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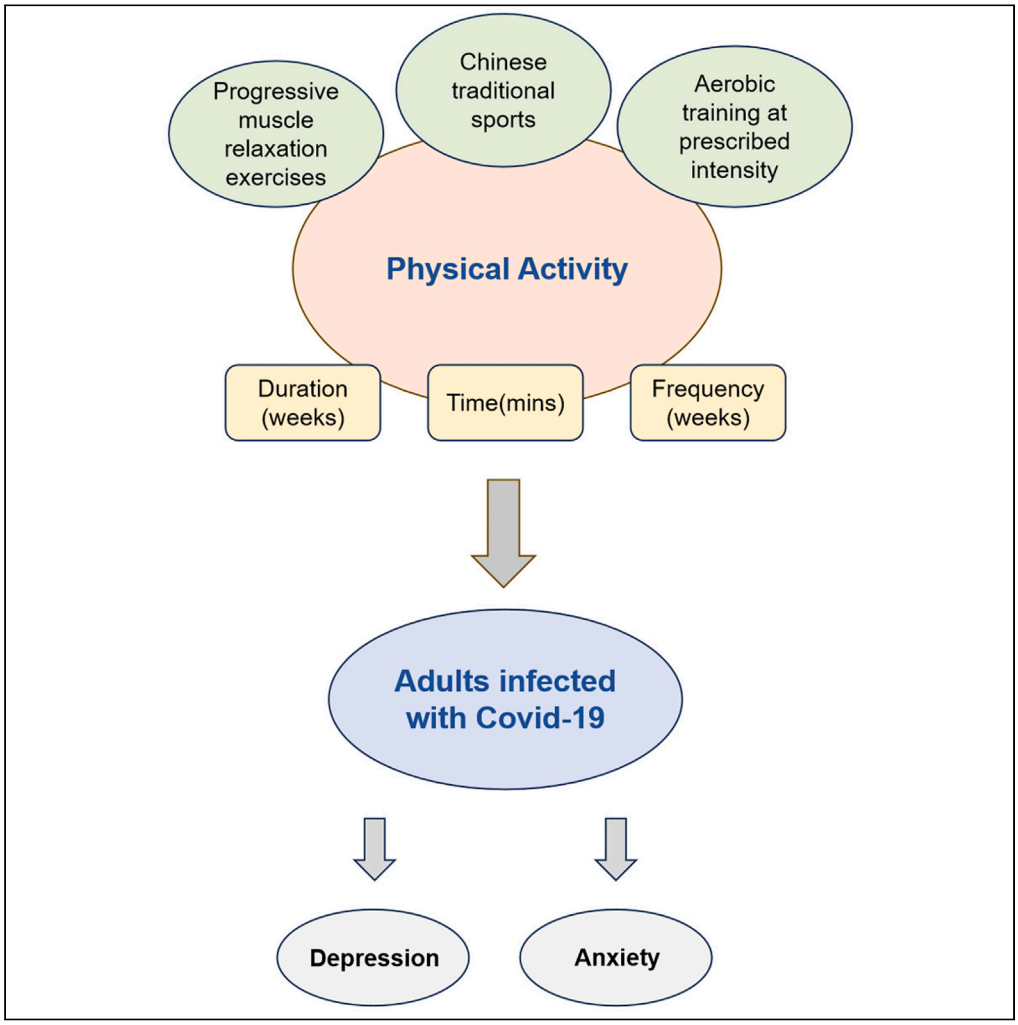


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## Highlights

Physical activity significantly enhances mental health in adults with COVID-19

Interventions with ≤5 sessions per week were more effective than those with >5 sessions

Interventions ≤2 weeks best improved depression; 3 ≤ 7 weeks best reduced anxiety

30 < 60 min interventions best improved anxiety; ≥60 min best improved depression

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# Effect of physical activity on anxiety and depression in COVID-19 adults: A systematic review and meta-analysis

Qingyuan Luo,[1,5] Peng Lan,[1,5] YuanZheng Lin,[2,5] Peng Zhang,[3,5] and Xiujie Ma[1,4,6,*]

## SUMMARY

**While the benefits of physical activity on mental health are well-known, systematic reviews and meta-analyses on its impact on mental illness in adults with COVID-19 are scarce. This study of 25 randomized controlled trials shows that physical activity significantly reduces anxiety (standardized mean difference [SMD] = −0.915; 95% confidence interval [CI] = −1.182 to −0.648; $I^2$ = 82.0%; $p < 0.001$) and depression (SMD = −0.752; 95% CI = −1.034 to −0.470; $I^2$ = 81.4%; $p < 0.001$). Traditional Chinese ethnic sports are notably effective. Interventions under 3 weeks best reduce depression, while 3 ≤ 7 weeks optimally reduce anxiety. Sessions ≤5 times weekly, with 30 ≤ 60 min for anxiety and >60 min for depression, yield the best outcomes. These results highlight the specific effectiveness of physical activity in alleviating anxiety and depression in COVID-19 patients.**

## INTRODUCTION

As of July 12, 2023, more than 774 million confirmed cases of COVID-19 have been reported to the World Health Organization (WHO) globally, with over 7 million deaths recorded.[1] The ongoing global COVID-19 pandemic has profoundly impacted both the physical and mental well-being of the population. The measures implemented in response to COVID-19, including quarantines, have led to a decline in physical activity levels among the public, resulting in heightened psychological stress and an increase in negative emotions.[2,3] Consequently, this has contributed to a spectrum of mental health problems, with depression and anxiety notably affected.[4,5] Research indicates a substantial surge in depression and anxiety associated with COVID-19. Studies reveal that during COVID-19 isolation, the prevalence of depression and anxiety has risen 2.5 to 3 times compared to pre-pandemic levels. Moreover, more than 70% of individuals report experiencing significant depressive symptoms and even suicidal ideation.[6,7]

During the COVID-19 pandemic, the WHO recommends that individuals confined to their homes engage in at least 150 min of moderate-intensity physical activity per week. This recommendation aims to reduce the risk of anxiety, depression, and enhance overall mental health.[8] Furthermore, the WHO advises including muscle-strengthening activities targeting major muscle groups on at least two days per week. These activities not only improve and maintain musculoskeletal health but also enhance an individual's resilience during the pandemic. Notably, patients with COVID-19 who adhere to these physical activity guidelines are significantly less likely to require ICU admission and have a reduced mortality rate compared to those who do not meet these recommendations.[9,10] Regular physical activity significantly ameliorates psychopathological and physiological issues, particularly anxiety and depression, even in infected patients.[11–13] Research consistently reveals that patients infected with COVID-19 commonly experience significant anxiety, depression, and other psychiatric disorders, which significantly heighten the risk of mortality.[14,15] While the majority of patients infected with COVID-19 recover within a few weeks, a subset of patients continues to experience persistent symptoms. This condition, known as "prolonged neo-coronavirus" or "chronic neo-coronavirus," persists regardless of age, gender, or other comorbidities.[16] A cohort study involving patients recovering from COVID-19 infection demonstrated that survivors continue to manifest a range of comorbidities beyond the six-month mark. These include fatigue, sleep difficulties, anxiety, depression in mental health, as well as muscle weakness, headaches, and alterations in taste perception affecting physical health.[17,18]

Thus far, while the epidemiological and clinical characteristics, pathogenesis, and complications of COVID-19 patients have been extensively documented,[19,20] the long-term implications of psychiatric disorders linked to the disease remain uncertain. Consequently, this study aimed to explore how physical activity impacts the mental health, specifically depression and anxiety, of adults infected with COVID-19. To investigate this question, we conducted a meta-analysis to assess the impact of physical activity. First, we outline the materials and

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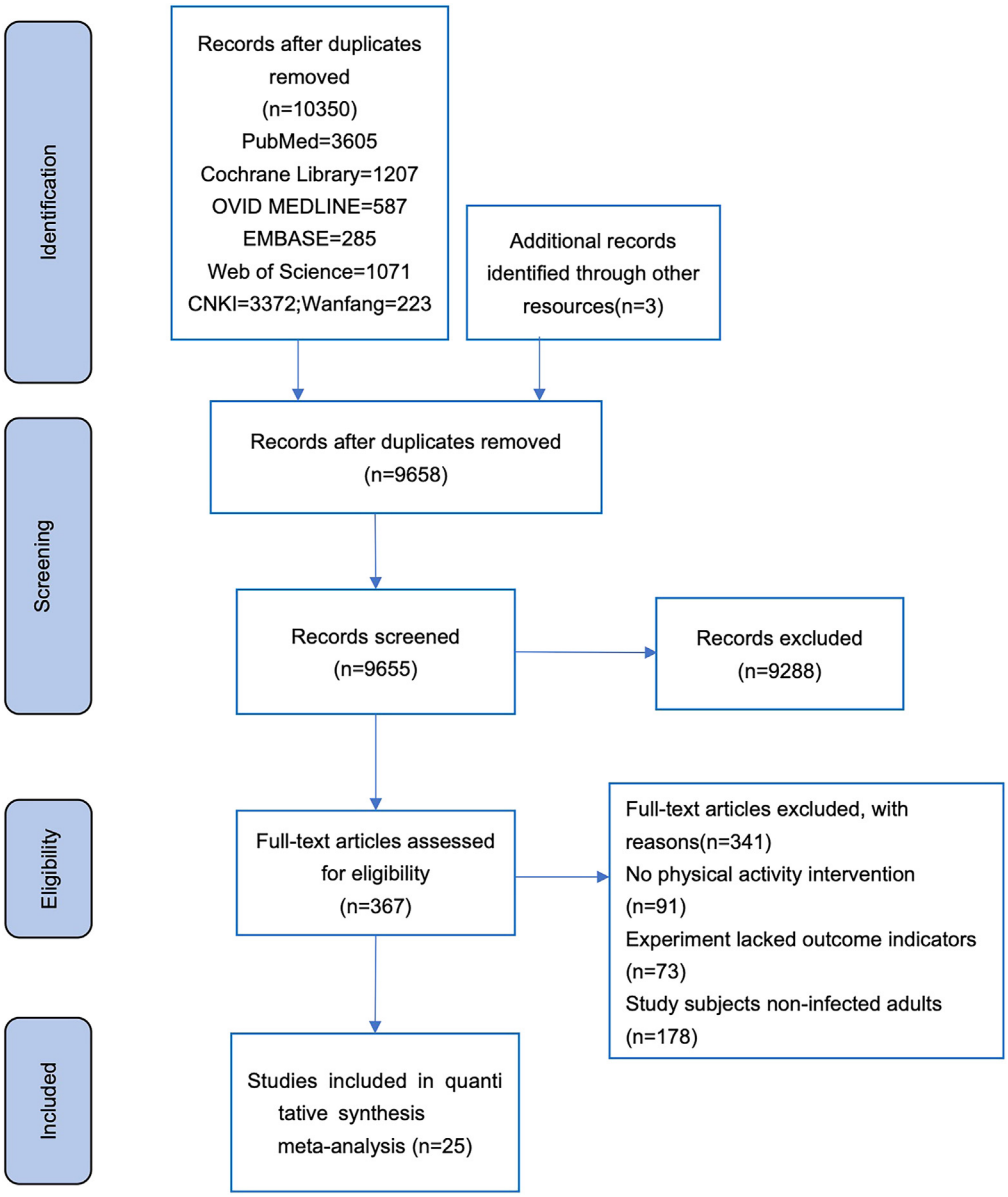


**Figure 1. Flow of study selection**

methods utilized in the meta-analysis. Second, we present the results of the meta-analysis. Additionally, we engage in a comprehensive discussion of the meta-analysis results, establishing links with previous research. Finally, we summarize the study's limitations and present our conclusions.

## RESULTS

### Studies selection

A total of 10,350 publications were retrieved from the database. During the initial screening, duplicate publications were removed, and titles and abstracts were reviewed to exclude 9,983 studies. Among these, duplicates accounted for 695 publications, while 9,288 studies were deemed irrelevant. The remaining 367 publications underwent further screening by reading the full text. Out of these, 341 studies were eliminated due to various reasons: absence of physical activity interventions (91), lack of outcome indicators in the experiments (73), and studies involving subjects other than infected adults (178). Additionally, 25 meta-analysis publications were screened as outlined in Figure 1. Among them, 25 experiments provided data for the meta-analysis, briefly characterized as follows in Table 1.

**Table 1. Included trial characteristics**

| Trial ID | Country | N | Age mean (range) | Gender, % Female | T | C | Recruitment setting | Depression and anxiety inclusion criteria | Depression and anxiety outcome measures | Research type |
|---|---|---|---|---|---|---|---|---|---|---|
| Lin X et al.[21] | China | 80 | 29–79 | 46.25 | 40 | 40 | (1) Meet the diagnostic criteria for mild COVID-19; (2) age over 18 years | HAMA ≥ 14 | HAMA | RCT |
| Zhang Y et al.[22] | China | 28 | 39–62 | 39.29 | 14 | 14 | (1) COVID-19 infected patients; (2) agreed to participate in this study and signed an informed consent form | NR | SAS SDS | RCT |
| Wang X et al.[23] | China | 60 | 18–75 | 46.7 | 30 | 30 | (1) Participants aged between 18 and 80 years; (2) positive throat swab result for the 2019-nCoV nucleic acid test | HAMA ≥ 14 HAMD ≥ 17 | HAMA HAMD | RCT |
| Yin L et al.[24] | China | 40 | 20–66 | 47.5 | 20 | 20 | (1) Individuals meeting the diagnostic criteria for COVID-19; (2) individuals exhibiting symptoms such as anxiety and depression | SAS ≥ 53 SDS ≥ 50 | SAS SDS | RCT |
| Chen X et al.[25] | China | 29 | 39–84 | 55.17 | 14 | 15 | (1) Met the diagnostic criteria for generalized COVID-19 patients; (2) provided informed consent and volunteered to participate | SAS ≥ 50 SDS ≥ 50 | SAS SDS | RCT |
| Li J et al.[26] | China | 93 | 43–74 | 45.2 | 47 | 46 | (1) Confirmed diagnosis of COVID-19; (2) individuals with normal communication abilities; (3) age 18 years or older | PHQ-9 ≥ 5 GAD-7 ≥ 5 | PHQ-9 GAD-7 | RCT |
| Cai G et al.[27] | China | 60 | 24–61 | 43.33 | 30 | 30 | (1) COVID-19 patients; (2) age < 80 | HAMD-24 > 8 | HAMD | RCT |
| Ma Z et al.[28] | China | 70 | 25–48 | 55.71 | 35 | 35 | (1) COVID-19 patients; (2) age ≥ 18 | PHQ-9>4 | PHQ-9 | RCT |
| Rutkowski S et al.[29] | Polish | 32 | 52–63 | 68.75 | 16 | 16 | (1) Aged between 40 and 80 years; (2) diagnosed with coronavirus disease-19 (COVID-19), including both women and men | HADS-A>8 HADS-D>8 | HADS-A HADS-D | RCT |
| Jung J H et al.[30] | South Korea | 109 | 28–68 | 48.5 | 52 | 57 | (1) Confirmed diagnosis of COVID-19; (2) aged at least 18 years | SAS>44 SDS>49 PHQ>4 | SAS SDS PHQ-9 | RCT |
| Zhang H et al.[31] | China | 40 | 33–51 | 40 | 20 | 20 | (1) Clinically confirmed COVID-19 diagnosis; (2) capability to walk independently and engage in physical activities; (3) willingness to participate voluntarily in this study | SAS ≥ 50 SDS>40 | SAS SDS | RCT |
| Şahın H et al.[32] | Turkey | 42 | 49–72 | 33.33 | 21 | 21 | (1) Patients in the post-acute phase of COVID-19, characterized by persistent symptoms lasting for at least 4 weeks after symptom onset | HADS-A ≥ 11 HADS-D ≥ 11 | HADS SF-36 | RCT |

(*Continued on next page*)

**Table 1. *Continued***

| Trial ID | Country | N | Age mean (range) | Gender, % Female | T | C | Recruitment setting | Depression and anxiety inclusion criteria | Depression and anxiety outcome measures | Research type |
|---|---|---|---|---|---|---|---|---|---|---|
| Jimeno-Almazán A et al.[33] | Spanish | 38 | 33–56 | 76.32 | 19 | 19 | (1) Individuals aged 18 years or older; (2) confirmed microbiological diagnosis of COVID-19 with persistent symptoms indicative of a chronic phase | GAD-7 ≥ 10<br>PHQ-9 ≥ 10 | SF-12<br>GAD-7<br>PHQ-9 | RCT |
| Özlü İ, Öztürk Z et al.[34] | Turkey | 67 | 21–49 | 44.78 | 33 | 34 | (1) Inclusion criteria required a confirmed diagnosis of COVID-19; (2) participants were required to be 18 years of age or older; (3) participants had to have no visual or hearing impairment; (4) participation was voluntary | SAS ≥ 20<br>TAS ≥ 20 | STAI<br>(SAS; TAS) | RCT |
| Ibrahim An A et al.[35] | Saudi Arabia | 48 | 57–68 | 56.94 | 24 | 24 | (1) Participants had a confirmed COVID-19 infection; (2) participants were between the ages of 60 and 80 years old | HADS-A<br>HADS-D | SF-36<br>HADS | RCT |
| Liu K et al.[36] | China | 51 | > 20 | 45.10 | 25 | 26 | (1) Participants with a confirmed diagnosis of COVID-19 | STAI>20 | STAI | RCT |
| Liu K et al.[37] | China | 72 | 61–78 | 31.94 | 36 | 36 | (1) A verified diagnosis of COVID-19; (2) aged 65 years or older; (3) a brief mental state examination (MMSE) score greater than 21 | SAS ≥ 20<br>SDS ≥ 20 | SF-36<br>SDS<br>SAS | RCT |
| Xiao C et al.[38] | China | 79 | 47–72 | 44.30 | 39 | 40 | (1) COVID-19 patients; (2) capable of following verbal instructions during training; (3) hospitalized for a duration exceeding 7 days | GAD-7 ≥ 5<br>PHQ-9 ≥ 5 | PSQI<br>GAD-7<br>PHQ-9 | RCT |
| Wang X et al.[39] | China | 177 | 18–60 | 37.28 | 96 | 21 | (1) Male or female aged 18 to 60 years; (2) positive COVID-19 nucleic acid test | GAD-7 ≥ 5<br>PHQ-9 ≥ 10 | GAD-7<br>PHQ-9 | RCT |
| Espinoza-Bravo C et al.[40] | Spanish | 43 | 20–60 | 79.06 | 21 | 22 | (1) Be between 20 and 60 years of age; (2) at least 6 weeks post-infection; (3) have a device with internet access | HADS-A ≥ 11<br>HADS-D ≥ 11 | HADS-A<br>HADS-D | RCT |
| Tanhan A et al.[41] | Turkey | 36 | 33–75 | 53.12 | 16 | 16 | (1) COVID-19 is in category 4, 5, 6; (2) able to use the computer remotely | HADS-A ≥ 8<br>HADS-D ≥ 8 | HADS-A<br>HADS-D | RCT |
| Chinvararak C et al.[42] | Thailand | 74 | 24–40 | 75.67 | 38 | 36 | (1) COVID-19 patients and age ≥ 18; (2) those with symptoms such as anxiety and depression | DASS-A ≥ 8<br>DASS-D ≥ 10 | DASS-21<br>PHQ-9 | RCT |
| Önal R et al.[43] | Turkey | 41 | 28–55 | 85.36 | 26 | 15 | (1) COVID-19 patients; (2) between 25 and 65 years of age | NR | BDI<br>SF-36 | PCT |
| Xing H et al.[44] | China | 154 | 29–55 | 57.79 | 74 | 80 | (1) COVID-19 patients; (2) 18 to 65 years old | NR | HAMD-A | RCT |
| Merellano-Navarro E et al.[45] | Brazil | 67 | 37–59 | 64.17 | 14 | 21 | (1) In COVID-19 recovery period; (2) age 30–69 | NR | DASS-21A<br>DASS-21D | RCT |

HAMA, Hamilton anxiety scale; HAMD, Hamilton depression scale; PHQ-9, Patient Health Questionnaire-9; GAD-7, generalized anxiety disorder scale; SAS, self-rating anxiety scale; SDS, self-rating depression scale; HADS, Hospital Anxiety and Depression Scale, HADS-A for anxiety and the HADS-D for depression; SF-36, 36-item Short-Form Health Survey; SF-12, health related quality of life by the 12-item Short Form Survey; STAI, State-Trait Anxiety Inventory; TAS, Trait Anxiety Scale; BDI, Beck Depression Inventory; PSQI, Pittsburgh sleeps quality index scale; CPDI, COVID-19 Peritraumatic Distress Index; DASS, Depression, Anxiety and Stress Scale; NR, not reported or unclear; T, test group; C, control group.

### Characteristics of eligible studies

Our systematic evaluation included 25 articles. Eight of them were published in Chinese,[21–28] and 17 were in English.[29–45] The study sites were in China,[21–28,31,36–39,44] Poland,[29] South Korea,[30] Turkey,[32,34,41,43] Spain,[33,40] Saudi Arabia,[35] Thailand,[42] and Brazil.[45] The sample sizes ranged from 29 to 177, with a total of 1,630 participants covering 18–84 years old. The included studies were RCT trials, and all reported inclusion criteria for depression and anxiety, except for studies in Turkey,[43] China,[22,44] and Brazil,[22] where studies[21,34,36,44] addressed only anxiety indicators and studies[27,28] addressed only depression indicators. The remaining 19 studies addressed both depression and anxiety indicators.

### Interventions and controls

Table 2 summarizes the characteristics of the physical activity interventions in all the included experiments. Ten studies involved interventions with traditional Chinese ethnic sports (Ba Duan Jin and Yi Jin Jing),[21–25,27,28,31,39,44] six studies involved progressive muscle relaxation exercises,[26,34,36–38,42] and nine studies specified aerobic versus anaerobic intensity.[29,30,32,33,35,40,41,43,45] The duration of the interventions in the included experiments ranged from 5 days to 12 weeks, with single interventions lasting 20–60 min and a minimum of 2 interventions per week. Supervisors and qualified trainers for the conduct of the experiments were specified in all but some studies.[28,34,35,44,45] In terms of exercise mode, all experiments except some studies[35–38,44,45] were conducted with individuals performing the exercise alone. Regarding the design of the experimental and control groups, the control group, with the exception of study,[37] did not undergo any rehabilitation interventions, while the control group in all other studies adopted the intervention activities of conventional medical care or WHO's rehabilitation guidelines.

### Risk of bias

Figures 2 and 3 illustrate the assessment of bias risks among the included studies. All trials analyzed exhibited an "unclear" risk of bias. Among the included studies, 14 reported the generation of random sequences,[21–26,29–35,37] while 5 employed random number tables,[22–25,29] and 2 utilized convenience sampling.[26,31] Additionally, 6 studies utilized computer-generated randomization,[33,37,39,42,45] 2 employed block randomization,[30,44] and 2 utilized simple randomization.[21,34] One study employed the ranked block group method,[35] while 4 did not specify a specific randomization method.[28,32,41,43] Notably, only 4 studies reported allocation concealment.[26,35,39,44]

### Meta-analysis of outcome indicators

#### *Physical activity compared to no intervention control*

The meta-analysis comprised a total of 25 experiments ($n$ = 1660), wherein the physical activity experimental group and the no intervention control group were evaluated using standardized mean difference (SMD). The analysis was conducted utilizing a random-effects model due to high heterogeneity ($I^2$ > 50%). Depression and anxiety states were assessed post-physical activity intervention in 26 experiments, revealing statistically significant improvements with physical activity compared to the no physical activity intervention control group. For anxiety symptom improvement, SMD = −0.915; 95% confidence interval (CI) = −1.182 to −0.648; $I^2$ = 82.0%; $p$ < 0.001; Z = 6.72 (refer to Figure 4). Regarding depressive symptom improvement, SMD = −0.752; 95% CI = −1.034 to −0.470; $I^2$ = 81.4%; $p$ < 0.001; Z = 5.222 (refer to Figure 5). However, it is important to note the high heterogeneity among the included experiments, likely attributed to the diverse control interventions and measurement tools utilized.

#### *Regression analysis*

The covariates (intervention program, number of exercise sessions per week, duration of a single exercise session, and number of weeks of duration) may influence the efficacy of physical activity in mitigating depression and anxiety. Hence, this paper conducts subgroup analyses regressing these covariates. Tables 3 and 4 present the results of covariate regression analyses for the alleviation of depression and anxiety through physical activity. Regarding anxiety alleviation, the intervention program (95% CI = −0.2632808 to 0.4993545, $p$ = 0.524), number of weekly exercise sessions (95% CI = −0.334951 to 0.7355642, $p$ = 0.442), duration of a single exercise session (95% CI = −0.7553053 to 0.5005878, $p$ = 0.675), and duration in weeks (95% CI = 0.8290981 to 0.9058052, $p$ = 0.927) did not yield significant effects. Similarly, for depression alleviation, neither the intervention program (95% CI = −0.3140492 to 0.7549539, $p$ = 0.395), number of exercise sessions per week (95% CI = −0.6611024 to 0.7587443, $p$ = 0.886), duration of a single exercise session (95% CI = −1.028739 to 0.6883309, $p$ = 0.680), nor the duration in weeks (95% CI = −0.9729155 to 1.46662, $p$ = 0.674) demonstrated significance.

#### *Sub-group analysis*

In order to further examine the impact of physical activity interventions on anxiety and depression among infected adults, we categorized the included literature into four subgroups based on intervention programs, duration in weeks, single workout duration, and frequency of workouts per week, considering the variations in study characteristics. The subgroup analyses, detailed in Tables 5 and 6, yielded the following findings. (1) Various intervention programs contributed to anxiety and depression alleviation, with ethnic traditional sports from China demonstrating significantly greater efficacy compared to other interventions. (2) Regarding intervention duration, improvements in anxiety symptoms were most pronounced within three to seven weeks, while shorter intervention durations (less than two weeks) were more effective for depression. (3) In terms of single intervention duration, periods ranging from 30 ≤ 60 min were most effective for anxiety, whereas

**Table 2. Physical activity characteristics**

| Trial ID | Physical activity arms and content | Setting | Duration | Session (Min) | Sessions per week | Control arm |
|---|---|---|---|---|---|---|
| Lin X et al.[21] | (1) SNC; (2) Ba Duan Jin lung exercise | S Q I | 4 weeks | 40–60 min | 5 | (1) CAU |
| Zhang Y et al.[22] | (1) SNC; (2) Yi Jin Jing | S Q G&I | 1 week | 60 min | ≥3 | (1) CAU |
| Wang X et al.[23] | (1) Ba Duan Jin; (2) FEMT | S Q I | 2 weeks | 60 min | 7 | (1) CAU |
| Yin L et al.[24] | (1) Ba Duan Jin; (2) FEMT | S Q I | 2 weeks | 60 min | 5 | (1) CAU |
| Chen X et al.[25] | (1) SNC; (2) bedtime Ba duan Jin | S Q I | 3 weeks | 40–60 min | ≥10 | (1) CAU |
| Li J et al.[26] | (1) PMRT | S Q I | 8 weeks | 45 min | 7 | (1) CAU |
| Cai G et al.[27] | (1) Yi Jing Jin | S Q I | 6 weeks | 30 min | 7 | (1) CAU |
| Ma Z et al.[28] | (1) Ba Duan Jin | U Q G | 4 weeks | 30 min | 7 | (1) CAU |
| Rutkowski S et al.[29] | (1) 60–80% maximum exercise intensity | S Q I | 3 weeks | 30 min | 5 | (1) Traditional medicine |
| Jung J H et al.[30] | (1) Craft activities; (2) trained in exercises | S Q I | 8 days | 40 min | 7 | (1) CAU |
| Zhang H et al.[31] | (1) Ba Duan Jin; (2) FEMT | S Q I | 8 weeks | 60 min | 5 | (1) CAU<br>(2) Daily activities and exercise |
| Şahın H et al.[32] | (1) SHEP | S Q I | 8 weeks | 50–60 min | 5–7 | (1) CAU |
| Jimeno-Almazán A et al.[33] | (1) CTR; (2) TR; (3) LTC | S Q I | 8 weeks | 30–60 min | 6 | (1) CAU |
| Özlü İ, Öztürk Z et al.[34] | (1) PMTT | U NR I | 5 days | 40–60 min | 5 | (1) CAU |
| Ibrahim An A et al.[35] | (1) MIAE (group M); (2) LIAE (group L) | NR | 10 weeks | 45 min | 4 | (1) CAU |
| Liu K et al.[36] | (1) PMRT; (2) deep breathing | S Q NR | 5 days | 20–30 min | 5 | (1) CAU |
| Liu K et al.[37] | (1) Respiratory rehabilitation | S Q NR | 6 weeks | 20 min | 7 | (1) Did interventions |
| Xiao C et al.[38] | (1) SNC; (2) PMRT | S Q NR | 1 week | 30 min | 7 | (1) CAU |
| Wang X et al.[39] | (1) Ba Duan Jin; (2) FEMT | S Q G | 1 week | 30 min | 7 | (1) CAU |
| Espinoza-Bravo C et al.[40] | (1) Functional exercise | S Q I | 8 weeks | 20–40 min | 2 | (1) Aerobic Exercise |
| Tanhan A et al.[41] | (1) Telerehabilitation program | S Q I | 8 weeks | 30–40 min | 3 | (1) Physiotherapy; (2) Rehabilitation Department |
| Chinvararak C et al.[42] | (1) PRMT; (2) breathing exercises | S Q I | 12 weeks | 20–25 min | 7 | (1) CAU |
| Önal R et al.[43] | (1) Yoga; (2) breathing exercises | S Q I | 8 weeks | 60 min | 2 | (1) CAU |
| Xing H et al.[44] | (1) Yi Jing Jin | U Q NR | 1 week | 20 min | 7 | (1) Basic nursing health education |
| Merellano-Navarro E et al.[45] | (1) Moderate-intensity intermittent hypoxic training | S NR NR | 8 weeks | 50 min | 3 | (1) CAU |

PMRT, progressive muscle relaxation training; FEMT, five elements music therapy; SNC, standard nursing care; SHEP, structured home exercise program (incorporating breathing exercises, strength training, and regular exercise regimen); CTR, concurrent training regimen; TR, rraining resistance; LTC, light-intensity training continuous; MIAE, moderate-intensity aerobic exercise; LIAE, low-intensity aerobic exercise. Respiratory rehabilitation = (1) respiratory muscle training, (2) cough exercise, (3) diaphragmatic training, (4) stretching exercise, (5) home exercise. Telerehabilitation program = (1) pulmonary exercises, (2) aerobic exercises, (3) strengthening exercises. CAU, care as usual; (S) supervised or unsupervised (U), qualified coach (Q), group (G) or individual (I); NR, not reported or NR, not reported or unclear; UHEP, unguided home exercise programs (breathing exercises, strength training, regular exercise programs, etc).

durations of 60 min or more were optimal for depression. (4) The frequency of weekly interventions also played a role, with five or fewer sessions per week showing superior outcomes for anxiety and depression compared to five or more sessions.

## DISCUSSION

The systematic review and meta-analysis conducted in this study aimed to analyze relevant experiments involving adults with COVID-19 infection, to elucidate the impact of physical exercise on the mental well-being of these individuals, and to propose effective exercise regimens for

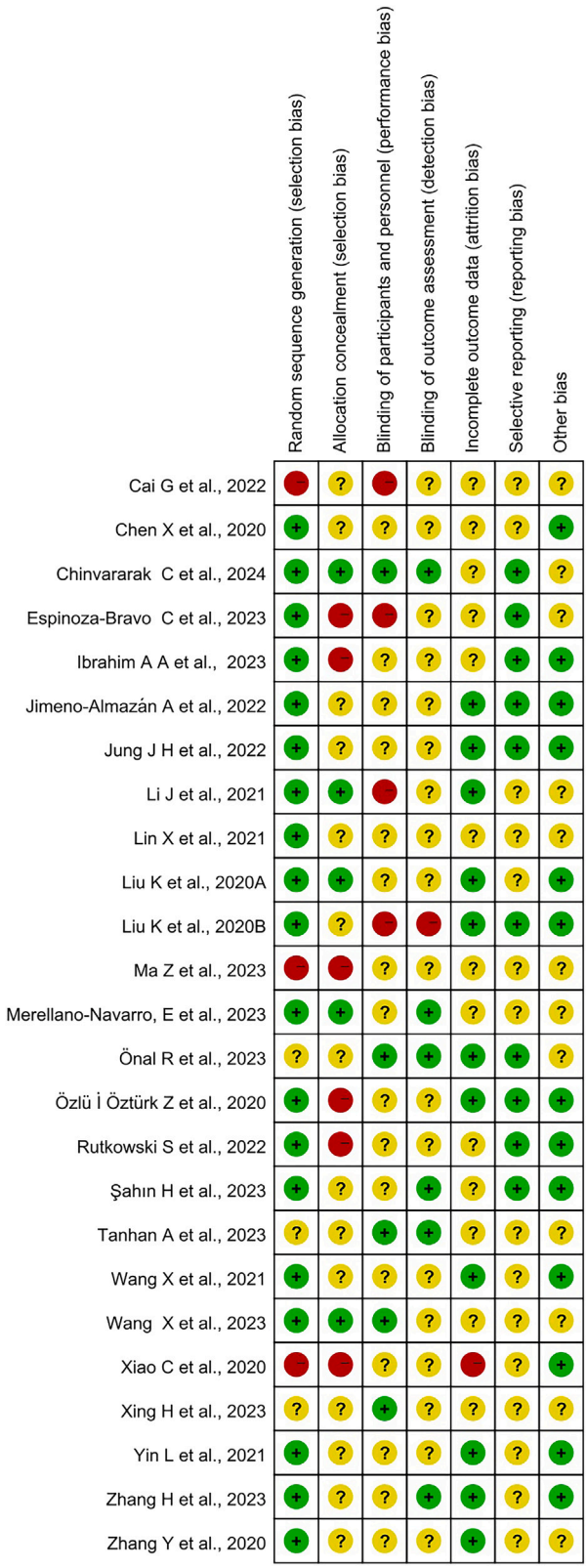


**Figure 2. Risk of bias ratings**

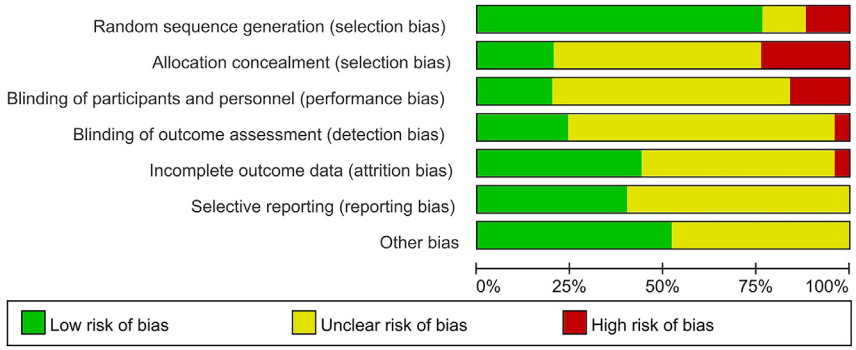


**Figure 3. Risk of bias graph**

alleviating mental health issues among adults with COVID-19 infection. The findings revealed that physical activity is beneficial in mitigating mental health disorders among adults with COVID-19 infection, with various forms of physical activity demonstrating varying degrees of improvement in mental disorders (anxiety: SMD = −0.915; 95% CI = −1.182 to −0.648, $p < 0.001$; depression: SMD = −0.752; 95% CI = −1.034 to −0.470; $p < 0.001$).

The results of this systematic evaluation are consistent with the findings of existing studies that there is a significant association between physical exercise and mental health during COVID-19.[46–48] It has been pointed out that taijiquan from China has a significant effect on

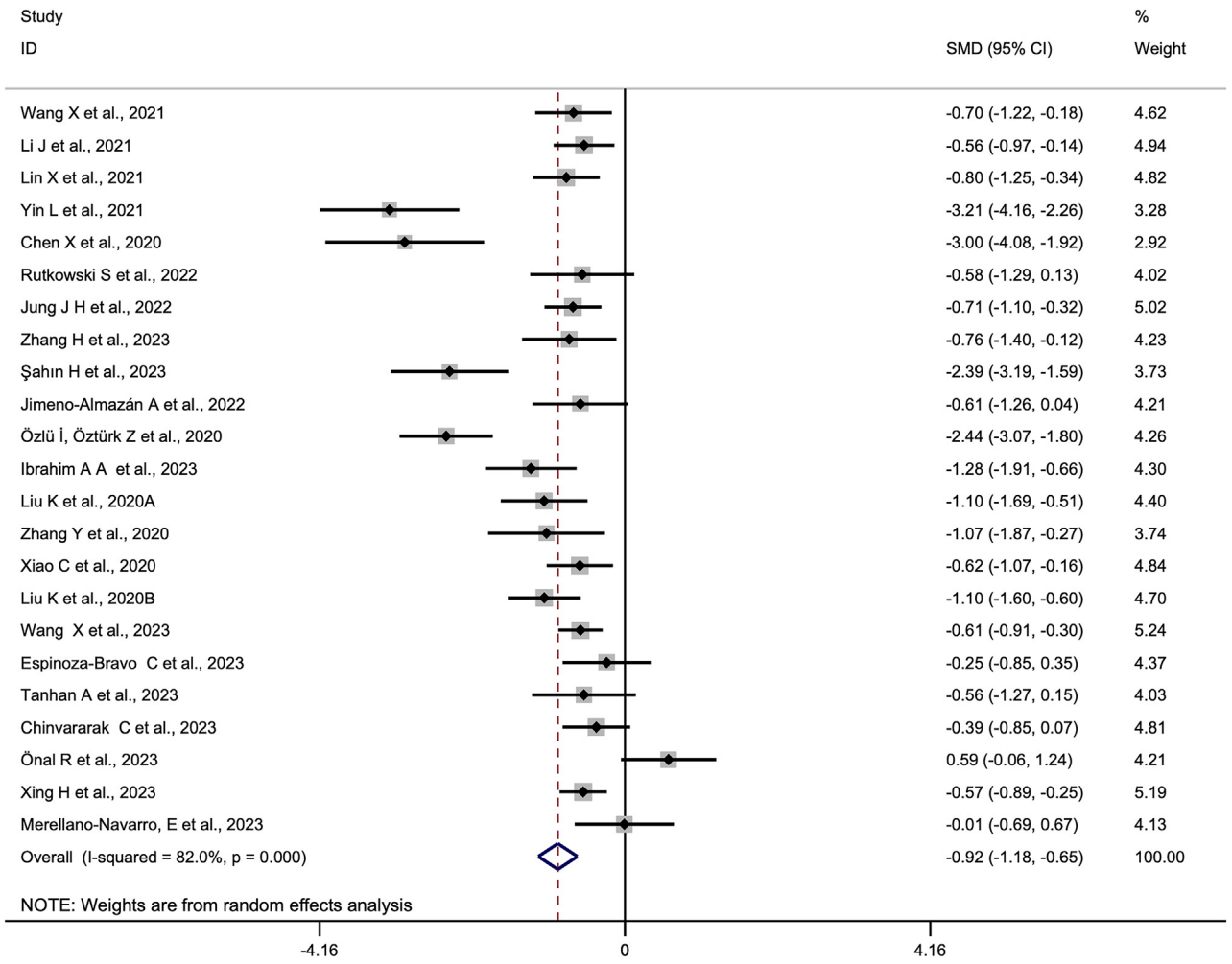


**Figure 4. Effects on anxiety disorders**

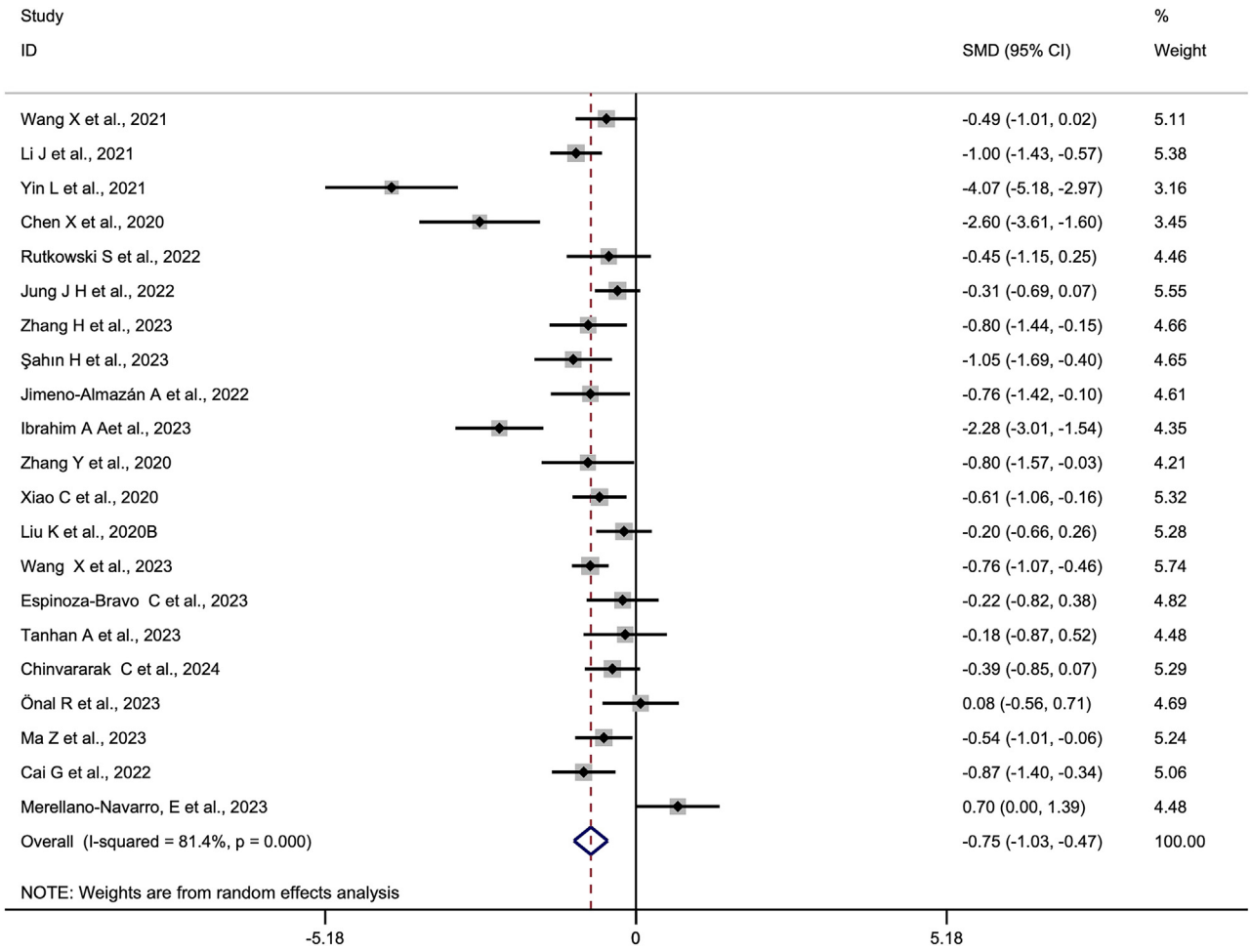


**Figure 5. Effects on depression**

improving patients' mental health,[49] especially during COVID-19, and Chinese ethnic traditional sports programs have a greater psychological improvement effect on patients compared with other sports.[50] This also supports the results of our subgroup analysis that Chinese ethnic traditional sports programs are more effective than other interventions in enhancing patients' mental health. In terms of patient depression, the ethnic traditional sports program from China had a better improvement effect than the other physical activity interventions included, which is in line with existing findings that ethnic traditional sports from China have the best improvement effect on depression in patients.[51,52] Our subgroup analysis of the number of weeks of intervention revealed that for anxiety disorders, the intervention time within $3 \leq 7$ weeks had the best improvement effect on patients. And this is supported by existing studies,[53] whereas for depression, intervention weeks of 2 weeks and less had a better improvement effect than other intervention times, which is also supported by existing studies, which state that just 60 min of PA of any intensity per week reduced the incidence of depression cases by 12% but had no relationship with anxiety.[54] This result may be due to the fact that depression and anxiety have different mechanisms of action on the body.[47] In our subgroup analysis of the single

**Table 3. Regression analysis of anxiety disorders**

| _ES | COEF. | SE | t | p>\|t\| | 95% CI |
|---|---|---|---|---|---|
| Intervention projects | 0.1180368 | 0.1815001 | 0.65 | 0.524 | −0.2632808 to 0.4993545 |
| Frequency (week) | 0.2003066 | 0.2547727 | 0.79 | 0.442 | −0.334951 to 0.7355642 |
| Time (min) | −0.1273588 | 0.2988909 | −0.43 | 0.675 | −0.7553053 to 0.5005878 |
| Duration (weeks) | 0.0383535 | 0.4128909 | 0.09 | 0.927 | 0.8290981 to 0.9058052 |
| _cons | −1.448003 | 1.153787 | −1.26 | 0.226 | −3.872019 to 0.9760125 |

**Table 4. Regression analysis for depression**

| _ES | COEF. | SE | t | p>\|t\| | 95% CI |
|---|---|---|---|---|---|
| Intervention projects | 0.2204523 | 0.2521346 | 0.87 | 0.395 | −0.3140492 to 0.7549539 |
| Frequency (weeks) | 0.0488209 | 0.3348845 | 0.15 | 0.886 | −0.6611024 to 0.7587443 |
| Time (mins) | −0.1702043 | 0.4049875 | −0.42 | 0.680 | −1.028739 to 0.6883309 |
| Duration (weeks) | 2468522 | 0.5753878 | 0.43 | 0.674 | −0.9729155 to 1.46662 |
| _cons | −1.46692 | 1.875549 | −0.78 | 0.446 | −5.442906 to 2.509065 |

intervention duration, a single session lasting between 30 and 60 min proved most effective in alleviating anxiety compared to other durations, consistent with prior research: for COVID-19 patients, engaging in group home-based recreational exercise for 30–60 min, twice a week, was identified as one of the most effective strategies for anxiety relief.[55,56] Concerning depression, a single session lasting 60 min or more displayed the greatest efficacy when compared to other single-session durations. Once again, our findings align with research from the COVID-19 period, which reported that a single exercise session lasting 60 min or longer was significantly associated with a reduced risk of depression.[57] Moreover, our subgroup analyses consistently revealed that for both depression and anxiety, the effectiveness of interventions was greater when conducted five or fewer times per week compared to more frequent interventions. This phenomenon may be attributed to the inverted U-shaped relationship between physical activity and mental health, where excessively high levels of physical activity can compromise the resilience of COVID-19-infected patients.[50] A study examining the effects of traditional Chinese sports on mental health corroborates these findings. Similarly, a meta-analysis of traditional Chinese ethnic sports aimed at improving mental health revealed a negative correlation between the duration of physical activity and mental health improvements.[58] This association may be due to the potential susceptibility of individuals engaged in prolonged physical activity to upper respiratory tract diseases and the subsequent impact on cellular immune function, ultimately counteracting the positive effects of physical activity on mental health.[59]

The prevalence of psychological distress among COVID-19-infected patients has been reported as follows: 36% for psychological distress in general, 22% for anxiety disorders, and 21% for depression.[60] Notably, physical activity has been demonstrated to play a significant moderating role in reducing anxiety and depression levels among these patients, alongside marked improvements in physiological and biochemical indicators, including adrenaline, heart rate, norepinephrine, and cortisol levels.[61,62] The underlying physiological and biochemical mechanisms responsible for mediating the effects of exercise on mental health are multifaceted. These include the release of endorphins,[63] modulation of inflammatory processes,[64] and regulation of the stress response through the hypothalamic-pituitary-adrenal (HPA) axis.[65] Mental health challenges observed in COVID-19 patients primarily stem from the detrimental impact of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on the body's internal milieu, characterized by cytopathic damage and viral replication, thereby creating a pro-inflammatory environment. The dysregulation and signaling of inflammatory cytokines within this environment can significantly elevate the risk of mental illness.[66,67] In line with previous research findings, heightened levels of the pro-inflammatory cytokine (CRP) have been consistently and positively correlated with a higher susceptibility to mental health disorders.[68]

Long-term exercise training has been empirically substantiated as an effective avenue for enhancing mental health. Physical activity primarily operates through the modulation of neuroinflammation, oxidative stress, serotonin (5-HT), and its receptors, among other mechanisms.[69] Research has elucidated that the Chinese national traditional sports program can effectively reduce levels of interleukin-6 (IL-6), downregulate pro-inflammatory gene expression including C-reactive protein, and mitigate the production of pro-inflammatory cytokines

**Table 5. Subgroup analysis of anxiety disorders**

| Group | Sub-group | K | N | SMD | 95% CI | p | $I^2$ |
|---|---|---|---|---|---|---|---|
| Interventions | Chinese traditional sports | 8 | 608 | −1.175 | −1.646 to −0.704 | 0.000 | 84.3% |
| | Progressive muscle relaxation exercises | 6 | 436 | −1.003 | −1.520 to −0.487 | 0.000 | 84.5% |
| | Aerobic training at prescribed intensity | 9 | 456 | −0.628 | −1.101 to −0.155 | 0.000 | 80.7% |
| Duration (weeks) | ≤2 | 9 | 765 | −1.127 | −1.550 to −0.703 | 0.000 | 85.7% |
| | 3 ≤ 7 | 4 | 213 | −1.239 | −1.951 to −0.528 | 0.002 | 80.4% |
| | ≥8 | 10 | 552 | −0.599 | −1.010 to −0.188 | 0.000 | 78.5% |
| Time (mins) | ≤30 | 6 | 462 | −0.695 | −0.922 to −0.467 | 0.234 | 26.8% |
| | 30 < 60 | 12 | 829 | −1.027 | −1.426 to −0.628 | 0.000 | 84.5% |
| | ≥60 | 5 | 209 | −0.987 | −1.991 to 0.017 | 0.000 | 90.7% |
| Frequency (weeks) | ≤5 | 12 | 573 | −0.931 | −1.438 to −0.424 | 0.000 | 86.3% |
| | > 5 | 11 | 927 | −0.867 | −1.153 to −0.581 | 0.000 | 75.2% |

**Table 6. Subgroup analysis of depression**

| Group | Sub-Group | K | N | SMD | 95% CI | *p* | $I^2$ |
|---|---|---|---|---|---|---|---|
| Interventions | Chinese traditional sports | 8 | 504 | −1.214 | −1.752 to −0.677 | 0.000 | 85.5% |
| | Progressive muscle relaxation exercises | 5 | 427 | −0.500 | −0.778 to −0.223 | 0.086 | 51.0% |
| | Aerobic training at prescribed intensity | 8 | 347 | −0.514 | −1.094 to −0.065 | 0.000 | 83.4% |
| Duration (weeks) | ≤2 | 6 | 493 | −0.994 | −1.572 to −0.415 | 0.000 | 87.7% |
| | 3 ≤ 7 | 5 | 263 | −0.820 | −1.402 to −0.239 | 0.001 | 79.3% |
| | ≥8 | 10 | 522 | −0.587 | −1.023 to −0.150 | 0.000 | 80.9% |
| Time (mins) | ≤30 | 4 | 257 | −0.409 | −0.657 to −0.162 | 0.670 | 0.0% |
| | 30 < 60 | 12 | 812 | −0.771 | −1.134 to −0.408 | 0.000 | 81.6% |
| | ≥60 | 5 | 209 | −1.132 | −2.137 to −0.126 | 0.000 | 90.5% |
| Frequency (weeks) | ≤5 | 9 | 375 | −0.840 | −1.585 to −0.094 | 0.000 | 89.9% |
| | > 5 | 12 | 903 | −0.694 | −0.920 to −0.468 | 0.003 | 61.2% |

by monocytes. These actions contribute to the stabilization of mental health among individuals.[70,71] Early studies have also underscored the role of endorphin-mediated exercise in promoting increased neurogenesis within the adult hippocampus, resulting in reductions in anxiety and depression-related behaviors.[72,73] Endorphins, released during physical activity, play a pivotal role in nervous system regulation and the maintenance of brain health,[74] although the precise underlying mechanisms warrant further exploration in future investigations. Additionally, it is imperative to recognize the integral role played by the HPA axis in individuals grappling with anxiety and depression.[75] Dysfunctions within the HPA axis can give rise to symptoms such as fear, sympathetic disorganization, hypervigilance, and psychiatric disorders, including anxiety and depression, which have been extensively documented in the academic community.[76,77] The mechanism behind these disorders involves physical and psychological stress experiences triggering activation of the HPA axis.[78] This activation leads to the secretion of corticotropin-releasing hormone (CRH) and arginine vasopressin (AVP) via small cell neurons in the paraventricular nucleus of the hypothalamus. These neuropeptides, in turn, stimulate the synthesis and release of adrenocorticotropic hormone (ACTH) from the anterior lobe of the pituitary gland. Ultimately, this cascade results in the synthesis of adrenocortical glucocorticoids, such as cortisol in humans, which can profoundly impact mood and behavior.[75,79,80] However, it is noteworthy that physical exercise can significantly ameliorate the dysfunction observed in the HPA axis among individuals with psychological disorders. It accomplishes this by increasing the secretion of CRH, restoring impaired responsiveness to glucocorticoids, and enhancing pituitary size and activity, among other functions.[81,82] By doing so, physical exercise contributes to the regulation of mental health among patients. The current study also affirms the positive impact of physical exercise on mental health, specifically in terms of anxiety and depression, among adult patients recovering from COVID-19 infection. Nonetheless, it is essential to acknowledge that this study did not delve into the intrinsic mechanisms affected by physical exercise in these patients. Therefore, future research endeavors should aim to elucidate the precise effects of specific interventions on intrinsic mechanisms among COVID-19-infected patients. Such investigations will be instrumental in formulating tailored exercise prescriptions for enhancing mental health following COVID-19 infection.

## Conclusions

Meta-analysis of this paper shows that physical exercise can significantly improve anxiety and depression in adult patients who have been infected with COVID-19. Specifically, an ethnically traditional sports program from China had the best effect on improving anxiety and depression in patients during COVID-19. Interventions of less than 3 weeks had the best effect on improving depression, and interventions of 3–7 weeks had the best effect on improving anxiety. Interventions of 5 or fewer sessions in a week were better than 5 or more sessions. Single interventions in the time period 30 to 60 min were best for anxiety improvement, while single interventions of 60 min or more were best for depression improvement. It is important to note: For the specific effects of the intrinsic mechanisms in humans with post-intervention follow-up results, this study has not been obtained. In addition, the methodological quality and number of included trials limited our ability to draw conclusions about their validity, and larger and higher quality RCTs are needed in the future to validate the current findings.

## Limitations of the study

While this study encompassed randomized controlled trials across multiple international settings, including China, Poland, South Korea, Turkey, Spain, Saudi Arabia, Brazil, and Thailand, it is imperative to acknowledge the potential influence of various factors on the study's outcomes. Specifically, these factors include the overall quality of the evidence base, the geographical distribution of trials, and the unique nature of COVID-19. The study's findings may have been influenced by these factors, emphasizing the need for future research to address these nuances for a more comprehensive understanding of the impact of physical activity interventions on the mental and physical health of COVID-19-infected individuals.

## RESOURCE AVAILABILITY

### Lead contact

Further information and requests for resources should be directed to and will be fulfilled by the lead contact, Xiujie Ma (ma.xiujie@outlook.com).

### Materials availability

This study did not generate new unique reagents.

### Data and code availability

- All data reported in this paper will be shared by the lead contact upon request.
- This paper does not report original code.
- Any additional information required to reanalyze the data reported in this paper is available from the lead contact upon request.

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This study represents the inaugural comprehensive meta-analysis of physical activity interventions aimed at enhancing the mental well-being of adult COVID-19 patients. It furnishes a dependable intervention regimen demonstrably effective in ameliorating the mental health challenges encountered by this population.

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## AUTHOR CONTRIBUTIONS

Conceptualization, X.M. and Q.L.; methodology, X.M.; software, Q.L.; validation, Y.L., P.L., and Q.L.; formal analysis, Q.L. and P.Z.; investigation, Q.L. and X.M.; resources, Q.L.; data curation, Q.L., P.L., and X.M.; writing – original draft preparation, Q.L.; writing – review & editing, Q.L. and X.M.; visualization, Y.L.; supervision, P.L. and P.Z.; project administration, X.M.; funding acquisition, X.M. All authors read and approved the final manuscript.

## DECLARATION OF INTERESTS

The authors declare no conflict of interests.

## STAR★METHODS

Detailed methods are provided in the online version of this paper and include the following:

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# STAR★METHODS

## KEY RESOURCES TABLE

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---|---|---|
| Deposited data | | |
| International prospective register of systematic reviews | PROSPERO | https://www.crd.york.ac.uk/PROSPERO/ |
| Studies For Meta-analysis | PubMed, Embase, Cochrane Library, Web of Science, Ovid Medline, CNKI, Wan Fang | https://doi.org/10.7910/DVN/NJHKHY |
| Software and algorithms | | |
| Review Manager5.4 | Downloaded Review Manager software | https://training.cochrane.org/online-learning/core-software/revman |
| EndNote X9.1 | Thomson Scientific | https://endnote.com/downloads |
| STATA 17.0 | Stata Corp LLC | https://www.stata.com/ |

## EXPERIMENTAL MODEL AND STUDY PARTICIPANT DETAILS

### Experimental model

As this study is a systematic review and meta-analysis, it does not use experimental models typical in the life sciences.

### Subject details

Our systematic evaluation included 25 articles. Eight of them were published in Chinese,[21–28] and 17 were in English.[29–45] The study sites were in China,[21–28,31,36–39,44] Poland,[29] South Korea,[30] Turkey,[32,34,41,43] Spain,[33,40] Saudi Arabia,[35] Thailand,[42] and Brazil.[45] The sample sizes ranged from 29 to 177, with a total of 1,630 participants covering 18 to 84 years old. The included studies were RCT trials, and all reported inclusion criteria for depression and anxiety, except for studies in Turkey,[43] China,[22,44] and Brazil,[22] where studies[21,34,36,44] addressed only anxiety indicators and studies[27,28] addressed only depression indicators. The remaining 19 studies addressed both depression and anxiety indicators.

## METHOD DETAILS

### Sources and methods

This study is registered in the PROSPERO platform with the registration ID CRD42023440487.

### Searching strategy

We conducted a comprehensive literature search across Chinese and English databases, including PubMed, Embase, the Cochrane Library, Web of Science core databases, Ovid Medline, CNKI, and Wanfang, exclusively selecting studies published between January 1, 2020, and January 10, 2024.

The specific keywords were as follows, using Cochrane Library as an example.

#1 MeSH descriptor: [Exercise] explode all trees

#2 Exercises or Physical or Physical Activities or Exercise, Physical or Activities, Physical or Physical Exercises or Activity, Physical or Exercises or Physical Activity or Physical Exercise or Acute Exercise or Acute Exercises or Exercise, Acute or Exercises, Acute or Training, Exercise or Exercise Trainings or Exercise Training or Trainings, Exercise or Exercises, Isometric or Isometric Exercises or Exercise, Isometric or Isometric Exercise or Aerobic Exercise or Exercises, Aerobic or Exercise, Aerobic or Aerobic Exercises (Word variations have been searched)

#3 MeSH descriptor: [COVID-19] explode all trees

#4 COVID-19 PandemicCOVID-19 Pandemic or Pandemic, COVID-19 or COVID 19 Pandemic or COVID-19 Pandemics or COVID 19 Virus Disease or Coronavirus Disease-19 or Coronavirus Disease 2019 or 2019 nCoV Disease or SARS-CoV-2 Infection or Virus Disease, COVID-19 or COVID 19 or COVID 19 Virus Infection or Disease, COVID-19 Virus or COVID19 or COVID-19 Virus Diseases or COVID-19 Virus Disease or SARS-CoV-2 Infections or Disease 2019, Coronavirus or Infection, SARS-CoV-2 or 2019 Novel Coronavirus Infection or SARS Coronavirus 2 Infection or COVID-19 Virus Infection or Coronavirus Disease 19 or 2019 Novel Coronavirus Disease or SARS CoV 2 Infection or Virus Infection, COVID-19 or COVID-19 Virus Infections or Severe Acute Respiratory Syndrome Coronavirus 2 Infection or 2019 nCoV Infection or Infection, COVID-19 Virus; (Word variations have been searched)

#5 #1 or #2
#6 #3 or #4
#7 MeSH descriptor: [Randomized Controlled Trial] explode all trees
#8 MeSH descriptor: [Mental Health] explode all trees
#9 Hygiene, Mental or Health, Mental or Mental Hygiene (Word variations have been searched)
#10 #8 or #9
#11 MeSH descriptor: [Depression] explode all trees
#12 Emotional Depression or Symptom, Depressive or Depressive Symptom or Depressive Symptoms or Depression, Emotional) (Word variations have been searched (Word variations have been searched)
#13 #11 or #12
#14 MeSH descriptor: [Anxiety] explode all trees
#15 Anxieties, Social or Anxiety, Social or Social Anxiety or Social Anxieties or Hypervigilance or Anxiousness or Angst or Nervousness (Word variations have been searched)
#16 #14 or #15
#17 #5 and #6 (Word variations have been searched)
#18 #10 or #13 or #16
#19 #17 and #18 (Word variations have been searched)

### Eligibility criteria

Inclusion Criteria: (1) Studies with controlled experimental groups. (2) Studies that incorporate measures of depression and anxiety. (3) Studies involving individuals infected with COVID-19 who are older than 18 years of age. (4) Participants with no history of psychiatric diagnosis. (5) Studies that include physical activity as an intervention. (6) Articles published between January 1, 2020 and January 10, 2024.

Exclusion Criteria: (1) Literature that could not be retrieved. (2) Repeatability studies. (3) Synthesis and observational or cross-sectional studies. (4) No clear report. (5) Infected persons younger than 18 years of age. (6) Non-COVID-19 infected persons.

Two authors independently conducted the initial screening of studies by reviewing titles and abstracts, removing duplicate entries from the selected literature. Subsequently, they confirmed the eligibility of studies according to the criteria outlined in this paper. In instances where a disagreement between the two authors arose during the literature selection process, the third author acted as an arbitrator to resolve the matter (see below table).

**Inclusion and exclusion**

| Inclusion criteria | Exclusion criteria |
|---|---|
| 1. Studies with controlled experimental groups | 1. Literature that could not be retrieved |
| 2. Studies that incorporate measures of depression and anxiety | 2. Repeatability studies |
| 3. Studies involving individuals infected with COVID-19 who are older than 18 years of age | 3. Synthesis and observational or cross-sectional studies |
| 4. Participants with no history of psychiatric diagnosis | 4. No clear report |
| 5. Studies that include physical activity as an intervention | 5. Infected persons younger than 18 years of age |
| 6. Articles published between January 1, 2020 and January 10, 2024 | 6. Non-COVID-19 infected persons |

### Data extraction

Two authors conducted independent literature screening, data extraction, and cross-checking. In cases where outcome data were presented graphically or if the final intervention results were not provided, we reached out to the trial authors for numerical data. The extracted information encompassed the following: 1. Basic study information (e.g., first author, publication date, country, sample size). 2. Fundamental characteristics of study participants (e.g., age, gender). 3. Details of the intervention (e.g., intervention program, duration, frequency per week, and length of each intervention). 4. Instruments utilized for assessing mental health. 5. Outcome metrics, including measurements of depression, anxiety, and other psychological aspects. In instances where disagreements arose between the two reviewers, a third author was consulted to resolve them.

## QUANTIFICATION AND STATISTICAL ANALYSIS

### Quality assessment

We meticulously followed all steps outlined in the PRISMA statement to ensure transparency throughout our review process.[83] This methodological approach guided our study search, the establishment of inclusion criteria, and the final selection of studies for the review,

thereby minimizing susceptibility to internal or external sources of bias. We conducted the meta-analysis using Stata 17.0 and assessed the overall quality of evidence using Review Manager 5.4.

## Statistical analysis

We employed Review Manager 5.4 and Stata 17.0 for conducting heterogeneity testing, data merging, forest plotting, and risk of bias assessment. The outcome indicators in the literature encompassed continuous outcome variables, and the units of the original study outcome indicators varied. Consequently, we selected SMD and 95% Confidence Interval (CI) for the combined effect size statistics of the effect scale indicators. Specifically, we categorized $|SMD| \leq 0.1$ as a small effect size, $0.10 \leq |SMD| \leq 0.34$ as a small-to-medium effect size, $0.35 \leq |SMD| \leq 0.64$ as a medium effect size, and $0.65 \leq |SMD| \leq 1.19$ as a large effect size. An $|SMD| \geq 1.20$ represented a very large effect size.[84] To assess inter-study heterogeneity, we employed the Q statistic, with a significance level set at $p < 0.05$. Quantitative evaluation of heterogeneity utilized the $I^2$ values, where 0% indicated no heterogeneity, $\geq 25\%$ signified mild heterogeneity, $\geq 50\%$ indicated moderate heterogeneity, and $\geq 75\%$ represented high heterogeneity. We employed a random-effects model for data merging when the $I^2$ value indicated moderate heterogeneity or higher. Conversely, a fixed-effects model was applied when heterogeneity was low. In cases where a trial reported multiple physical activity groups compared to the control condition, we combined these groups to prevent data loss and potential issues with the unit of analysis.[85]