REVIEW

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Imboden C[1], Claussen MC[1,2,3], Seifritz E[2], Gerber M[4]

Physical Activity for the Treatment and Prevention of Depression: A Rapid Review of Meta-Analyses

Körperliche Aktivität für die Behandlung und Prävention der Depression: Übersichtsarbeit von Meta-Analysen

1. PRIVATE CLINIC WYSS, *Münchenbuchsee, Switzerland*
2. UNIVERSITY OF ZURICH, *Department of Psychiatry, Psychotherapy and Psychosomatics, Psychiatric University Hospital Zurich, Zurich, Switzerland*
3. PSYCHIATRIC SERVICES GRISONS, *Chur, Switzerland*
4. UNIVERSITY OF BASEL, *Department of Sport, Exercise and Health, Basel, Switzerland*

Summary

› **Aim:** We conducted an umbrella review of 55 meta-analyses to summarize current evidence on the effects of exercise on depression.

› **Results:** Aerobic, resistance or combined exercise for several weeks as well as mind-body exercise has shown to yield significant moderate effects on depression severity in adult patients, including the elderly. The effect diminishes when only high-quality studies are analyzed but reaches similar magnitude of other efficacious treatments. Additionally, exercise showed positive effects on sleep, cardiorespiratory fitness and quality of life in depressed patients. In children and adolescents and during the peripartum period, exercise interventions have been found have small-to-moderate effects, but studies varied in methodology and methodical quality could be improved (heterogeneous samples, blinding). Regular physical activity has been shown to have a protective effect on incident depression in adults, reducing odds by 17 to 21%. In children and adolescents, the effect tends to be smaller. Across 15 meta-analyses in samples with physical diseases, exercise-regimes have been shown to have positive effects on depressive symptoms in chronic conditions (such as pain, obesity or cardiovascular disease), cancer survivors, and in post-stroke, neurological and cardiovascular conditions, as well as in diabetes, chronic kidney disease, arthritis and HIV.

› **Discussion:** Exercise and physical activity have a wide range of benefits for depression and depressive symptoms in at-risk populations. Further research is needed to find optimal dose and duration of exercise-treatment and ways to sustainably increase physical activity in psychiatric populations and patients with chronic diseases.

KEY WORDS:
Exercise, Aerobic, Resistance, Depressive Symptoms, At-Risk Population

Zusammenfassung

› **Problemstellung:** Eine Übersicht von 55 Meta-Analysen soll die aktuelle Evidenz der Effekte von Sport auf die Depression untersuchen.

› **Resultate:** Aerobes sowie Krafttraining oder Kombinationen inklusive achtsamkeitsorientierte Sportinterventionen zeigten signifikante moderate Effekte auf depressive Symptome bei Erwachsenen und älteren Patienten. Dieser wird kleiner, wenn nur Studien mit hoher Qualität analysiert werden, bleibt aber ähnlich effektiv wie andere wirksame Interventionen. Zusätzliche Effekte auf den Schlaf, die Lebensqualität sowie kardiorespiratorische Fitness bei depressiven Patienten konnten bestätigt werden. Bei Kindern und Jugendlichen sowie während dem Peripartum erreicht körperliche Aktivität kleine bis moderate signifikante Effekte auf depressive Symptome; allerdings sind die untersuchten Interventionen heterogener und die Methodik könnte verbessert werden (z.B. unterschiedliche Populationen, mangelnde Verblindung). Regelmässige körperliche Aktivität zeigte eine Odds-Reduktion von 17 bis 21% bezüglich des Risikos, im späteren Verlauf eine Depression zu entwickeln, mit einem kleineren Effekt bei Kindern und Jugendlichen. In 15 Meta-Analysen in Populationen mit körperlichen Erkrankungen hat regelmässiges Training positive Effekte auf depressive Symptome bei allgemeinen chronischen Erkrankungen (wie Schmerzen, Übergewicht oder Kardiovaskuläre Erkrankungen), Krebs-Überlebenden, post-Stroke, neurologischen und kardiovaskulären Erkrankungen, Diabetes, chronischer Niereninsuffizienz, Arthritis und HIV-positiven Erwachsenen zeigen können.

› **Diskussion:** Sport und körperlicher Aktivität haben breite positive Wirkungen auf die Depression und depressive Symptome in Risikopopulationen. Es besteht ein Bedarf an weiteren Studien, um optimale Dosen und Dauer von Sportinterventionen zu klären und Methoden zu entwickeln, körperliche Aktivität in psychiatrischen Populationen und Menschen mit chronischen Erkrankungen nachhaltig zu fördern.

SCHLÜSSELWÖRTER:
Sport, aerobes Training, Krafttraining, depressive Symptome, Risikopopulationen

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CORRESPONDING ADDRESS:
Dr. med. Christian Imboden
Medical Director, Private Clinic Wyss
Fellenbergstrasse 34
3053 Muenchenbuchsee, Switzerland
✉: christian.imboden@pkwyss.ch

Introduction

Depression is one of the leading causes for disability worldwide (51) and adds up to the highest economic burden of all brain disorders including psychiatric disorders in Switzerland (49). With current treatment-options, there is still a high rate of non-remitters (74), and new pharmacological targets outside of the monoaminergic system are scarce. Additionally, patients with somatic diseases are at increased risk for depressive symptoms worsening psychosocial functioning and quality of life (50). Therefore, alternative treatments are needed to reduce the burden of depression. Exercise treatment defined as structured training regimes over several weeks may be such an option with a vast array of additional health benefits (6). Meanwhile, a considerable body of evidence has arisen, supporting the prescription of physical activity (PA) in patients with mental disorders, especially major depressive disorder (MDD).

Methods and Objectives

With this umbrella review, we aim at summarizing the current evidence on the effects of exercise on depression, by reviewing previously published meta-analyses. We focus on (i) regular exercise-regimes for several weeks as treatment for depression and special domains of depression including special populations such as children and adolescents, older adults, and women during the peripartum period. (ii) Studies on the preventive effect of exercise on incident depression were also included in this review. Additionally, we (iii) summarize the effects of exercise on depressive symptoms in various physical diseases associated with high rates of depression.

Meta-analyses were identified in PubMed by combining the search-terms "meta-analysis" AND "exercise" AND "depression" (in all fields). During the first round of the selection-process, titles were screened for eligibility (meta-analyses of studies on effects of exercise in samples of depressed people or exercise to prospectively prevent depression), in a second round, we read the abstracts of the provided articles to decide if the paper should be included in this review. Meta-analyses were included if they examined a regime of exercise for several weeks in populations with (i) a diagnosis of depression by clinical interview or depression-scores above cut-off in widely used symptom-scales; (ii) examined studies providing quantitative measures of depressive symptoms in at-risk populations for depression including various physical diseases; (iii) examined the preventive effect of exercise in the general population or at-risk populations. All included studies are summarized in Table 1 (see supplemental material online) to 5 providing an overview of the included samples, the methods of the analyzed studies and the pooled main effects on depression.

Our initial search yielded 568 publications. Screening of the titles resulted in 76 publications eligible to be included in this review. After reading the abstracts, we excluded 21 papers resulting in 55 meta-analyses included in this review.

Results

Exercise as a Treatment for Depression

Treatment of Depression and Depressive Symptoms in Adult Populations

Aerobic and/or Resistance Exercise

We identified 11 meta-analyses of studies evaluating the effect of various regimes of exercise treatment for depression without mind-body interventions such as yoga. Most publications focused on trials assessing either aerobic or resistance exercise or a combination of the two (20, 40, 44, 46, 47, 59, 63, 67). All included studies evaluated supervised exercise on several days per week for a range of weeks in patients with clinical depression or depressive symptoms versus heterogenous control groups. In most studies, controls were not allowed to exercise (non-active or passive controls). Effects were significant in most studies, and the effect sizes were of moderate magnitude. In comparison to active treatments such as antidepressants or psychotherapy, exercise was not superior but reached comparable effects (46, 47, 59). Three meta-analyses performed a sub-analysis of studies meeting high methodological standards (adequately concealed random allocation, blinded outcome assessment, intention-to-treat-analysis) and reported smaller effects, which did not reach statistical significance (20, 40, 46). However, those studies often included efficacious control-conditions such as antidepressant medication, and therefore, support the clinical efficacy of exercise. Rethorst et al. (59) found larger effects in patients with clinical depression than in non-clinical populations, and Schuch et al. (63) reported larger effects in patients with diagnosed major depressive disorder (MDD) compared to non-clinical samples or dysthymia, and if participants engaged in at least moderate-to-vigorous intensity exercise programs.

One meta-analysis only included studies evaluating the effects of aerobic exercise versus inactive controls in clinical population with diagnosis of MDD (k=11). This meta-analysis found a moderate effect in favor of aerobic exercise, which remained stable if only studies with low risk of bias (PEDro score≥6) were included (53). The meta-analysis of Nebiker et al. (56) compared studies on the effects of aerobic/endurance exercise versus resistance/neuromuscular training separately in populations with a diagnosis of depression and found significant effects for both types with larger effects for neuromuscular training. Effects stayed significant if only studies with low risk of bias were included (PEDro score≥6). One recent meta-analysis (14) focused purely on k=4 trials evaluating the effects of resistance training with minimal or no warm-up versus controls without additional PA and reported non-significant effects. However, they found a very high level of heterogeneity in the included studies and therefore advised to interpret the results with caution. An overview of these meta-analyses can be found in Table 1 (see supplemental material online).

Mind-Body Exercise for Depression

Mind-body exercise is combining PA with elements of mindfulness. We identified 4 meta-analyses of studies including yoga, qigong and tai chi interventions. Mind-body exercise was applied over a heterogenous duration from 1 up to 10 weeks. All included meta-analyses found positive significant effects on depressive symptoms. Cramer et al. (22) analyzed k=12 studies in samples of depressed patients comparing yoga versus treatment as usual (TAU), relaxation and aerobic exercise and found yoga to be significantly superior in alleviating depressive symptoms versus all control interventions with moderate-to-large effect sizes. However, they concluded that most studies were of low methodological quality. Guo and coworkers (34) performed a meta-analysis of studies evaluating the effects of qigong in patients with MDD and found a moderate effect in favor of qigong. Another meta-analysis evaluated the effects of yoga on depressive symptoms in samples with various mental disorders and reported a moderate effect in favor of yoga (10). Seshadri et al. (66) restricted their meta-analysis to studies with outpatients with MDD and analyzed studies on the effects of exercise (aerobic and resistance), tai chi and yoga. They found a significant overall effect of moderate-to-large size for exercise and yoga, but not for tai chi. If only studies with the lowest risk of bias were included, the effect diminished to a small-to-moderate effect, but still was statistically significant. Details of the studies are shown in Table 1 (see supplemental material online).

Effects on Various Symptoms Associated with Depression

Studies reporting the effects of regular exercise on cardiorespiratory fitness (CRF) in samples with a clinical diagnosis of MDD or depressive symptoms above cut-off in clinical scales were analyzed by Stubbs et al. (69). In their meta-analysis of k=7 studies, they found a significant increase of CRF of moderate effect size (Hedges' g=0.64). The effect persisted if only high-quality studies were analyzed, but the authors did not provide the criteria for "high-quality studies". If restricted to patients with MDD, the effect was slightly smaller (g=0.41), but still significant. Schuch and coworkers (64) performed a meta-analysis of k=6 exercise-studies reporting measures of quality of life (QoL) ›

in depressed patients. Overall QoL was found to increase significantly (SMD [standardized mean difference]=0.39) as were physical (SMD=0.53) and psychological (SMD=0.54) domains of QoL. Dropout rates of exercise interventions for depression were analyzed by Stubbs et al. (71). In their meta-analysis of k=40 studies (N=1720), they found an overall dropout rate of 18%. The rate tended to be higher in control groups and if patients suffered from higher depressive symptoms at baseline. If exercise-treatment was supervised by trained specialists, dropout rate was significantly lower. Sun et al. (72) conducted a meta-analysis on the effects of exercise on cognitive symptoms across various cognitive domains in patients with MDD. They included k=9 studies (N=642) and found no evidence for a beneficial effect of exercise on global cognition nor any of the included sub-domains. However, in subgroup analyses, they found significant small effects on cognition by low intensity exercise (SMD=0.34) and mind-body exercise (SMD=0.33). Brupbacher et al. (13) conducted a network meta-analysis of studies assessing sleep quality across exercise trials in patients with unipolar depression. They found moderate-to-large effects for vigorous aerobic exercise, mind-body exercise and resistance training (with larger effects for vigorous resistance training), but not for moderate aerobic exercise. Two meta-analyses evaluated the effect of regular exercise on resting levels of brain-derived neurotrophic factor (BDNF) in patients with MDD. Both reported no significant effects across k=5 (45) and k=6 (24) studies, respectively. Beserra at al. (7) conducted a meta-analysis on the effects of exercise on cortisol levels and found a moderate and borderline-significant effect on the reduction of cortisol levels (SMD=-0.65). However, the assessment of cortisol was heterogenous across included studies. A detailed overview of studies reported in this section is provided in Table 2 (see supplemental material online).

Effects on Depression or Depressive Symptoms in Special Populations

Children and Adolescents

Three of the four meta-analyses on the effect of exercise interventions in children and adolescents included healthy volunteers or at-risk populations for depression (3, 11, 16). Interventions were heterogenous and included educational lessons on benefits of PA as an addition in one meta-analysis (11). Most meta-analyses found significant small-to-moderate effects of exercise on depressive symptoms. Carter et al. (16) conducted a sub-analysis of studies with clinical samples only and reported a significant effect of exercise on depressive symptoms (SMD=-0.43). A further sub-analysis of high-quality studies only (score ≥5 on Delphi list) found non-significant effects. Bailey et al. (3) restricted their meta-analysis to samples of adolescents (12-25 years) and reported a significant large effect (SMD=-0.82) that was slightly smaller if restricted to clinical samples (SMD=-0.72). Only one meta-analysis was restricted to participants with depression scores above cut-off or clinical diagnosis of depression (2). They reported a small-to-moderate effect of exercise interventions in a small number of studies (k=4, SMD=-0.59). Two authors concluded that the overall quality of evidence should considered as low to very low (2, 3). An overview of the presented meta-analyses can be found in Table 3 (see supplemental material online).

Peripartum Period

We identified 6 meta-analyses on the effects of exercise during the peripartum period. Two papers analyzed the effect of exercise on depressive symptoms in samples of healthy pregnant women (23, 54). Davenport et al. (23) included k=13 studies on exercise interventions alone or in combination with co-interventions (educational, counselling, diet) during pregnancy and found a significant small effect on antenatal depressive symptoms with a 67% reduction of odds for depression. Nakamura et al. (54) included (i) studies with exercise interventions during pregnancy and the postpartum period and (ii) observational studies measuring PA during pregnancy. For (i) intervention-studies, they reported a significant small-to-moderate effect on postpartum depressive symptoms that was even stronger in studies with moderate-to-high exercise intensities (SMD=-0.70). In (ii) observational studies, PA failed to show an effect on depressive symptoms. Therefore, an active approach to increase PA might be beneficial.

Of the four other papers, three included studies in healthy pregnant and/or postpartum women or a mix of healthy participants and such with a diagnosis of depression (15, 52, 57). Generally, significant small-to-moderate effects of exercise interventions on postpartum depressive symptoms could be found that were larger, if restricted to samples with postpartum depression or depressive symptoms (52, 57). If restricted to studies with low risk of bias, the effect tended to be smaller but still significant (15). Pritchett et al. (58) restricted their analysis to trials in depressed postpartum women and reported a significant small-to-moderate effect on depressive symptoms that was even larger in trials with exercise-only interventions compared to exercise with co-interventions such as counselling and educational programs.

Older Adults

Three meta-analyses were found on the effects of exercise interventions in populations aged ≥60 years with depression or measures of depressive symptoms. In a meta-analysis restricted to depressed patients, Bridle et al. (9) reported a significant small effect of mixed exercise interventions (endurance/strength). Rhyner and Watts (60) found a significant small-to-moderate effect on depressive symptoms in a much broader sample of k=41 studies including non-depressed patients and mind-body interventions. In a sub-analysis, they found the effects to be larger if restricted to samples with clinical diagnosis of depression. Klil-Drori et al. (42) performed an analysis of k=9 studies restricted to aerobic or resistance interventions that lasted at least 8 weeks in samples of adults ≥60 years and a depression scale as primary outcome (no diagnosis required). They reported a significant moderate effect on depressive symptoms and found high risk of bias in k=5 studies.

Finally, Leng et al. (48) found significant small positive effects of exercise interventions on depressive symptoms and QoL in patients with a diagnosis of dementia or mild cognitive impairment (MCI).

Effects of Exercise on Incidence of Depression

Two meta-analyses were restricted to prospective cohort-studies on the protective effect of self-reported PA on incidence depression and found a comparable odds reduction of 17 to 21% (25, 62). Schuch and coworkers (62) restricted their meta-analysis to k=49 studies with a follow-up of at least 1 year and included populations across all age groups. The effect tended to be higher in adults (22% odds-reduction) and elderly (21% odds-reduction) compared to children and adolescents (10% odds-reduction). A broader sample of studies (k=111) was considered by Dishman et al. (25). They reported higher effects on incidence depression if exercise was of at least moderate intensity or met public health recommendations.

Korczak et al. (43) analyzed k=50 studies restricted to samples of children and adolescents. However, they included both cross-sectional and longitudinal studies, which complicates

Table 4

Meta-analyses on the effects of physical activity on incidence of depression or depressive symptoms (prevention). r=Correlation coefficient; OR=Odds ratio; Bold=Significant effects (p<0.05).

AUTHORS, YEAR	DESIGNS OF INCLUDED STUDIES	MEASUREMENT OF PHYSICAL ACTIVITY	MEASUREMENT OF DEPRESSIVE SYMPTOMS	NUMBER OF STUDIES (K)	NUMBER OF PARTICIPANTS (N)	EFFECTS (95% CI)
Korczak et al. (2017)	Cross-sectional (k=36) and longitudinal (k=14) studies in children and adolescents (8-19 years)	Mostly self-report: frequency only (k=15), intensity (k=7), frequency and intensity (k=27). k=1 study with accelerometer data	Depressive symptoms: Interview (k=4), self-report questionnaires (k=46)	50	89,894	**r=-0.17 (-0.23, -0.10)** **Cross-sectional only: r=-0.17 (-0.23, -0.10)** **Longitudinal only: r=-0.07 (-0.10, -0.04)**
Schuch et al. (2018)	Prospective cohort designs ≥1 year, across all ages with absence of depression / depressive symptoms at baseline. Average follow-up: 7.4 years	Mostly self report, k=1 study with accelerometer data	Incident depression: Diagnostic interview, cutoff in depression-scale, physician diagnosis	49	266,939	**OR=0.83 (0.79, 0.88)** **Youths: OR=0.90 (0.83, 0.98)** **Adults: OR=0.78 (0.70, 0.87)** **Elderly: OR=0.79 (0.72, 0.86)** Moderate to high methodological quality of included studies.
Dishman et al. (2021)	Prospective cohort designs in adults without depression / depressive symptoms at baseline	Self-report	(i) Incident depression (diagnostic interview, cutoff in depression-scale, physician diagnosis. (ii) increased subclinical depressive symptoms in validated questionnaire	111	>3 million	**OR=0.79 (0.75, 0.82)** Similar results for diagnosis of depression & subclinical symptoms. Lower odds if exercise was moderate to vigorous or met public health recommendations.

conclusion regarding the direction of the effects. In their meta-analysis, they found a small but significant effect of PA on depressive symptoms (r=-0.17) that was higher in cross-sectional studies than in longitudinal. An overview of the meta-analyses presented in this section can be found in Table 4.

Effects of Exercise on Depresssive Symptoms in Patients with Physical Diseases

We identified 15 meta-analyses on the effect of regular exercise in groups of patients with various physical diseases. All of these meta-analyses yielded positive results in favor of exercise-treatment as described in detail in Table 5 (see supplemental material online). Small-to-moderate effects were found in samples of adults with a variety of chronic diseases if compared to non-active controls (5, 36). Small-to-moderate positive effects were reported in two meta-analyses of samples of cancer survivors (12, 21), adults after a stroke (26), and patients with various neurological disorders (1) or multiple sclerosis alone (27). Across cardiovascular disorders, effects of exercise interventions tend to be of moderate-to-large magnitude, including exercise-based rehabilitation in samples of acute myocardial infarction (75) and regular exercise for patients with heart failure (61, 73). However, the meta-analysis in acute myocardial infarction included only k=2 non-RCT trials (75). In samples of adults and adolescents with diabetes (55), exercise reduced depressive symptoms with a moderate effect and lead to a mean reduction of 2.9 points on the Beck Depression Inventory (BDI). Even larger effects were reported in meta-analyses on the effects of exercise in chronic kidney disease in hemodialysis (28, 68); Ferreira et al. (28) found an effect of a mean difference of -6.95 points on the BDI if exercise was compared to non-active controls. Kelley et al. (41) reported a moderate effect of exercise in patients with arthritis. Finally, exercise treatment has shown to yield large positive effects on depressive symptoms in adults living with human immunodeficiency virus (HIV) (35).

Discussion

In this umbrella review, we found a solid body of evidence supporting an antidepressant effect of exercise-treatment including mind-body exercise in adult patients including the elderly with depression. Although effects are found to be smaller and partly non-significant in high-quality studies (20, 40, 44, 46), this still supports the use of exercise as treatment option in depression since most high-quality studies included efficacious treatments as control conditions. Additionally, the recent meta-analysis by Morres et al. (53) found exercise to have significant moderate effects in studies with low risk of bias. Several of the studies considered in the meta-analyses have included patients that were concomitantly treated with antidepressants and/or psychotherapy. However, possible interaction effects of exercise with standard treatment have not been reported and might be an area of interest for future analyses. Exercise has also shown to have beneficial effects on sleep quality, CRF and QoL in depressed populations. However, effects on cognitive impairment caused by depression might be questionable and might be restricted to low-intensity and mind-body exercise. This stands in contrast to findings in patients with schizophrenia where high-intensity exercise tends to have larger effects on cognitive symptoms (29). Effects on BDNF or the stress-axis in depressed populations are not supported by the current body of evidence. However, the studies on cortisol vary in methodology, making it difficult to interpret the results. Further studies should include dynamic tests of the stress-axis such as the cortisol awakening reaction (CAR) or a diurnal slope. However, currently available results are conflicting (30, 38).

Further research should focus on possible mediating factors linking exercise with the amelioration of depressive symptoms. Possible targets might be CRF and sleep. Indeed, CRF as measured by VO_2max has shown to be significantly associated with improvement of depressive symptoms in secondary ›

analyses (33, 38). Regarding sleep, there is evidence that improvement of depression related insomnia by itself leads to strong antidepressant effects (8). However, to our knowledge, there is no published data supporting a mediating role of sleep concerning the antidepressant effects of exercise.

In samples of children and adolescents, beneficial effects of exercise in depression is supported by sound empirical evidence. However, since the overall quality of evidence is considered as rather low, further high-quality trials in clinical samples are needed. The same applies for the peripartum period: most studies included additional elements rendering it difficult to isolate the effect of exercise by itself. Nonetheless, an active approach to increase PA in depressed or at-risk pregnant women might be an advisable strategy. According to the evidence from meta-analyses, in patients suffering from chronic physical conditions, especially cardiovascular disease, aiming at reaching public health recommendations concerning PA seems advisable and might help to reduce depressive symptoms and hence increase wellbeing.

Since comorbid psychiatric disorders such as anxiety disorders or substance use disorders increase the risk of treatment resistant depression (17), it might be of interest to control for comorbid disorders in future trials on exercise for depression.

There is an ongoing debate on the optimal dose and duration of exercise interventions. For the treatment of depression, the guidance paper of the European Psychiatric Association (EPA) (70) recommends interventions of 2 to 3 supervised exercise sessions per week of 45-60 minutes duration and of moderate intensity with aerobic or a combination of aerobic and resistance training for several weeks. Studies conducted in samples of moderately to severely depressed inpatients have shown that exercise treatment is also feasible in severely depressed patients if they receive proper support and exercise under supervised conditions (39, 65).

Regular PA has shown to reduce odds for depression by >20%. However, there are findings suggesting that this applies only to PA during leisure time and not work-related or household PA (4). Since predisposition for depression or preexisting depressive symptoms might influence PA behaviors, questions arise concerning the directionality of this association. Shedding light onto this question, a recent genetics-study robustly supported the hypothesis that PA protects from incident depression (19) and not vice versa. Since exercise interventions tend to lose their effect once they are stopped (46), supporting a physically active lifestyle beyond structured exercise-treatments in patients with depression or at-risk for depression becomes increasingly important an might help to reduce relapse-rates (37). This could be achieved by implementing assessment of PA and specified PA-counselling methods for patients with depression into routine care. An approach including motivational and volitional strategies has proven to be a promising method to increase PA in a sustainable way (31). Since such a strategy could increase PA of depressed patients as well (18), a multi-site trial evaluating a motivational and volitional PA counselling in moderately to severely depressed patients is currently underway (32).

Conflict of Interest

The authors have no conflict of interest.

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