[New 2015]

Psychological therapies for people with dementia who have associated depression [New 2015].

SCOPING QUESTION: For people with dementia and comorbid depression, do psychological interventions (including cognitive behavioural therapy, behavioural activation, interpersonal therapy and counseling) produce any benefit and/or harm compared to controls? (Update of 2010 mhGAP 2010)

BACKGROUND

Depression is a common problem in older age, with a particularly high prevalence among people with dementia. In a recent study, the prevalence of depression in those with very mild Alzheimer's disease (AD) (Clinical Dementia Rating (CDR)=0.5) was 32.1%, and 39.6% in mild AD (CDR=1) (Karttunen et al., 2011). The prevalence of major depression tends to decrease as dementia severity increases (Forsell et al., 1998; Rubin et al., 2001). Depression in dementia has been associated with decrease in quality of life, increased need for institutionalization, greater health care utilization, higher mortality rates and increased caregiver burden (Verkaik et al., 2007).

The authors of the most recent Cochrane review (Bains et al., 2002) concluded that despite widespread prescription of antidepressants for depression in dementia, the evidence to support this practice was weak. They acknowledged that this conclusion was based on a few trials with small sample sizes, mainly investigating classes of antidepressants not often used in clinical practice. The authors highlighted the need for more definitive research to clarify efficacy. In the light of recent evidence from larger, better designed and reported trials of newer classes of antidepressant medications used to treat depression in dementia (i.e., Selective Serotonin Reuptake Inhibitor (SSRI) and Noradrenaline and Selective Serotonin Antidepressant (NASSA) has proven that there is evidence that these medications lack efficacy for the treatment of depression in dementia, while being associated with significant adverse effects. An important outcome of this review is that antidepressant medications are no longer considered as the first line of treatment for depression in dementia.

Much less attention has been given to the evaluation of psychological interventions as possible treatments for depression and anxiety in dementia. Psychological treatments may include cognitive behavioural therapy, problem solving therapies, interpersonal therapy or integrative therapeutic techniques. The aim of this scoping question is to identify current evidence on the effectiveness of these interventions for people with depression and anxiety in dementia.

[New 2015]

PART 1: EVIDENCE REVIEW

Population/ Intervention / Comparison / Outcome (PICO)

1. **Population:** Adults with depression and dementia
2. **Interventions:** Psychological interventions (including cognitive behavioural therapy, behavioural activation, interpersonal therapy, and counseling
3. **Comparison:** Control (including usual care or enhanced usual care or attention-control educational programs or diagnostic feedback)
4. **Outcomes:**

1. **Critical** – Depression symptoms

2. **Important** – Patient quality of life, activities of daily living (ADLs), neuropsychiatric symptoms and cognition

Search strategy

A recent relevant Cochrane Collaboration systematic review (6) was identified following a search conducted using Medline with the following:

1. search terms ((("Depression"[Mesh] OR "Depressive Disorder"[Mesh]) AND ("Dementia"[Mesh] OR "Alzheimer Disease"[Mesh])) AND ("Cognitive Therapy"[Mesh] OR "Psychotherapy"[Mesh])

Included in GRADE tables or footnotes

2. Orgeta V, Qazi A, Spector AE, Orrell M (2014). Psychological treatments for depression and anxiety in dementia and mild cognitive impairment. Cochrane Database of Systematic Review.1:CD009125. doi:10.1002/14651858.CD009125.pub2.

[New 2015]

PICO Table

Intervention	Comparison	Outcomes	Systematic reviews used for GRADE	Justification for systematic review used
Psychological interventions	Control (i.e., usual care, or enhanced usual care, or attention-control educational programs, or diagnostic feedback)	Depression symptoms Patient quality of life Activities of daily living Neuropsychiatric symptoms Cognition	Orgeta V et al. (2014).	Systematic review relevant to the area

Narrative description of the study that went into analysis

The Cochrane systematic review was carried out to assess the effectiveness of psychological interventions in reducing anxiety and depression in people with dementia or mild cognitive impairment (MCI). The systematic review authors searched the Cochrane Dementia and Cognitive Improvement Group Specialized Register and additional sources for both published and unpublished data. They included randomized controlled trials (RCTs) comparing a psychological intervention with usual care or a placebo intervention (i.e., social contact control) in people with dementia or MCI. Two review authors worked independently to select trials and to extract data and assess studies for risk of bias, using a data extraction form. They contacted authors when further information was not available from the published articles.

Six RCTs involving 439 participants with dementia were included in the review, but no studies of participants with MCI were identified. The studies included people with dementia living in the community or in nursing home care and were carried out in several countries. Trials either restricted recruitment to patients with mild or mild to moderate dementia or had a preponderance of low levels of severity among those recruited. In only two trials were participants selected on the basis of clinically significant psychological morbidity. Only one of the studies was classified as low risk of bias. Five studies were at unclear or high risk of bias due to uncertainties around randomization, blinding and selective reporting of results. The studies used the different psychological approaches of cognitive behavioural therapy (CBT), interpersonal therapy and counseling. Two studies were of multimodal interventions including a specific psychological therapy. The comparison groups received usual care, attention-control educational programs, diagnostic feedback or services slightly above usual care.

The authors concluded that psychological interventions added to usual care can reduce symptoms of depression and clinician-rated anxiety for people with dementia; thus, psychological interventions have the potential to improve patient well-being. Further high quality studies are needed to investigate which treatments are most effective and to evaluate the effect of psychological interventions in people with MCI.

[New 2015]

GRADE Table

Table 1. Psychological interventions vs. controls for treatment of depression and anxiety in dementia

Authors: M Prince and M Harper
Question: **Are psychological interventions effective for the treatment of depression and anxiety in dementia compared to controls?**
Bibliography: Orgeta V, Qazi A, Spector AE, Orrell M (2014). Psychological treatments for depression and anxiety in dementia and mild cognitive impairment. Cochrane Database of Systematic Reviews.1:CD009125. doi:10.1002/14651858.CD009125.pub2.

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Psychological interventions	Control	Relative (95% CI)	Absolute		
Depression symptoms (follow-up 5/12 months; measured with Geriatric Depression Scale (15 or 30 item version), or Cornell Scale for Depression in Dementia; better indicated by lower values)												
5	Randomized trials	Serious[1]	No serious inconsistency	Serious[2]	No serious imprecision	None	216	223	-	SMD 0.22 lower (0.41 to 0.03 lower)	□□□□ LOW	CRITICAL
Self-rated quality of life (measured with Quality of Life in Alzheimer disease (QOL-AD) scale; better indicated by higher values)												
3	Randomized trials	No serious risk of bias	No serious inconsistency	Serious[2]	Serious[3]	None	161	173	-	MD 0.37 higher (0.01 lower to 1.75 higher)	□□□□ LOW	IMPORTANT
Activities of daily living (measured with Bristol Activities of Daily Living (BADLS) and Alzheimer's Disease Cooperative Study Activities of Daily Living Scale (ADSC-ADL); better indicated by higher values)												
2	Randomized trials	Serious[1]	No serious inconsistency	Serious[2]	No serious imprecision	None	150	163	-	SMD 0.13 lower (0.35 lower to 0.09 higher)	□□□□ LOW	IMPORTANT
Neuropsychiatric symptoms (measured with Neuropsychiatric Inventory (NPI) and NPI-Q; better indicated by lower values)												
2	Randomized trials	Serious[1]	Serious[4]	Serious[2]	Serious[3]	None	150	161	-	SMD 0.06 higher (0.16 lower to 0.28 higher)	□□□□ VERY LOW	IMPORTANT

Cognition (measured with Mini Mental State Examination (MMSE); better indicated by higher values)												
4	Randomized trials	Serious[5]	No serious inconsistency	Serious[2]	Serious[3]	None	191	190	-	MD 0.80 lower (1.7 lower to 0.11 higher)	⨁◯◯◯ VERY LOW	IMPORTANT

[1] Cochrane rated aspects of risk of bias unclear in at least one of the studies included.
[2] In only two of the trials were participants selected on the basis of clinically significant psychological morbidity (anxiety symptoms). For the other four trials, no mention is made in the Cochrane Review of selection being based either upon elevated or clinically significant symptoms of depression or anxiety.
[3] WHO guidance: Downgrade if CI crosses line of no effect.
[4] I squared value 68%.
[5] Cochrane rated two of the four studies as "unclear" with regards to bias (includes Burgener et al., 2008; Burns et al., 2005 cited in the review), which carry a weighting of 17.8%.

Additional evidence not mentioned in GRADE tables (including footnotes)

Meta-analysis carried out in the Cochrane Review also showed a positive effect of psychological treatments on clinician-rated anxiety (2 trials, 65 participants, MD -4.57; 95% CI -7.81 to -1.32, low quality evidence), but not on self-rated anxiety (2 trials, SMD 0.05; 95% CI -0.44 to 0.54) or carer-rated anxiety (1 trial, MD -2.40; 95% CI -4.96 to 0.16). Results showed no difference between the psychological intervention and treatment as usual on caregivers' self-rated depressive symptoms 0.07, 95% CI -0.14, 0.29. There were no reports of adverse events.

Other relevant trials not included in the Cochrane Review

Teri L, Logsdon RG, Uomoto J, McCurry SM (1997). Behavioral treatment of depression in dementia patients: a controlled clinical trial. Journal of Gerontolology, Series B: Psychological Sciences & Social Sciences.52(4):159-66.

This study comprises an RCT testing the effectiveness of behavioural activation treatments applied by the caregiver in reducing levels of depression symptoms in depressed AD patients. Participants had a mean MMSE score of 16.5, suggesting mild to moderate dementia severity. There were 72 participants randomly assigned to two treatment conditions (one focusing on increasing pleasant events (n=23) and the other problem-solving issues of concern (n=19)) compared to two control groups (typical care (n=10) and wait list (n=20)). All depression outcomes favoured the treatment groups to a statistically significant degree. Standardized mean differences indicated a 4- to 5-point net benefit on the Hamilton Depression Rating Scale and a 4-point net benefit on the Cornell Scale for Depression in Dementia. Clinically significant improvement was observed in 50% of participants (in terms of pleasant events) and 68% (in terms of problem-solving), compared to 20% improvement in the two control groups.

Burgener SC, Yang Y, Gilbert R, Marsh-Yant S (2008). The effects of a multimodal intervention on outcomes of persons with early-stage dementia. American Journal of Alzheimer's Disease and Other Dementias.23(4):382-394. doi:10.1177/1533317508317527.

This is a very small RCT of a multi-modal intervention that included group CBT, along with Taiji exercises and support groups for people with early stage AD. Outcomes (including cognitive functioning, physical functioning, depression and self-esteem) were assessed at 20 weeks and after the full 40 weeks of the intervention. At 20 weeks, the treatment group (n = 24) performed better than the control group receiving educational programs (n=19) on mental ability and self-esteem, with gains in balance also being evident.

Logsdon RG, Pike KC, McCurry SM, Hunter P, Maher J, Snyder L, Teri L (2010). Early-stage memory loss support groups: outcomes from a randomized controlled clinical trial. Journal of Gerontolology, Series B: Psychological Sciences & Social Sciences.65(6):691-697. doi:10.1093/geronb/gbq054.

This study comprises an RCT comparing a 9-session structured early-stage dementia support group program (n=96) to a wait-list control group (n=46). MMSE scores for the intervention group was 23.2 (4.7) and for the control group was 24.0 (3.8). The support group program focused on coping with memory problems, daily living, self-esteem, relationship and health, legal and financial concerns. The main outcomes were quality of life, mood, communication, stress, self-efficacy and assessment of memory-related behaviour problems. Intervention participants report significant improvement in quality of life, while the wait-list control group reported decreased quality of life (β=1.74, p<0.001, R^2=0.05, effect size d=0.44). Similar results were found for depressive symptoms.

PART 2: FROM EVIDENCE TO RECOMMENDATIONS

Summary of evidence table

Outcome	Various psychological interventions *(Number of studies, mean difference [95% CI], quality)*
Depression symptoms in those with dementia who have clinically significant depression	5 studies, MD 0.22 lower (0.41 lower to 0.03 lower), LOW quality
Patient quality of life	3 studies, MD 0.37 higher (0.01 lower to 1.75 higher), LOW quality
Activities of daily living	2 studies, SMD 0.13 lower (0.35 lower to 0.09 higher),

	LOW quality
Neuropsychiatric symptoms	2 studies, SMD 0.06 higher (0.16 lower to 0.28 higher), VERY LOW quality
Cognition	4 studies, MD 0.80 lower (1.7 lower to 0.11 higher), VERY LOW quality

[New 2015]

Evidence to recommendation table

Benefits	There is limited evidence that the use of psychological treatments (including cognitive behavioural therapy, interpersonal therapy or counseling techniques) may reduce symptoms of depression and anxiety in those with depression in dementia. However, it is noteworthy that the majority of the participants included in the Orgeta et al. (2014) Cochrane review were not reported to have a clinical diagnosis of depression, but were assessed for depressive symptoms. Effect sizes were consistent between trials using different psychological interventions, but were of small size and marginal clinical significance. Behavioural activation interventions administered with a caregiver may be more effective in relieving depression symptoms among people with dementia; however, this finding comes from only one small RCT.
Harms	None identified.
Summary of the quality of evidence	The quality of evidence is very low to low.

Value and preferences	
In favour	Depression is common among people with dementia and is associated with significant adverse effects, including decrease in quality of life, increased need for institutionalization, greater health care utilization, higher mortality rates and increased caregiver burden. Psychological therapies may be preferred to antidepressant medication, which has been shown to lack efficacy. High levels of treatment adherence were reported in most of the trials included in the Cochrane Review.

Against	Most of the participants of the trials included in the Cochrane Review had mild to moderate dementia. The ability of patients with more severe dementia to access and participate in these therapies must be considered questionable.
Uncertainty or variability?	There is some uncertainty with regards to the value of psychosocial interventions for people with more severe dementia.

Feasibility (including resource use considerations)	Most of the interventions evaluated in the trials that were included in the Cochrane Review were resource intensive, with between 6 and 48 therapeutic sessions (6, 10, 10, 12, 20, 48 sessions) lasting from 30-60 minutes each. Professional specialist psychotherapists working in secondary care settings in high-income countries administered the interventions. These approaches would likely be unfeasible in most low resource settings. They might be adapted as briefer interventions to be administered by suitably trained and supported non-specialists, but such approaches have not been developed or evaluated. Behavioural activation administered by a caregiver would be more feasible in low resource settings; however, the effectiveness of this intervention is supported in only one small RCT.
Uncertainty or variability?	There is major variability with regards to the feasibility of these interventions in LAMICs due to resource constraints.

[New 2015]

Recommendation and remarks

Recommendation

People with dementia and mild to moderate symptoms of depression may be offered psychological interventions (such as cognitive behavioural therapy [CBT], interpersonal therapy [IPT], structured counselling and behavioural activation therapy), in non-specialized health care settings under supervision of a specialist.

Rationale: Depression is common among people with dementia and is associated with significant adverse effects, including decrease in quality of life, increased need for institutionalization, greater health care utilization, higher mortality rates and increased caregiver burden. There is limited low quality evidence that the use of psychological treatments may reduce symptoms of depression in this population. Delivery of these interventions requires adequate training and supervision of non-specialist health care provider.

Remarks

Psychological interventions may not be feasible as a treatment for people with severe dementia and symptoms of depression due to impaired cognitive function.
It is possible to train non-specialist health care workers to provide psychological treatments with the close supervision of a specialist.
None of the primary studies available on psychological interventions were carried out in low- or middle-income countries.
The type of psychosocial intervention offered should be based upon the capacity of health care workers and patient preferences.

Judgements about the strength of a recommendation

Factor	Decision
Quality of the evidence	¡ High ¡ Moderate **X Low** ¡ Very low
Balance of benefits versus harms	**X Benefits clearly outweigh harms** ¡ Benefits and harms are balanced ¡ Potential harms clearly outweigh potential benefits
Values and preferences	¡ No major variability **X Major variability**
Resource use	¡ Less resource-intensive **X More resource-intensive**
Strength	**CONDITIONAL**

OTHER REFERENCES

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