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Effectiveness of comprehensive care programs for patients with multiple chronic conditions or frailty: A systematic literature review

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ABSTRACT

Objective

To describe comprehensive care programs targeting multimorbid and/or frail patients and to estimate their effectiveness regarding improvement of patient and caregiver related outcomes, healthcare utilization and costs.

Methods

Systematic search in six electronic databases for scientific papers published between January 2011 and March 2014, supplemented by reference tracking. Wagner's Chronic Care Model (CCM) was used to operationalize comprehensive care. The quality of the included studies was assessed, and a best-evidence synthesis was applied.

Results

Nineteen publications were included describing effects of eighteen comprehensive care programs for multimorbid or frail patients, of which only one was implemented in a European country. Programs varied in target groups, settings, interventions and number of CCM components addressed. Providing

comprehensive care might result in more patient satisfaction, less depressive symptoms, a better health-related quality of life or functioning of multimorbid or frail patients, but the evidence is insufficient. There is no evidence that comprehensive care reduces the number of primary care or GP visits or healthcare costs. Regarding the use of inpatient care, the evidence was insufficient. No evidence was found for a beneficial effect of comprehensive care on caregiver-related outcomes.

Conclusion

Despite the fact that over the years several (good-quality) studies have been performed to estimate the value of comprehensive care for multimorbid and/or frail patients, evidence for their effectiveness remains insufficient. More good-quality studies and/or studies allowing meta-analysis are needed to determine which specific target groups at what moment will benefit from comprehensive care. Moreover, evaluation studies could improve by using more appropriate outcome measures, e.g. measures that relate to patient-defined (personal) goals of care.

1. INTRODUCTION

Due to rapid aging 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 [1] and [2]. An increasing proportion of these chronically ill people suffer from multimorbidity [3] and [4], defined as the co-occurrence of two or more chronic or long-term conditions within the same person [5] and [6]. Especially among older people, the prevalence of multimorbidity is high: among people over age 65 it is estimated at about 65%, and among people over age 85 at about 85% (e.g. [7], [8] and [9]). Among this latter age group, frailty – defined as a state of vulnerability resulting from cumulative physiological declines in reserve capacity and fitness across multiple body systems [10] – is also quite common, with estimated prevalence rates of about 30% [11]. As frailty is related to the natural process of aging, the prevalence of this condition is also expected to further increase in the near future. Although multimorbidity and frailty are distinct concepts, populations of people with multimorbidity respectively frailty are partly overlapping, and in practice it is not always possible to disentangle these concepts due to the various definitions that are being used in the literature [12] and [13].

Additionally, both people with multimorbidity and people with frailty (or people with both) have complex health and social care needs, and as such may benefit from similar comprehensive care approaches [14]. Compared to people with one chronic disease, people with multimorbidity more often experience problems related to mobility, self-care and performance of usual activities as well as pain or discomfort and cognitive problems [15]. Multimorbidity may also cause poor quality of life and distress, and increases the risk of disability and mortality [8], [16] and [17]. Frailty has been found to result in an increased use of primary, hospital and nursing home care as well as of community services (e.g. [18] and [19]).

Traditional disease-specific care delivery models do not fit with the comprehensive needs of people with multimorbidity and frailty, and have been blamed for resulting in the provision of inadequate and inefficient care for these people, due to a lack of

coordination and evidence-based knowledge [20], [21], [22], [23], [24] and [25]. In addition to the reported suboptimal quality of care for people with multimorbidity and frailty, concerns have been raised about the financial sustainability of health and social care in many western countries because of the expected increase of (older) people with complex chronic conditions in the near future (e.g. [26] and [27]). Innovative patient-centered, but also efficient and preferably cost-effective approaches of care delivery are therefore urgently needed [28] and [29]. Over the last years, care delivery for people with (multiple or complex) chronic conditions or frailty has gradually shifted from a mostly disease-specific approach to a more integrated or comprehensive approach in which the multiple health and social care needs of these people are addressed. Comprehensive care has been widely acknowledged as the best way forward to achieve good quality and cost-effective care for people with multiple chronic or complex conditions [30], [31] and [32]. Comprehensive care programs can be defined as those initiatives that proactively seek to structure and coordinate care and improve health outcomes while constraining healthcare expenditures [33]. Many different terms are being applied to comprehensive care including integrated care, guided care, case management, and shared care. Core elements of these initiatives are: (a) a well-coordinated and proactive approach to health and social care needs, often including comprehensive needs assessment, (b) patient-centeredness by involving patients in decision-making and planning their care process, and by taking their individual needs into account, (c) (simultaneous) delivery of multiple interventions, and (d) involvement of professionals from multiple disciplines. In 2012, de Bruin and colleagues performed a systematic literature review to gain insight into the characteristics and effectiveness of these new comprehensive care programs for patients with multimorbidity or frailty [33]. They found 28 programs, of which only four came from European countries. Regarding their effects, the results were mixed and the quality of many studies lagged behind. This made the authors to conclude that it was too early to draw firm conclusions regarding the effectiveness of comprehensive care, and that more rigorous evaluation studies were needed to determine what constitutes best care for the increasing number of people with multiple chronic conditions. More recently, many comprehensive care programs for people with multiple chronic conditions have been developed in European countries [34] and [35], and we expect similar developments to have taken place outside Europe. Moreover, we expect that the lessons that could be learned from earlier reviews would result in an increased number of good-quality studies evaluating the effectiveness of such programs. Based on these considerations and the urgency to strengthen the evidence-base for comprehensive care for people with multiple chronic conditions, we decided to repeat the previous systematic literature review using more recent studies. As such, the current study aims to provide more insight into the effectiveness of comprehensive care programs for people with multimorbidity or frailty. Since both people with multimorbidity and people with frailty have complex health and social care needs, they might benefit from similar comprehensive care approaches. For this reason, we decided to focus in our systematic literature review on comprehensive care programs for both target groups. Additionally, it appeared that – although theoretically distinct concepts – it is not always possible to distinguish

multimorbidity from frailty due to the various definitions that are being used in the literature [33].

2. METHODS

2.1. Study design and search strategy

We focused on English language papers published between January 2011 (end of the inclusion period of studies described in the previous review [33]) and March 2014. The search was conducted in the databases Medline, Cochrane, Cinahl, EMBASE, PsycINFO, and SciSearch. Keywords used to search these databases were similar to the previous review: 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, the internet was searched manually in case the papers identified by our database search described the design or a pilot of an intervention study. In those cases, information about the current status of these studies was collected.

2.2. Study selection

Four reviewers worked in pairs and independently reviewed the titles and abstracts 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 [36], [37], [38], [39] and [40], the Chronic Care Model (CCM) was used as a conceptual framework to describe the identified programs [32] and [41]. According to this model, a comprehensive care program should ideally address six interrelated components. The first two components mainly refer to the context in which care is provided: (1) a health care system that endorses the improvement of chronic care by supporting improvement at all levels of its organization, promoting effective improvement strategies aimed at comprehensive system change and providing incentives based on quality care; (2) community resources and policies that can support or expand a health system's care for chronically ill patients. Health systems can for instance form partnerships with community organizations to support and develop interventions that fill gaps in needed services and encourage patients to participate in (effective) community programs. The other four components 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 and better collaboration; (5) decision support, by the implementation of evidence-based guidelines and protocols to provide good care, and (6) development of clinical information systems to facilitate a smooth delivery of care and to support care providers and patients [42] and [43]. 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 described program met our operational definition of a comprehensive care program; (2) the aim of the program was to provide care for patients with multiple chronic diseases and/or frailty; and (3) the study described in the paper was an intervention study evaluating the effectiveness of a program. Duplicate studies were removed.

2.3. Data extraction, quality assessment, and data analysis

Four researchers 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 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.

Cost estimates were adjusted for cross-country purchasing power differences (PPP), using 2011 US\$ PPP, and for inflation, using Gross Domestic Product prices in order to make meaningful comparisons across studies [44]. Four studies did not report the year of data collection. For these studies the year of publication was used as reference year.

The methodological quality of the selected studies was also scored by two researchers separately, based on six items adapted from two quality criteria lists [45] and [46] (Table 1). Similar to previous reviews [33] and [47], our list only included criteria that in our opinion were most relevant for studies on comprehensive care. Each criterion was rated as ‘+’ (criterion fulfilled), ‘-’ (criterion not fulfilled), or ‘?’ (criterion not reported). Since we did not use a complete standardized set of quality assessment criteria, we provided a total quality sum-score (ranging from 0 to 6) per study, which was determined by counting the number of criteria scored positively. We considered the quality of a study as low if the total quality sum-score was lower than 3, moderate if it was 3, good if it was 4 or 5, and high if it was 6.

[TABLE 1]

2.4. Best evidence synthesis

To draw conclusions regarding the effectiveness of comprehensive care programs, a best-evidence analysis was applied in line with previous studies [33], [48], [49] and [50]. We distinguished four levels of evidence:

1. Strong evidence: consistent evidence for a beneficial effect of comprehensive care across multiple studies with good or 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 good or high quality sum-score;
3. Insufficient evidence: inconsistent evidence for a beneficial effect of comprehensive care across multiple studies;
4. No evidence: only few (<3) studies available and/or consistent evidence for no effect of comprehensive care across multiple studies.

Results were considered consistent when at least 75% of the studies showed results in the same direction. Findings of studies with good or high quality sum-scores were valued more than findings of studies with low or moderate quality sum-scores.

3. RESULTS

3.1. Study retrieval

Our literature search yielded 2611 potentially relevant publications. On the basis of their titles and abstracts, 80 publications were selected for full-text screening, of which 18 were included. One paper was added after reference tracking, resulting in a total of 19 publications describing 18 different studies/programs [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [64], [65], [66], [67] and [68]. Reasons for exclusion are shown in Fig. 1.

[FIGURE 1]

3.2. Study characteristics

Study designs and length of follow-up:

Of the 18 studies, seven were randomized controlled trials [53], [56], [58], [59], [60], [65] and [68], five pretest–post-test studies [51], [54], [57], [62] and [67], three cluster randomized controlled trials [52], [61] and [64], two post-test only studies [55] and [63], and one was a quasi-randomized controlled trial [66] (Table 2 and Appendix 1). Sample size varied from 47 to 1682 subjects [54] and [55], and the mean sample size was 497 (SD = 465.37). Twelve studies had a total follow-up of 12 months or less [53], [55], [56], [59], [60], [62], [63], [64], [65], [66], [67] and [68], five studies had a total follow-up of longer than 12 months [51], [52], [57], [58] and [61], and one study did not report length of follow-up [54].

[TABLE 2]

Methodological quality of studies:

Two studies fulfilled all quality criteria (sum-score of 6; [53] and [64]) based on what could be retrieved from the information provided in the papers (Table 1). Six studies were of good quality, i.e. they had a quality sum-score of 5 [58] and [61] or 4 [59], [60], [65] and [68]. We will refer to these eight studies as ‘studies with a relatively high quality sum-score’ or ‘studies of relatively high quality’ (the remaining ten studies we will refer to as ‘studies of relatively poor quality’). The observed minimum quality sum-score was 0 (n = 4; [54], [55], [57] and [67]).

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 [52], [53], [56], [57], [58], [59], [60], [61], [63], [64], [65], [66] and [68]. Usual care was mostly described as normal access to services available to frail older and/or multimorbid people, routine home, primary, and hospital care. In two of these studies [57] and [58], the usual care conditions were not or only poorly described (Table 2 and Appendix 1). Five studies did not include a usual care condition, but evaluated the effect of comprehensive care programs over time [51], [54], [55], [62] and [67].

3.3. Program characteristics

Target populations:

The 18 comprehensive care programs were implemented in the USA (n = 12), Canada (n = 3), Australia (n = 1), Japan (n = 1), and the Netherlands (n = 1). Twelve programs focused on frail elderly who were (at risk of) using long-term care or medical services or had difficulty in self-managing medications [52], [53], [55], [57], [58], [59], [61], [62], [63], [66] and [67]. Three programs focused on older people with (a combination of) specific chronic conditions such as diabetes mellitus and heart failure [56], [64] and [65], two programs focused on frequently admitted and/or complex patients (not necessarily frail/older) [51] and [54], and one program focused on kidney disease patients (not necessarily frail/older) with diabetes and/or cardiovascular disease [68] (Table 2 and Appendix 1).

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 2 and Appendix 1). Consequently, the type of care that was provided also differed widely between the programs. In some programs new partnerships between primary, secondary, home health and/or community care were established such as the Program of Research to Integrate Services for the Maintenance of Autonomy (PRISMA) and the Primary Interdisciplinary Elder Care at Home (PIECH) program [57] and [62]. Other programs were initiated from the hospital, and entailed care coordination around hospital discharge such as the program with a care transitions coordinator [55] or hospital care provision in the community setting, such as for instance the Hospital to Home program [67].

Contents:

Table 2 and Appendix 1 illustrate the diversity in the comprehensive care programs with regard to the number of included interventions and related CCM components: two CCM components (n = 7), three CCM components (n = 5), four CCM components (n = 4), and five CCM components (n = 2). All comprehensive care programs included interventions related to innovations or changes in the delivery system design, such as appointing case managers, establishing multi-professional care groups or implementing individualized care plans. The majority of comprehensive care programs (n = 11) additionally provided decision support for healthcare providers by implementing evidence-based guidelines or training teams to implement new protocols. Nine programs included interventions to provide self-management support, such as involving patients in the design of their care plan and educating patients to improve self-management. Interventions related to involve community resources (e.g. establishing access to community services and partnerships with local service centers; n = 9) or to improve or change clinical information systems (e.g. introducing electronic patient records and computerized clinical charts; n = 7) were less frequently observed. Only one program included interventions related to changes or innovations in the health

system component. These interventions included installing committees to support new partnerships, employing management teams to support process and quality improvement, and enabling infrastructure for innovations in chronic care [57].

3.4. Impact of comprehensive care programs

Table 2 and Appendix 1 present all outcomes. Here below we describe the outcomes that were reported in at least three studies in two parts: patient outcomes (paragraph 3.4.1) and healthcare utilization and costs (paragraph 3.4.2). Only two (poor-quality) studies reported on the effectiveness of programs regarding caregiver-related outcomes (Table 2 and Appendix 1). The outcomes described below are also shown in two summarizing figures: Fig. 2 (patient outcomes) and Fig. 3 (healthcare utilization and costs). More detailed information about the differences in outcomes between comprehensive care and usual care, or changes over time, are presented in (online) Appendices 2 and 3.

[FIGURE 2]

[FIGURE 3]

3.4.1. Patient outcomes

Patient satisfaction:

Three studies measured the effect of comprehensive care on patients' satisfaction with the care they received [57], [59] and [67] of which only one had a relatively high-quality sum-score, whereas the other two studies were of relatively poor quality. The relatively high-quality study reported a greater increase in satisfaction with home care in the comprehensive care group than in the usual care group [59]. One of the other studies reported a comparable beneficial effect with regard to satisfaction with the health services received [57], but the third study failed to show a beneficial effect of comprehensive care on patients' overall satisfaction with the care program or their satisfaction with home care and community services [67].

Health-related quality of life:

Effects on health-related quality of life were reported in nine studies [53], [56], [57], [58], [60], [61], [64], [67] and [68], of which six had a relatively high-quality sum-score. Six studies reported no beneficial effects of comprehensive care. One (relatively poor-quality) study found lower follow-up numbers of participants reporting unmet needs (i.e. disabilities not compensated by adequate resources) in the comprehensive care group than in the usual care group [57]. In two studies (one of relatively high quality [60] and one of relatively poor quality [67]), a beneficial effect of comprehensive care was found on both physical and mental health.

Depressive symptoms:

Four (all relatively high-quality) studies estimated the effect of comprehensive care on depressive symptoms [53], [58], [60] and [61]. Three studies reported no differences between comprehensive care and usual care groups [53], [58] and [61],

and one [60] reported a larger reduction of depressive symptoms in the comprehensive care group compared with a usual care group.

Functional status:

Seven studies evaluated effects of comprehensive care on patients' functional status [53], [56], [57], [58], [60], [61] and [66], of which four had a relatively high-quality sum-score. Four of the seven studies reported no beneficial effect of comprehensive care [56], [58], [61] and [66]. One (good-quality) study found that patients' physical performance improved more in the comprehensive care group than in the usual care group [60], whereas another (relatively poor-quality) study found less functional decline in the comprehensive care group than in the usual care group, but no beneficial effect of comprehensive care with respect to functional autonomy [57]. The last (relatively high-quality) study found a beneficial effect of comprehensive care on physical performance, but not on performance of activities of daily living [53].

Mortality:

Mortality was evaluated in five studies [53], [56], [58], [64] and [68], of which four were of relatively high quality [53], [58], [64] and [68]. None of the studies reported a significant difference between comprehensive care and usual care groups in mortality rates.

3.4.2. Healthcare utilization and costs

Use of outpatient healthcare services:

Three studies estimated the effects of providing comprehensive care on the number of primary care or GP visits by multimorbid or frail people [52], [64] and [68], of which two were of relatively high quality [64] and [68]. In all three studies, a comparison with usual care was made. None of them showed significant effects. Regarding other types of outpatient care, the number of studies estimating such outcomes (e.g. outpatient visits to medical specialists, use of home care) was too low ($n < 3$) to be able to indicate whether comprehensive care affects the utilization of outpatient healthcare services.

Use of inpatient healthcare services:

Fifteen studies assessed the use of inpatient healthcare services by multimorbid or frail patients [51], [52], [53], [54], [55], [56], [57], [58], [59], [62], [63], [64], [66], [67] and [68]. Five studies were of relatively high quality [53], [58], [59], [64] and [68]. In ten of these studies, a comparison was made between comprehensive care and usual care, including four relatively high-quality studies [53], [58], [59] and [64]. Different indicators of inpatient healthcare utilization (e.g. number of hospital [re]admissions [52], [53], [55], [58], [62], [64], [66], [67] and [68], time to admission [53], length of stay [51], [52], [54], [56], [62] and [66], number of ED visits [52], [54], [57], [62], [64], [67] and [68], and number of institutionalized patients [53], [58] and [63]) were studied. Comprehensive care favored usual care in only two studies, of which one had a relatively poor- [57] and the other a relatively high-quality sum-score [59]. This latter study showed a lower proportion of patients

who had at least one hospital inpatient day during the course of study among the comprehensive care group. The other study showed a lower increase over time in the proportion of patients visiting an ED in favor of the comprehensive care group. In six studies no difference between the comprehensive care groups and the usual care groups were found for any indicator [52], [53], [58], [63], [66] and [68]. Two studies found opposite effects, favoring the usual care group [56] and [64]. The five studies that did not compare comprehensive care with usual care [51], [54], [55], [62] and [67] were all of relatively poor quality; they all showed a reduced use of inpatient healthcare (hospital (re)admission rates, number of hospital days and ED visits) after implementing comprehensive care with the situation before.

Costs:

Results on healthcare costs were reported in eight studies [51], [56], [58], [59], [62], [66], [67] and [68], of which three were of relatively high quality [58], [59] and [68]. One study (with a relatively high-quality sum-score) reported a beneficial effect of comprehensive care: the yearly costs of visiting an integrated clinic (\$1648 per patient) were lower than the yearly costs of visiting separate clinics (\$2818 per patient) [68]. One (uncontrolled) study of relatively poor quality showed a reduction of total costs and of costs related to unplanned hospitalizations and ED visits to be reduced after 12 months (−\$27,200 and −\$20,377 respectively per patient) and 24 months (−\$42,697 and −\$25,761 respectively per patient) [51], whereas another (uncontrolled) relatively poor-quality study reported substantial cost savings (−\$2151 per patient per year) due to prevention of hospital readmissions [67]. In three studies, two of relatively poor [56] and [66] and one of relatively high quality [59], no difference in costs were found between comprehensive care and usual care. One (relatively high-quality) study found higher total costs of long-term care in the comprehensive care group (−\$3506 per patient over two years) than in the usual care group (−\$2534 per patient over two years) [58]. One (relatively poor-quality) study did not report outcomes regarding costs [62].

3.4.3. Summary of the best-evidence synthesis

Considering the results on patient outcomes as summarized in Fig. 2, it seems that providing comprehensive care to patients with multimorbidity or frailty could result in patients experiencing better quality of care, a better health-related quality of life or functional status and less depressive symptoms, but the evidence is insufficient. There is no evidence that providing comprehensive care results in lower mortality rates.

Considering the results on healthcare utilization and costs as summarized in Fig. 3, there is no evidence that providing comprehensive care to patients with multimorbidity or frailty results in a reduction of the number of primary care or GP visits by these patients. Whether providing comprehensive care reduces the use of inpatient care (hospitalization, use of ED visits) by patient with multiple chronic conditions is unclear; the evidence is insufficient. No evidence was found for a beneficial effect of comprehensive care on caregiver-related outcomes. Furthermore, we found no evidence that comprehensive care is accompanied with lower costs, but

in fact, there were too little studies of good quality to draw conclusions in this respect.

4. DISCUSSION

Three years after the systematic literature review of de Bruin and colleagues [33], we repeated their approach with more recent studies [51], [52], [53], [54], [55], [56], [57], [58], [59], [60], [61], [62], [63], [64], [65], [66], [67] and [68] assessing the effectiveness of comprehensive care programs for people with multimorbidity or frailty on a wide range of outcome measures. We expected to be able to draw more firm conclusions about the effectiveness of such programs. Particularly in view of the increasing number of comprehensive care programs that have been developed for people with multiple chronic conditions in recent years, and the expected higher quality of the evaluation studies.

Despite the substantial number of such programs found in European countries, as described in earlier studies [34] and [35], and the increased number of relatively high-quality evaluation studies we found over 3 years, evidence for beneficial effects is still limited, which confirms earlier findings in this area (e.g. [6]). Regarding patient outcomes, there is insufficient evidence for a beneficial effect of comprehensive care on multimorbid or frail patients' satisfaction with care, their quality of life, depressive symptoms and functional status, whereas we found no evidence at all for a beneficial effect on mortality rates. No evidence was found for a beneficial effect of comprehensive care on caregiver-related outcomes. Regarding the impact of comprehensive care on healthcare utilization and costs, there is no evidence that the provision of comprehensive care results in a reduced number of primary care or GP visits by people with multimorbidity or frailty or in cost savings, and insufficient evidence was found that comprehensive care results in a reduced use of inpatient care. This is in contrast with the findings of Bruin and colleagues, who found moderate evidence for a beneficial effect of comprehensive care on inpatient healthcare utilization and healthcare costs, and insufficient evidence regarding outpatient healthcare utilization [33].

Concerning the outcomes focussing on healthcare utilization, one could question whether it is realistic to expect a reduction of healthcare utilization in general, given the high needs for care and support of these patients. However, a reduction of unplanned hospital admissions, readmissions and ED visits seems to be a valid goal to strive for, when developing and implementing comprehensive care. We therefore consider these types of healthcare utilization here in more detail. Regarding hospital admissions, none of the included studies distinguished between planned and unplanned admissions, so we could not draw any conclusions in this respect. Hospital readmissions had been evaluated in four studies [52], [55], [66] and [67], but none of these studies were of relatively high quality. ED visits had been evaluated in seven studies [52], [54], [57], [62], [64], [67] and [68], of which only two were of relatively high quality. The relatively high-quality study [68] found no difference in ED visits between comprehensive care and usual care, and the relatively high-quality study [64] showed more ED visits among patients receiving comprehensive care compared with usual care. It is clear that, like in the previous review of de Bruin and colleagues, the relatively poor quality of many studies hindered us to draw firm conclusions. Apart from that, our review did not show any

result whatsoever that justifies a belief in a beneficial effect of comprehensive care on healthcare utilization by multimorbid or frail people nor on its costs.

4.1. Methodological considerations

It should be acknowledged that it is difficult to explain our inconsistent findings. Differences were observed in program characteristics and contexts in which these programs were implemented. As suggested in earlier studies [61], [69], [70] and [71], in some countries or regions the difference between the comprehensive care program and usual care may have been small because of developments in usual care toward improving care (e.g. initiating multidisciplinary collaboration). As such, the added value of comprehensive care in terms of the selected outcome measures may have been more difficult to demonstrate. However, since the usual care conditions are often not well-described in the included studies it is difficult to establish whether this might explain the inconsistent findings. The lack of contrast between comprehensive care programs and usual care might also result from the opposite: that the comprehensive care programs have not always been implemented so well as they had been designed. It has been widely acknowledged that there are structural, organizational, and professional barriers to implementation of care innovations such as comprehensive care [71], [72] and [73]. These factors might have played a role in the studies that were included in this review too. However, as also mentioned in earlier studies [33] and [72], barriers and facilitators regarding implementation are often hardly described and it remains therefore unclear whether these have played a role.

Furthermore, studies were included regardless of how ‘multimorbidity’ and ‘frailty’ were operationalized. As such, target groups of the included comprehensive care programs varied significantly. We further observed a wide variety in outcome measures and instruments used in the included evaluation studies. Consequently, there were not sufficient studies with enough data to perform a meta-analysis. We therefore decided to perform a best evidence synthesis of the results to be able to summarize available evidence in a structured way.

Remarkably few studies from European countries could be included in both the previous review of de Bruin et al. [33] (n = 4) and the current one (n = 1), whereas the development and implementation of comprehensive care programs for people with multiple chronic conditions in European countries seems to be well underway [34] and [35]. This discrepancy may be partly explained by the fact that both reviews only included English language papers. However, our experience from the EC funded ICARE4EU project [74] and SUSTAIN project [75] also makes us to suspect that many comprehensive care programs targeting people with multiple chronic conditions in European countries have not been thoroughly evaluated or described in the literature yet [35].

4.2. Recommendations

Based on the current evidence, we still cannot draw firm conclusions on the effectiveness of comprehensive care for people with multiple chronic conditions. Patient-reported outcome measures may be the ones most likely to be positively influenced by the provision of comprehensive care. Nevertheless, the patient-reported outcome measures that have most often been used in evaluation studies may not always be the most appropriate ones to estimate the effects of comprehensive care programs for people with multimorbidity or frailty. For instance, improving

physical functioning may not always be a realistic goal to strive for in these patients. And expecting a reduction of depressive symptoms is not relevant if depressive complaints are not an issue for individual patients or if the interventions selected for a patient, do not aim to alleviate depressive symptoms. It is therefore recommended, in line with Smith and colleagues [6], to tailor interventions within comprehensive care programs to the individual needs of patients. Moreover, we recommend evaluating the effects of comprehensive care on outcome measures that really matter to patients. As such, it may be worthwhile to develop and use valid instruments that assess personal goal attainment of patients with multiple chronic conditions [76] and [77].

Since it is still difficult to establish which target groups will benefit from comprehensive care most, it is further recommended to increase the samples sizes of future evaluation studies. This will allow us to perform sub-group analyses, so that more insight can be gained in which patients (with specific socio-economic or illness related characteristics, but also with specific preferences and competencies) might benefit from a specific approach. Future program evaluations could benefit from cross-country agreement on the use of a confined set of internationally validated outcome measures, in addition to more program-specific outcomes measures, if necessary. Agreement on outcomes measures might also help to apply meta-analysis, which may especially be useful when sample sizes of separate studies are low. The Joint Action on chronic diseases and promoting healthy aging across the life cycle (JA-CHRODIS [78]) and/or the European Innovation Partnership on Active and Healthy Ageing [79], both initiatives of the European Commission, could provide an acknowledged platform for such arrangements at a European level. These European initiatives might also facilitate the exchange of knowledge about the effects of comprehensive care programs implemented in European countries. Also other European wide projects such as the ICARE4EU project [74] and the SUSTAIN project [75] will contribute to the knowledge base. These projects will provide starting-points for how to improve current practice in comprehensive care and how to transfer lessons learned to other health systems and regions. Particularly because it is expected that the cross-country comparisons that are central in these projects may help us to further understand why programs do not always live up to their promise (e.g. are programs or program components not effective, are programs not provided to the right target group, are programs not correctly implemented, which barriers hamper successful implementation etc.). Such knowledge is of utmost importance for policy-makers and decision-makers tasked with designing, establishing and maintaining systems of comprehensive care so that they can make more evidence-informed decisions.

5. CONCLUSION

This review revealed no indications that implementing programs providing comprehensive care for people with multimorbidity or frailty results in a reduction of health services utilization or costs. Providing comprehensive care might increase multimorbid or frail patients' satisfaction with care and improve their health-related quality of life or functional status, but evidence for this is still insufficient. Comprehensive or integrated care programs are nowadays more often implemented in European countries or regions, but this is not reflected yet in a substantial number of well-designed evaluation studies from European countries. Moreover, the quality

of the evaluation studies in general lags behind, which hampers making progress in developing comprehensive care for people with multiple chronic conditions that is really evidence-based. To promote the performance of evaluation studies focusing on the effectiveness of European programs, and to enhance their quality and cohesion, researchers in European countries need to collaborate and exchange their knowledge and experience. The findings of and experiences with the European DISMEVAL project regarding the evaluation of chronic disease management programs [80] may be useful to apply to the evaluation of comprehensive or integrated care programs for multimorbid or frail people as well. The JA-CHRODIS could serve as a platform for collaboration and knowledge exchange for this purpose.

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APPENDIX A.

Supplementary data Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.healthpol.2016.04.002>.

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TABLES AND FIGURES

Table 1

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) [51]	—	—	?	+	—	—	1
Boult et al. (2011) [52]	+	+	?	+	?	?	3
Cameron et al. (2013) [53]	+	+	+	+	+	+	6
Davis et al. (2013) [54]	—	—	?	—	—	—	0
Fleming and Haney (2013) [55]	—	—	?	—	—	—	0
Gharacholou et al. (2012) [56]	+	+	—	?	?	+	3
Hébert et al. (2010) [57]	—	—	?	—	—	—	0
Kono et al. (2012) [58]	+	+	?	+	+	+	5
Levine et al. (2012) [59]	+	+	?	+	—	+	4
Marek et al. (2013) [60]	+	—	?	+	+	+	4
Metzelthin et al. (2013) [61]	+	+	?	+	+	+	5
Rosenberg (2012) [62]	—	—	?	+	—	—	1
Schulz et al. (2011) [63]	—	—	+	—	—	—	1
Wade et al. (2011) [64]	+	+	+	+	+	+	6
Wakefield et al. (2011) [65]	+	+	+	+	—	—	4
Wald et al. (2011) [66]	+	+	—	—	—	—	2
Watkins et al. (2012) [67]	—	—	—	—	—	—	0
Weber et al. (2012) [68]	+	—	+	—	+	+	4

‘+’ – criterion fulfilled; ‘—’ – criterion not fulfilled; ‘?’ – lack of information.

^a Was the method of randomization adequate?

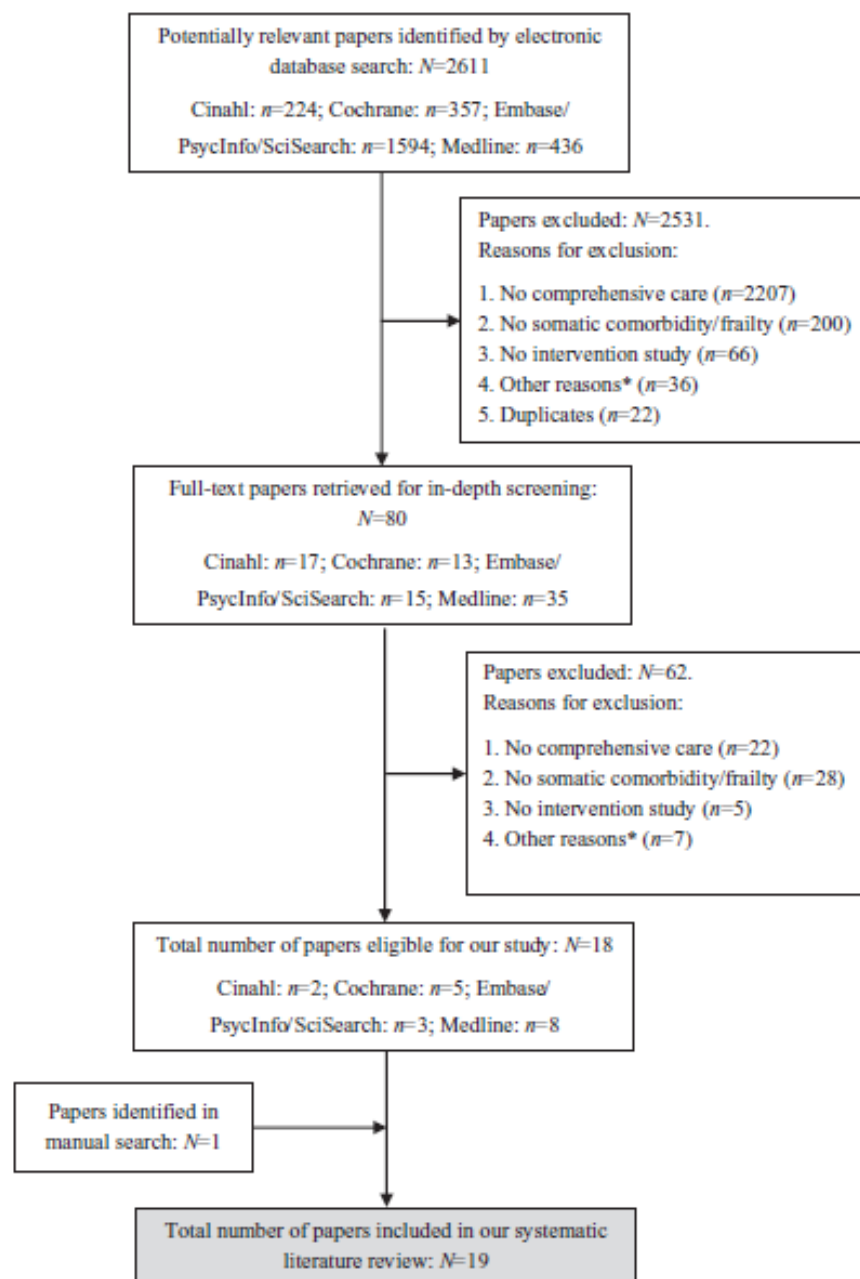
^b Were the groups similar at baseline regarding the most important prognostic indicators?

^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?



* 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.

Fig. 1. Flow diagram of literature screening process.

Table 2

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

Author (year)	Length of follow-up (months)	Setting	Study population and design	Chronic care components in comprehensive care program ^a	Usual care	Study parameters and outcomes ^b
Berry et al. (2013) [51]	24	Integrated health system, USA	The most complex (1–2% of patients; cohort study (pretest–posttest; N= 373).	– community resources – self management support – delivery system design – clinical information system	N.A.	(<i>p not reported</i>) – Decline in length of hospital stay. – Decrease in unplanned charges. – Decrease in total charges.
Boult et al. (2011) [52]	20	Primary health care, USA	Older adults at high risk of using health services heavily; cRCT (N= 850; CC= 446, UC= 404).	– community resources – self management support – delivery system design – clinical information system	Patients continued to receive care from their established primary care physicians.	– No effect regarding the use of health care services, except for a reduction in the use of home health care.
Cameron et al. (2013) [53]	3, 12	Clinical service (community and hospital settings), Australia.	Frail older people, not usually living in a residential aged care facility; RCT (N= 216; CC= 107, UC= 109).	– community resources – delivery system design – decision support	Health and aged care services normally available to older people.	– Lower prevalence of frailty in the CC group than in the UC group. – No effect with respect to depressive symptoms and health-related quality of life. – Mobility remained relatively stable in the CC group, whereas it declined substantially in the UC group. – No major effects with respect to number of deaths, hospital admissions, permanent admissions to nursing care facilities, and time to admission.
Davis et al. (2013) [54]	N.R.	Hospital, USA	Frequently admitted patients in a safety net primary care clinic; Cohort study (pretest–posttest; N= 47)	– self management support – delivery system design	N.A.	(<i>preliminary data; p not reported</i>) – Reduction in hospital days. – Reduction in ED visits.
Fleming and Haney (2013) [55]	12	Home health and hospice organization, USA	Frail older patients who were discharged from the hospital; Cohort study (posttest only; N= 682)	– self management support – delivery system design	N.A.	(<i>p not reported</i>) – Slight reduction in 12-month average hospital readmission rate
Gharacholou et al. (2012) [56]	12	Veterans Affairs medical centers (inpatient and outpatient), USA	Elderly who were previously hospitalized (>2 days expected length of stay) and diagnosed with heart failure; RCT (N= 309; CC= 155, UC= 154)	– community resources – delivery system design – decision support	Standard diagnostic and treatment approaches	– Improvement for physical functioning and basic ADL at hospital discharge but not at follow-up. – No effects regarding bodily pain, vitality, physical role, general health, social functioning, emotional role, and mental health. – Longer length of stay. – No effects regarding total costs and mortality rates.
Hébert et al. (2010) [57]	48	Primary, secondary, home health and community care, Canada	Older people at risks of functional decline; Quasi-experimental pretest–posttest matched comparison study (N= 1501; CC= 728, UC= 773)	– health system – community resources – delivery system design – decision support – clinical information system	N.R.	– Lower annual incidence of functional decline. – Lower prevalence of unmet needs. – Higher satisfaction and empowerment. – Increase in caregiver burden. – Lower number of visits to emergency rooms than expected (i.e. compared to usual care).

Table 2 (Continued)

Author (year)	Length of follow-up (months)	Setting	Study population and design	Chronic care components in comprehensive care program ^a	Usual care	Study parameters and outcomes ^b
Kono et al. (2012) [58]	24	Preventive care, Japan	Ambulatory frail elders who have been certified for care (facilities) at home, but who are not yet utilizing any long-term care services; RCT (N= 323; CC= 161, UC= 162)	– community resources – delivery system design	N.R.	– No effect regarding living state. – No effects regarding ADL, depression, and social support were found. In participants with <i>ADL dependency at baseline</i> , ADL and depression deteriorated more in the control group than in the intervention group. – Total long-term care services costs were higher in the intervention group.
Levine et al. (2012) [59]	12	Management services organization (medical groups and independent physician networks), USA	Frail older adults with multiple chronic conditions at high risk for use of medical services; RCT (N= 298; CC= 156, UC= 142)	– community resources – self management support – delivery system design – decision support – clinical information system	Standard care (i.e. usual primary care, home healthcare, hospice, ED, and hospital care)	– Higher mean satisfaction with care. – Less likely to be admitted to the hospital. – No effect in terms of costs of care.
Marek et al. (2013) [60]	12	Medicare-certified home healthcare agencies, USA	Frail older adults having difficulty in self-managing medications; RCT (N= 414; CC1= 152, CC2= 137, UC= 125)	– self management support – delivery system design – decision support – clinical information system	No intervention beyond the baseline pharmacy screen	– Better clinical outcomes (i.e. depression, physical performance, cognition, physical and mental quality of life)
Metzelthin et al. (2013) [61]	6, 12, 24	Primary care, the Netherlands	Community dwelling frail older people; cRCT (N= 346; CC= 193, UC= 153)	– self management support – delivery system design – decision support	Care as usual	– No effect regarding disability. – No effects regarding social participation, social support, depression, and fear of falling.
Rosenberg (2012) [62]	12	Primary/community care, Canada	Frail elderly adults living in the community; prospective cohort study (N= 248)	– community resources – delivery system design	N.A.	– Reduction in hospital admissions and hospital days. – No reduction in ED contacts.
Schulz et al. (2011) [63]	12	Community care, USA	Community-dwelling elderly/disabled clients who prefer to receive their prescriptions in the community; Cohort study (N= 1073; CC= 273, UC= 800)	– self management support – delivery system design	Standard care, i.e. prescriptions were dispensed in traditional prescription vials	– Fewer nursing home admissions (<i>p not reported</i>)

Wade et al. (2011) [64]	6	Specialized hospital care, USA	Elderly suffering from heart failure; cRCT (N= 316; CC= 164, UC= 152)	- self management support - delivery system design - decision support - clinical information system	Nurse case management only (vs. telehealth system with nurse case management in CC program)	- No effect with regard to health related quality of life (physical and mental). - No effects regarding acute care hospitalizations, hospital days, ED visits, cardiovascular admissions, primary care visits, and prescriptions (i.e. cardiac glycosides, antianginal agents, beta blockers, ACE inhibitors/angiotension II receptor antagonists, and diuretics). - No effect with regard to mortality. More cardiology visits and angiotension receptor antagonist prescription purchases.
Wakefield et al. (2011) [65]	12	Primary care at a Veterans Affairs (VA) Medical Center, USA	Veterans with comorbid type 2 diabetes and hypertension; RCT (N= 302; CC1 [low intensity]= 102, CC2 [high intensity]= 93, UC= 107)	- delivery system design - clinical information system	Follow-up appointments with the primary care clinic in the usual manner (incl. access to a nurse care manager)	- Decreased HbA1c during the 6-month intervention period, but not at 6 months follow-up. Decreased systolic blood pressure (in the high intensity group). - No effect of adherence.
Wald et al. (2011) [66]	Discharge and 30 days	Inpatient general medical services, USA	Elderly medical inpatients; qRCT (N= 217; CC= 122, UC= 95)	- delivery system design - decision support	Usual care lacked the interdisciplinary team approach of the CC program	- No effects regarding falls, discharge location, length of stay or 30-day readmission rates. - No effect regarding mean charges.
Watkins et al. (2012) [67]	30-120	Home environment, post-discharge from a non-trauma hospital, USA	Older patients discharged from acute hospital or inpatient rehabilitation facility, at risk for hospital readmission; Cohort study (N= 292)	- community resources - delivery system design - decision support	N.A.	- Increase regarding quality of life (physical and mental). - No comparative data on reduction of hospital readmissions and post-discharge ED visits is provided. - Cost savings due to prevention of hospital readmissions.
Weber et al. (2012) [68]	12	Hospital, Canada	Kidney disease patients with diabetes and/or cardiovascular disease; RCT (N= 139; CC= 70, UC= 69)	- delivery system design - decision support	Continued attendance at each separate multidisciplinary clinic, blood work, investigations, and follow-up as usual	- No effects regarding experienced symptoms. - No effects regarding hospital admissions and 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). - Lower yearly costs of visiting an integrated clinic than visiting separate clinics.

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; N.A.= not applicable; N.R.= not reported; ED= emergency department; ADL= activities of daily living.

^a According to the Chronic Care Model, a comprehensive care program should ideally address the following six interrelated components: (1) health system, (2) community resources, (3) self management support, (4) delivery system design, (5) decision support, (6) clinical information system.

^b The comprehensive care is the reference point.

Note: Appendix 1 provides a more complete overview of the studies, especially with regard to the content of the integrated care programs and the study outcomes.



Fig. 2. Summary of reported effects of comprehensive care programs on patient outcomes: (a) based on all studies included and (b) based on studies with relatively high-quality sum-score.



Fig. 3. Summary of reported effects of comprehensive care programs on healthcare utilization and costs: (a) based on all studies included and (b) based on studies with a relatively high-quality sum-score.