Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle

REPORT ON REVIEW OF THE MEDICAL LITERATURE AND CARE APPROACHES, ADMINISTRATIVE DATABASES ANALYSES

WP6, Task 2

CHRODIS
ADDRESSING CHRONIC DISEASES & HEALTHY AGEING ACROSS THE LIFE CYCLE

This document arises from the EU CHRODIS Joint Action which has received funding from the European Union, in the framework of the Health Programme (2008-2013). Sole responsibility lies with the author and the Executive Agency for Health and Consumers is not responsible for any use that may be made of the information contained therein

WORK PACKAGE 6: TASK 2

Comprehensive care programs for patients with multiple chronic conditions and/or frailty: A systematic literature review (update)

Hopman, E.P.C. [1], de Bruin, S.R.[2], Forjaz, J.[3], Rodriguez Blazquez, C.[3], Tonnara, G.[4], Lemmens, L.C.[2], Onder, G.[4], Rijken, P.M.[1]

[1] Netherlands Institute for Health Services Research (NIVEL), P.O. Box 1568, 3500BN, Utrecht, The Netherlands

[2] National Institute for Public Health and the Environment, Centre for Prevention and Health Services Research, P.O. Box 1, 3720 BA Bilthoven, The Netherlands

[3] Instituto de Salud Carlos III, Calle Sinesio Delgado, 4, 28029 Madrid, Spain

[4] Università Cattolica del Sacro Cuore, Largo A. Gemelli, 1, 20123 Milano, Italy

Correspondence to:

(E.P.C.) Petra Hopman

Netherlands Institute for Health Services Research (NIVEL)

P.O. Box 1568

3500 BN, Utrecht

The Netherlands

E-mail: P.Hopman@nivel.nl

Tel.: +31 30 2729763

Fax: +31 30 2729729

Introduction

Due to rapid ageing and greater longevity of the Western population as well as increasing improvement of medical care, a growing number of people are living with a chronic condition [Eurostat, 2010; Busse et al., 2010]. An increasing proportion of these chronically ill people is multimorbid [Boyd & Fortin, 2010; Uijen & van der Lisdonk, 2008], which refers to the co-occurrence of two or more chronic or long-term conditions within the same person [Bower et al., 2011; Smith et al., 2012]. Especially among older people the prevalence of multi-morbidity is very high: among people over age 65 the proportion of individuals with multiple chronic conditions is estimated at about 65%; among people over age 85 at about 85% [e.g. Marengoni et al., 2011; Vogeli et al., 2007].

People suffering from multiple chronic conditions often experience a poor quality of life, disability, psychological distress, and an increased mortality risk [Marengoni et al., 2011; Fortin et al., 2006]. In order to adequately address the complex healthcare needs of (elderly) people with multi-morbidity, the delivery of integrated care from different care sectors (e.g. medical care, home help, and psychological support) is required. Most current care delivery models however are disease-specific and therefore not adapted to the needs of people with multiple chronic conditions. For people with multimorbidity, a disease-specific approach incorporates the threat of a too narrow focus on their health and participation problems, a lack of evidence regarding treatment and subsequently also a lack of decision support (clinical practice guidelines may contradict each other and do not sufficiently address aspects of multi-morbidity), inadequate coordination of care, interference of medicines and suboptimal use due to poly-pharmacy, and interference of advised self-care for co-existing diseases [e.g. Boyd et al., 2005; van Weel & Schellevis, 2006; Greβ et al., 2009]. Coordination of care is difficult, and healthcare providers often fail to meet the integral healthcare demand of multimorbid patients [Greß et al., 2009; Vogeli et al., 2007]. Moreover, chronic illness care puts a high burden on financial and human resources. Increasing healthcare expenditures and the pressure on healthcare labour markets raise concern about its sustainability. Therefore innovation of chronic illness care in order to provide good quality care (with limited resources) is urgently needed.

More and more, comprehensive care programs are implemented in healthcare systems worldwide to address the integral healthcare demand of multimorbid patients [Versnel et al., 2011; Boult et al., 2009; Boyd et al., 2005]. Comprehensive care programs generally address multiple healthcare needs of people with multimorbidity, functional disabilities, and/or high healthcare utilization, and healthcare services are provided by multiple healthcare providers [Boult et al., 2009]. Comprehensive care programs are patient centered and aim to structure and coordinate delivery of healthcare services [Versnel et al., 2011; Boult et al., 2009; Boyd et al., 2005]. By improving quality and continuity of care, these programs aim to improve patient health outcomes, whilst making efficient use of healthcare resources [Greβ et al., 2009; Mattke et al., 2007; Wagner et al., 2005].

In 2012, de Bruin and colleagues performed a systematic literature review in order to systematically describe the effectiveness of existing comprehensive care programs and to define the program characteristics that may be related to positive care outcomes [de Bruin et al., 2012]. They studied 28 comprehensive care programs for multimorbid patients and found that programs varied in the target patient groups, implementation settings, number of included interventions, and number of CCM components to which these interventions related.

Regarding the programs’ impact on patients and caregivers, *moderate evidence* was found for a beneficial effect of comprehensive care on inpatient healthcare utilization and healthcare costs, health behavior of patients, perceived quality of care, and satisfaction of patients and caregivers. *Insufficient evidence* was found for a beneficial effect of comprehensive care on health-related quality of life in terms of mental functioning, medication use, and outpatient

Co-funded by
the Health Programme
of the European Union

healthcare utilization and healthcare costs. *No evidence* was found for a beneficial effect of comprehensive care on cognitive functioning, depressive symptoms, functional status, mortality, quality of life in terms of physical functioning, and caregiver burden. De Bruin et al. [de Bruin et al., 2012] stated that, because of the heterogeneity of comprehensive care programs, it was too early to draw firm conclusions regarding their effectiveness, and that more rigorous evaluation studies would be necessary to determine what constitutes best care for the increasing number of people with multiple chronic conditions.

(...)

Co-funded by
the Health Programme
of the European Union

2. Methods

2.1 Study design and search strategy

We conducted a systematic literature review focusing on English language papers published between January 2011 and March 2014. The year 2011 was used as a starting point, since the former systematic literature review focused on the years 1995-2010 [de Bruin et al., 2012]. The search was conducted in the databases Medline, Cochrane, Cinahl, EMBASE, PsycINFO, and SciSearch. The following keywords were used to search these databases: *case management, comprehensive healthcare, critical pathways, disease management, continuity of patient care, patient care management, planning or team, patient-centered care, delivery of integrated healthcare, guided care, integrated care, managed care (programs), shared care, transmural care* and variations of the keywords *chronic disease, chronic illness, co-morbidity, frailty, multimorbidity, multiple chronic conditions*, and specific chronic conditions. These search terms were combined with variations of the following search terms: *benefits, effects, effectiveness, efficacy, impact, outcomes*, and specific (health) outcomes. In addition to the search in the electronic databases, the internet was searched in case the papers identified by our electronic database search described the design or a pilot of an intervention study. In those cases, the internet was consulted for information about the current status of these studies.

2.2 Study selection

Four reviewers worked in pairs and independently reviewed the title and abstract of the papers extracted by the search for their relevance. When considered relevant by both reviewers, the full-text paper was retrieved. Any disagreement between the reviewers was resolved by consensus. In line with earlier studies [Tsai at el., 2005; Zwar et al., 2006; Adams et al., 2007; de Bruin et al., 2011; Lemmens et al., 2011], the Chronic Care Model (CCM) of Wagner was used as a conceptual framework to describe comprehensive care programs [Wagner et al., 2001; Wagner et al., 2005]. According to this model, a comprehensive care program ideally contains six interrelated components. The first two components, mainly referring to the context in which chronic care is provided, are (1) a health care system that is open to provide high-quality chronic care and (2) links towards community resources and policies. The other four components, related to the delivery of care, are: (3) self-management support to activate patients and their families to cope with the challenges of living with and the treatment of a chronic illness and to improve the confidence and skills of the patients in managing their chronic illness; (4) change in the delivery system design that ensures effective delivery of care by for example working in multidisciplinary teams; collaboration in multidisciplinary teams; (5) decision support; by the implementation of evidence-based guidelines and protocols to provide the chronically ill with good care and (6) development of clinical information systems as a tool for the care team for implementing reminder systems and provide information about patients. A program was considered comprehensive if it included interventions that could be related to at least two components of the CCM, since, according to the model, components must be interrelated.

Papers were eligible if they met the following inclusion criteria: (1) the program described in the paper met our operational definition of a comprehensive care program; (2) the aim of the program was to treat patients with multiple chronic conditions and/or frailty; (3) the study described in the paper was an intervention study evaluating the effectiveness of a comprehensive care program. Duplicate studies were removed.

2.3 Data extraction, quality assessment, and data analysis

Four authors (PH, GT, JF, CR) worked in pairs to extract relevant data from the studies included. Data extracted from the papers were: (1) study design; (2) length of follow-up of

Co-funded by
the Health Programme
of the European Union

study; (3) target population of the program; (4) setting in which the program had been implemented; (5) content of the program described in terms of the CCM components; (6) characteristics of the usual care condition; and (7) study outcomes. Our analyses were descriptive and qualitative in nature.

Four authors (PH, GT, JF, CR) worked in pairs to score the methodological quality of the selected studies, based on six items adapted from two quality criteria lists [Verhagen et al., 1998; Van Tulder et al., 2003] (Table 2). Similar to the criteria list used in previous reviews [Peikes et al, 2009; de Bruin et al., 2012], our list only included criteria that in our opinion were most relevant for studies on comprehensive care. Each criterion was rated as '+' (i.e. criterion fulfilled), '-' (i.e. criterion not fulfilled), '?' (i.e. criterion not reported), or 'N.A' (i.e. not applicable). Since we did not use a complete standardized set of quality assessment criteria, we decided not to assign an overall quality rating per study. Hence, we only provide a total quality sum-score (ranging from 0 to 6) per study that was determined by counting the number of criteria scored positively.

Best evidence synthesis

To draw conclusions regarding the effectiveness of comprehensive care programs, in line with earlier studies a best-evidence analysis was applied [Hoogendoorn et al., 2000; Singh et al., 2008; Proper et al., 2011]. We distinguished four levels to rate the strength of evidence for each of the outcomes:

1. Strong evidence: consistent evidence for a beneficial effect of comprehensive care across multiple studies with high quality sum-scores;
2. Moderate evidence: consistent evidence for a beneficial effect of comprehensive care across multiple studies, including at least one study with a high quality sumscore and studies with lower quality sum-scores;

3. Insufficient evidence: inconsistent evidence for a beneficial effect of comprehensive care across multiple studies;
4. No evidence: only few studies available and/or consistent evidence for no effect of comprehensive care across multiple studies.

Similar to previous reviews that applied a best-evidence synthesis [Hoogendoorn et al., 2000; Proper et al., 2011; de Bruin et al., 2012] results were considered consistent when at least 75% of the studies showed results in the same direction. Findings of studies with relatively higher quality sum-scores were valued more than findings of studies with relatively lower quality sum-scores.

Results

3.1 Study retrieval

Our literature search yielded 2611 potentially relevant publications. On the basis of their title and abstract, 80 papers were selected by the reviewers to be retrieved full-text for in-depth screening. This screening process resulted in 19 publications for inclusion in our study. The addition of one paper from our manual search resulted in a total of 20 publications that were classified as eligible for our review. Reasons for exclusion are shown in Figure 1.

>>INSERT FIGURE 1 ABOUT HERE<<

3.2 Study characteristics

3.2.1. Study designs and length of follow-up. The 20 included publications described 19 different studies i.e. seven randomized controlled trials, six pretest-post-test studies, three cluster randomized controlled trials, two post-test only studies, and one quasi randomized controlled trial (Table 1). Across all studies, sample size varied from 47 to 1682 subjects. Of the studies with a longitudinal design, eleven studies had a follow-up of ≤12 months, five studies had a follow-up of >12 months, and one study (presenting preliminary data) did not report follow-up length.

3.2.2. Methodological quality of studies. Two studies fulfilled all quality criteria (i.e. sum-score of 6) based on what could be retrieved from the information provided in the papers (Table 2). The observed minimum sum-score was 0 (*n* = 4). The quality criteria 'randomization' and 'drop-out rate' were most frequently scored positively. The quality criteria 'randomization', 'similarity at baseline', 'application of intention-to-treat-analysis', and 'adjustment for confounders' were not applicable for studies with a non-experimental design (*n* = 8).

>>INSERT TABLE 1 ABOUT HERE<<

3.2.3. Usual care conditions. In two thirds of the studies (*n* = 13) the effects of comprehensive care programs were compared with those of care as usual (i.e. no comprehensive care). In three of these studies, the usual care conditions were not or only poorly described (Table 1). Usual care was mostly described as normal access to services available to frail older and/or multimorbid people, routine home, primary, and hospital care.

3.3. Program characteristics

3.3.1. Target populations. The 19 comprehensive care programs were implemented in the USA (n = 12), Canada (n = 3), Australia (n = 1), Japan (n = 1), Taiwan (n = 1), and the Netherlands (n =1). Thirteen comprehensive care programs focused on frail older people who were (at risk of) using long-term care or medical services or had difficulty in self-managing medications [Boult et al., 2011; Cameron et al., 2013 ; Fleming & Haney, 2013; Hébert et al., 2010; Kono et al., 2012; Lee et al., 2011; Levine et al., 2012; Metzelthin et al., 2013; Rosenberg, 2012; Schulz et al., 2011; Wald et al., 2011; Watkins et al., 2012]. Three programs focused on older people with (a combination of) specific chronic conditions such as diabetes mellitus and heart failure [Gharacholou et al., 2012; Wade et al., 2011; Wakefield et al., 2011], two programs focused on frequently admitted and/or complex patients (not necessarily frail/older) [Berry et al., 2013; Davis et al., 2013], and one programs focused on kidney disease patients (not necessarily frail/ older) with diabetes and/or cardiovascular disease [Weber et al., 2012] (Table 1).

3.3.2. Settings. The settings in which the comprehensive care programs were implemented varied from home care organizations and community centers to primary care practices, hospitals, specialized clinics (e.g. geriatric clinics and Veterans Affairs medical centers), and managed care organizations (Table 1). Consequently, the type of care that was provided also differed widely between the programs.

3.3.3. Contents. Table 1 presents the contents of the comprehensive care programs included in our review. The table illustrates the diversity in the comprehensive care programs with regard to the number of included interventions and the number of related CCM components. We observed comprehensive care programs that included interventions related to *one* CCM components (*n*=2), *two* CCM components (*n*=5), *three* CCM components (*n*=6), *four* CCM components (*n*=4), and *five* CCM components (*n*=2).

All comprehensive care programs included interventions related to the CCM component *delivery system design*. Examples are employing a case manager, working in multidisciplinary teams, designing individualized care plans, and making home visits to patients. The majority of comprehensive care programs (*n*=12) additionally included interventions related to the CCM component *decision support*. Interventions to support healthcare providers' decision-making included implementing evidence-based guidelines, and training teams to implement

Co-funded by
the Health Programme
of the European Union

new protocols. Nine comprehensive care programs included interventions related to the CCM component *self-management support,* such as involving patients in the design of their care plan and educating patients to improve self-management. Interventions related to the CCM components *community resources* (e.g. establishing access to community resources and partnerships with local community service centers; *n*=8) and *clinical information systems* (e.g. electronic patient records and computerized clinical charts; *n*=6) were less frequently observed. A small minority of the comprehensive care programs (*n*=1) included interventions related to the CCM component health system. Examples of such interventions are installing committees to support new partnerships, employing management teams to support process and quality improvement, and enabling infrastructure for innovations in chronic care.

3.4. Impact of comprehensive care programs

Table 1 presents all outcomes reported in the studies included. Only outcomes that were reported in *at least three studies* are described in the text. In describing the effect of comprehensive care programs, we distinguish patient related outcomes (paragraph 3.4.1), informal and professional caregiver related outcomes (paragraph 3.4.2), and healthcare utilization and costs (paragraph 3.4.3). More detailed information about the actual differences between comprehensive care groups and usual care groups or about actual changes over time are provided in Table 3a (patient related outcomes) and Table 3b (healthcare utilization). Quality of reporting on baseline and follow-up scores on the clinical patient outcomes widely varied across studies.

>>INSERT TABLE 2 ABOUT HERE<<

3.4.1. Patient related outcomes

Co-funded by
the Health Programme
of the European Union

Fifteen studies evaluated the effect of comprehensive care on patient related outcomes (Table 1). We distinguish the effect on physical health status and physical functioning (paragraph 3.4.1.1), mental health status, cognitive and emotional functioning (paragraph 3.4.1.2), social functioning, social participation, and social support (paragraph 3.4.1.3), general health status and health related quality of life (paragraph 3.4.1.4), and on patient satisfaction and empowerment (paragraph 3.4.1.5).

3.4.1.1. Physical health status, physical functioning

Activities of daily living. Four studies evaluated the effect of comprehensive care on activities of daily living (Table 3a) [Gharacholou et al., 2012; Kono et al., 2012; Lee et al., 2011; Metzelthin et al., 2013]. Four studies reported no differences between comprehensive care and usual care groups. One study reported a significant difference between baseline and follow-up for the comprehensive care group [Lee et al., 2011]. Considering these findings, there is *no evidence* for a beneficial effect of comprehensive care programs on activities of daily living.

Mortality. Mortality was evaluated in five studies [Cameron et al., 2013; Gharacholou et al., 2012; Kono et al., 2012; Wade et al., 2011; Weber et al., 2012]. None of these studies reported a significant difference between comprehensive care and usual care groups. Therefore, *no evidence* for a beneficial effect of comprehensive care programs on (a reduction of) mortality was found.

Physical health status. Four studies evaluated the effect of comprehensive care on physical health status [Dorman-Marek et al., 2013; Wade et al., 2011; Watkins et al., 2012; Weber et al., 2012]. Three studies reported a significant effect of the comprehensive care program (two studies reported a significant group×time interaction and one study reported a significant time effect within the comprehensive care group) [Dorman-Marek et al., 2013; Wade et al., 2011; Watkins et al., 2012]; two of these studies had a high quality sum-score (Table 2).

Co-funded by
the Health Programme
of the European Union

Considering these findings, there is *strong evidence* for a beneficial effect of comprehensive care on physical health status.

Physical performance/functioning. Five studies evaluated the effect of comprehensive care on physical performance/functioning using one or more indicators [Cameron et al., 2013; Dorman-Marek et al., 2013; Gharacholou et al., 2012; Hébert et al., 2010; Lee et al., 2011]. Four studies reported a significant effect of the comprehensive care program. Of these studies, one reported a significant time effect within the comprehensive care group [Lee et al., 2011]. However, one study reported a significant difference between the comprehensive care and usual care groups at follow-up for only one (out of two) indicators [Hébert et al., 2010], and two studies reported a significant group×time interaction for only one (out of two) indicators or comprehensive care groups [Cameron et al., 2013; Dorman-Marek et al., 2013]. Considering these findings, there is *insufficient evidence* for a beneficial effect of comprehensive care on physical performance/functioning.

3.4.1.2. Mental health status, cognitive and emotional functioning

Depressive symptoms. Five studies measured the effect of comprehensive care on depressive symptoms [Cameron et al., 2013; Dorman-Marek et al., 2013; Lee et al.2011; Kono et al., 2012; Metzelthin et al., 2013]. Three studies reported no differences between comprehensive care and usual care groups. Two studies, however, reported a significantly larger reduction of depressive symptoms in the comprehensive care group than in the usual care group [Dorman-Marek et al., 2013] or a significant difference between baseline and follow-up for the comprehensive care group [Lee et al.2011]. Considering these findings, there is *insufficient evidence* for a beneficial effect of comprehensive care on (reduction of) depressive symptoms.

Mental health status. Mental health status was evaluated in four studies [Dorman-Marek et al., 2013; Gharacholou et al., 2012; Wade et al., 2011; Watkins et al., 2012]. Three studies reported a significant effect of the comprehensive care program (two studies reported a significant group×time interaction and one study reported a significant time effect within the comprehensive care group) [Dorman-Marek et al., 2013; Wade et al., 2011; Watkins et al., 2012]; two of these studies had a high quality sum-score (Table 2). Considering these findings, there is *strong evidence* for a beneficial effect of comprehensive care on mental health status.

>>INSERT TABLE 3a ABOUT HERE<<

3.4.1.3. Social functioning, social participation, and social support

Only one study measured the effect of comprehensive care on *social functioning* [Gharacholou et al., 2012], one study measured the effect of comprehensive care on *social participation* [Metzelthin et al., 2013], and *social support* was evaluated in two studies [Kono et al., 2012; Metzelthin et al., 2013]. None of these studies reported a significant difference between comprehensive care and usual care groups and/or an effect of comprehensive care over time. Considering these findings, there is *no evidence* for a beneficial effect of comprehensive care on social functioning, social participation, and social support.

3.4.1.4. General health status, health related quality of life

Only one study measured the effect of comprehensive care on *general health* [Gharacholou et al., 2012], one study measured the effect of comprehensive care on *health related quality of life* [Cameron et al., 2013], and one study measured the effect of comprehensive care on *unmet needs* [Hébert et al., 2010]. Two of these studies reported no significant difference between comprehensive care and usual care groups and/or an effect of comprehensive care over time. One study reported a significant group effect at follow-up [Hébert et al., 2010].

Co-funded by
the Health Programme
of the European Union

Considering these findings, there is *no evidence* for a beneficial effect of comprehensive care programs on general health status and health related quality of life.

3.4.1.5. Patient satisfaction and empowerment

No evidence was found for a beneficial effect of comprehensive care programs on *patient empowerment*, since only one study measured the effect of comprehensive care on this outcome measure [Hébert et al., 2010]. However, five studies measured the effect of comprehensive care on *patient satisfaction* [Berry et al., 2013; Fleming & Haney, 2013; Hébert et al., 2010; Levine et al., 2012; Watkins et al., 2012]. Three studies reported no differences between comprehensive care and usual care groups. Two studies reported a significant difference between comprehensive care and usual care groups [Hébert et al., 2010; Levine et al., 2012]. Considering these findings, there is *insufficient evidence* for a beneficial effect of comprehensive care programs on patient satisfaction.

3.4.2. Informal and professional caregiver related outcomes

No evidence was found for a beneficial effect of comprehensive care programs on *informal caregiver related outcomes* since no studies were found that evaluated this outcome measure. Four studies measured the effect of comprehensive care on *professional caregiver related outcomes*. More specifically, one study measured the amount of time that was being saved [Berry et al., 2013], one study measured physician satisfaction [Fleming & Haney, 2013], one study measured caregiver burden (Hébert et al., 2010], and one study measured recognition of abnormal functional and cognitive status [Wald et al., 2011]. Only two studies reported a significant effect of the comprehensive care program [Berry et al., 2013; Wald et al., 2011], therefore *insufficient evidence* was found for a beneficial effect of comprehensive care programs on professional caregiver related outcomes.

Co-funded by
the Health Programme
of the European Union

>>INSERT TABLE 3b ABOUT HERE<<

3.4.3. Healthcare utilization and healthcare costs

Fifteen studies evaluated the effect of comprehensive care on healthcare utilization (paragraph 3.4.3.1) and/or healthcare costs (paragraph 3.4.3.2) (Table 1).

3.4.3.1. Healthcare utilization

Hospital care utilization. Fourteen studies measured the effect of comprehensive care on hospital care utilization using one or more of the following indicators: number of hospital (re)admissions, hospital stay (days), time to admission, and number of ED visits (Table 3b) [Berry et al., 2013; Boult et al., 2011; Cameron et al., 2013 ; Davis et al., 2013; Fleming & Haney, 2013; Gharacholou et al., 2012; Hébert et al., 2010; Kono et al., 2012; Levine et al., 2012; Rosenberg, 2012; Wade et al., 2011; Wald et al., 2011; Watkins et al., 2012; Weber et al., 2012]. Five studies reported a significant effect of the comprehensive care program. Of these studies, two reported a significant difference between the comprehensive care and usual care groups at follow-up [Gharacholou et al., 2012; Levine et al., 2012] and one reported a significant time effect within the comprehensive care group [Rosenberg, 2012]. However, one study reported a significant group×time interaction as well as a non-significant time effect for the comprehensive care group (the group×time interaction could be explained by a significant time effect for the usual care group) [Hébert et al., 2010]. Another study reported a significant group effect at follow-up for only two (out of eight) indicators [Wade et al., 2011]. Considering these findings, there is *insufficient evidence* for a beneficial effect of comprehensive care on (reduced) hospital care utilization.

Co-funded by
the Health Programme
of the European Union

Community and institutional long-term care services utilization. Four studies evaluated the effect of comprehensive care on community and institutional long-term care services utilization [Kono et al., 2012; Cameron et al., 2013; Boult et al., 2011; Schulz et al., 2011]. No study reported any effect of comprehensive care. Considering these findings, there is *no evidence* for a beneficial effect of comprehensive care programs on (reduced) utilization of community and institutional long-term care services.

Primary care utilization. Primary care was evaluated in three studies [Boult et al., 2011; Wade et al., 2011; Weber et al., 2012]. Since no study reported an effect of comprehensive care, there is *no evidence* for a beneficial effect of comprehensive care programs on (reduced) primary care utilization.

Specialist care utilization. Three studies measured the effect of comprehensive care on the use of specialist care using one or more indicators [Boult et al., 2011; Wade et al., 2011; Weber et al., 2012]. Two of these studies reported no differences between comprehensive care and usual care groups (over time), and one study reported a significant difference between the comprehensive care and usual care groups at follow-up for only one (out of two) indicators [Wade et al., 2011]. Therefore, there is *no evidence* for a beneficial effect of comprehensive care programs on (reduced) utilization of specialist care.

3.4.3.2 Healthcare costs. Eight studies evaluated the effect of comprehensive care on healthcare costs [Berry et al., 2013; Gharacholou et al., 2012; Kono et al., 2012; Levine et al., 2012; Rosenberg, 2012; Wald et al., 2011; Watkins et al., 2012; Weber et al., 2012]. Three studies reported a positive effect of the comprehensive care program on healthcare costs [Berry et al., 2013; Watkins et al., 2012; Weber et al., 2012] and one study reported a negative effect (i.e. costs were higher in the comprehensive care group) [Kono et al., 2012). Four studies reported no effect [Gharacholou et al., 2012; Levine et al., 2012; Rosenberg, 2012;

Co-funded by
the Health Programme
of the European Union

Wald et al., 2011]. It should be noted that not all studies provided exact data and/or statistically tested whether differences (between groups, or over time) were significant. However, considering these findings there is *insufficient evidence* for a beneficial effect of comprehensive care programs on healthcare costs.

4. Discussion

This systematic literature review summarizes available information about the characteristics of comprehensive care programs for people with multiple chronic conditions and about their impact on patients and caregivers. There is a vast amount of literature on comprehensive care. However, most literature focuses on comprehensive care programs for people with a single disease [e.g. Mattke et al., 2007; Tsai at el., 2005; Zwar et al., 2006; Adams et al., 2007; Ofman et al., 2004; Singh, 2008; Weingarten et al., 2002; Goetzel et al., 2005]. Our work focuses on comprehensive care programs for people with multiple diseases, and therefore adds to the current literature. A key publication and starting point for the current review is the literature review of de Bruin and colleagues (2012), who studied 28 comprehensive care programs for multimorbid patients. Based on their findings, the authors concluded that although “a broad array of comprehensive care programs is available to multimorbid patients (...) because of the heterogeneity of the programs it is as yet too early to draw firm conclusions regarding their effectiveness”. In order to do so, it should be clear “which patient groups benefit most from comprehensive care and which program characteristics contribute most to positive effects of comprehensive care” [de Bruin et al., 2012].

With the current review we aim to elaborate on this review by describing the number, characteristics, and impact of present comprehensive care programs, thereby further contributing to a scientific basis for the improvement of care for patients with multimorbidity.

We conducted a thorough systematic review of nineteen studies that examined different comprehensive care programs for multimorbid patients. These programs varied in the target patient groups, implementation settings, number of included interventions, and number of CCM components to which these interventions related. Although again, evidence regarding the effectiveness of comprehensive care is rather inconsistent, *strong* evidence was found for a beneficial effect of comprehensive care on physical and mental health status. *Insufficient* evidence was found for a beneficial effect of comprehensive care on physical performance and functioning, (the reduction of) depressive symptoms, patient satisfaction and empowerment, professional caregiver related outcomes, (reduced) hospital care utilization, and health care costs. *No* evidence was found for a beneficial effect of comprehensive care on activities of daily living, (reduced) mortality, social functioning, social participation, and social support, general health status, health related quality of life, professional caregiver related outcomes, (reduced) utilization of community and institutional long-term care services, primary care, and specialist care.

In line with the former literature review [de Bruin et al., 2012], the majority of comprehensive care programs reviewed in our study incorporated interventions related to three or more CCM components. >>*Describe (and elaborate on) nature and scope of the programs in terms of the CCM components. Also, try to find a pattern (i.e. number and/or type of CCM components) among successful comprehensive care programmes.*

Mention the study's limitations (those of de Bruin et al [2012] were that the included scientific papers were written in the English language only what might have caused them to miss relevant comprehensive care programs, and that they could not use a complete standardized tool to assess the methodological quality of the included studies). Also argue for more heterogeneity in (the use of) outcome measures (patient related and health care utilization), so that programs can be better compared in terms of their effectiveness.<<

References

de Bruin SR, Versnel N, Lemmens LC, Molema CCM, Schellevis FG, Nijpels G, Baan CA. Comprehensive care programs for patients with multiple chronic conditions: A systematic literature review. Health Policy 107 (2012) 108–145.

Eurostat, http://epp.eurostat.ec.europa.eu/portal/page/portal/health/public_health/ data_public_health/ database (Table People having a long-standing illness or health problem, by sex, age and income quintile, year: 2010).

Busse, R., Blümel, M., Scheller-Kreinsen, D., & Zentner, A. (2010). Tackling chronic disease in Europe. Strategies, interventions and challenges. Observatory Studies Series no. 20. World Health Organization, on behalf of the European Observatory on Health Systems and Policies Series.

Boyd, C. & Fortin, M. (2010). Future of multimorbidity research: How should understanding of multimorbidity inform health system design? *Public Health Reviews*, *32*, 451–74.

Uijen A. A. & van de Lisdonk, E. H. (2008). Multimorbidity in primary care: Prevalence and trend over the last 20 years. *European Journal of General Practice*, *14(1)*, 28-32. doi:10.1080/13814780802436093.

Bower, P., Macdonald, W., Harkness, E., Gask, L., Kendrick, T., Valderas, J.M., Dickens, C., Blakeman, T., & Sibbald, B. (2011). Multimorbidity, service organization and clinical decision making in primary care: a qualitative study. *Family Practice, 28(5)*, 579-87.

Smith, S.M., Soubhi, H., Fortin, M., Hudon, C., & O'Dowd, T. (2012). Managing patients with multimorbidity: systematic review of interventions in primary care and community settings. *Cochrane Database of Systematic Reviews 2012 (4).* Art. No.: CD006560. DOI: 10.1002/14651858.CD006560.pub2.

Co-funded by
the Health Programme
of the European Union

Marengoni, A., Angleman, S., Melis, R., Mangialasche, F., Karp, A., Garmen, A., Meinov, B. et al. (2011). Aging with multi-morbidity: a systematic review of the literature. *Aging Research Reviews, 10*, 430-439 (DOI: 10.1016/j.arr2011.03.003).

Vogeli, C., Shields, A.E., Lee, T.A., Gibson, T.B., Marder, W.D., Weiss, K.B., et al. (2007). Multiple chronic conditions: prevalence, health consequences, and implications for quality, care management, and costs. *Journal of General Internal Medicine, 22 (Suppl. 3)*, 391-395.

Fortin M, Bravo G, Hudon C, Lapointe L, Almirall J, Dubois MF, et al. Relationship between multimorbidity and health-related quality of life of patients in primary care. Quality of Life Research 2006;15:83–91.

Boyd, C.M., Darer, J., Boult, C., Fried, L.P., Boult, & L., Wu, A.W. (2005). Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases. Implications for pay for performance. *Journal of the American Medical Association, 294*, 716-724.

van Weel, C. & Schellevis, F.G. (2006). Comorbidity and guidelines: conflicting interests (Comment). *The Lancet, 367*, 550-551.

Greß S, Baan CA, Clanan M, Dedeu T, Groenewegen P, Howson H, et al. Co-ordination and management of chronic conditions in Europe: the role of primary care—position paper of the European forum for primary care. Quality in Primary Care 2009;17:75–86.

Versnel N, Welschen LM, Baan CA, Nijpels G, Schellevis FG. The effectiveness of case management for comorbid diabetes type 2 patients; the CasCo study. Design of a randomized controlled trial. BMC Family Practice 2011;12, http://dx.doi.org/10.1186/471-2296-12-68.

Boult C, Green AF, Boult LB, Pacala JT, Snyder C, Leff B. Successful models of comprehensive care for older adults with chronic conditions: evidence for the institute of medicine’s “retooling for an Aging America” report. Journal of the American Geriatrics Society 2009;57:2328–37.

Mattke S, Seid M, Ma S. Evidence for the effect of disease management: is $1 billion a year a good investment? American Journal of Managed Care 2007;13:670–6.

Tsai AC, Morton SC, Mangione CM, Keeler EB. A meta-analysis of interventions to improve care for chronic illnesses. American Journal of Managed Care 2005;11:478–88.

Zwar N, Harris M, Griffiths R, Roland M, Dennis S, Powell Davis G, et al. APHCRI stream four: a systematic review of chronic disease management. Canberra: Australian Primary Health Care Research Institute (APHCRI); 2006.

Adams SG, Smith PK, Allan PF, Anzueto A, Pugh JA, Cornell JE. Systematic review of the chronic care model in chronic obstructive pulmonary disease prevention and management. Archives of Internal Medicine 2007;167:551–61.

De Bruin SR, Heijink R, Lemmens L, Struijs JN, Baan CA. Impact of disease management programs on healthcare expenditures for patients with diabetes, depression, heart failure or chronic obstructive pulmonary disease: a systematic review of the literature. Health Policy 2011;101:105–21.

Lemmens K, Lemmens L, Boom J, Drewes H, Meeuwissen J, Steuten L, et al. Chronic care management for patients with COPD: a critical review of available evidence. Journal of Evaluation in Clinical Practice 2011, http://dx.doi.org/10.1111/j.1365-2753.2011.01805.x.

Wagner EH, Austin BT, Davis C, Hindmarsh M, Schaefer J, Bonomi A. Improving chronic illness care: translating evidence into action. Health Affairs (Millwood) 2001;20:64–78.

Wagner EH, Bennett SM, Austin BT, Greene SM, Schaefer JK, Vonkorff M. Finding common ground: patient-centeredness and evidencebased chronic illness care. Journal of Alternative and Complementary Medicine 2005;11(Suppl. 1):S7–15.

Verhagen AP, de Vet HC, de Bie RA, Kessels AG, Boers M, Bouter LM, et al. The Delphi list: a criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. Journal of Clinical Epidemiology 1998;51:1235–41.

Van Tulder M, Furlan A, Bombardier C, Bouter L. Updated method guidelines for systematic reviews in the cochrane collaboration back review group. Spine (Phila Pa 1976) 2003;28:1290–9.

Peikes D, Chen A, Schore J, Brown R. Effects of care coordination on hospitalization, quality of care, and health care expenditures among Medicare beneficiaries: 15 randomized trials. JAMA 2009;301:603–18.

Hoogendoorn WE, van Poppel MN, Bongers PM, Koes BW, Bouter LM. Systematic review of psychosocial factors at work and private life as risk factors for back pain. Spine (Phila Pa 1976) 2000;25:2114–25.

Singh AS, Mulder C, Twisk J, Van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. Obesity reviews 2008;9:474–88.

Proper KI, Singh AS, van Mechelen W, Chinapaw MJ. Sedentary behaviors and health outcomes among adults: a systematic review of prospective studies. American Journal of Preventive Medicine 2011;40:174–82.

Berry LL, Rock BL, Smith Houskamp B, Brueggeman J, Tucker L. Care coordination for patients with complex health profiles in inpatient and outpatient settings. Mayo Clinic Proceedings, 2013, 88(2), 184-194.

Boult C, Reider L, Leff B, Frick KD, Boyd CM, Wolff JL, Frey K, Karm L, Wegener ST, Mroz T, Scharfstein DO. The effect of guided care teams on the use of health services:

results from a cluster-randomized controlled trial. Archives of internal medicine, 2011, 171(5), 460-466.

Cameron ID, Fairhall N, Langron C, Lockwood K, Monaghan n, Aggar c, Sherrington C, Lord SR, Kurrle SE. A multifactorial interdisciplinary intervention reduces frailty in older people: randomized trial. BMC Medicine, 2013, 11, 65-xx.

Davis E, Janssen J, Johnson A, Fontil V, Aronson L, Handley MA, Ebeling F, Tang L, Evans L, Gupta R, Horton C. Primary care-based complex care management: Using an interdisciplinary geriatric approach to improve care for frequently admitted patients in a safety net primary care clinic. Journal of General Internal Medicine, 2013, 28(3), 445.

Dorman Marek K, Stetzer F, Ryan PA, Denison Bud L, Adams SJ, Schlidt A, Lancaster R, O'Brien AM. Nurse care coordination and technology effects on health status of frail older adults via enhanced self-management of medication. Nursing Research, 2013, 62(4), 269-278.

Fleming MO & Haney TT. Improving patient outcomes with better care transitions: The role for home health. Cleveland Clinic Journal of Medicine, 2013, 80 Electronic Suppl 1:eS2-6.

Gharacholou SM, Sloane R, Cohen HJ, Schmader KE. Geriatric inpatient units in the care of hospitalized frail adults with a history of heart failure. International Journal of Gerontology, 2012, 6(2), 112-116.

Hébert R, Raiche M, Dubois MF, Gueye NR, et al. (2010). Impact of PRISMA, a coordination-type integrated service delivery system for frail older people in Quebec (Canada): A quasi-experimental study. Journals of Gerontology. Series B (Psychological Sciences and Social Sciences) 2010:107-18.

Kono A, Kanaya Y, Fujita T, Tsumura C, Kondo T, Kushiyama K, Rubenstein LZ. Effects of a preventive home visit program in ambulatory frail older people: a randomized control trial. Journal of Gerontology Series A: Biological Sciences & Medical Sciences, 2012, 67(3), 302-309.

Lee WJ, Peng LN, Cheng YY, Liu CY, Chen LK, Yu HC. Effectiveness of short-term interdisciplinary intervention on postacute patients in Taiwan. Journal of the American Medical Directors Association, 2011, 12(1), 29-32.

Levine S, Steinman BA, Attaway K, Jung T, Enguidanos S. Home care program for patients at high risk of hospitalization. American Journal of Managed Care, 2012, 18(8), 269-276.

Metzelthin SF, van Rossum E, de Witte LP, Ambergen AW, Hobma SO, Sipers W, Kempen GI. Effectiveness of interdisciplinary primary care approach to reduce disability in community dwelling frail older people: Cluster randomised controlled trial. British Medical Journal, 2013, 347, f5264.

Rosenberg T. Acute hospital use, nursing home placement, and mortality in a frail community-dwelling cohort managed with primary integrated interdisciplinary elder care at home. Journal of the American Geriatric Society, 2012, 60(7), 1340-1346.

Schulz RM, Porter C, Lane M, Cornman C, Branham L. Impact of a medication management system on nursing home admission rate in a community-dwelling nursing home-eligible Medicaid population. American Journal of Geriatric Pharmacotherapy, 2011, 9(1), 69-79.

Wade MJ, Desai AS, Spettell CM, Snyder AD, McGowan-Stackewicz V, Kummer PJ, Maccoy MC, Krakauer RS. Telemonitoring with case management for seniors with heart failure. American Journal of Managed Care, 2011, 17(3), 71-79.

Wakefield BJ, Holman JE, Ray A, Scherubel M, Adams MR, Hillis SL, Rosenthal GE. Effectiveness of home telehealth in comorbid diabetes and hypertension: a randomized, controlled trial. Telemedicine and e-Health, 2011, 17(4), 254-261.

Wald HL, Glasheen JJ, Guerrasio J, Youngwerth JM, Cumbler EU. Evaluation of a hospitalist-run acute care for the elderly service. Journal of Hospital Medicine, 2011, 6(6), 313-321.

Watkins L. An evidence-based strategy for transitioning patients from the hospital to the community. North Carolina Medical Journal, 2012, 73(1), 48-50.

Watkins L, Hall C, Kring D. Hospital to home: A transition program for frail older adults. Professional Case Management, 2012, 17(3), 117-123.

Weber C, Beaulieu M, Djurdjev O, Er L, Taylor P, Ignaszewski A, Burnett S, Levin A. Towards rational approaches of health care utilization in complex patients: An exploratory randomized trial comparing a novel combined clinic to multiple specialty clinics in patients with renal disease-cardiovascular disease-diabetes. Nephrology Dialysis Transplantation, 2012, 27(3), iii104-iii110.

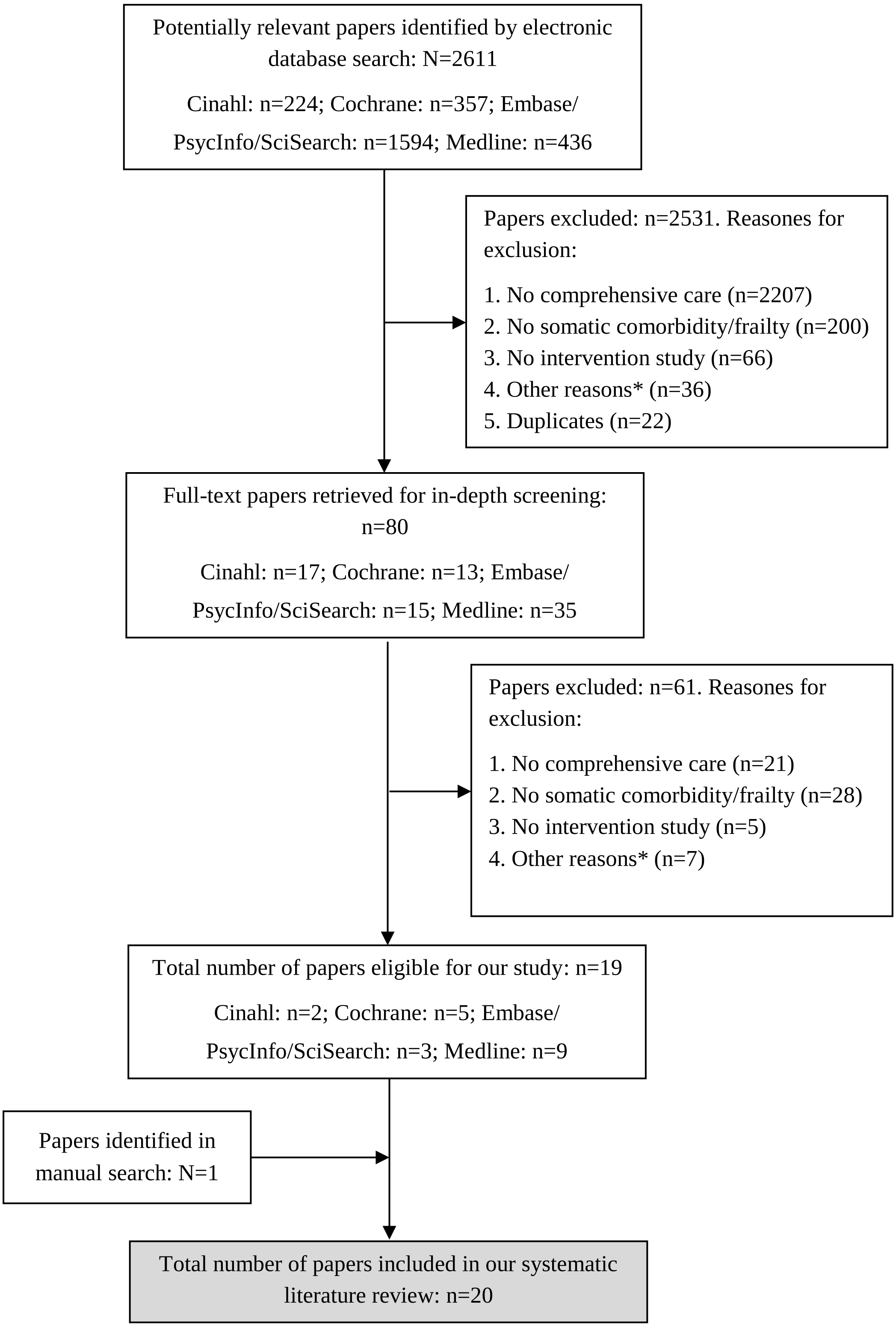
Ofman JJ, Badamgarav E, Henning JM, Knight K, Gano Jr AD, Levan RK, et al. Does disease management improve clinical and economic outcomes in patients with chronic diseases? A systematic review. American Journal of Medicine 2004;117:182–92.

Singh D. How can chronic disease management programmes operate across care settings and providers? Birmingham: World Health Organization; 2008.

Weingarten SR, Henning JM, Badamgarav E, Knight K, Hasselblad V, Gano Jr A, et al. Interventions used in disease management programmes for patients with chronic illness-which ones work? Meta-analysis of published reports. British Medical Journal 2002;325:925.

Goetzel RZ, Ozminkowski RJ, Villagra VG, Duffy J. Return on investment in disease management: a review. Health Care Financing Review 2005;26:1–19.

Figure 1: Flows diagram of literature screening process



* e.g. papers were not written in English, papers could not be retrieved, identified documents were non-scientific papers, papers described the design of an intervention study only.

Table 1: Characteristics and results of studies evaluating the impact of comprehensive care programs for frail and/or multimorbid patients

Study #1	*Author(s):* Berry et al. (2013)
	Study design (N): Cohort study (pretest-posttest; *N*=373)
	Follow-up: 24 months (2009-2011)
	Setting: Gundersen Health, an independent, integrated health system operating a 325-bed hospital, a level II trauma center, and 35 outpatient clinics in 19 counties in a 150-mile radius in three states (USA).
	Target population: The most complex (1-2% of) patients due to multiple diseases, use of multiple health care professionals, medication management issues, multiple inpatient admissions, multiple urgent care/emergency department visits, lack of social support, financial limitations, and cognitive deficits.
	Control condition: N.A.
Intervention / comprehensive care program:	*CR:* Social workers partner with the care coordination nurses when patients have nonmedical needs that undermine their health goals and may require community resources that they can help the patient obtain. Social workers or care coordinators may also play a 'mediator' role - for example, when family members disagree on a patient's care plan.
	SMS: Acting as a partner and advocate, the care coordinator helps the patient understand his or her medical conditions, counsels the patient on whether symptoms require immediate attention, shows patients how to follow a clinician's instructions

Co-funded by
the Health Programme
of the European Union

	(including medication use), and teaches family members about home care.
	DSD: Gundersen’s care coordination program spans the continuum of inpatient and outpatient settings. Nurse and social worker teams proactively collaborate with multiple practitioners to provide care to the most complex patients. The care coordinators work holistically with patients for months or years. The care coordinators are often the first to identify subtle changes in a patient’s condition. They alert clinicians to changes, brief emergency department physicians, and monitor transitions (eg, from hospital to short-term nursing home stay).
	CIS: Patients’ EMRs are tagged so that the coordinator is alerted to scheduled and unscheduled interventions. The scheduling tool in the EMR allows care coordinators to simultaneously view their patients’ clinic appointments, hospital admissions, and urgent care and emergency department visits in one place. The EMR is also formatted to enable a patient’s various health care practitioners to view the care coordinator’s notes in a single tab, thereby aiding the practitioners in comprehending the patient’s “whole” story efficiently.
Results:	*Patients:* In an internal survey of **patient satisfaction** (not specified in article) conducted during a 15-month period from 2005 to 2006, care coordination patients consistently indicated high satisfaction with their ability to better manage their own health care, improvement in the quality of their lives, and having their health care needs met.
	Professional caregivers: A 2012 Gundersen survey asked physicians whether care coordination **saved them time** and, if so, to

	estimate how many minutes were saved per patient per month. In all, 138 physicians (nearly 40% of respondents) indicated that care coordination saved them at least 30 minutes per patient per month -- the highest estimated time-saving option listed in the survey.
	Healthcare utilization and healthcare costs: The **mean length of a hospital stay** decreased by 39% at 12 months post-enrollment and by 46% at 24 months post-enrollment. **Unplanned charges** (from the emergency department and inpatient hospitalizations; $13,893,894 at 12 months pre-enrollment) decreased by 51% (to $6,751,079) at 12 months post-enrollment and by a cumulative 64% (to $4,959,045) at 24 months post-enrollment. **Total charges** ($24,400,637 at 12 months pre-enrollment) decreased by 39% (to $14,959,923) at 12 months post-enrollment and by a cumulative 60% (to $9,658,234) at 24 months post-enrollment.
Study #2	*Author(s):* Boult et al. (2011)
	Study design (N): cRCT (*N*=850; CC=446, UC=404)
	Follow-up: 20 months (2006-2008)
	Setting: Three health care systems in Baltimore (Maryland-Washington DC, USA).
	Target population: Older adults (≥65 years) at high risk of using health services heavily.
	Control condition: Patients in the usual care group continued to receive care from their established primary care physicians.

Intervention / comprehensive care program:	Guided care was provided by a team that includes a specially trained registered nurse, two to five physicians, and members of a primary care office staff. This team provided the following eight clinical services:
	CR: Facilitation of access to appropriate community resources (1).
	SMS: Creation of an evidence-based care guide and a patient-friendly version called an action plan (2), use of motivational interviewing to promote patient self-management (3), education and support of family caregivers (4).
	DSD: Guided care was provided by a team that includes a specially trained registered nurse, two to five physicians, and members of a primary care office staff. Monitoring of the patient on a monthly basis (5), smoothing the patient's transitions among sites of care (6), and coordination of the efforts of all the patient's providers of care (7).
	DS: Performing a comprehensive assessment at home (8).
Results:	*Healthcare utilization and healthcare costs:* No differences in the **use of health care services** were found between guided care and usual care patients, except for the 29.7% reduction in the **use of home health care** by guided care patients (OR, 0.70; 95% CI,0.53-0.93). In the highest-risk (of using health care services in the future) subgroup, there were no statistically significant differences between the study groups' use of health services.
Study #3	*Author(s):* Cameron et al. (2013)
	Study design (N): RCT (*N*=216; CC=107, UC=109)

	Follow-up: 3 and 12 months (2011)
	Setting: Division of Rehabilitation and Aged Care Services (DRACS) at Hornsby Ku-ring-gai Health Service (Sydney, Australia). DRACS is a large clinical service that has programs operating both in the community and hospital settings.
	Target population: Older people (≥70 years) with three or more of the CHS frailty criteria, not usually living in a residential aged care facility, without moderate or severe cognitive impairment or an illness likely to be associated with a life expectancy of <12 months.
	Control condition: Usual care, as received by the control group, consisted of those health and aged care services that would normally be available to older people (i.e. general practitioner and medical specialist consultations, and nursing and allied health interventions as appropriate).
Intervention / comprehensive care program:	*CR:* Where the participant was socially isolated, options to encourage greater social engagement were identified, such as participation in day activity groups and telephone contact with a volunteer.
	DSD: Case management by the physiotherapist, and regular case conferences involving the physiotherapist, geriatrician, rehabilitation physician, nurse and dietician, facilitated coordination of the delivery of the intervention. For all participants, additional interventions were provided or recommended based on a comprehensive geriatric evaluation, for example review by the study geriatrician or rehabilitation physician, follow-up of chronic diseases, treatment of pain, and management of other

	identified conditions such as urinary incontinence.
	DS: The CHS frailty components that were present in each participant were specifically targeted. If the participant met the weight loss criterion, a dietician evaluated nutritional intake. Home-delivered meals were recommended if appropriate clinical criteria applied. In addition, if the participant’s body mass index was <18.5 kg/m2, or mid-upper arm circumference was <the 10th percentile (using Australian age and gender specific norms), nutritional supplementation was offered using commercially available, high energy, high protein supplements. If the exhaustion criterion was met and the Geriatric Depression Scale score was high, the study team considered referral to a psychiatrist or psychologist. Participants who met the weakness, slowness or low energy expenditure criteria received up to 10 home-based physiotherapy sessions and performed a home exercise program, over the course of 12 months.
Results:	*Patients:* There was a lower **prevalence of frailty** and a lower **number of frailty criteria** in the intervention group compared with the control group at 12 months. **Mobility** remained relatively stable in the intervention group, whereas it declined substantially in the control group. There were no major differences between the groups with respect to **depressive symptoms** and **health related quality of life**.
	Healthcare utilization and healthcare costs: There were no major differences between the groups with respect to **number of deaths**, **hospital admissions**, **permanent admissions to nursing care facilities**, and **time to admission**).

Study #4	*Author(s):* Davis et al. (2013)
	Study design (N): Cohort study (pretest-posttest; *N*=47)
	Follow-up: N.R.
	Setting: General Medicine Clinic (GMC) at San Francisco General Hospital (USA).
	Target population: Frequently admitted patients in a safety net primary care clinic.
	Control condition: N.A.
Intervention / comprehensive care program:	GMC Complex Care Management Program:
	SMS: The health coach proactively coaches patients toward care plan goals.
	DSD: The GMC Complex Care Management Program is an interdisciplinary team embedded in San Francisco General Hospital (GMC). The nurse and health coach have frequent contact with primary care providers and round weekly with the program physician, social worker, and coordinator. Patients have direct phone access to the team. A patient advisory board provides input on program design and services.
Results:	*Healthcare utilization and healthcare costs:* Preliminary data show a reduction in **hospital days** by 35% and **ED visits** by 55% as compared to the year prior to enrollment.
Study #5	*Author(s):* Dorman-Marek et al. (2013)

	Study design (N): RCT (*N*=414; CC1 [MD.2 medication-dispensing machine]=152, CC2 [medplanner]=137, UC=125)
	Follow-up: 12 months (2006-2010)
	Setting: Three Medicare-certified home healthcare agencies in Milwaukee County, Wisconsin, USA).
	Target population: Frail* older adults having difficulty in self-managing medications. **Inclusion criteria: (a) age of 60 years or older, (b) Medicare primary payer, (c) impaired ability to manage medications and/or impaired cognitive functioning but able to follow directions with prompting. Exclusion criteria: (a) terminal diagnosis or hospice care that would make attrition likely and (b) use of other device for medications (such as pager as a prompt).*
	Control condition: The control group received no intervention beyond the baseline pharmacy screen.
Intervention / comprehensive care program:	*SMS:* Nurse care coordinators provided education and tools for the participants to manage their chronic conditions. Self-regulation was enhanced through the use of the MD.2 machine or medplanner that provided prompts for medication administration as well as feedback on missed doses. Nurse care coordination enhanced participants' ability to communicate with multiple physicians, pharmacies, social service agencies, and other individuals or organizations involved in the their healthcare.
	DSD: After obtaining written consent, a pharmacist and an advanced practice nurse reviewed all medications identified by the participant with corresponding medical diagnoses. They used the program FirstDataBank to identify drug interactions, and

	Beers criteria for inappropriate medication use in the older adults. A team of nurse providers delivered nurse care coordination to both intervention groups. The advanced practice nurse reviewed initial care plans and documentation for each visit and made monthly or as-needed supervisory visits to observe implementation of the research intervention and educate research staff.
	DS: Individual and family self-management theory (IFSMT; Ryan & Sawin, 2009) guided this study.
	CIS: The CareFacts (2012) computer system, designed for documentation against participant-specific intervention protocols, was used for clinical documentation.
Results:	*Patients:* Participants who received nurse care coordination and the medplanner had significantly better clinical outcomes (i.e. **depression**, **physical performance**, **cognition**, **physical and mental quality of life**) than the control group, but the addition of the MD.2 to nurse care coordination did not result in better clinical outcomes.
Study #6	*Author(s):* Fleming & Haney (2013)
	Study design (N): Cohort study (posttest only; *N*≈1682[*]). [*]*Calculated by subtracting the 12-month sum of readmissions (N=225) from the 12-month sum of referrals (N=1907).*
	Follow-up: 12 months (2011-2012)
	Setting: Amedisys, a home health and hospice organization (USA).

	Target population: Older/frail* patients who were discharged from the hospital (to their home). **Not specified*
	Control condition: N.A.
Intervention / comprehensive care program:	*SMS:* Coaching focuses on the patient's diagnoses and capabilities, with discussion of diet and lifestyle needs and identification of 'red flags' about each condition. The CTC asks the patient to describe his or her treatment goals and care plan. Ideally, the patient or a family member puts the goals and care plan in writing in a notebook in the patient's own words; this strategy makes the goals and plan more meaningful and relevant to the patient. The diagnoses are also written in the notebook along with a list of the patient's medications that describes what each drug is for, its exact dosage, and instructions for taking it. The CTC revisits this information at each encounter with the patient and caregiver. At the time of hospital discharge, the CTC arranges the patient's appointment with the primary care physician and records this in the patient's notebook. The date and time for the patient's first home nursing visit is also arranged and recorded so that the patient and caregiver know exactly when to expect that visit.
	DSD: The care transitions coordinator (CTC; a registered nurse) meets with the patient and physician(s) as soon as possible upon his or her referral to home care to plan the transition home from the facility and determine the resources needed once home. The CTC becomes the patient's 'touchpoint' for any questions or problems that arise between the time of discharge and

Co-funded by
the Health Programme
of the European Union

	the time when an home health nurse visits the patient’s home. The CTC communicates the patient's clinical needs and personal goals to the home care nurse.
Results:	*Patients:* The 12-month average **hospital readmission rate** (as calculated month by month) in the last 6 months of the study decreased from 17% to 12%. During this period patient **satisfaction** was enhanced, according to internal survey data (no data reported).
	Professional caregivers: During this period physician **satisfaction** was enhanced, according to internal survey data (no data reported).
Study #7	*Author(s):* Gharacholou et al. (2012)
	Study design (N): RCT (*N*=309; CC=155, UC=154)
	Follow-up: 12 months
	Setting: This study was a secondary analysis of 309 inpatients from a Veterans Administration (VA) Cooperative study (1995-1999; USA). The parent trial was a VA multicenter 2x2 factorial study, randomizing 1388 participants to inpatient Geriatric Evaluation and Management (GEM) or an inpatient usual care (UC), and, upon hospital discharge, to either geriatric outpatient clinic or usual outpatient care. The 11 centers that participated in the study were chosen from Veterans Affairs medical centers with established inpatient and outpatient programs of geriatric evaluation and management.

	Target population: Age ≥65 years, previously diagnosed with heart failure, and hospitalized on a medical or surgical ward with an expected length of stay ≥2 days.
	Control condition: Inpatients randomized to UC received all standard diagnostic studies and treatment approaches as appropriate for the medical condition that prompted hospitalization. However, the distinguishing feature between UC and GEM was the absence of the multi-disciplinary approach for geriatric evaluation and management to patients in the UC group.
Intervention / comprehensive care program:	*CR:* The patient's social situation was assessed in order to identify social support and community resources.
	DSD: The geriatric intervention consisted of core multidisciplinary teams providing GEM. The inpatient and outpatient team members included a geriatrician, a nurse, and a social worker, who followed standard protocols for GEM. Specific instructions included obtaining a history and performing a physical examination; screening for geriatric syndromes; assessing functional, cognitive, affective, and nutritional status; evaluating the primary caregiver's capabilities; and assessing the patient's social situation. After formulation of the treatment plan, the multidisciplinary team would meet at least twice a week to review the plan.
	DS: GEM was provided according to VA standards and consistent with care guidelines.
Results:	*Patients:* GEM patients had higher mean change scores for **physical functioning** and **basic activities of daily living** at hospital discharge, which remained significant after adjusting for baseline health-related quality of life (HRQOL) scores and in-

	hospital days. Outcomes were not significantly different at 1 year. No differences were found between the GEM and AC groups regarding **bodily pain**, **vitality**, **physical role**, **general health**, **social functioning**, **emotional role**, and **mental health**.
	Healthcare utilization and healthcare costs: **Length of stay** for GEM was greater than usual care. **Total costs** at 1 year were not different (*p* = 0.9). **Mortality rates** at 1 year were high and similar in both the groups.
Study #8	*Author(s):* Hébert et al. (2010)
	Study design (N): Quasi-experimental pretest-posttest matched comparison study (*N*=1501; CC=728, UC=773)
	Follow-up: 48 months (2001-2005)
	Setting: Primary, secondary, home health and community care in three areas of the Eastern Townships region in the Province of Québec, Canada.
	Target population: Older people (≥75 years) were randomly selected from the Québec Medicare list to receive the 6-item Sherbrooke Postal Questionnaire (SPQ), a tool screening individuals at risks of functional decline. Those screening positive were invited to participate.
	Control condition: N.R.
Intervention / comprehensive	Program of Research to Integrate Services for the Maintenance of Autonomy (PRISMA) model:
	HS: Coordination was established at the strategic level (governance), by creating a Joint Governing Board (JGB) of all health

care program:	care and social services organizations and community agencies (public, private, and voluntary). On this board, the decision makers agree on policies and orientations and what resources to allocate to the integrated system.
	CR: At the tactical level (management), a service coordination committee, mandated by the JGB and comprising public and *community service representatives* together with older people, monitored the service coordination mechanism and facilitated adaptation of the service continuum.
	DSD: A case manager (CM) was responsible for conducting a thorough assessment of the patient's needs, planning the required services, arranging patient admission to these services, organizing and coordinating support, directing the multidisciplinary team of practitioners involved in the case, and advocating, monitoring, and reassessing the patient as frequently as necessary according to the needs (minimally twice a year). The CM worked for the Local JGB and was legitimate for work in all institutions and services of the area. The CM could be a nurse, a social worker, or another health professional and was specifically trained. The CM worked closely with the Primary Care Physician (PCP), and the relationship between the CM and PCP had been evaluated as part of the implementation study.
	DS: Callers to a 'single entry point' portal were screened using a brief 7-item questionnaire that evidences good levels of sensitivity and specificity in identifying significantly disabled older people. A detailed assessment of disabilities was then undertaken for those screened positive; individuals deemed eligible for ISD are then referred to a case manager. Furthermore,

	a single assessment instrument (SMAF, a 29-item scale developed according to the World Health Organization classification of disabilities) allowed for evaluating the needs of clients in all organizations and by all the professionals working either in home care organizations or in hospitals and institutions.
	CIS: The PRISMA model includes a computerized clinical chart to facilitate communication between organizations and professionals.
Results:	*Patients:* Over the last 2 years (when the implementation rate was over 70%), there were fewer cases of **functional decline** in the experimental group. In the fourth year of the study, the annual incidence of functional decline was lower in the experimental group, whereas the **prevalence of unmet needs** in the comparison region was nearly double the prevalence observed in the experimental region. **Satisfaction** and **empowerment** were significantly higher in the experimental group.
	Professional caregivers: There was a significant increase in **caregiver's burden** in the experimental group (26%, $p<0.001$), whereas the increase was near significant in the comparison group (7.7%, $p=0.098$). The difference of pattern in the two groups was significant ($p=0.013$).
	Healthcare utilization and healthcare costs: For health services utilization, a lower **number of visits to emergency rooms** and **hospitalizations** than expected was observed in the experimental cohort.
Study #9	*Author(s):* Kono et al. (2012)

	Study design (N): RCT (*N*=323; CC=161, UC=162)
	Follow-up: 24 months (2008-2010)
	Setting: Preventive care in three suburban municipalities of Izumiotsu, Sennan, and Misaki, in Osaka, Japan.
	Target population: Ambulatory frail elders (≥65 years) who have been certified for care in the two lowest LTCI* care levels, but who are not yet utilizing any long-term care services. **In the Japanese Long-Term Care Insurance (LTCI) system, all people aged 65 years or older could be certified as Support Level 1 or 2 if they need any support for living at home or Care Level 1, 2, 3,4, or 5, if they need continuous care at homes or care facilities. Elders certified as 'Support Level 1' are the mildest frail and those as 'Care Level 5' are the most severe frail.*
	Control condition: N.R.
Intervention / comprehensive care program:	*CR:* Provide information regarding social or healthcare resources, consult social welfare professionals, coordination of social welfare financial services, apply for recertification to local government department, introduce to public guardianship services for protecting elderly rights.
	DSD: Routine preventive home visits are performed every six months for two years by community care nurses, care managers, or social workers. Principally, home visitors assess comprehensive care needs based on structured assessments, list health and social problems or difficulties, and provide subsequent specific recommendations for each individual elder in the intervention

	group. Comprehensive care needs for elders are categorized into five levels: ‘self-care only’, ‘needs attention from non-professional community members’, ‘needs attention from community care professionals’, ‘needs care management or community-based care services’, ‘needs urgent care’.
	DS: Assessment elements of locomotion, daily activities, social contacts or relationships with other people, and health conditions are suggested by the principles of the Ministry of Health, Labor and Welfare for care management targeted to elders in Support Levels 1 or 2.
Results:	*Patients:* Significant differences in the **living state** were not found. Significant changes over the study period regarding **activities of daily living (ADL)**, **depression**, and **social support** were not found between the groups. In *participants with ADL dependency at baseline* (n=205), **activities of daily living** and **depression** deteriorated significantly more in the control group than in the intervention group (2 year follow-up).
	Healthcare utilization and healthcare costs: Total long-term care services **costs** over 2 years in the intervention group (36,001 credits = around\378,010) were higher than in the control group (26,022 credits = around\273,231) (nonsignificant).
Study #10	*Author(s):* Lee et al. (2011)
	Study design (N): Prospective cohort study (*N*= 251)
	Follow-up: 4-12 weeks (2006-2008)

	Setting: Community hospital (post-acute care) in Yi-Lan County, Taiwan.
	Target population: Frail older patients[*] admitted to a community hospital with acute or post-acute conditions. [*] *Inclusion criteria: (1) >65 years; (2) medically stable, requiring no intensive medical, laboratory, or oxygen support; and (3) presence of acute functional decline during hospitalizations. Exclusion criteria: (1) admission for elective procedures, (2) acute conditions related to terminal illness, (3) malignancy, and (4) patients who were considered to have a low potential for functional recovery.*
	Control condition: N.A.
Intervention / comprehensive care program:	*DSD:* Once patients were admitted to the PAC unit, the case manager, a senior nurse, completed comprehensive geriatric assessment within 72 hours, and the interdisciplinary team took charge of further treatment.
Results:	*Patients:* Improvement was significant in various dimensions, including **cognition**, **physical function**, **depression**, **ambulation**, **nutrition**, and **pain**.
Study #11	*Author(s):* Levine et al. (2012)
	Study design (N): RCT (*N*=298; CC=156, UC=142)
	Follow-up: 12 months (2008-2009)

Co-funded by
the Health Programme
of the European Union

	Setting: The home care intervention study was conducted within a management services organization that manages and operates medical groups and independent physician networks nationally. The study was conducted among three Los Angeles County regions (USA) of the management services organization.
	Target population: Frail older adults* with multiple chronic conditions at high risk for use of medical services **An assessment tool identified frail older adults at high risk for use of medical services by using an algorithm that considered variables such as age, sex, number of medications, number and types of chronic conditions, and use of EDs and inpatient hospital services.*
	Control condition: Patients assigned to the usual care group received the standard care for which they were eligible, provided by their medical group. That included the usual primary care, home healthcare, hospice, ED, and hospital care.
Intervention / comprehensive care program:	The Choices for Healthy Aging (CHA) program:
	CR: A physician with a nurse care manager, medical assistant, and social worker acted as personal care advocates of the patients, facilitating coordination of appointments with specialists and other service providers.
	SMS: Goals of the CHA program included patient-specific health education and self-management or caregiver management of the disease.
	DSD: Within 5 days of a patient consenting to the program, an initial home visit was made by a home care physician, nurse care

	manager, and social worker. The physician conducted an initial medical assessment, a medication review and provided acute treatment needed for stabilization and palliation. The nurse followed with patient and family education, advance care planning, assessment of medications management need, and treatment adherence of patients. The social worker conducted a biopsychosocial evaluation, including an assessment of the patient's living condition, level of caregiver support, and mental status. Follow-up visits were conducted at least once a month. The clinical team conducted weekly meetings to ensure continuity of care and coordinated treatment plans. The home care physician was available to visit 24 hours a day, 7 days a week, and also made regularly scheduled home visits as medically appropriate. Patients and caregivers were provided with the physician's cell phone number.
	DS: The CHA program was adapted from an evidence-based home-based palliative care program found to be effective in improving patient satisfaction, decreasing deaths in the hospital, and reducing cost of care among patients in the last year or two of life.
	CIS: The medical team collected data in an electronic database. Also, an assessment tool was initially used to identify frail older adults at high risk for use of medical services by using an algorithm that considered variables such as age, sex, number of medications, number and types of chronic conditions, and use of EDs and inpatient hospital services
Results:	*Patients:* The intervention group reported significantly higher mean **satisfaction with care** than the usual care group.

	Healthcare utilization and healthcare costs: CHA patients were less likely than usual care patients to be **admitted to the hospital**. There were no differences in terms of **costs of care** between the home care and usual care groups.
Study #12	*Author(s):* Metzelthin et al. (2013)
	Study design (N): cRCT (*N*= 346; CC=193, UC=153)
	Follow-up: 6, 12, and 24 months (2009-2011)
	Setting: Twelve general practices in the south of the Netherlands.
	Target population: Community dwelling frail (score ≥5 on Groningen Frailty Indicator) older (≥ 75 years) people. Excluded were those who were terminally ill or confined to bed, had severe cognitive or psychological impairments, or were unable to communicate in Dutch.
	Control condition: N.R.
Intervention / comprehensive care program:	The 'Prevention of Care' (PoC) approach:
	SMS: The PoC approach stimulates self-management skills and encourages active involvement in decision making.
	DSD: After the postal screening for frailty using the Groningen Frailty Indicator (step 1), frail older people and their informal caregiver, if available, receive a home visit by the practice nurse who does a multidimensional assessment focusing on existing problems in daily activities and on risk factors for disability (step 2). On the basis of the assessment phase, a preliminary

	treatment plan is formulated (step 3) by the general practitioner, the practice nurse and, eventually, occupational and physical therapist, and, if necessary, other healthcare professionals. During a second home visit by the practice nurse (step 4), a final treatment plan is formulated, including a list of goals, strategies, and actions that meet the older person's needs. Subsequently, the treatment starts (step 5).
	DS: The intervention protocol offers recommendations and guidelines for the execution of the treatment plan. The practice nurse is also the case manager and, along with the frail older person and the informal caregiver, regularly evaluates the achievement of goals, the implementation of strategies in daily life, and the need for support in the following period (step 6).
Results:	*Patients:* Mixed model multilevel analyses showed no significant differences between the two groups with regard to **disability** (primary outcome) and secondary outcomes (i.e. **social participation**, **social support**, **depression**, and **fear of falling**). Subgroup analyses confirmed these results.
Study #13	*Author(s):* Rosenberg (2012)
	Study design (N): Prospective cohort study (*N*= 248)
	Follow-up: 12 months (2009-2011)
	Setting: Primary/community care in Victoria, British Columbia (Canada).
	Target population: Frail elderly adults (not specified) who were living in the community and not in nursing homes.

	Control condition: N.A.
Intervention / comprehensive care program:	Primary Interdisciplinary Elder Care at Home (PIECH):
	CR: Team members recommended home support services. Patients purchased these services from private agencies unrelated to the PIECH service, or the regional health authority provided them after referral to a community case-manager.
	DSD: All individuals received a comprehensive geriatric assessment from the primary care physician and nurse when enrolled that included a medical history and examination, functional review, standardized scales, and comprehensive laboratory testing. Healthcare directives were discussed and documented with most individuals. The regional laboratory performed laboratory monitoring, including electrocardiograms, in the home for people who were unable to get out. On average, a nurse saw stable individuals routinely in their homes monthly to monitor their health status and medication administration, and the physician saw them every 2 to 3 months. Community care nurses from the regional long-term care program provides long-term procedural services (e.g., skin ulcer treatment). The physician referred individuals to the physical therapist (PT) on as-needed basis. A group of family doctors from local clinics provided after-hours telephone coverage as part of a regional call service.
Results:	*Healthcare utilization and healthcare costs:* For all patients, there was a significant reduction in **hospital admissions** (39.7%) and **hospital days** (37.6%). No significant reduction in **ED contacts** was found. For active patients (i.e. individuals remaining in the practice for the entire period; n=198 [80%]), there was a significant reduction in **hospital admissions** (59.5%) and

	hospital days (61.7%). No significant reduction in **ED contacts** was found. The model did not increase **direct community medical care costs** (no data reported).
Study #14	*Author(s):* Schulz et al. (2011)
	Study design (N): Cohort study (*N*=1073; CC=273, UC=800)
	Follow-up: 12 months (2006-2008)
	Setting: Community care (USA; not specified).
	Target population: Community-dwelling elderly/disabled clients (not specified) in a state Medicaid home and community-based waiver program (for persons eligible for nursing home care), who prefer to receive their services (prescriptions) in the community.
	Control condition: Clients in the control group received standard care (ie, their prescriptions were dispensed in traditional prescription vials, and they did not participate in the coordinating service).
Intervention / comprehensive care program:	*SMS:* A calendar card, in which a client's medicines were dispensed instead of in prescription bottles.
	DSD: A coordinating service that facilitated communication among clients or caregivers, case managers, and providers to address medication adherence and management issues.
Results:	*Healthcare utilization and healthcare costs:* Participants in the control group were 2.94 times more likely to be **admitted to a**

	nursing home compared to participants in the intervention group.
Study #15	*Author(s):* Wade et al. (2011)
	Study design (N): cRCT (*N*=316; CC=164, UC=152)
	Follow-up: 6 months (2008-2009)
	Setting: Specialized care in New Jersey, New York, or Pennsylvania (USA).
	Target population: Elderly (not specified) suffering from heart failure. *Inclusion: medical claims for chronic HF in medical claims in the past 3 years, inpatient admission or ≥2 ED visits for any cause within the 6 months before identification, and high risk for a subsequent admission or ED visit based on the health plan's proprietary predictive model. Exclusion: claims or utilization records indicating a terminal condition, end-stage renal disease, dementia, use of a ventricular assist device, active listing for cardiac transplantation, completed heart transplant, or requirement for chronic or ongoing intravenous HF medication.*
	Control condition: Nurse case management (CM) only: case managers worked closely with the members, physicians, subspecialty providers, and others to facilitate care to manage the complex cardiac, oncologic, psychiatric, social, other medical, and/or end-of-life needs of the participants. They identified needs were addressed on scheduled calls with the member. Common issues covered included health education, safety and emergency measures, medication regimen, and care

	coordination needs.
Intervention / comprehensive care program:	Telehealth system with nurse case management (THCM):
	SMS: Educational content was also available to participants on demand through the HGS.
	DSD: The Intel Health Guide System (HGS)-mediated data flow between the participants and case managers catalyzed frequent case management interactions between the participant, his or her case manager, and the participant's physician.
	DS: Alerts to the case manager occurred when measurements or response violated threshold values set in alignment with the Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure blood pressure guidelines HF management guidelines and the physician's care plan. Case managers modified members' care protocols and thresholds as needed.
	CIS: The telehealth system consisted on a touch screen, a remote patient management unit placed in the member's home, and a case manager user interface accessed via secure Internet link through a broadband connection. The system was also programmed to ask members about their health status, activities, and medication adherence, and to offer and show educational videos. Participants in THCM transmitted their weight and blood pressure as often as every weekday. Periodically, they were asked to input responses about medication adherence, exercise, and any recent ED visits or hospital stays. Case managers were instructed to check the Web-based clinical user interface for alerts on each member's condition and to respond with care

	coordination assistance as needed.
Results:	*Patients:* Change in **health status** scores from the beginning to the end of the study did not differ significantly between the groups.
	Healthcare utilization and healthcare costs: Regarding the main outcomes (i.e. **admission to an acute care hospital**, an **ED visit**, or **death** during the measurement period), no significant differences were found between the THCM and CM groups, whether analyzed as intention-to treat or as-treated. The THCM and CM groups did not differ significantly in measures of **hospital days**, **cardiovascular admissions**, **primary care visits**, and annualized months of **prescriptions** filled for diuretics or angiotensin-converting enzyme inhibitors. **Cardiology visits** and angiotensin receptor antagonist **prescription** purchases were more frequent for THCM than for CM members. Mean acute **hospital days** per member per year dropped 42% from approximately 10 days in the baseline year to 5.41 days during THCM and 6.44 for CM.
Study #16	*Author(s):* Wakefield et al. (2011)
	Study design (N): RCT (*N*=302; CC1 [low intensity]=102, CC2 [high intensity]=93, UC=107)
	Follow-up: 12 months (2005-2007)
	Setting: Primary care at the Iowa City Veterans Affairs (VA) Medical Center, which provides primary, secondary, and tertiary medical, surgical, psychiatric, and neurological care to more than 36,000 veterans residing in eastern Iowa and western Illinois

	(USA).
	Target population: Veterans with comorbid type 2 diabetes and hypertension (HTN) being treated by a VA primary care provider.
	Control condition: Usual care subjects scheduled follow-up appointments with the primary care clinic in the usual manner. These subjects had access to their nurse care manager employed by the medical center.
Intervention / comprehensive care program:	*DSD:* Both intervention groups received care management from a study nurse. Each weekday, the study nurse reviewed responses from intervention group subjects and determined whether the subject needed follow-up (additional health information, increased monitoring, compliance strategies, problem resolution facilitation, or contact with the subject's physician).
	DS: The study team (nurses, a physician, and a certified diabetes educator) developed a branching disease management algorithm based on DM and HTN guidelines from the VA, American Diabetes Association, and the American Heart Association.
	CIS: The intervention combined close surveillance via a home telehealth device and nurse care management over a 6-month time period. Within the intervention group, patients were assigned to high- and low-intensity data transmission levels (varied the amount of monitoring and education content transmitted to patients) to ascertain differences in outcomes over and above

	patient transmission of blood glucose (BG) and blood pressure (BP) measurement to the nurse. Trended data on BP, BG, and responses to prompts were viewed via a secure Web site by the nurse. These data enabled the nurse to efficiently provide close surveillance.
Results:	*Patients:* Intervention subjects experienced decreased **A1c** during the 6-month intervention period compared with the control group, but 6 months after the intervention was withdrawn, the intervention groups were comparable with the control group. For **systolic blood pressure (SBP)**, the high-intensity subjects had a significant decrease in SBP compared with the other groups at 6 months and this pattern was maintained at 12 months. **Adherence** improved over time for all groups, but there were no differences among the three groups.
Study #17	*Author(s):* Wald et al. (2011)
	Study design (N): qRCT (*N*=217; CC=122, UC=95)
	Follow-up: Discharge and 30 days (readmission rate; 2007-2008)
	Setting: Inpatient general medical services of the Anschutz Inpatient Pavilion (AIP) of the University of Colorado Hospital (UCH), USA.
	Target population: Medical inpatients age ≥70 years.
	Control condition: Usual care consisted of either a hospitalist, a general internist, or an internal medicine subspecialist attending

	physician, with one medical resident, one intern, and medical students admitting every fourth day. The general medical teams attended daily discharge planning rounds with a discharge planner and social worker focused exclusively on discharge planning. The content of teaching rounds on the general medical services was largely left to the discretion of the attending physician.
Intervention / comprehensive care program:	Hospitalist-run Acute Care for the Elderly (Hospitalist-ACE):
	DSD: The Hospitalist-ACE unit implemented an interdisciplinary team approach. The Hospitalist- ACE model of care consisted of clinical care provided by a hospitalist attending with additional training in geriatric medicine, administration of standardized geriatric screens assessing function, cognition, and mood, 15 minute daily interdisciplinary rounds focusing on recognition and management of geriatric syndromes and early discharge planning, and a standardized educational curriculum for medical residents and medical students addressing hazards of hospitalization. Interdisciplinary rounds were attended by Hospitalist-ACE physicians, nurses, case managers, social workers, physical or occupational therapists, pharmacists, and volunteers. Rounds were led by the attending or medical resident.
Results:	*Professional caregivers*: Hospitalist-ACE patients had significantly greater **recognition of abnormal functional status** (65% versus 32%, *p*< 0.0001), **recognition of abnormal cognitive status** (57% versus 36%, *p*=0.02), and greater **use of 'Do Not Attempt Resuscitation' (DNAR) orders** (39% versus 26%, *p*=0.04). No differences were found regarding the **use of physical**

	restraints, and **sleep aids.**
	Healthcare utilization and healthcare costs: No differences were found between intervention and control group regarding **falls**, **discharge location**, **length of stay**, **mean charges** ($24,617 ± $15,828 versus $21,488 ± $13,407, *p*=0.12), or **30-day readmission rates**.
Study #18	*Author(s):* Watkins et al. (2012)
	Study design (N): Cohort study (*N*=292)
	Follow-up: 30-120 days (2009-2011)
	Setting: Home environment, post-discharge from a non-trauma hospital in southeastern USA.
	Target population: Older patients (≥65 years) discharged from acute hospital or inpatient rehabilitation facility, at risk for hospital readmission (i.e. meeting ≥2 of 11 risk factors: [1] ≥2 documented chronic conditions, [2] physical disability or functional decline requiring assistance with activities of daily living, [3] history of falling in the past year requiring medical evaluation or treatment, [4] >8 medications at admission or discharge, [5] cognitive decline or depression, [6] >3 physician visits in the past 6 months, [7] ≥3 ED visits in the past 6 months, [8] ≥3 hospitalizations in the past year, [9] nutritional impairment, [10] history of hospitalization for hip fracture in the past year, or [11] limited social support.
	Control condition: N.A.

Intervention / comprehensive care program:	The Hospital to Home program:
	CR: In addition to the social work navigator, the Hospital to Home program contracted with a state-licensed home care agency to provide immediate home care services at discharge. These services may have included transportation home from the hospital and to doctor appointments as well as light housekeeping, laundry, meal preparation, prescription pickup, and grocery shopping.
	DSD: The navigator recommended in-home services at discharge. Within the first 72 hours, the navigator made a home visit to review the discharge orders and medications, confirm that services arranged prior to discharge were implemented, evaluate the home environment, help the patient and family identify other needs, and provide community resource referrals to meet those needs. Follow-up phone calls and other home visits are made by the navigator during the participant's enrollment.
	DS: The SF-36 was administered at the initial visit.
Results:	*Patients:* **Quality of life** significantly increased in all dimensions. Almost all (99%) participants were **satisfied** with the program.
	Healthcare utilization and healthcare costs: **Hospital readmissions** decreased by 61%. **Cost savings** by preventing readmissions correlated to a cost savings of $628,202 per year. No comparative data on reduction of **post-discharge ED visits** is provided.

Co-funded by
the Health Programme
of the European Union

Study #19	*Author(s):* Weber et al. (2012)
	Study design (N): RCT (*N*=139; CC=70, UC=69)
	Follow-up: 12 months (2005-2006)
	Setting: St. Paul’s Hospital in Vancouver, British Columbia, Canada.
	Target population: Kidney disease patients[*] with diabetes (DM) and/or cardiovascular disease (CVD). [*] *Included were patients attending the kidney care clinic (KCC) and also attending either a heart failure and/or diabetes clinic within or outside St Paul’s Hospital.*
	Control condition: Continued attendance at each separate multidisciplinary clinic (including the KCC) and received blood work, investigations and follow-up as per usual clinical practice of these areas.
Intervention / comprehensive care program:	*DSD:* Patients attended one integrated multidisciplinary clinic and were seen by the diabetes, cardiac or renal nurse, a dietician and pharmacist as well as by a nephrologist, cardiologist and/or endocrinologist at each clinic visit. Patients were discussed by all physicians and team members at the conclusion of the clinic visit, and a single letter describing follow-up for each condition was sent to the GP and all attending physicians.
	DS: Physician visits were determined based on major clinical issues identified. Patients received regular blood work, according to one protocol, based on dominant comorbidity and level of kidney function. Protocols had been vetted and approved by the

	multidisciplinary teams beforehand.
Results:	*Patients:* No difference **experienced symptoms**.
	Healthcare utilization and healthcare costs: No difference **in hospital admissions**, and no differences in clinical parameters (i.e. **number of visits to other specialists**, **the GP**, **and the ED**; **medication use**; **mortality rates**; **percentage of subjects commencing renal replacement therapy**). Differences in the **cost** of clinic visits alone were $86 400 per year in favor of the intervention (combined clinic) arm.

N = total number of patients allocated (to comprehensive or usual care) at study entry; cRCT = cluster-randomized controlled trial; RCT = randomized controlled trial; qRCT = quasi randomized controlled trial; CC = number of people receiving comprehensive care; US = number of people receiving usual care.

Six components of Wagner’s chronic care model: HS = health system; CR = community resources; SMS = self management support; DSD = delivery system design; DS = decision support; CIS = clinical information system.

N.A. = not applicable; N.R. = not reported

Table 2: Results of methodological quality assessment of included studies

Author (year)	Randomization[a]	Similar at baseline[b]	Compliance[c]	Drop-out rate[d]	ITT-analysis[e]	Adjustments for confounding variables in analysis[f]	Total score
Berry et al. (2013)	N.A.	N.A.	?	+	N.A.	N.A.	1
Boult et al. (2011)	+	+	?	+	?	?	3
Cameron et al. (2013)	+	+	+	+	+	+	6
Davis et al. (2013)	N.A.	N.A.	?	-	N.A.	N.A.	0
Dorman-Marek et al. (2013)	+	-	?	+	+	+	4
Fleming & Haney (2013)	N.A.	N.A.	?	N.A.	N.A.	N.A.	0
Gharacholou et al. (2012)	+	+	N.A.	?	?	+	3
Hébert et al. (2010)	N.A.	N.A.	?	-	N.A.	N.A.	0

Co-funded by
the Health Programme
of the European Union

Kono et al. (2012)	+	+	?	+	+	+	5
Lee et al. (2011)	N.A.	N.A.	N.A.	+	N.A.	N.A.	1
Levine et al. (2012)	+	+	?	+	-	+	4
Metzelthin et al. (2013)	+	+	?	+	-	+	4
Rosenberg (2012)	N.A.	N.A.	?	+	N.A.	N.A.	1
Schulz et al. (2011)	N.A.	N.A.	+	-	N.A.	N.A.	1
Wade et al. (2011)	+	+	+	+	+	+	6
Wakefield et al. (2011)	+	+	+	+	-	-	4
Wald et al. (2011)	+	+	N.A.	N.A.	-	-	2
Watkins et al. (2012)	N.A.	N.A.	N.A.	N.A.	N.A.	N.A.	0
Weber et al. (2012)	+	-	+	-	-	+	3

N.A. = not applicable; + = criterion fulfilled; − = criterion not fulfilled; ? = lack of information.

[a] Was the method of randomization adequate?

[b] Were the groups similar at baseline regarding the most important prognostic indicators?

[c] Was the compliance of patients acceptable in all groups (20% cut-off point)?

[d] Was the drop-out rate described and acceptable (40% cut-off point)?

[e] Did the analysis include an intention-to-treat analysis?

[f] Are adjustments made for confounding variables and/or differences in prognostic indicators at baseline?

*Table 3a: Patient related outcomes of studies evaluating impact of comprehensive care programs for multimorbid patients**

Study	Study design (*N*)[a]	Measuring instrument[b]	Comprehensive care group[c]		Usual care group		*p*
			Baseline	Follow-up	Baseline	Follow-up	
PHYSICAL HEALTH STATUS/FUNCTIONING							
Activities of daily living							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	ADL	3.2 (2.1)	change: 1.1	3.3 (2.2)	change: 0.8	0.24 (group×time)
Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	ADL	90.2 (11.7)	88.1 (14.7)	91.4 (12.2)	89.0 (18.7)	n.s. (group) n.s. (group×time)
		IADL	7.3 (3.5)	7.0 (3.8)	7.2 (3.7)	7.0 (4.0)	n.s. (group) n.s. (group×time)
Lee et al	Prospective	IADL	2.1 (2.4)	3.1 (2.7)	--	--	<0.001 (time)

(2011)	cohort study (*N*=251)						
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	GARS-ADL	17.97 (6.14)	18.31 (5.82)	16.54 (5.35)	16.73 (5.73)	0.07 (group×time)
		GARS-IADL	15.12 (5.96)	16.08 (6.35)	14.03 (5.86)	14.77 (5.86)	0.41 (group×time)
Ambulation							
Lee et al (2011)	Prospective cohort study (*N*=251)	TUG	19.9 (22.5)	12.9 (21.1)	--	--	<0.001 (time)
Bodily pain							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-Bodily pain	41.3 (28.6)	change: 15.5	44.5 (30.5)	change: 19.0	0.37 (group×time)

Lee et al (2011)	Prospective cohort study (*N*=251)	NRS	2.4 (3.1)	1.5 (2.0)	--	--	<0.001 (time)
Disability							
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	GARS	33.09 (11.52)	34.39 (11.58)	30.58 (10.62)	31.50 (10.92)	0.35 (group×time)
Fear of falling, fall rate							
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	Short FES-I	13.24 (5.39)	13.73 (5.75)	12.38 (4.72)	12.95 (5.29)	0.94 (group×time)
Wald et al. (2011)	RCT (*N*=217; CC=122, UC=95)	Fall rate (*N*/1000 patient days)	--	4.8	--	6.7	n.s. (group)

Co-funded by
the Health Programme
of the European Union

Frailty							
Cameron et al. (2013)	RTC (N=216; CC=107, UC=109)	mean CHS score	3.44 (0.65)	change: 0.80 (1.19)	3.45 (0.67)	change: 0.41 (1.02)	<0.01 (group×time)
		% frail patients (CHS criteria)	N.R.	66 (83%)	N.R.	81 (76%)	0.02 (group×time)
Nutritional status							
Lee et al (2011)	Prospective cohort study (N=251)	MNA	16.0 (3.9)	17.8 (3.5)	--	--	<0.001 (time)
Mortality							
Cameron et al. (2013)	RTC (N=216; CC=107,	Deaths (n)	--	12 (10.0%)	--	10 (8.26%)	0.64 (group)

	UC=109)						
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	Deaths (*n*)	--	29.0%	--	27.3%	0.73 (group)
Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	Deaths (*n*)	--	11 (6.8%)	--	20 (12.4%)	N.R.
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	Deaths (*n*)	--	6 (3.7%)	--	6 (3.9%)	0.96 (group)
Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Deaths (*n*)	--	11 (16%)	--	6 (12%)	n.s. (group)
Physical health status							
Dorman-Marek et al. (2013)	RCT (*N*= 414; CC1 [MD.2]=	SF-36-PCS	*MD.2:* 33.5 (9.48)	*MD.2 vs. planner*	35.7 (10.20)	--	*MD.2 vs. planner* 0.73 (group×time)

	152, CC2 [planner]= 137, UC=125)		*planner:* 34.2 (9.39)	change: 0.095 [-0.450;0.640] *planner vs. control* change: 1.390 [0.816;1.963]			*planner vs. control* <0.0001 (group×time)
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	SF-12-PCS	38.67 (N.R.)	39.19 (N.R.)	39.66 (N.R.)	42.05 (N.R.)	0.01 (group×time)
Watkins et al. (2012)	Cohort study. *N*=292	SF-36-PCS	25.79 (N.R.)	30.89 (N.R.)	--	--	<0.001 (time)
Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Reported symptoms (*n*)	N.R	N.R	N.R	N.R	0.40 (group)
Physical performance/functioning							

Co-funded by
the Health Programme
of the European Union

Cameron et al. (2013)	RTC (*N*=216; CC=107, UC=109)	SPPB	5.21 (1.89)	5.83 (2.82)	5.74 (2.12)	4.69 (2.91)	<0.001 (group×time)
		BI	93.9 (11.1)	89.5 (17.5)	92.5 (14.3)	86.1 (24.7)	0.79 (group×time)
Dorman-Marek et al. (2013)	RCT (*N*= 414; CC1 [MD.2]= 152, CC2 [planner]= 137, UC=125)	PPT	*MD.2:* 14.6 (5.06) *planner:* 14.2 (5.16)	*MD.2 vs. planner* change: 0.118 [-0.111;0.347] *planner vs. control* change: 1.009 [0.768;1.250]	15.8 (6.14)	--	*MD.2 vs. planner* 0.31 (group×time) *planner vs. control* <0.0001 (group×time)
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-Physical functioning	18.9 (21.7)	change: 3.3	24.5 (23.9)	change: -1.5	0.61 (group×time)

Hébert et al. (2010)	Quasi-experimental pretest-posttest matched comparison design (*N*=1501; CC=728, UC=773)	SMAF	17.0	25.9	18.1	26.6	0.68 (group×time)
		AIFD	--	254	--	391	<0.001 (group)
Lee et al (2011)	Prospective cohort study (*N*=251)	BI	47.1 (33.6)	66.2 (32.9)	--	--	<0.001 (time)
Role functioning due to physical state							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155,	SF-36-Physical	11.1 (22.8)	change: 25.0	16.6 (30.9)	change: 23.6	0.77 (group×time)

	UC=154)	role					
Vitality							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-Vitality	30.0 (21.3)	change: -0.4	33.3 (24.2)	change: 0.8	0.69 (group×time)
MENTAL HEALTH STATUS, COGNITIVE AND EMOTIONAL FUNCTIONING							
Cognitive functioning							
Dorman-Marek et al. (2013)	RCT (*N*= 414; CC1 [MD.2]= 152, CC2 [planner]= 137, UC=125)	MMSE	*MD.2:* 25.5 (3.33) *planner:* 25.0 (3.65)	*MD.2 vs. planner* change: 0.119 [0.005;0.244] *planner vs. control* change: 0.311 [0.180;0.442]	26.3 (3.17)	--	*MD.2 vs. planner* 0.06 (group×time) *planner vs. control* <0.0001 (group×time)

Lee et al (2011)	Prospective cohort study (*N*=251)	MMSE	13.4 (8.1)	15.9 (8.2)	--	--	<0.001
Depressive symptoms							
Cameron et al. (2013)	RTC (*N*=216; CC=107, UC=109)	GDS-SF	4.76 (3.18)	4.62 (3.33)	5.06 (3.19)	4.98 (3.16)	0.59 (group×time)
Dorman-Marek et al. (2013)	RCT (*N*= 414; CC1 [MD.2]= 152, CC2 [planner]= 137, UC=125)	GDS	*MD.2:* 4.4 (3.27) *planner:* 4.2 (3.16)	*MD.2 vs. planner* change: -0.045 [-0.204;0.114] *planner vs. control* change: 0.322 [0.155;0.490]	3.5 (3.16)	--	*MD.2 vs. planner* 0.56 (group×time) *planner vs. control* 0.0002 (group×time)

Co-funded by
the Health Programme
of the European Union

Lee et al (2011)	Prospective cohort study (*N*=251)	GDS-SF	1.2 (2.1)	0.8 (1.3)	--	--	<0.001
Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	GDS	7.1 (4.0)	7.1 (4.0)	7.0 (4.0)	7.2 (3.8)	n.s. (group) n.s. (group×time)
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	HADS-D	6.54 (3.77)	5.97 (4.18)	6.69 (4.35)	6.10 (3.78)	0.87 (group×time)
Mental health status							
Dorman-Marek et al. (2013)	RCT (*N*= 414; CC1 [MD.2]= 152, CC2 [planner]= 137, UC=125)	SF-36-MCS	*MD.2:* 48.3 (12.10) *planner:* 49.7 (12.08)	*MD.2 vs. planner* change: 0.241 [-0.450;0.940] *planner vs.*	54.12 (11.29)	--	*MD.2 vs. planner* 0.50 (group×time): *planner vs. control* <0.0001 (group×time)

				control change: 1.686 [0.949;2.423]			
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-Mental health	28.1 (24.7)	change: 1.0	67.0 (22.7)	change : -1.5	0.41 (group×time)
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	SF-12-MCS	54.60 (N.R.)	54.43 (N.R.)	56.33 (N.R.)	56.55 (N.R.)	0.04 (group×time)
Watkins et al. (2012)	Cohort study. *N*=292	SF-36-MCS	47.17 (N.R.)	52.22 (N.R.)	--	--	0.001 (time)
Role functioning due to emotional state							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155,	SF-36-Emotional	60.5 (44.0)	change: 17.3	64.7 (43.8)	change: 21.4	0.31 (group×time)

	UC=154)	role					
SOCIAL FUNCTIONING, SOCIAL PARTICIPATION, SOCIAL SUPPORT							
Social functioning							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-Social functioning	52.7 (34.3)	change: 13.7	49.8 (32.5)	change: 8.8	0.27 (group×time)
Social participation							
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	MSPP-CP-D	1.63 (1.48)	1.61 (1.33)	1.90 (1.63)	1.94 (1.70)	0.38 (group×time)
		MSPP-CP-F	0.36 (0.35)	0.33 (0.31)	0.46 (0.44)	0.44 (0.45)	0.32 (group×time)
		MSPP-FSP-D	0.61 (0.84)	0.58 (0.77)	0.73 (0.88)	0.71 (0.87)	0.57 (group×time)
		MSPP-FSP-F	0.38 (0.56)	0.34 (0.51)	0.45 (0.63)	0.45 (0.64)	0.31 (group×time)
Social support							

Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	SSS	6.8 (4.2)	7.1 (4.1)	6.6 (4.6)	7.3 (4.5)	n.s. (group) n.s. (group×time)
Metzelthin et al. (2013)	cRCT (*N*= 346; CC=193, UC=153)	SSL-I12	27.17 (6.30)	26.76 (5.98)	27.46 (6.06)	27.35 (6.27)	0.60 (group×time)
GENERAL HEALTH STATUS, HEALTH RELATED QUALITY OF LIFE							
General health							
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	SF-36-General health	28.0 (31.9)	change: -6.7	28.1 (24.7)	change: -6.4	0.92 (group×time)
Health related quality of life							
Cameron et al. (2013)	RTC (*N*=216; CC=107, UC=109)	EQ-5D VAS	58.2 (15.8)	57.5 (20.8)	57.9 (18.4)	57.7 (19.7)	0.91 (group×time)

Unmet needs							
Hébert et al. (2010)	Quasi-experimental pretest-posttest matched comparison design (*N*=1501; CC=728, UC=773)	Participants with unmet needs (i.e. disabilities not compensated by adequate resources; *n*/1000)	--	353	--	667	<0.001 (group)
PATIENT SATISFACTION, EMPOWERMENT							
Empowerment							
Hébert et al. (2010)	Quasi-experimental	HCEQ	7.78	7.71	8.26	7.29	<.0.01 (group×time)

	pretest-posttest matched comparison design (*N*=1501; CC=728, UC=773)						
Patient satisfaction							
Berry et al. (2013)	Cohort study (pretest-posttest design; *N*=373)	N.R.	--	--	N.R.	N.R.	N.R.
Fleming & Haney (2013)	Cohort study (posttest only; *N*≈1682).	N.R.	--	--	N.R.	N.R.	N.R.
Hébert et al. (2010)	Quasi-experimental	HCSQ	7.50	8.54	7.97	7.73	<.0.001 (group×time)

	pretest-posttest matched comparison design (*N*=1501; CC=728, UC=773)						
Levine et al. (2012)	RCT (*N*=298; CC=156, UC=142)	HCSM	N.R.	N.R. (CC>UC) change: 10.92	N.R.	N.R. (UC<CC) change: 1.93	0.03 (group) <0.005 (group×time)
Watkins et al. (2012)	Cohort study. *N*=292	OSP	--	4.85 (N.R.)	--	--	--
		OSN	--	4.92 (N.R.)	--	--	--
		OCLHA	--	4.83 (N.R.)	--	--	--
		OSCS	--	4.74 (N.R.)	--	--	--
CLINICAL OUTCOMES							
HbA1C/blood glucose							

Wakefield et al. (2011)	RCT (*N*=302; CC1 [low int.]=102, CC2 [high int.]=93, UC=107)	Blood glucose (HbA1C)	CC1: 7.2 CC2: 7.1	CC1 change: -0.17 CC2 change: -0.19	7.2	change: -0.33	0.01 (group: UC) 0.22 (group: CC1) 0.19 (group: CC2) n.s. (group×time FU)
Systolic blood pressure							
Wakefield et al. (2011)	RCT (*N*=302; CC1 [low int.]=102, CC2 [high int.]=93, UC=107)	Systolic blood pressure (SBP)	CC1: 136 CC2: 138	CC1 change: 0.76 CC2 change: -4.92	134	change: 3.34	0.09 (group: UC) 0.73 (group: CC1): 0.73 0.04 (group: CC2) *CC2 vs. UC:* 0.006 (group×time) *CC2 vs. CC1:* 0.08 (group×time)

---

* For these tables we used information that was provided in the original papers. In several papers, however, information was not complete, which explains why baseline, follow-up, and/or p-values are sometimes missing.

[a] RCT = randomized controlled trial; cRCT = cluster-randomized controlled trial; *N* = total number of patients allocated (to comprehensive or usual care) at study entry; CC = comprehensive care; US = usual care.

[b] ADL = activity of daily living; IADL = instrumental activity of daily living; GARS = Groningen Activity Restriction Scale (ADL and IADL = [instrumental] activities of daily living subscale); TUG = timed up-and-go test; SF-12/36 = Short Form Health Survey (12 or 36 items; PCS = Physical Component Summary; MCS = Mental Component Summary); NRS = Numerical Pain Rating Scale; Short FES-I = Short Falls Efficacy Scale - International; CHS = Cardiovascular Health Study; MNA = Mini Nutritional Assessment; SPPB = Short Physical Performance Battery; BI = Barthel-index; PPT = Physical Performance Test; SMAF = Functional Autonomy Measurement System; AIFD = Annual incidence of functional decline (i.e. institutionalization, death or loss of 5 points in SMAF score; n/1000); MMSE = Mini–Mental State Examination; GDS = Geriatric Depression Scale (-SF=short form); HADS = Hospital Anxiety and Depression Scale (-D = depression subscale); MSPP=Maastricht Social Participation Profile (CP-D=consumptive participation, diversity score; CP-F=consumptive participation, frequency score; FSP-D=formal social participation, diversity score; FSP-F=formal social participation, frequency score); SSS = Social Support Scale; SSL-I12 = Social Support List - Interaction version; EQ-5D VAS = EuroQOL five dimensions questionnaire visual analogue scale; HCEQ = Health Care Empowerment Questionnaire; HCSQ = Health Care Satisfaction Questionnaire; HCSM = Home Care Satisfaction Measure; OSP = ‘Overall satisfaction with the program’ (1-5, n=107); OSN = ‘Overall satisfaction with the navigator‘ (1-5, n=107); OCLHA = ‘Overall satisfaction with licensed home care agency‘ (1-5, n=107); OSCS = ‘Overall satisfaction with community services‘ (1-5, n=107).

[c] N.R. = not reported; n.s. = not significant (exact *p*-value not reported)

Co-funded by
the Health Programme
of the European Union

*Table 3b: Health care utilization of studies evaluating impact of comprehensive care programs for multimorbid patients**

Study	Study design (*N*)[a]	Measuring instrument[b]	Comprehensive care group[c]		Usual care group[c]		*p*
			Baseline *N* or %	Follow-up *N* or %	Baseline *N* or %	Follow-up *N* or %	
HOSPITAL CARE UTILIZATION							
Berry et al. (2013)	Cohort study (pretest-posttest design; *N*=373)	Hospital stay (days, *M*)	8.36 days	4.5 days	N.R.	N.R.	N.R.
Boult et al. (2011)	cRCT (*N*=850; CC=446, UC=404)	Hospital admissions (*n*)	--	MAC=0.70	--	MAC=0.72	n.s. (group)
		30-Day readmissions (*n*)	--	MAC=0.13	--	MAC=0.17	n.s. (group)
		Hospital days (*n*)	--	MAC=4.26	--	MAC=4.49	n.s. (group)
		ED visits (*n*)	--	MAC=0.44	--	MAC=0.44	n.s. (group)

Co-funded by
the Health Programme
of the European Union

Cameron et al. (2013)	RTC (*N*=216; CC=107, UC=109)	Hospital admissions (*n*)	--	*n*=74	--	*n*=67	0.32 (group)
		Time to admission	--	haz. ratio= 0.69	--	--	0.27 (group)
Davis et al. (2013)	Cohort study (pretest-posttest design; *N*=47).	Days in the hospital (*n* per year)	24.8	16.0	--	--	N.R.
		ED visits (*n*)	--	-55%	--	--	N.R.
Fleming & Haney (2013)	Cohort study (posttest only; *N*≈1682).	All-cause hospital readmissions	--	12%	--	--	N.R.
Gharacholou et al. (2012)	RTC (*N*=309; CC=155, UC=154)	Length of stay during index hospitalization (days, *n*)	--	24	--	17	0.03 (group)
Hébert et al. (2010)	Quasi-experimental	Participants with ≥1	46%	49%	32%	54%	n.s. (time[CC])

	pretest-posttest matched comparison design (*N*=1501; CC=728, UC=773)	ED visit					<0.001 (time[UC]) <0.001 (group×time)
Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	Participants admitted to the hospital (*n*)	0 (0%)	7 (4,4%)	0 (0%)	6 (3,7%)	N.R.
Levine et al. (2012)	RCT (*N*=298; CC=156, UC=142)	Proportion participants utilizing ≥1 hospital inpatient days	N.R.	25.6%	N.R.	37.1%	0.02 (group)
Rosenberg (2012)	Prospective cohort study (*N*= 248) *198 active and 50*	Hospital admissions (*n*)	116	70	--	--	0.004 (time)
		Hospital days (n)	1,700	1,061	--	--	0.04 (time)

	discharged patients at 12 month follow-up	Length of stay (days, *M*)	14.7	15.2	--	--	N.R.
		ED contacts (*n*)	120	95	--	--	0.20 (time)
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	Inpatient admissions (*n*)	--	57 (34.8%)	--	49 (32.2%)	0.53 (group)
		All-cause inpatient admissions (*M*)	--	1.21	--	1.19	0.95 (group)
		All-cause inpatient days (*M*)	--	5.41	--	6.44	0.42 (group)
		ED visits (*N*)	--	34 (20.7%)	--	20 (13.2%)	0.09 (group)
		All-cause ED visits (*M*)	--	0.67	--	0.43	0.05 (group)
		Cardiovascular inpatient admissions (*M*)	--	1.19	--	1.16	0.92 (group)

Co-funded by
the Health Programme
of the European Union

		Cardiovascular inpatient days (*M*)	--	5.40	--	6.39	0.44 (group)
		Cardiovascular ED visits (*M*)	--	3.86	--	3.03	0.04 (group)
Wald et al. (2011)	RCT (*N*=217; CC=122, UC=95)	Length of stay (days, *M*)	--	3.4 (2.7)	--	3.1 (2.7)	0.52 (group)
		30-Day readmission rate	--	12.3%	--	9.5%	0.51 (group)
		Discharges to home	--	68.8%	--	67.4%	0.84 (group)
		Discharges to home with services	--	14.0%	--	7.4%	0.12 (group)
Watkins et al. (2012)	Cohort study. *N*=292	Hospital readmissions	--	22%	--	--	--
		Post-discharge ED visits	--	28%	--	--	--

Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Hospital admissions	--	18%	--	20%	n.s. (group)
		ED admissions	--	29%	--	23%	N.R.
COMMUNITY AND INSTITUTIONAL LONG-TERM CARE SERVICES UTILIZATION							
Kono et al. (2012)	RCT (*N*= 323; CC=161, UC=162)	Institutionalized participants (e.g. nursing home or group home services, *n*)	0 (0%)	5 (3.1%)	0 (0%)	3 (1.9%)	N.R.
		Participants living at home (*n*)	161 (100%)	132 (82.0%)	162 (100%)	127 (78.4%)	n.s. (group×time)
Cameron et al. (2013)	RTC (*N*=216; CC=107, UC=109)	Permanent admissions to nursing care facilities (*n*)	--	*n*=16	--	*n*=21	N.R.
Boult et al. (2011)	cRCT (*N*=850;	Skilled nursing	--	MAC=0.20	--	MAC=0.25	n.s. (group)

	CC=446, UC=404)	facility admissions (*n*)					
		Skilled nursing facility days (*n*)	--	MAC=2.84	--	MAC=4.03	n.s. (group)
Schulz et al. (2011)	Cohort study (*N*=1073; CC=273, UC=800)	Participants with ≥1 nursing home admissions (*n*)	--	6 (2.2%)	--	40 (5.0%)	N.R.
PRIMARY CARE UTILIZATION							
Boult et al. (2011)	cRCT (*N*=850; CC=446, UC=404)	Primary care visits (*n*)	--	MAC=9.89	--	MAC=9.88	n.s. (group)
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	Primary care physician office visits (*M*)	--	1.95 (N.R.)	--	1.52 (N.R.)	0.23 (group)
Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	GP visits (*n*)	N.R	N.R	N.R	N.R	0.14 (group×time)

Co-funded by
the Health Programme
of the European Union

SPECIALIST CARE UTILIZATION							
Boult et al. (2011)	cRCT (*N*=850; CC=446, UC=404)	Specialists visits (*n*)	--	MAC=9.04	--	MAC=8.49	n.s. (group)
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	Specialist office visits (*M*)	--	10.04 (N.R.)	--	8.32 (N.R.)	0.05 (group)
		Cardiologist visits (*M*)	--	3.86 (N.R.)	--	3.03 (N.R.)	0.04 (group)
		Cardiothoracic visits (*M*)	--	0.05 (N.R.)	--	0.09 (N.R.)	0.07 (group)
Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Other specialists visits (*n*)	N.R	N.R	N.R	N.R	0.08 (group×time)
MEDICATION USE							
Wade et al. (2011)	RCT (*N*=316; CC=164, UC=152)	Prescriptions filled in prior year (%):					
		- Cardiac glycosides	15.2%	1.93%	25.7%	1.70%	0.55 (group)

		- Antianginal agents	28.7%	1.79%	27.6%	1.86%	0.86 (group)
		- Beta blockers	85.4%	8.48%	77.6%	6.97%	0.05 (group)
		- ACE inhibitors	54.3%	N.R	50.7%	N.R	N.R.
		- Angiotension II receptor antagonists	31.1%	2.59%	20.4%	1.39%	0.02 (group)
		- ACE inhibitors or angiotension II receptor antagonists	78.7%	4.59%	67.8%	3.80%	0.23 (group)
		- Diuretics	N.R	6.74%	N.R	5.46%	0.07 (group)
Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Medication use	N.R	N.R	N.R	N.R	n.s. (group)
HOME HEALTH CARE UTILIZATION							
Boult et al. (2011)	cRCT (*N*=850; CC=446, UC=404)	Home health care episodes (*n*)	--	MAC=0.99	--	MAC=1.30	<0.05 (group)
RENAL REPLACEMENT THERAPY (RRT)							

Weber et al. (2012)	RCT (*N*=139; CC=70, UC=69)	Dialysis rates (*n*)	--	22 (32%)	--	22 (32%)	n.s. (group)

---

[a] RCT = randomized controlled trial; cRCT = cluster-randomized controlled trial; *N* = total number of patients allocated (to comprehensive or usual care) at study entry; CC = comprehensive care; US = usual care.

[b] ED = emergency department; CHS = Cardiovascular Health Study

[c] MAC = mean annual per capita; N.R. = not reported; n.s. = not significant

* For these tables we used information that was provided in the original papers. In several papers, however, information was not complete, which explains why baseline, follow-up, and/or p-values are sometimes missing.