., Alvaro, R., Vellone, E., 2017. Psychometric characteristics of the caregiver burden inventory in caregivers of adults with heart failure. *Eur. J. Cardiovasc. Nurs.* 16 (6), 502–510.
- Hajat, C., Stein, E., 2018. The global burden of multiple chronic conditions: a narrative review. *Prev. Med. Rep.* 12, 284–293.
- Hamar, G.B., Rula, E.Y., Coberley, C., Pope, J.E., Larkin, S., 2015. Long-term impact of a chronic disease management program on hospital utilization and cost in an Australian population with heart disease or diabetes. *BMC Health Serv. Res.* 15, 174.
- Hawkins, M.A., Gathright, E.C., Gunstad, J., Dolansky, M.A., Redle, J.D., Josephson, R., Moore, S.M., Hughes, J.W., 2014. The MoCA and MMSE as screeners for cognitive impairment in a heart failure population: a study with comprehensive neuropsychological testing. *Heart Lung* 43 (5), 462–468.
- He, X., Li, J., Wang, B., Yao, Q., Li, L., Song, R., Shi, X., Zhang, J.A., 2017. Diabetes self-management education reduces risk of all-cause mortality in type 2 diabetes patients: a systematic review and meta-analysis. *Endocrine* 55 (3), 712–731.
- Huygens, M.W.J., Swinkels, I.C.S., de Jong, J.D., Heijmans, M.J.W.M., Friele, R.D., van Schayck, O.C.P., de Witte, L.P., 2017. Self-monitoring of health data by patients with a chronic disease: does disease controllability matter? *BMC Fam. Pract.* 18 (1), 40.
- Kennedy, A., Rogers, A., Bower, P., 2007. Support for self care for patients with chronic disease. *BMJ* 335 (7627), 968–970.
- Lai, D.W.L., 2012. Effect of financial costs on caregiving burden of family caregivers of older adults. *SAGE Open* 2 (4), 1–14.
- Lancaster, K., Abuzour, A., Khaira, M., Mathers, A., Chan, A., Bui, V., Lok, A., Thabane, L., Dolovich, L., 2018. The use and effects of electronic health tools for patient self-monitoring and reporting of outcomes following medication use: systematic review. *J. Med. Internet Res.* 20 (12), e294.
- Lee, Y., Tang, F., Kim, K.H., Albert, S.M., 2015. The vicious cycle of parental caregiving and financial well-being: A longitudinal study of women. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 70 (3), 425–431.
- Lochner, K.A., Goodman, R.A., Posner, S., Parekh, A., 2013. Multiple chronic conditions among medicare beneficiaries: state-level variations in prevalence, utilization, and cost, 2011. *Medicare Medicaid Res. Rev.* 3 (3), E1–E19.
- Lorini, S., De Maria, M., Ausili, D., Matarese, M., Vellone, E., 2019. Validity and reliability of the caregiver contribution to self-care chronic illness inventory (CC-SC-CII). Proceedings of the Euro Heart Care 2019. European Heart Association, Milan.
- Lyons, K.S., Sayer, A.G., 2005. Using multilevel modeling in caregiving research. *Ageing Ment Health* 9 (3), 189–195.
- Lyons, K.S., Vellone, E., Lee, C.S., Cocchieri, A., Bidwell, J.T., D'Agostino, F., Hiatt, S.O., Alvaro, R., Vela, R.J., Riegel, B., 2015. A dyadic approach to managing heart failure with confidence. *J. Cardiovasc. Nurs.* 30 (4 Suppl 1), S64–S71.
- Marengoni, A., Angleman, S., Melis, R., Mangialasche, F., Karp, A., Garmen, A., Meinow, B., Fratiglioni, L., 2011. Aging with multimorbidity: a systematic review of the literature. *Ageing Res. Rev.* 10 (4), 430–439.
- Marvardi, M., Mattioli, P., Spazzafumo, L., Mastroforti, R., Rinaldi, P., Polidori, M.C.,

- Cherubini, A., Quartesan, R., Bartorelli, L., Bonaiuto, S., Cucinotta, D., Di Iorio, A., Gallucci, M., Giordano, M., Martorelli, M., Masaraki, G., Nieddu, A., Pettenati, C., Putzu, P., Solfrizzi, V., Tammaro, A.E., Tomassini, P.F., Vergani, C., Senin, U., Mecocci, P. Study Group on Brain, A., Italian Society of Geriatrics, 2005. The caregiver burden inventory in evaluating the burden of caregivers of elderly demented patients: results from a multicenter study. *Aging Clin. Exp. Res.* 17 (1), 46–53.
- Mei, J., Tian, Y., Chai, X., Fan, X., 2019. Gender differences in self-care maintenance and its associations among patients with chronic heart failure. *Int. J. Nurs. Sci.* 6 (1), 58–64.
- Mirel, S., Pop, S., Onaca, E., Domnita, S., Mirel, V., 2011. The Use of Medical Devices in Self Monitoring of Chronic Diseases. In, pp. 48–53.
- Mori, Y., Futamura, A., Murakami, H., Kohashi, K., Hirano, T., Kawamura, M., 2015. Increased detection of mild cognitive impairment with type 2 diabetes mellitus using the Japanese version of the Montreal cognitive assessment: a pilot study. *Neurol. Clin. Neurosci.* 3 (3), 89–93.
- Nasreddine, Z.S., Phillips, N.A., Bedirian, V., Charbonneau, S., Whitehead, V., Collin, I., Cummings, J.L., Chertkow, H., 2005. The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J. Am. Geriatr. Soc.* 53 (4), 695–699.
- Novak, M., Guest, C., 1989. Application of a multidimensional caregiver burden inventory. *Gerontologist* 29 (6), 798–803.
- Orueta, J.F., Nuño-Solinis, R., Mateos, M., Vergara, I., Grandes, G., Esnaola, S., 2012. Monitoring the prevalence of chronic conditions: which data should we use? *BMC Health Serv. Res.* 12 (1), 365.
- Palladino, R., Tayu Lee, J., Ashworth, M., Triassi, M., Millett, C., 2016. Associations between multimorbidity, healthcare utilisation and health status: evidence from 16 European countries. *Age Ageing* 45 (3), 431–435.
- Polenick, C.A., Leggett, A.N., Webster, N.J., Han, B.H., Zarit, S.H., Piette, J.D., 2020. Multiple chronic conditions in spousal caregivers of older adults with functional disability: Associations with caregiving difficulties and gains. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 75 (1), 160–172.
- Raghupathi, W., Raghupathi, V., 2018. An empirical study of chronic diseases in the United States: a visual analytics approach. *Int. J. Environ. Res. Public Health* 15 (3), 431.
- Raudenbush, S.W., Bryk, A.S., Cheong, Y.F., Congdon, R.T., Du Toit, M., 2011. *HLM 7: Hierarchical Linear and Nonlinear Modeling*. Scientific Software International, Incorporated.
- Restrepo, R.D., Alvarez, M.T., Wittnebel, L.D., Sorenson, H., Wettstein, R., Vines, D.L., Sikkema-Ortiz, J., Gardner, D.D., Wilkins, R.L., 2008. Medication adherence issues in patients treated for COPD. *Int. J. Chron. Obstruct. Pulmon. Dis.* 3 (3), 371–384.
- Riegel, B., Barbaranelli, C., Sethares, K.A., Daus, M., Moser, D.K., Miller, J.L., Haedtke, C.A., Feinberg, J.L., Lee, S., Stromberg, A., Jaarsma, T., 2018. Development and initial testing of the self-care of chronic illness inventory. *J. Adv. Nurs.* 74 (10), 2465–2476.
- Riegel, B., Dickson, V.V., Faulkner, K.M., 2016. The situation-specific theory of heart failure self-care: revised and updated. *J. Cardiovasc. Nurs.* 31 (3), 226–235.
- Riegel, B., Jaarsma, T., Stromberg, A., 2012. A middle-range theory of self-care of chronic illness. *ANS Adv. Nurs. Sci.* 35 (3), 194–204.
- Riegel, B., Lee, C.S., Dickson, V.V., Carlson, B., 2009. An update on the self-care of heart failure index. *J. Cardiovasc. Nurs.* 24 (6), 485–497.
- Ruppar, T.M., Cooper, P.S., Mehr, D.R., Delgado, J.M., Dunbar-Jacob, J.M., 2016. Medication adherence interventions improve heart failure mortality and readmission rates: systematic review and meta-analysis of controlled trials. *J. Am. Heart Assoc.* 5 (6), e002606.
- Sayer, A.G., Klute, M.M., 2005. Analyzing Couples and Families: Multilevel Methods. In: Bengtson, V.L., Acock, A.C., Allen, K.R., Dilworth-Anderson, P., Klein, D.M. (Eds.), *Sourcebook of Family Theory & Research*. Sage Publications, Inc., pp. 289–313. doi:10.4135/9781412990172.d63.
- Sevinc, S., Samancioglu, S., 2017. Influence of caregiver on heart failure patients' disease beliefs and compliance. *Eur. J. Cardiovasc. Nurs.* 16, S27.
- Smith, M.L., Bergeron, C.D., Riggall, S.D., Meng, L., Towne Jr., S.D., Ahn, S., Ory, M.G., 2017. Self-care difficulties and reliance on support among vulnerable middle-aged and older adults with chronic conditions: a cross-sectional study. *Matrityas* 104, 1–10.
- Smith, S.M., O'Dowd, T., 2007. Chronic diseases: what happens when they come in multiples? *Br. J. Gen. Pract.* 57 (537), 268–270.
- Swinkles, J., Tilburg, T.V., Verbakel, E., Broese van Groenou, M., 2019. Explaining the gender gap in the caregiving burden of partner caregivers. *J. Gerontol. B Psychol. Sci. Soc. Sci.* 74 (2), 309–317.
- Tomlin, A., Sinclair, A., 2016. The influence of cognition on self-management of type 2 diabetes in older people. *Psychol. Res. Behav. Manag.* 9, 7–20.
- Trivedi, R.B., Bryson, C.L., Udriș, E., Au, D.H., 2012. The influence of informal caregivers on adherence in COPD patients. *Ann. Behav. Med.* 44 (1), 66–72.
- Uchmanowicz, I., Jankowska-Polanska, B., Mazur, G., Sivarajan Froelicher, E., 2017. Cognitive deficits and self-care behaviors in elderly adults with heart failure. *Clin. Interv. Aging.* 12, 1565–1572.
- Vellone, E., Riegel, B., Alvaro, R., 2019. A situation-specific theory of caregiver contributions to heart failure self-care. *J. Cardiovasc. Nurs.* 34 (2), 166–173.
- Vellone, E., Riegel, B., Cocchieri, A., Barbaranelli, C., D'Agostino, F., Glaser, D., Rocco, G., Alvaro, R., 2013. Validity and reliability of the caregiver contribution to self-care of heart failure index. *J. Cardiovasc. Nurs.* 28 (3), 245–255.
- Wakabayashi, R., Motegi, T., Yamada, K., Ishii, T., Gemma, A., Kida, K., 2011. Presence of in-home caregiver and health outcomes of older adults with chronic obstructive pulmonary disease. *J. Am. Geriatr. Soc.* 59 (1), 44–49.
- Watson, R., Modeste, N.N., Catolico, O., Crouch, M., 1998. The relationship between caregiver burden and self-care deficits in former rehabilitation patients. *Rehabil. Nurs.* 23 (5), 258–262.
- Wheeler, J.R., Janz, N.K., Dodge, J.A., 2003. Can a disease self-management program reduce health care costs? The case of older women with heart disease. *Med. Care* 41 (6), 706–715.
- World Medical Association, 2013. Declaration of Helsinki: ethical principles for medical research involving human subjects. *JAMA* 310 (20), 2191–2194.
- Zwerink, M., Brusse-Keizer, M., van der Valk, P.D., Zielhuis, G.A., Monnikhof, E.M., van der Palen, J., Frith, P.A., Effing, T., 2014. Self management for patients with chronic obstructive pulmonary disease. *Cochrane Database Syst. Rev.* 3, CD002990.