

[Physical activity](#)

Q 6: Is advice on physical activity better (more effective than/as safe as) than treatment as usual in adults with depressive episode/disorder with inactive lifestyles?

Background

The relationship between lack of regular physical activity and mental disorders has been subject of some documentation. In the United States National Comorbidity Survey, respondents were asked the question “How often do you get physical exercise, either on your job or in a recreational activity?”. In total, 60% of respondents identified themselves as getting regular physical exercise. Those who reported regular exercise were less likely to meet criteria in the previous year for diagnosis of DSM-III-R major depression (8% vs. 13%) and a similar pattern of findings were reported for a range of anxiety disorders. These rates remained significant when adjusted for demographic variables and comorbid physical and mental disorders (Goodwin, 2003).

Reviews exist on the short-term moderate effectiveness of advice by health staff to increase physical activity. The question is whether such advice leads to improvement of depressive symptoms and associated functioning.

Population/Intervention(s)/Comparison/Outcome(s) (PICO)

- Population:** adults with depressive episode/disorder
- Interventions:** advice on physical activity
- Comparison:** treatment as usual
- Outcomes:** symptom severity post intervention
functioning post intervention
symptom severity at 6 to 12 months follow-up
adverse effects (including tolerability)

[Physical activity](#)

List of the systematic reviews identified by the search process

INCLUDED IN GRADE TABLES OR FOOTNOTES

Hillsdon M et al (2002). Advising people to take more exercise is ineffective: a randomized controlled trial of physical activity promotion in primary care. *International Journal of Epidemiology*, 31:808-15.

Hillsdon M et al (2005). The effectiveness of public health interventions for increasing physical activity among adults: a review of the reviews. *NHS, Health Development Agency*, url: http://www.nice.org.uk/nicemedia/documents/physical_activity_adults_ebsummary.pdf

Mead et al(2008). Exercise for depression. *Cochrane Database of Systematic Review*, (4):CD004366.

EXCLUDED FROM GRADE TABLES AND FOOTNOTES

Carlson DL (1991). The effects of exercise on depression: a review and meta-regression analysis. Milwaukee: University of Wisconsin.
(reason for exclusion: outdated)

Craft LL, Landers DM (1998). The effects of exercise on clinical depression and depression resulting from mental illness: A meta-regression analysis. *Journal of Sport & Exercise Psychology*, 20:339–57.
(reason for exclusion: relatively outdated)

Lawlor DA, Hopker SW (2001). The effectiveness of exercise as an intervention in the management of depression: Systematic review and meta-regression analysis of randomized controlled trials. *British Medical Journal*, 322:763–67.
(reason for exclusion: relatively outdated)

NICE (2004). Depression: Management of depression in primary and secondary care. *National Clinical Practice Guideline Number 23*. The British Psychological Society & The Royal College of Psychiatrists.
(reason for exclusion: relatively outdated)

North TC, McCullagh P, Tran ZV (1990). Effect of exercise on depression. *Exercise & Sport Sciences Reviews*, 18:379–415.
(reason for exclusion: outdated)

Stathopoulou G et al (2006). Exercise interventions for mental health: a quantitative and qualitative review. *Clinical Psychology: Science and Practice*,13:179–93.

Physical activity

(reason for exclusion: this meta analysis only included studies published in peer-reviewed journals)

Sjosten N, Kivela SL (2006). The effects of physical exercise on depressive symptoms among the aged: a systematic review. *International Journal of Geriatric Psychiatry*, 21:410–8.

(reason for exclusion: older people only)

PICO Table

Serial no.	Intervention/Comparison	Outcomes	Systematic reviews used for GRADE	Explanation
1	Advice on physical activity/ usual care	symptom severity post intervention; functioning post intervention; symptom severity at 6 to 12 months follow-up; adverse effects (including tolerability)	Mead et al (2008)	The Mead et al (2008) review is a recent Cochrane review that includes both peer-reviewed as unpublished studies.

Narrative description of the studies that went into the analysis

The **Mead et al (2008)** Cochrane review covers 25 trials, which they describe as follows: Twenty-one trials recruited participants from non-clinical populations with most involving recruitment of participants through the media. Six trials recruited participants from clinical populations (i.e. hospital inpatients or out-patients). Twenty-one trials provided aerobic exercise, of which 13 trials provided running. Three provided treadmill walking, two provided walking, one provided aerobic training with an instructor, one provided aerobic dance and one which provided cycling on a stationary bike. Two provided mixed exercise i.e. endurance, muscle strengthening and stretching, one provided Tai-Chi, two provided resistance training, one provided Qigong exercises and one provided 'individually tailored' exercises. Two provided resistance training alone. Of the 13 trials with two arms, exercise was compared with waitlist or usual care in three trials, exercise was compared with a placebo intervention (e.g. social activity) in six trials, exercise was compared with cognitive-behavioural therapy (CBT) in two trials, two trials compared CBT plus exercise versus CBT alone and one trial compared exercise with bright light therapy. Of the 11 trials with three arms, one trial compared exercise versus exercise plus sertraline versus sertraline, three compared exercise versus wait list versus a placebo intervention (e.g. social activity), two compared exercise versus usual care versus CBT, one compared exercise versus CBT versus both exercise and CBT, one compared exercise versus low-intensity-CBT versus high-intensity-CBT, one compared exercise versus a placebo versus CBT, one compared high intensity resistance training versus low intensity resistance training versus usual care and one compared running versus weight-lifting versus wait-list. Of the 25 trials, 14 were from US , 1 from Canada , 3 from the UK, 1 from Australia, 2 from Hong Kong, 1 from Norway , 1 from Germany, 1 from Russia and 1 from Thailand.

Physical activity

In all studies the author of the trial described the participants as having depression (by any method of diagnosis and with any severity of depression). The effects of exercise on depressive symptoms in participants with emotional distress (but not fulfilling a diagnosis of depression) or those who are healthy were not included in this review. The review describes neither baseline severity of depression nor comorbidity with anxiety symptoms.

GRADE Tables

Table 1

Author(s) Van Ommeren. Mark, Barbui, Corrado

Date: 2009-06-04

Question: Should advice on physical activity vs usual care be used for depressive episode/disorder?

Settings:

Bibliography: Mead GE et al (2008). Exercise for depression. *Cochrane Database of Systematic Reviews*, (3):CD004366.

Quality assessment							Summary of findings				Quality	Importance
							No of patients		Effect			
No of studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	advice on physical activity	usual care	Relative (95% CI)	Absolute		
depression symptom level post intervention (Better indicated by lower values)												
23 ¹	randomized trials	very serious ²	very serious ³	very serious ⁴	no serious imprecision	none ⁵	476 ¹	431 ¹	-	SMD 0.82 lower (1.12 to 0.51 lower) ⁶	VERY LOW	CRITICAL
depression symptom level (+6 months follow-up (follow-up 9-26 months; Better indicated by lower values)												
5	randomized trials	serious ⁷	no serious inconsistency ⁸	very serious ⁴	no serious imprecision	none ⁹	108	110	-	SMD 0.44 lower (0.71 to 0.18 lower)	VERY LOW	IMPORTANT
functioning post intervention (Better indicated by lower values)												

Physical activity

0	no evidence available					none	0	0	-	MD 0 higher (0 to 0 higher)		IMPORTANT
adverse events												
5 ¹⁰	randomized trials					none	0/0 (0%)	0/0 (0%)	RR 0 (0 to 0)	0 fewer per 1000 (from 0 fewer to 0 fewer)		IMPORTANT
								0%		0 fewer per 1000 (from 0 fewer to 0 fewer)		

¹ Analysis 1.1, p.51 Mead et al (2008).

² Drop out was above 30% in 6 studies (see Table 1 page 11). Mead et al (2008) explicitly aimed to determine the influence of study quality, in particular allocation concealment, blinding and intention to treat analyses on effect sizes. When only those trials with adequate allocation concealment, intention to treat analysis and blinded outcome assessors were included, the effect size was moderate and not statistically significant (N = 3, n = 226; SMD -0.42 (95% CI -0.88, 0.03).

³ I-squared is 76% .

⁴ The question is about health workers' advising physical activity, while the research is on participants randomized to a physical activity treatment condition. Advising doctors to instruct patients on undertaking more physical activity may not necessarily change behaviour (Hillsdon et al, 2002). A recent review of eight reviews which examined the effectiveness of physical activity interventions in primary healthcare settings found that brief advice from a health professional, supported by written materials is likely to be effective in producing modest effects on physical activity for up to three months (Hillsdon et al 2005).

⁵ Visual inspection of the Funnel plot does not suggest strong asymmetry and Beggs test was not statistically significant. (see last paragraph on page 9 and plot on page 10, Mead et al (2008)).

⁶ In contrast to the significant effect size across the 23 studies, the effect size is moderate and not significant for the 3 studies with the strongest methodological features (see analysis 6.6).

⁷ Drop out is above 30% for 1 of 5 studies, i.e the Klein study (see Analysis 1.2 Table 1 pages 11-12 Mead et al (2008)).

⁸ I-squared is 0% (Analysis 1.2 Mead et al (2008)).

⁹ There are too few studies to detect any study bias.

¹⁰ Meta-analyses was not performed on adverse events/drop-outs. Yet, four of five trials reported a lack of difference in adverse events between groups (page8 Mead et al (2008)).

Reference List

Carlson DL (1991). The effects of exercise on depression: a review and meta-regression analysis. Milwaukee: University of Wisconsin.

Craft LL, Landers DM (1998). The effects of exercise on clinical depression and depression resulting from mental illness: A meta-regression analysis. *Journal of Sport & Exercise Psychology*, 20:339–57.

Goodwin RD (2003). Association between physical activity and mental disorders among adults in the United States. *Preventive Medicine*, 36:698-703.

Hillsdon M et al (2002). Advising people to take more exercise is ineffective: a randomized controlled trial of physical activity promotion in primary care. *International Journal of Epidemiology*, 31:808-15.

Physical activity

Hillsdon M et al (2005). The effectiveness of public health interventions for increasing physical activity among adults: a review of the reviews. *NHS, Health Development Agency*, url: http://www.nice.org.uk/nicemedia/documents/physical_activity_adults_ebsummary.pdf

Lawlor DA, Hopker SW (2001). The effectiveness of exercise as an intervention in the management of depression: Systematic review and meta-regression analysis of randomized controlled trials. *British Medical Journal*, 322:763–67.

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NICE (2004). Depression: Management of depression in primary and secondary care. *National Clinical Practice Guideline Number 23*. The British Psychological Society & The Royal College of Psychiatrists.

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Stathopoulou G et al (2006). Exercise interventions for mental health: a quantitative and qualitative review. *Clinical Psychology: Science and Practice*, 13:179–93.

Sjosten N, Kivela SL (2006). The effects of physical exercise on depressive symptoms among the aged: a systematic review. *International Journal of Geriatric Psychiatry*, 21:410–8.

From evidence to recommendations

Factor	Explanation
Narrative summary of the evidence base	In individuals with depressive episode/disorder there is very low quality evidence favoring advice on physical activity over treatment as usual in reducing depression symptoms post treatment (N = 23; n = 907; SMD = -0.82; 95% CI, -1.12 to -0.51) and at 9-26 months follow-up (N = 5; n = 218; SMD = -0.44; 95% CI, -0.71 to -0.18). When only those trials with adequate allocation concealment, intention to treat analysis and blinded outcome assessors were included, the effect size for post intervention symptom improvement was moderate and not

[Physical activity](#)

	statistically significant (N = 3, n = 226; SMD -0.42 (95% CI -0.88, 0.03).
Summary of the quality of evidence	<p>The quality of the evidence was very low for symptom improvement.</p> <p>The outcomes functioning and adverse effects were not meta-analyzed</p>
Balance of benefits versus harms	The reviewed studies suggest a large effect but better studies found a moderate effect that was not statistically significant. Data on adverse effects were not meta-analyzed but 4 of 5 trials that reported adverse effects found no statistical differences. The overall balance appears favourable for physical activity.
Define the values and preferences including any variability and human rights issues as relevant to application in nonspecialized settings in low and middle income countries.	<p>The Global Strategy for Diet and Physical Activity for Health - requested by WHO's member states in 2002 and adopted at the World Health Assembly in May 2004 - describes how community and individual strategies to increase participation in physical activity can help in the fight to reduce the burden of chronic disease. The strategy document suggests roles for WHO member states, United Nations agencies, civil society and the private sector, to help to reduce the occurrence of non-communicable diseases by increasing levels of physical activity and improving diets for both children and adults.</p> <p>Of note, physical activity may involve behavioural activation and may lead to feelings of relaxation - which are interventions covered in separate scoping documents. Possibly any effects of physical activity is related to the amount of behavioural activation involved.</p>
Define the costs and resource use and any other relevant feasibility issues as relevant to application in nonspecialized settings in low and middle income countries	<p>The majority of studies in the Mead et al(2008) are from high income countries and involve aerobic exercise. The generalizability of these findings to low income settings is unknown. It is not known that what extent health worker advice to do exercise to improve depression will be accepted by service users in low income settings, which may vary.</p> <p>There is cultural variability in perception of the value of physical activity, which may lead to variability in uptake and successful implementation on this intervention in different settings. It is not known that what extent health worker advice to do exercise to improve depression will be accepted by service users in low income settings.</p> <p>The intervention is unlikely appropriate for those engaged in physical labour.</p>
Final recommendation	

Physical activity

Advice on physical activity should be encouraged as part of treatment for adults with depressive episode/disorder with inactive lifestyles. In moderate and severe depression, this intervention should be considered as adjunct to antidepressants or brief structured psychological treatments.
Strength of Recommendation: STANDARD

Limitations

The comparative effectiveness of physical activity versus other psychological or pharmacological interventions was not assessed.

Update of the literature search – June 2012

In June 2012 the literature search for this scoping question was updated. The following systematic reviews were found to be relevant without changing the recommendation:

NICE Clinical Guidelines. CG90. Depression in adults: The treatment and management of depression in adults. Appendix 19: Clinical evidence forest plots. National Institute for Health and Clinical Excellence, 2010.

Herring MP, Puetz TW, O'Connor PJ, Dishman RK. Effect of Exercise Training on Depressive Symptoms Among Patients With a Chronic Illness Arch Intern Med. 2012;172(2):101-111