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REVIEW ARTICLE

Effectiveness of late-life depression interventions on functional limitations: A systematic review

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ABSTRACT: *Depression is one of the most prevalent mental disorders in older adults and leads to considerable decreases in health, well-being, and impaired functioning. Intervention studies have focused on the effects on symptomatic recovery, and most do not include functional recovery as an outcome. Reduction of functional limitations as a treatment goal in old-age psychiatry aligns with the values of older persons. The objective of this review was therefore to evaluate the effectiveness of late-life depression interventions on functional limitations. This systematic review identified 15 randomized controlled trials in which the effectiveness of different interventions on functional limitations was evaluated in patients with late-life depression. The interventions were categorized into four categories: psychological interventions, drug treatment, physical exercise, and collaborative care. Multicomponent and collaborative-care interventions appear to be the most promising for improvement of functional limitations, particularly in primary care and community-dwelling populations of older persons with symptoms of depression. There is, however, a lack of evidence regarding studies in specialized mental health care.*

KEY WORDS: *depression, mental health recovery, nursing care, psychiatry, systematic review.*

INTRODUCTION

Depression is one of the most prevalent mental disorders and leads to considerable decreases in health, well-being, and daily functioning (disability). While the largest proportion of the years of life lived with disabilities (YLDs) due to depressive disorders occurs at working ages, the Global Burden of Disease studies shows that depression in later life still accounts for 6.1 million YLDs among persons aged 65 years and over (Ferrari *et al*. 2013). This will only increase over the next decades due to a shifting demographical balance. Pooled prevalence rates of depressive disorder vary from 1.8% to 7.2% among community-dwelling older adults (Beekman *et al*. 1999; Luppa *et al*. 2012). The prognosis of depression deteriorates with increasing age (Schaakxs *et al*. 2018). Meta-analyses of randomized controlled trials on the effectiveness of antidepressants demonstrated significantly lower effect-sizes in older adults compared to younger adults (Tedeschini *et al*. 2011). This is further substantiated in a meta-regression analyses of studies in older depressed samples, which shows that increasing age is associated with lower treatment responses (Calati *et al*. 2013). Despite the lack of direct comparisons between younger and older adults within stratified randomized controlled trials, comparisons of the course of depression between

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younger and older adults indicate a more adverse course of depression in later life (Schaakxs *et al*. 2018). Even when symptomatic recovery is achieved, it is not always accompanied by functional recovery (Collard *et al*. 2018; Lenze *et al*. 2005; Wassink-Vossen *et al*. 2019).

The concept of functioning, functional limitations or disability, pertains to how people function in everyday life, in the performance of activities, and in the areas of life in which they participate (Bickenbach 2012). This differs from concepts such as quality of life and well-being because these are broad concepts that may be affected by disability, but that also depend on people's assessment of several other factors (Hudelson 1994). Worldwide, more than 46% of persons aged 60 years and over have disabilities and more than 250 million older persons experience moderate to severe disability (United Nations, Department of Economic & Social Affairs, Population Division 2015). Poor functional recovery after treatment of depression may be explained by shared determinants such as chronic medical illnesses and cognitive impairment (Alexopoulos 2005; Baune *et al*. 2007; Comijs *et al*. 2011), as well as by a two-way association between late-life depression and functional limitations (Lenze *et al*. 2001): depression negatively impacts functioning (Cronin-Stubbs *et al*. 2000) and functional limitations are associated with persistent depression (Lenze *et al*. 2001; Licht-Strunk *et al*. 2007).

From the patient's perspective, functional recovery is regarded as an important treatment outcome (Zimmerman *et al*. 2006). In the recent years, there has been a call for a reformulation of the concept of 'health' as the ability to adapt and self-manage in the face of social, physical and emotional challenges (Huber *et al*. 2011). Both patient organizations as well as governmental institutions argue for new approaches that are tailored to improve mental health care and reinforce self-management by patients (European Commission 2020; Mind 2020; Rijksoverheid 2020). For patients, the core of recovery is not the absence of an illness, for example depression, but rather the ability to 'rise above the diagnostic label' (Boevink 2012). Primary outcomes of depression treatment studies mainly focus on remission and severity of depressive symptoms, even though outcome measures such as functional limitations may be of equal, if not higher importance. To date, reviews of intervention studies in late-life depression have focused on the effect on symptomatic recovery and did not include functional recovery as an outcome (Langlieb & Guico-Pabia 2010), or found limited effect on functional disability in older adults with physical comorbidities (Frost *et al*. 2019). Such knowledge would be relevant, because the addition of interventions with a positive effect on functional recovery could improve the prognosis of late-life depression.

An important step is to review and assess the effect of late-life depression interventions on functional limitations, while also taking the quality of the studies into account. The objective of this review was therefore to evaluate the effectiveness of late-life depression interventions on functional limitations.

METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Moher *et al*. 2015). The research objectives, search strategy, and data-extraction sheets were a prior approved by all authors and have not been adapted during the study period.

Inclusion and exclusion criteria

This review considered intervention studies with a randomized controlled design, including older adults with depressive disorders and with functional limitations/recovery as primary or secondary outcome. Inclusion criteria for the studies were: (a) older adults with a mean age ≥65 years; (b) with any type of depressive disorders/symptoms confirmed by a (self-report) depression scale, by the International Statistical Classification of Diseases (ICD 10) or the Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria; (c) receiving interventions (any dosage or duration) for depression, (d) with outcome measured as functional limitations/disability. Studies into patient samples with another illness as the primary diagnosis (e.g. bipolar disorder, psychosis, dementia, stroke survivors, diabetes, heart failure, cancer) or other subgroups (e.g. war veterans) were excluded.

Study outcome

Because depression is related to functional decline across several domains, the outcome of interest was a change in functional status, measured by any self-reported or observer-rated functional disability scale. Studies that only used quality of life measures were not included.

Search strategy

Studies were identified through a systematic literature search including articles up until April 2021 The databases PubMed and CINAHL served as the primary source for original studies. Search terms included keywords for depression in combination with keywords for functional limitations and clinical trials: ((‘Depression’[Mesh] OR ‘Depressive Disorder, Treatment-Resistant’[Mesh] OR ‘Depressive Disorder, Major’[Mesh]) AND ‘Aged’[Mesh]) AND (‘Clinical Trials as Topic’[Mesh] OR ‘Controlled Clinical Trial’ [Publication Type]) AND (functional limitations OR WHODAS OR Sheehan OR impairment OR disability). Only articles that were written in English or Dutch were included. We did not pose any restriction with respect to year of publication.

Study selection

All studies were selected and evaluated for eligibility based on the title and abstract, independently by two authors (Author 1 and Author 4). Subsequently, full-text evaluation of the studies was performed by the same two authors. In the rare case of disagreement, a third author (Author 2) was included in the discussion and consensus was reached.

Quality assessment

Studies that met the inclusion criteria were evaluated in terms of methodological quality using the Cochrane Risk of Bias assessment tool (RoB 2), which addresses specific domains that may influence the risk of bias in an RCT (Higgins *et al*. 2011). The five domains for individually randomized trials are: (1) bias arising from the randomization process; (2) bias due to deviations from intended interventions; (3) bias due to missing outcome data; (4) bias in measurement of the outcome; and (5) bias in selection of the reported result. The tool includes algorithms that map responses to signalling questions onto a proposed risk-of-bias judgement for each domain. These domain-level judgements provide the basis for an overall risk-of-bias judgement for the specific trial result being assessed. The overall risk-of-bias levels are: (1) low risk of bias (the study is considered to be at low risk of bias for all domains for this result); (2) some concerns (the study is considered to raise some concerns in at least one domain for this result, but not to be at high risk of bias for any domain); or (3) high risk of bias (the study is considered to be at high risk of bias in at least one domain for this result, or the study is considered to have concerns regarding multiple domains that substantially lower confidence in the result) (Higgins *et al*. 2019). The quality appraisal was also independently conducted by two authors (Author 1 and Author 4).

Data extraction

Participants and study characteristics including mean age, gender distribution, recruitment setting and depression measure were extracted from the selected studies. Change in functional limitations (pre-post-test and between groups) was assessed using the functional-limitations scales that were applied. Information related to the therapy including setting, content, duration and frequency of sessions, control condition and mode of delivery were also extracted from the included studies.

In the case of more than one intervention group (e.g. in-person problem solving therapy (PST) and PST via telephone or two types of exercise versus medication), all treatment groups were reviewed separately with regard to the effect on functional limitations. Studies were grouped by type of intervention.

RESULTS

Search results

The search strategy yielded 510 articles in PubMed and 478 in CINAHL. After removing duplicates, 583 records remained. The initial title and abstract screening led to the exclusion of 170 out of 220 articles that did not meet the inclusion-criteria. We examined 50 full-text articles, of which ten articles were included (exclusion reasons: no formal measure of depression (n = 2); subgroup (n = 1); no formal measure of functional limitations (n = 9); only baseline measures of functional limitations available (n = 4); only physical functioning was measured (n = 2); adult population (n = 8); no subgroup analysis of older population (n = 9); design was not an RCT (n = 2); meta-analysis (n = 2); double study (n = 1)).

In the selected articles, the Short Form Health Survey questionnaire (SF-36/12 or RAND) from the Medical Outcome Study was frequently used to measure disability (Tarlov *et al*. 1989). After this observation, a post-hoc search was conducted including terms of (SF or RAND) and (rehabilitation). The (SF or RAND) search resulted in five additional studies.

This led to the selection of fifteen RCTs on interventions in late-life depression with effectiveness on functional limitations as the outcome measure (see Fig. 1: flowchart).

Study characteristics

Fifteen studies included a total of $n = 4285$ participants, which varied for each study from $n = 25$ (Alexopoulos *et al*. 2003) to $n = 1801$ (Unutzer *et al*. 2002). Six studies included community-dwelling older adults (Brenes *et al*. 2007; Choi *et al*. 2014, 2020; Gitlin *et al*. 2013; Huang, *et al*. 2015b; Kiosses *et al*. 2010), five studies were conducted in primary care (Gilbody *et al*. 2017; van Marwijk *et al*. 2008; Unutzer *et al*. 2002; Williams *et al*. 2000) of which one in combination with a mental health care institute (Neviani *et al*. 2017) and two studies were conducted in a nursing home/senior centre (Gitlin *et al*. 2013; Rondanelli *et al*. 2011). The majority of the studies took place in the USA. Five out of fifteen in other countries: Italy (Neviani *et al*. 2017; Rondanelli *et al*. 2011), The Netherlands (van Marwijk *et al*. 2008), the United Kingdom (Gilbody *et al*. 2017) and Taiwan (Huang *et al*. 2015b). Table 1 summarizes the description included studies.

Population

The mean age of the populations varied from 65 (Choi *et al*. 2014) to 78 years (Rondanelli *et al*. 2011) with varying sex distribution from 41% women (Williams *et al*. 2000) to 100% (Rondanelli *et al*. 2011). Six studies included participants with major depression (Alexopoulos *et al*. 2003, 2011, 2015; Kiosses *et al*. 2010; van Marwijk *et al*. 2008; Neviani *et al*. 2017), two studies focused on a combination of major depression and/or dysthymia (Rondanelli *et al*. 2011; Unutzer *et al*. 2002), one study included participants with minor depression or dysthymia (Williams *et al*. 2000), one study included

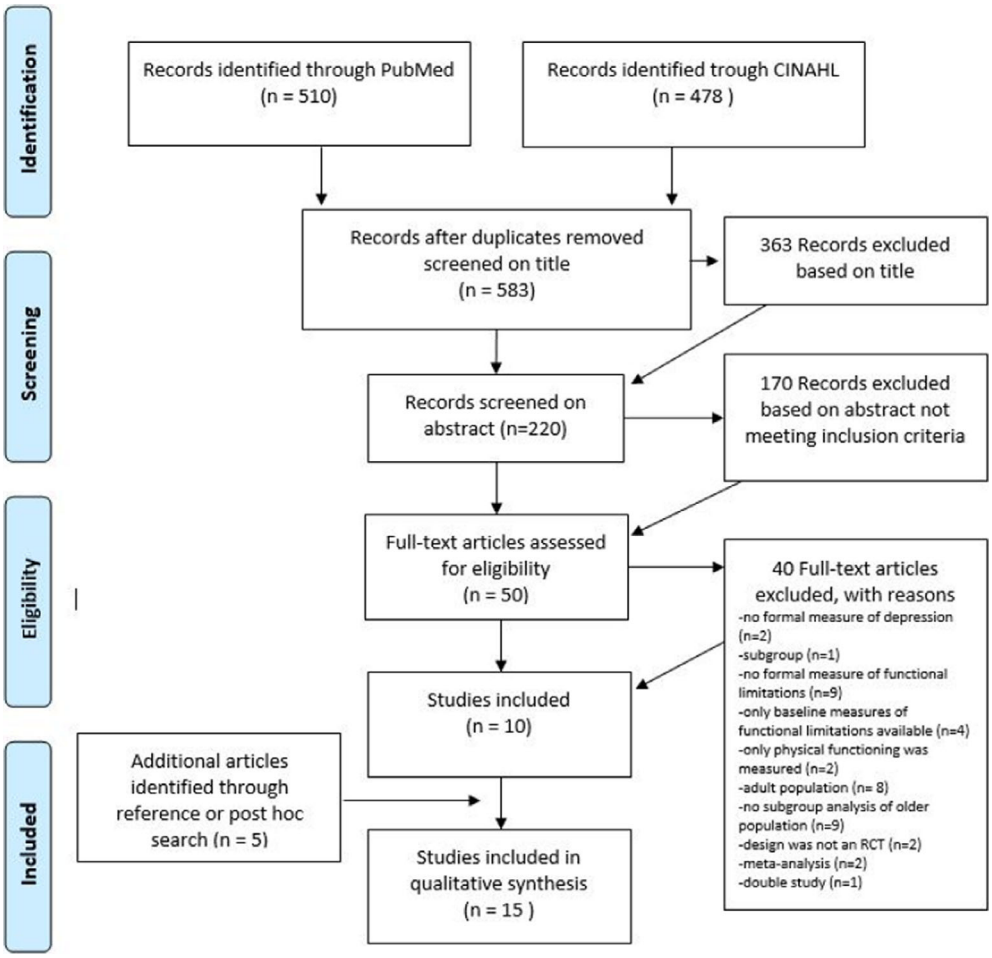

FIG. 1 Flowchart of the study selection.

TABLE 1 *Summary of included studies*

First author, year of publication	Total *N*	Type of study	Population main inclusion criteria: depression(measurement)	Characteristics		Setting (Recruitment)/ country	Outcome on functioning	Assessment time
				Mean age Years (SD)	Gender % women			
Alexopoulos *et al.* (2003)	25	RCT	major depression (HDRS)	74 (7.3)	74%	University intervention research centre (unknown) USA	WHODAS	Baseline, 12 weeks
Alexopoulos *et al.* (2011)	221	RCT	major depression (SCID, HDRS) executive dysfunction	73 (7.7)	unknown	University intervention research centre (unknown) USA	WHODAS	Baseline, weekly until week 12, 24, 36 weeks
Alexoploulos *et al.* (2015)	39	RCT	major depression (SCID)	IG:: 73 (8.0) CG: 73 (7.7)	IG: 72%. CG: 73%	University intervention research centre (unknown) USA	WHODAS	Baseline, 6, 9 weeks
Brenes *et al.* (2007)	37	RCT	2–4 symptoms of depression (PHQ-9)	IG1: 76 (6.4) IG2: 74 (7.8) CG: 74 (5.8)	IG1: 73%. IG2: 64%. CG: 50%	Community (newspaper/ads/flyers) USA	a. SF-36 physical b. SF-36 mental c. Q FAST	Baseline, 4 months
Choi *et al.* (2014)	158	RCT	depression (HDRS = ≥15)	65 (9.2)	78%.	Community (aging service agencies) USA	WHODAS	Baseline, 12, 36 weeks,
Choi *et al.* (2020)	277	RCT	severe depressive symptoms (HDRS = ≥15)	67.5 (8.9)	69.7%	Community (aging service agencies) USA	WHOAS	Baseline, 12, 24, 36 weeks
Gilbody *et al.* (2017)	705	RCT	subthreshold depression (MINI)	77 (7.1)	58%.	primary care (GP) England	a. SF-12 physical b. Sf-12 mental	Baseline, 4, 12 months
Gitlin *et al.* (2013)	208	RCT	depressive symptoms (PHQ-9 = ≥5)	77 (7.1)	58%.	Community/senior center (ads/ brochure) USA	Q FAST	Baseline 4, 8 months
Huang *et al.* (2015)	57	RCT	depressive mood (GDS-15 = ≥5);	77 (5.9)	52.6%.	community (mail/poster) Taiwan	SF-36	Baseline, 3, 6, 9 months
Kiosses *et al.* (2010)	30	RCT	major depression (SCID and HDRS = ≥17)	IG: 80 (8.5) CG: 78 (8.1)	IG: 67%. CG: 73%	Research centre (advertisement/ home delivered meals program) USA	SDS	Baseline, 6,12 weeks

(*Continued*)

TABLE 1 (Continued)

First author, year of publication	Total *N*	Type of study	Population main inclusion criteria: depression(measurement)	Characteristics		Setting (Recruitment)/ country	Outcome on functioning	Assessment time
				Mean age Years (SD)	Gender % women			
Marwijk *et al.* (2008)	145	RCT	major depression (GDS-15 = 'positive' and diagnose by PRIME-MD)	65.6 (8.7)	83%	Primary care (screening GP) Netherlands	SF	Baseline, 2,6,12 months
Neviani *et al.* (2017)	121	RCT	Major Depression (HDRS = >18)	75	71%	Mental Health and Primary Care, (GP and psychiatrist) Italy	BDQ	Baseline, 24 weeks
Rondanelli, *et al.* (2011)	46	RCT	Major Depression or Dysthymia (DSM-IV clinical diagnosis by senior psychiatrist)	IG: 85 (6.9) CG: 83 (7.3)	100%;	Nursing home (psychiatrist) Italy	SF-36	Baseline, 8 weeks
Unutzer *et al.* (2002)	1801	RCT	major depression or dysthymia (SCID)	71 (7.5)	65%	primary care (GP) USA	SDS	Baseline, 3, 6, 12 month
Williams *et al.* (2000)	415	RCT	minor depression or dysthymia (PRIME-MD and HDRS = ≥10)	71 (range 60-95)	41%	Primary care (research psychiatrist/ psychologist) USA	SF-36 Physical SF-36 Mental	Baseline, 11 weeks

Abbreviations: BDQ: Brief Disability Questionnaire; CG: control group; GDS-15: Geriatric Depression Scale; HAMD: Hamilton Depression Rating Scale; MCI: Mild Cognitive Impairment; PRIME-MD: PRIMary care Evaluation of Mental Disorders. Outcome (disability scales) - SDS: Sheehan Disability Scale; Q FAST: physical disability questionnaire adopted from The Fitness Arthritis and Seniors Trial (FAST). Characteristics - IG: intervention group; SF-36/SF-12: Healthy survey short form; Type of study - RCT: Randomized Controlled Trial. Population inclusion criteria – SCID: Structured Clinical Interview for DSM-4; WHODAS: World Health Organization Disability Assessment Schedule.

participants with subthreshold depression (Gilbody *et al*. 2017), three studies included elderly with depressive symptoms and excluded persons with major depression (Brenes *et al*. 2007; Huang *et al*. 2015b) or severe mental illness in the past (Gitlin *et al*. 2013). Depression was mainly determined by screening questionnaires (Patient Health Questionnaire (PHQ-9) (Brenes *et al*. 2007; Gitlin *et al*. 2013); Geriatric Depression Scale (GDS-15) (Huang *et al*. 2015b; van Marwijk *et al*. 2008)), rating scales (Hamilton Depression Rating Scale (HDRS) (Alexopoulos *et al*. 2003, 2011; Choi *et al*. 2014, 2020; Kiosses *et al*. 2010; Neviani *et al*. 2017; Neviani *et al*. 2017; Williams *et al*. 2000)), or diagnostic interviews by research assistants (Structured Clinical Interview for DSM Disorders (SCID) (Alexopoulos *et al*. 2011, 2015; Kiosses *et al*. 2010; Unutzer *et al*. 2002); Mini-International Neuropsychiatric Interview (MINI) (Gilbody *et al*. 2017); Primary Care Evaluation of Mental Disorders (PRIME-MD) (van Marwijk *et al*. 2008; Williams *et al*. 2000)). One study included participants with a clinical diagnosis of depression diagnosed by a senior psychiatrist (Rondanelli *et al*. 2011).

Outcome measurements

The functional limitations outcome was defined as functional impairment (Unutzer *et al*. 2002), functional status (Williams *et al*. 2000), functional difficulty (Gitlin *et al*. 2013), disability (Alexopoulos *et al*. 2003, 2011, 2015; Choi *et al*. 2014, 2020; Neviani *et al*. 2017), physical and emotional functioning (Brenes *et al*. 2007) or health related functions in measuring quality of life (Gilbody *et al*. 2017; Huang *et al*. 2015b; Rondanelli *et al*. 2011). The outcome measurements that were used for functional improvement varied. Six studies used any form of the SF questionnaire (Brenes *et al*. 2007; Gilbody *et al*. 2017; Huang *et al*. 2015b; van Marwijk *et al*. 2008; Rondanelli *et al*. 2011; Williams *et al*. 2000), five studies used the World Health Organization Disability Assessment Schedule (WHODAS) (Alexopoulos *et al*. 2003, 2011, 2015; Choi *et al*. 2014, 2020), two studies used the Sheehan Disability Scale (SDS) (Kiosses *et al*. 2010; Unutzer *et al*. 2002), two studies used the Questionnaire from The Fitness Arthritis and Seniors Trial (Q FAST) (Brenes *et al*. 2007; Gitlin *et al*. 2013) and Neviani *et al*. (2017) used the Brief Disability Questionnaire (BDQ). See Table 1 for a summary of the characteristics of the included studies. For a more elaborate description of the instruments that were used with references, see Box 1: Description of instruments used to measure disability.

Risk of bias

Overall, most studies had an unclear or high risk of bias (n = 13), largely due to limited reporting of the randomization process (n = 10), missing outcome data (n = 10), and doubts regarding the selection of reported results (n = 8). Studies were most commonly at a low risk of bias for outcome assessment (n = 14). However, it should be noted that due to the nature of the psychological interventions, blinding of the participants and research staff was not possible in most of the studies. In the end, only two studies were classified with a low risk of bias. The final judgement of the risk-of-bias tool across all included studies is summarized in Table 2. The complete summary of the risk-of-bias assessment of the studies is included in Fig. 2a,b: Risk-of-bias summary. Individual risk-of-bias ratings are discussed throughout the synthesis for each outcome.

Synthesis of the effect of interventions on functioning

The interventions were grouped into psychological interventions (Alexopoulos *et al*. 2003, 2011, 2015; Choi *et al*. 2014, 2020; Huang *et al*. 2015b; Kiosses *et al*. 2010; Williams *et al*. 2000), drug treatment (Brenes *et al*. 2007; Rondanelli *et al*. 2011; Williams *et al*. 2000), exercise (Brenes *et al*. 2007; Huang *et al*. 2015b in combination with medication (Neviani *et al*. 2017) and any type of collaborative care (Gilbody *et al*. 2017; Gitlin *et al*. 2013; van Marwijk *et al*. 2008; Unutzer *et al*. 2002).

The interventions evaluated were compared to a variation of control conditions, including active controls: problem solving therapy (Alexopoulos *et al*. 2015), supportive therapy/care calls (Alexopoulos *et al*. 2003, 2011; Choi *et al*. 2014, 2020; Kiosses *et al*. 2010), and sertraline (Neviani *et al*. 2017), as well as inactive control conditions: care as usual (Brenes *et al*. 2007; Gilbody *et al*. 2017; Huang *et al*. 2015b; van Marwijk *et al*. 2008; Unutzer *et al*. 2002), waiting list (Gitlin *et al*. 2013), and placebo (Rondanelli *et al*. 2011; Williams *et al*. 2000). Eight out of fifteen studies measured follow-up results, defined as ≥12 weeks after conclusion of the intervention. Only one study showed long-term effectiveness compared to the control group up to eight months post-intervention (Gilbody *et al*. 2017) (see Table 2).

BOX 1 DESCRIPTION OF USED INSTRUMENTS TO MEASURE FUNCTIONAL LIMITATIONS IN INCLUDED STUDIES

Description of used instruments to measure disability			
Instrument	Abb.	Description	Reference
36-Item Short Form Survey	SF-36	General measure of quality of life and functioning that yields a profile of 8 scores. Relevant domains include emotional role and social role functioning. Instrument has 8 domains in total, and can generate 8 scaled scores, as well as mental component and physical component summary scores. Validated in LDD	Tarlov *et al.* (1989)
World Health Organization Disability Assessment Schedule	WHODAS	Global measure of daily functioning in six domains: cognition, mobility, self-care, getting along with people, life activities (household and work/school), and participation. Degree of difficulty for each item rated on a 5-point scale. Validated in LLD	Chwastiak *et al.* (2003)
Sheehan Disability Scale	SDS	Brief self-report scale that assesses impairment in work/school, social life, and home/family life. Participants rank their perceived degree of impairment in each domain on a 10-point scale. Not validated in LLD	Sheehan *et al.* (1996)
Questionnaire from The Fitness Arthritis and Seniors Trial	Q-fast	A self-report 23-item questionnaire developed for The Fitness Arthritis and Seniors Trial (FAST). Measures physical disability in 5 domains: ambulations and stair climbing, transfer activities, upper extremity tasks, basic and complex activities of daily living. Degree of difficulty for each item rated on a 5-point scale. Not validated in LLD	Ettinger *et al.* (1997)
Brief Disability Questionnaire	BDQ	Adapted from the Medical Outcomes Survey Short Form and evaluates the restrictions in everyday activities due to depression, including physical activities, hobbies, daily routines, lack of motivation, and efficiency for home, school or work activities. Total scores range from 0 to 24, with greater scores indicating higher levels of disability. Not validated in LLD	Von Korff *et al.* (1996)

LDD, Late-life depression.

Psychological interventions

Eight studies examined interventions based on cognitive-behavioural therapy (CBT) principles, embedded in problem solving therapy, including three main steps: (1) patient symptoms are linked to their everyday problems, (2) the problems are clarified and (3) patients learn skills to improve their ability to deal with specific everyday problems. Results on PST were mixed. Huang *et al.* (2015b) studied PST provided by a psychiatric nurse and found that PST was not effective in the short or long term, whereas Alexopoulos *et al.* (2003) found that the PST group had lower disability scores as compared to the control group, after twelve weeks. The six remaining studies showed a positive effect of PST on short-term disability (12 weeks) compared with supportive therapy (Alexopoulos *et al.* 2011; Choi *et al.* 2014, 2020; Huang *et al.* 2015b; Kiosses *et al.* 2010), and equal effectiveness when compared with engagement (Alexopoulos *et al.* 2015). Williams *et al.* (2000) found an effect of PST on only mental functioning in a small subpopulation. Kiossen *et al.* (2010) found that augmentation of PST with environmental adaptation tools and caregiver participation was more effective in lowering disability than supportive therapy. Two studies (Choi *et al.* 2014, 2020) compared two interventions (video conferenced PST and in-person PST and video conferenced PST and behavioural activation) with care calls, and found that PST and behavioural activation were more effective than care calls. There were no differences in the effects on disability between in-person PST and care calls. None of the studies had a low risk of bias (Table 2). The overall effect of the interventions was not persistent, since no long-term effectiveness was found in most of the studies that measured follow-up results (Alexopoulos *et al.* 2011; Choi *et al.* 2014; Huang *et al.* 2015b), only Choi *et al.* (2020) found a persisting effect at 36 weeks.

Drug treatment

Three studies measured the effect of medication on functioning in late-life depression. Two studies compared medication with a placebo (Rondanelli *et al.*

TABLE 2 *Summary of results grouped by type of intervention*

First author, year of publication	Intervention duration		Outcome functioning	Assessment time	Analysis[†]	Results	Effect +/-	Quality ROB[‡]
	Intervention (*n*)	Control (*n*)						
Psychological interventions								
Alexopoulos *et al.* (2003)	12 weekly sessions Problem solving therapy (*n* = 12)	Supportive therapy (*n* = 13)	WHODAS	Baseline, 12 week	Mixed effect models	Significant time-by-treatment interaction ($F_{[1,22]}$ = 4.44); that is, PST led to a more rapid improvement in WHODAS-II scores. The effect size for the time-by-treatment interaction was 0.58; *P* = <0.05. The PST group had less disability (higher WHODAS-II scores) at the end of treatment than the ST group ($t_{[23]}$ = 4.69); *P* = <0.001	+	🟡
Alexopoulos *et al.* (2011)	12 weekly sessions Problem-solving therapy (*n* = 110)	Supportive Therapy (*n* = 111)	WHODAS	Baseline, weekly until week 12, 24, 36 weeks	Mixed effect models	After 12 weeks: PST participants had a significantly higher reduction in disability (total WHODAS scores) over 12 weeks than ST participants (Est. = −0.1824; *T* = −2.51; df = 202; *P* = 0.01). After 36 weeks: no significant difference between groups in the course of disability after treatment (group by time interaction: *t* = 0.16, df = 1, 142; *P* = 0.66).	−	🟡
Alexoploulos *et al.* (2015)	9 weekly sessions		WHODAS	Baseline, 6, 9 weeks	Mixed effect linear regression models	Both treatments reduced WHODAS; the effect of week was $F_{(2,234)}$ = 35.73, *P* < 0.001.	+	🔴
	Engagement in meaningful, rewarding activities (*n* = 39)	Problem-solving therapy (*n* = 97)				The week x treatment interaction was not significant: $F_{(2,234)}$ = 0.08; *P* = 0.93. The difference between groups (after controlling for other variables) at week 9 was 0.16 WHODAS points; $t_{(234)}$ = 0.11 with a Cohen's d = 0.02; 95% CI: −0.35 to 0.39; *P* = 0.91.	−	
Choi *et al.* (2014)	6 sessions 1) video conferenced problem-solving therapy (*n* = 58)	Care calls (*n* = 12)	WHODAS	Baseline, 12, 36 weeks	Mixed effect regression	1) 0-12 weeks: group by time interaction effect: *B* (SE): −0.31 (0.14); 95% CI = −0.60, −0.03; *t* = −2.16; *P* = 0.03	+	🟡
	2) Face-to-face problem-solving therapy at home (*n* = 63)	Care calls (*n* = 12)				2) 0–12 weeks: group by time interaction effect: *B* (SE): −0.09 (0.14); 95% CI = −0.36, 0.19; *t* = −0.60; *P* = 0.55	−	
						1/2) 12–36 weeks: Group by time interaction effects were nonsignificant for both groups.	−	
Choi *et al.* (2020)	5 weekly sessions		WHODAS	Baseline, 12, 24, 36 weeks	Mixed effect regression	1) Compared with participants in the AC group, participants in the tele-BA group had significantly reduced WHODAS scores across all follow-up assessments estimate, –3.91 (95% CI –5.93 to –1.89); *P* < 0.001	+	🔴
	1) video conferenced BA by lay counselors (*n* = 90)	AC: Telephone support calls by research assistants (*n* = 94)				2) Compared with participants in the AC group, participants in the tele-PST group	+	

(*Continued*)

TABLE 2 (Continued)

First author, year of publication	Intervention duration: Intervention (*n*)	Intervention duration: Control (*n*)	Outcome functioning	Assessment time	Analysis[†]	Results	Effect +/-	Quality ROB[‡]
						had significantly reduced WHODAS scores across all follow-up assessments estimate, –3.80 (95% CI –5.81 to –1.80); $P < 0.001$		
	2) video conferenced PST by clinicians (*n* = 93)	AC: Telephone support calls by research assistants (*n* = 94)				1/2) tele−BA and tele−PST did not significantly differ on decreased WHODAS scores across all follow−up assessments. Follow−up means estimated: tele−BA (18.3 [95%CI, 16.9 to 19.7]) and tele−PST (18.4 [95%CI, 17.0 to 19.8]) $P = 0.92$.	–	
Huang *et al.* (2015)	12 weeks		SF-36	Baseline, 3, 6, 9 months	GEE	3 months: group by time interaction $B = 0.96$; SE = 3.76; 95% Wald CI = −6.315 to 8.337; Wald $\square^2 = 0.065$; $P = 0.80$	–	!
	Cognitive behavioral therapy (*n* = 18)	Usual care (*n* = 20)				6/9 months: no effect	–	
Kiosses *et al.* (2010)	12 weeks		SDS	Baseline, 6,12 weeks	Mixed effect models	3 Months: treatment by time interaction ($F = 7.32$, df = 1, 47.1, $P = 0.01$).	+	
	Problem adaptation therapy (*n* = 15)	Supportive therapy (*n* = 15)						
Williams *et al.* (2000)	11 weeks: 6 treatment sessions		a) SF 36 Ph	Baseline, 11 weeks	Mixed models of covariance	a) no effect (NR)	–	
	Problem solving therapy (*n* = 138)	Placebo (*n* = 140)	b) SF-36 M			b)[§] minor depression in the lowest tertile of baseline functioning : 4.7 (1.96) points; $P = 0.02$	+	
						b)[§] minor depression intermediate: 2.9 (1.60) $P = >0.05$ and high baseline function: 1.4 (1.84) $P = >0.05$	–	
						b)[§] For dysthymia patients no significant improvement: (NR); $P = >0.05$	–	
Medication								
Brenes *et al.* (2007)	16 weeks		a) SF 36 Ph	Baseline, 4 months	ANCOVA	a)No effect (NR)	–	
	Sertraline (*n* = 11)	Usual care calls (*n* = 39)	b) SF-36 M			b) No effect (NR)	–	
			c) Q FAST			c) Trend towards a negative effect (ES = 0.35; $P = 0.27$).	–	
Rondanelli, *et al.* (2011)	8 weeks		a) SF 36 Ph	Baseline, 8 weeks	ANCOVA	a) Two months: mean intervention group = 49.7; difference (95% CI): 15.9 (9.9 to 21.9) $P = <0.001$	+	!
	Omega 3 supplements (*n* = 22)	Placebo (*n* = 24)	b) SF-36 M			b) Two months: mean intervention group = 66.6; difference (95% CI): 18.3 (12.9 to 23.7) $P = <0.001$	+	
Williams *et al.* (2000)	11 weeks		a) SF 36 Ph	Baseline, 11 weeks	Mixed models of covariance	a) No effect	–	
	Paroxetine (*n* = 137)	Placebo (*n* = 140)	b) SF-36 M			b)[§] dysthymia, in highest tertile of baseline functioning: 5.8 (2.02) $P = 0.01$;	+	
						b)[§] dysthymia, and intermediate baseline functioning: 4.4 (1.74) $P = 0.03$;	+	
							–	

(*Continued*)

TABLE 2 (Continued)

First author, year of publication	Intervention duration: Intervention (n)	Intervention duration: Control (n)	Outcome functioning	Assessment time	Analysis[†]	Results	Effect +/-	Quality ROB[‡]
						b)[§] dysthymia in low baseline functioning: 2.7 (2.17) P = >0.05;		
						b)[§] minor depression in the lowest tertile of baseline functioning 4.7 (2.03) P = 0.02;	+	
						b)[§] minor depression intermediate: 2.3 (1.65) and high baseline function: 0.2 (1.96) P = >0.05;	–	
Physical exercise								
Brenes *et al.* (2007)	16 weeks		a) SF 36 Ph	Baseline, 4 months	ANCOVA	a) No effect (NR)	–	🔴
	Exercise (n = 14)	Usual care calls (n = 12)	b) SF-36 M			b) Significant improvement (E = 0.95; P = 0.02).	+	
			c) Q FAST			c) Trend towards a positive effect (ES = −0.22; P = 0.19).	–	
Huang *et al.* (2015)	12 weeks		SF-36	Baseline, 3, 6, 9 months	GEE	Three months: group by time B = 12.68; SE = 3.18; 95% Wald CI = −6.457 to 18.911; Wald $\square^2$ = 15.938; P = <0.001	+	🟡
	Exercise (n = 19)	Usual care (n = 20)				Six/nine months: no effect	–	
Neviani *et al.* (2017)	24 weeks		BDQ	Baseline, 24 weeks	GLM	1) Four months: changes were not significantly greater (P = 0.32).	–	🔴
	1) Sertraline + thrice weekly non-progressive exercise (n = 37)	Sertraline (n = 42)				2) Four months: greater declines (effect size = −0.31; P = 0.02).	+	
	2) Sertraline + plus thrice-weekly progressive aerobic exercise. (n = 42)	Sertraline (n = 42)						
Collaborative care (see Box 2 **for further description of the interventions)**								
Gilbody *et al.* (2017)	8 weekly sessions		a) SF 36 Ph	Baseline, 4, 12 months	Linear mixed effect models	a) Four months: better physical functioning (mean score difference, −2.83 [95% CI, −4.03 to −1.62]; d = 0.2; P < 0.001.)	+	🔴
	Collaborative care (n = 344)	Usual care (n = 361)	b) SF-36 M			a) Twelve months: better physical functioning (mean score difference, −1.67 [95% CI, −3.06 to −0.27]; d = 0.1; P = 0.02)	+	
						b) Four months: better mental functioning (mean score difference, −1.88 [95% CI, −3.29 to −0.47]; d = 0.2; P = 0.01)	+	
						b) Twelve months: better mental functioning mean score difference, −2.15 [95% CI, −3.70 to −0.59]; d = 0.2; P = 0.007)	+	

(*Continued*)

TABLE 2 (Continued)

First author, year of publication	Intervention duration		Outcome functioning	Assessment time	Analysis[†]	Results	Effect +/-	Quality ROB[‡]
	Intervention (*n*)	Control (*n*)						
Van Marwijk *et al.* (2008)	6 months		a) SF-36 Ph	Baseline, 2,6,12 months	Analysis of variance	a) Two, six, twelve: no effect (NR)	–	🔴
	Multi component disease management (*n* = 70)	Usual care (*n* = 75)	b) SF-36 M			b) Two, six, twelve months: no effect (NR)	–	
Unutzer *et al.* (2002)	12 months		SDS	Baseline, 3, 6, 12 month	Mixed effect models	Intervention group had less health related functional impairment than control group at the three timepoints (adjusted analysis for intervention vs usual care: between-group difference or OR (95% CI); *t*; *P* value). Baseline: 0.10 (−0.12 to 0.35); *t* = 0.978; *P* = 0.33		🟢
	Collaborative care management (*n* = 906)	Usual care (*n* = 895)				Three months: −0.67 (−0.9 to −0.4); *t* = −5.06; *P* = <0.001	+	
						Six months: −0.35 (−0.6 to −0.05); *t* = −2.3; *P* = 0.02	+	
						Twelve months: −0.94 (−1.19 to −0.64; *t* = −6.65; *P* = <0.001	+	
Gitlin *et al.* (2013)	10 sessions		Q-FAST		Mixed effect models	Improvement in intervention group compared with control for functional difficulties at four months: mean difference (95% CI) 0.2 (−0.3 – 0.0); *P* = 0.02	+	🟢
	Multi component home based intervention (*n* = 106)	Wait-list (*n* = 102)				No additional gain after eight months in intervention group: mean difference (95% CI) 0.1 (0.0 to 0.2) *P* = 0.148	–	

Abbreviations: BA: behavioural activation; Interventions – AC: attention control; PATH: problem adaptation therapy; Ph = Physical domain); PST: problem solving therapy; Q FAST: physical disability questionnaire adopted from The Fitness Arthritis and Seniors Trial (FAST); SDS: Sheehan Disability Scale; SF-36/SF-12: Healthy survey Short Form (M = Mental domain; ST: supportive therapy. Outcome measurement – BDQ: Brief Disability Questionnaire; WHODAS: World Health Organization Disability Assessment Schedule.

[†]Analyses: ANCOVA = Analysis of covariance; GEE = Generalized estimated equations; GLM = Generalized linear models.

[‡]Quality ROB: The overall risk-of-bias judgements are: + (=Low risk of bias)! (=Some concerns); or – (= High risk of bias).

[§]Because baseline mental functioning component scores interacted significantly with treatment assignment and diagnosis, these results are presented separate in mean (SE); *P*.

FIG. 2 (a, b) Risk-of-bias summary.

2011; Williams *et al*. 2000) and one with care as usual, where antidepressant use was an exclusion criterion in the control group (Brenes *et al*. 2007). Both Brenes *et al*. (2007) and Williams *et al*. (2000) examined selective serotonin reuptake inhibitors (SSRI's), specifically sertraline and paroxetine. The sertraline condition group (Brenes *et al*. 2007) experienced slight declines in physical functioning. This negative effect was not statistically significant. Paroxetine (Williams *et al*. 2000) was beneficial for mental health functioning only (and not physical functioning), in the middle and highest functioning groups of patients with dysthymia and in the lowest functioning group of patients with minor depression. Both studies were qualified as presenting a

BOX 2 DESCRIPTION OF INCLUDED COLLABORATIVE CARE INTERVENTIONS (SEE TABLE 2)

First author, year of publication	Intervention	Components
Gilbody *et al.* (2017)	*Collaborative care:* One face-to-face and four to six telephone calls by a case manager (mental health nurse or psychologist) corresponding with GP or psychiatrist	(1) support; (2) symptom monitoring; (3) structured behavioural activation program; (4) medication (continuation)
Gitlin *et al.* (2013)	*Multi component home based intervention:* Up to ten 1-hour in-home sessions. First weekly then biweekly for up to four months by social workers	(1) care management (systematic unmet care needs assessment; (2) referral and linkage involving resource identification; (3) linking participants to social and medical services; (4) education instructing in symptom recognition, stress reduction techniques; (5) behavioural activation (goals and plan of action)
Van Marwijk *et al.* (2008)	*Multi component disease management:* Once every two weeks during first two months, then monthly for four months by general practitioner	(1) standard screening/diagnosing depression; (2) education and information; (3) drug therapy; (4) supportive counselling
Unutzer *et al.* (2002)	*Collaborative care management*: Face-to-face or telephone calls. In acute treatment phase biweekly, in relapse prevention phase monthly by care managers/ depression clinical specialist (DCS) (nurses/ psychologists). And treatment by general practitioner or specialist in stepped care model	(1) multidisciplinary collaboration on a common definition of the problem; (2) development of therapeutic alliance; (3) personalized treatment plan; (4) proactive follow-up and outcome monitoring by depression care manager; (5) targeted use of specialty consultation; (6) protocols for stepped care/treatment (medication/psychotherapy)

high risk of bias. Rondanelli *et al.* (2011) found that omega-3 supplements had a positive effect on mental and physical functioning after two months. Risk of bias was with some concerns.

Physical exercise

Three studies examined the effects of physical exercise on functional limitations. Two studies compared physical exercise with usual care (Brenes *et al.* 2007; Huang *et al.* 2015b), and Neviani *et al.* (2017) compared two types of exercise combined with an SSRI (sertraline), in comparison with medication alone. Simple exercise routines with 150 min/week (cardiovascular and muscle strength exercises) had an effect on mental and physical functioning after three months, but no long-term effect was found (Huang *et al.* 2015b). A similar intervention of aerobic and resistance training three times a week showed a short-term effect on mental functioning, but no effect on the physical domain of the SF (Brenes *et al.* 2007). This intervention did, however, have an effect on functional limitations measured with the FAST questionnaire (see Table 2). Likewise, Neviani *et al.* (2017) showed a short-term effect on functional limitations of progressive exercise three times a week. Non-progressive exercise did not have an effect on functional limitations. The risk-of-bias of these studies was with some concerns (Huang *et al.* 2015b; Neviani *et al.* 2017), or high risk of bias (Brenes *et al.* 2007).

Collaborative care

Studies were included in the collaborative-care category when the intervention was either a multicomponent mono-disciplinary intervention (Gilbody *et al.* 2017; Gitlin *et al.* 2013; van Marwijk *et al.* 2008) or a multidisciplinary treatment (Unutzer *et al.* 2002) (see Table 2 for the components of the interventions). Four studies examined collaborative care, varying from eight weekly sessions (Gilbody *et al.* 2017) to a twelve-month programme (Unutzer *et al.* 2002) and compared this intervention with usual care (Gilbody *et al.* 2017; van Marwijk *et al.* 2008; Unutzer *et al.* 2002) or a waiting-list control condition (Gitlin *et al.* 2013). All four studies were conducted in primary care. The effect on functional recovery was positive in three out of four studies (Gilbody *et al.* 2017; Gitlin *et al.* 2013; Unutzer *et al.* 2002) (see Table 2). All three of the studies with a positive effect on functioning included case management (by a mental health nurse, psychologist or social worker) and a multidisciplinary approach as components of the collaborative-care programme. Two of these studies had a low risk

of bias (Gitlin *et al*. 2013; Unutzer *et al*. 2002), while the third study had some concerns (Gilbody *et al*. 2017). The mono-disciplinary disease management programme by van Marwijk *et al*. (2008) did not find an effect on functional status and also had some concerns regarding risk of bias.

DISCUSSION

Principal findings

This systematic review identified fifteen RCTs in which the effectiveness of interventions on reducing functional limitations was evaluated in patients with late-life depression. These RCTs evaluated a total of 20 interventions that could be categorized into four categories: psychological interventions, drug treatment, physical exercise and collaborative care. We found that the studies in the collaborative-care interventions groups showed the most similar results with regard to the effect on functional limitations in late-life depression. Studies on psychological interventions, drug treatment and physical activity showed mixed results and no definite conclusions could be drawn with regard to their impact on functional recovery in late-life depression.

Efficacy of the interventions

Patients with late-life depression often suffer from comorbid physical diseases (Schaakxs *et al*. 2018) and geriatric syndromes such as frailty (Collard *et al*. 2014), loneliness (Peerenboom *et al*. 2015) and bereavement (Shah & Meeks 2012). Despite the complicating nature of these comorbid diseases and syndromes, they are rarely, if ever, taken into account in antidepressant drug treatment trials for late-life major depression (Benraad *et al*. 2016). It is likely that a disease-oriented approach does not suit the complexity of these interrelated problems well. This may explain why mono-disciplinary interventions, regardless of whether they were psychotherapy, drug treatment or physical activity, were not consistently associated with functional improvement. In a collaborative-care approach, the focus is on functioning and quality of life instead of solely on managing symptoms, and this review showed that this approach improves functioning in addition to generating symptomatic improvement.

Collaborative care requires that four key criteria are met: (1) a multi-professional approach to patient care, (2) a structured management plan, (3) scheduled patient follow-ups, and lastly, (4) enhanced inter-professional communication (Gunn *et al*. 2006), whereas disease specific treatment can still be highly variable. The collaborative-care studies included in this review were indeed heterogeneous with respect to depression-specific treatment, but consisted of multi-component and/or multidisciplinary interventions. Since the addition of a case manager was part of the intervention in all studies with a positive effect on functioning, this implies that coordination and supervision of care is an important element in improving functional abilities in late-life depression.

The only study in which a collaborative-care intervention did not improve functional limitations was based on care provided by the general practitioner according to the current guidelines at that time (van Marwijk *et al*. 2008). This stepped-care approach focuses on reducing symptoms (including drug-therapy, supportive counselling, education and information) and can be regarded as disease-oriented care. While no effect on functional status was observed, they did find an effect on reduction of symptoms of depression.

Two explanations can be put forward for the lack of impact on functional status. First, it could be argued that the guideline cannot be regarded as a structured management plan, especially because implementation of depression guidelines in clinical practice is generally questionable (Bruijniks *et al*. 2018; Sinnema *et al*. 2013, 2015). Second, because the general practitioner was a key person in this study, not only for providing care according to current guidelines, but also for to identifying the need of involvement of others and coordination of care, one may question whether this role for coordination of care and inter-professional communication was actually taken on. Therefore, it is likely that the key criteria of collaborative care were not met in this study.

Kiosses *et al*. (2010) studied PST and found that it effectively reduced functional limitations. When looking into the content of their intervention, it was noted that the environment of patients was also actively included in the treatment. We therefore make a case for categorizing this study as collaborative care instead of psychological treatment, because the intervention targeted multiple domains and met the key criteria of collaborative care.

The overarching conclusion points towards the integration of interventions such as psychological treatment into a collaborative-care framework to increase effectiveness. This could also be applied to other interventions in the physical exercise and medication categories. The mixed results with regard to the effect on functional status imply that these interventions may

be beneficial for a subgroup of depressed older persons. However, when personalized into a collaborative-care approach and augmented with specific interventions targeting the prevalent old-age phenomena, these interventions can be an important part of old-age psychiatric care with prolonged treatment results leading towards functional improvement.

This is in line with a recent review and meta-analysis by Frost *et al*. (2019) in which they studied the effect of non-pharmacological interventions on depressive symptoms and functioning in older persons with physical comorbidities. They found that PST had an effect on depressive symptoms, but not on functioning. With regard to collaborative care, they found that it did not reduce depressive symptoms, but that scores on the subscale of mental functioning improved. The participants in the studies who were included in the meta-analysis by Frost *et al*. (2019) probably had higher levels of frailty and had more somatic diseases, when compared to the studies that were included in the this review.

Methodological considerations

Population

The majority of the studies included in the present review recruited patients from community-dwelling samples or primary care (n = 13). Only two studies were conducted in a nursing home or senior centre. In the past ten years, the attention on functional status has increased, in particular due to patient involvement in treatment and shared decision-making in primary care (Archer *et al*. 2012; Kirkham *et al*. 2016). Nevertheless, the inclusion of functional status as an outcome measure is still uncommon (Beyer & Johnson 2018; Cuijpers *et al*. 2020; Huang *et al*. 2015a) in clinical trials in the area of mental health care.

The definition of depression varied from depressive symptoms to full-blown depressive disorder. The majority of the studies included participants with depressive symptoms and did not conduct a formal diagnostic procedure. This could imply that the most depressed and frail elderly were not included in the studies. Research by Markle-Reid *et al*. (2013) showed that the frail group benefits most from nurse-led collaborative care. The current findings are therefore likely to underrepresent the actual effect of the interventions on functional status in late-life depression.

Measuring functional disability/recovery

Very few functional assessment instruments have been validated in patients with late-life depression, and the available data are mixed. The variation in measurement of daily functioning outcomes in the old-age population was recently acknowledged in a meta-analysis by Bingham *et al*. (2018). Of the 21 functional assessment instruments identified by this meta-analysis, only two have been formally validated in a depressed elderly population, that is the 36-Item Short Form Survey (SF-36) (Tarlov *et al*. 1989) and the Performance Assessment of Self-Care Skills (PASS) (Rogers *et al*. 2010). We included fourteen RCTs in which five different instruments were used to measure functioning, of which only the SF-36 was validated in patients with late-life depression. This may have led to a lower sensitivity to detect subtle changes in functional status in older persons with late-life depression living in the community or with good physical health. In this regard, the WHODAS was recommended for research and clinical purposes, as well as the Late-Life Function and Disability Instrument (LLFDI) (Bingham *et al*. 2018; Karp *et al*. 2009).

Strengths and limitations

Although this review was performed in accordance with the highest scientific standards (Higgins *et al*. 2019), some limitations should be noted. First, to increase generalizability, studies on subgroups of depressed older persons were excluded from this review; for example depression in patients with cardiovascular diseases or in patients with cognitive impairment. The reverse of this decision is that we may have missed important information regarding interventions that target functional limitations in older adults with multimorbidity. Secondly, the data were too heterogeneous to perform a quantitative meta-analysis with respect to various levels of depressive symptoms, and the study populations had different characteristics, that is nursing home residents (Gitlin *et al*. 2013; Rondanelli *et al*. 2011), and community-dwelling depressed elderly (Brenes *et al*. 2007; Choi *et al*. 2014, 2020; Gitlin *et al*. 2013; Huang *et al*. 2015b; Kiosses *et al*. 2010). Thirdly, because the topic of functional limitations is on the verge of nursing and medical care, we searched the primary database of medicine (PubMed) and the primary database of nursing (CINAHL). However, we may have missed articles that were only available through other databases. Lastly, most of the studies included in this review were conducted in primary care. Although this can be explained by the lack of attention given to functioning in specialized mental

health care, the results cannot be generalized to these populations.

Quality of studies

The majority of the studies presented with an unclear or high risk of bias. Only two collaborative-care studies showed a low risk of bias. The findings should therefore be weighted accordingly. This implies that the results from the physical exercise, medication, psychological treatment and the remaining collaborative-care studies were interpreted more cautiously.

Clinical relevance/future recommendations

The complexity of late-life antidepressant treatment is reflected in adverse course trajectories and low remission rates. The need for additional treatment options is high, and these additional treatments should consider old-age phenomena such as frailty and multimorbidity to improve functional recovery. Future studies should combine interventions within a collaborative-care approach. Collaborative care can be regarded as a complex intervention that contains several interacting components and demands for a different research approach than a straight forward RCT. Methodologies of complex intervention studies allow multiple interaction and synergetic components to be taken into account (Craig *et al*. 2008).

Validated measurement instruments of functional limitations are available, and nurses can use these measures broadly as an outcome of care and treatment in their daily work and in practice-oriented research.

The addition of a case manager is an important intervention to improve coordination of care in the medical, psychological and social domains. This is of utmost importance in an old-age population with comorbid mental and physical illnesses, especially because the prevalence of frailty and cognitive impairment is high in populations with multimorbidity, and two-way associations with functional status have been observed.

CONCLUSIONS

Targeting functional recovery as a treatment goal opens up new opportunities for increasing the success of antidepressant treatment in late-life depression. Collaborative-care interventions seem most promising for improvement of functional limitations, particularly in primary care and community-dwelling populations of older persons with depressed symptoms. However, there is a lack of evidence regarding studies in specialized mental health care. Most importantly, reduction of functional limitations as a treatment goal in old-age psychiatry aligns with the values of older persons.

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