Effects of music therapy on COVID-19 patients’ anxiety, depression, and life quality
A protocol for systematic review and meta-analysis
Xiaomei Chen, MBa, Haiying Li, MBb, Xiaoying Zheng, MBc, Jiaqi Huang, MBd,e

Abstract
Background: Whether music therapy improves coronavirus disease 2019 (COVID-19) patients’ anxiety, depression, and life quality are still controversial. Therefore, to provide evidence-based medical evidence for clinical non-pharmacological interventions, we performed a meta-analysis of randomized controlled trials of music therapy for COVID-19 patients’ anxiety, depression, and life quality.

Methods: Cochrane Central Register of Controlled Trials Repositories, PubMed, Embase, Web of Science and Chinese Science Citation Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Scientific Journal Database, and Wan-Fang database were searched to identify studies on the evaluation of the effectiveness of the music-based intervention on COVID-19 patients’ anxiety, depression, and life quality from inception to May 2021. Two researchers independently carried out data extraction and literature quality evaluation of the quality and the meta-analysis on the included literature was performed with Revman5.3 software.

Results: The results of this meta-analysis will be submitted to a peer-reviewed journal for publication.

Conclusion: This study will provide reliable evidence-based evidence for the effects of music therapy on COVID-19 patients’ anxiety, depression, and life quality.

Abbreviation: COVID-19 = coronavirus disease 2019.

Keywords: coronavirus disease 2019, meta-analysis, music therapy, protocol

1. Introduction
In December 2019, a severe acute respiratory syndrome coronavirus 2, characterized by pneumonia, broke out in Wuhan, China, known as coronavirus disease 2019 (COVID-19). The disease is transmitted from person to person through the respiratory tract and contact with infected people, and all people are generally susceptible. The incubation period is generally from 1 to 14 days, and up to now, there exists no effective antiviral therapy.

Prevention and isolation are the 2 most effective protective measures. To prevent the wider spread of the epidemic, confirmed cases have been isolated for treatment and suspected cases have been self-quarantined for observation. Isolated people often have psychological stress reactions to various factors. When focusing on the prevention and control of COVID-19 clinically, our attention should also be paid to psychological intervention for different groups of people.

As an interdisciplinary subject, music therapy integrates medicine, music, and psychology together. Meanwhile, being a non-drug intervention method, it has been increasingly applied in clinical practice by researchers. Therefore, music therapy may be used as a non-pharmacological intervention for psychological intervention in COVID-19 patients. However, there is still insufficient clinical evidence to support it. A meta-analysis was conducted to further evaluate the effects of music therapy intervention on COVID-19 patients’ anxiety, depression, and life quality.

2. Methods

2.1. Protocol
Under the guidance of the preferred reporting items for systematic reviews and meta-analysis protocols, this protocol of systematic review and meta-analysis was conducted to further evaluate the effects of music therapy intervention on COVID-19 patients’ anxiety, depression, and life quality.
review and meta-analysis has been drafted.\cite{18} The research framework has been registered on the open science framework (OSF) (Registration Number: DOI 10.17605/OSF.IO/VKF8X).

2.2. Ethics
Since this is a protocol with no patient recruitment and personal information collection, the approval of the ethics committee is not required.

2.3. Eligibility criteria
2.3.1. Types of studies. We will collect all randomized controlled trials.

2.3.2. Participants. COVID-19 patients.

2.3.3. Interventions. Patients in the control group were given routine treatment, while patients in the experimental group accepted music therapy on the basis of routine treatment.

2.3.4. Outcome index. Any rating scale that describes anxiety, depression, and life quality.

2.4. Exclusion criteria
(1) Studies without a control group. (2) Review articles, techniques, case reports, letters to the editor, and editorials are excluded.

2.5. Search strategy
Computer was used to retrieve Cochrane Central Register of Controlled Trials Repositories, PubMed, Embase, Web of Science and Chinese Science Citation Database, China National Knowledge Infrastructure, Chinese Biomedical Literature Database, Chinese Scientific Journal Database, and Wan-Fang database. The retrieval time limit was between the establishment of the database and May 2021. Taking PubMed as an example, the retrieval strategy is displayed in Table 1.

2.6. Data screening and extraction
The literature selection process is listed in Figure 1. Two authors independently searched and screened relevant papers. EndNote X7 software was utilized to delete the duplicates. The titles and abstracts of all searched papers were checked for eligibility. Relevant papers were selected, and then the full-text papers were subsequently assessed by the 2 authors. Finally, a panel meeting was convened for resolving the disagreements about the inclusion of the papers.

We developed a data abstraction form to extract all useful data: (i) the characteristics of papers (authors, publish year, and country); (ii) the characteristics of participators (sample size, mean age, sex ratio, and study period); (iii) study design (random allocation, allocation concealment, masking, selection process of participators, and loss to follow-up); (iv) music therapy process (music therapy method, music therapy period, music therapy frequency, minutes per session, and the treatment measures in the control group); and (v) outcome measures (anxiety, depression, and life quality score).

2.7. Quality evaluation
Two authors independently assessed the risk of bias of included studies using Cochrane Collaboration’s risk of the bias assessment tool, and all disagreements were resolved by discussing with a third author.

2.8. Statistical analysis
Rev-Man 5.3 software was applied for the meta-analysis. The pooled effects were estimated using the standardized mean differences and its 95% confidence interval (95% CI). Heterogeneity between studies was assessed by I-square ($I^2$) and Q-statistic ($P < .10$), and a high $I^2$ (≥50%) was recognized as heterogeneity. If $P≥.1$ and $I^2 ≤ 50\%$, there was no statistical heterogeneity among the results of the studies, and a fixed-effect model (Mantel–Haenszel method) was adopted for analysis, otherwise a random-effect model was used.

2.8.1. Dealing with missing data. If there are insufficient or missing data in the literature, the authors will be contacted via email. If the data are still not available, only the currently available data will be analyzed and the potential impacts will be discussed.

2.8.2. Subgroup analysis. According to the duration of intervention and severity of illness, subgroup analysis will be carried out.

2.8.3. Sensitivity analysis. We also performed sensitivity analyses to test the robustness of the results by re-estimating the pooled effects with a fixed-effect or random-effect model.

2.8.4. Publication bias. If the number of studies included in an outcome indicator is no less than 10, a funnel chart will be used to assess publication bias.\cite{19}

3. Discussion
Clinical observation revealed that COVID-19 patients had different degrees of diarrhea, nausea, decreased appetite, rash, and other adverse reactions during antiviral treatment.\cite{20,21} At the same time, to cutoff the transmission route, the confirmed patients accepted isolation treatment and other prevention and control measures, which leads to anxiety, stress, loneliness, depression, and despair.\cite{20} Excessively negative emotions can result in obsessive thinking, and, in severe cases, psychopathy seriously affects the treatment and recovery of COVID-19 patients. In this study, the principles and methods of evidence-based medicine were applied to evaluate the effectiveness of music therapy, so as to further clarify the effects of music therapy on
COVID-19 patients’ anxiety, depression, and life quality to provide a basis for clinical application.

**Author contributions**

**Conceptualization:** Jiaqi Huang, Xiaomei Chen, and Haiying Li.

**Data curation:** Jiaqi Huang, Xiaomei Chen, Haiying Li, and Xiaoying Zheng.

**Funding acquisition:** Jiaqi Huang.

**Funding support:** Jiaqi Huang.

**Project administration:** Jiaqi Huang.

**Resources:** Xiaoying Zheng.

**Software operating:** Xiaomei Chen.

**Supervision:** Jiaqi Huang and Xiaoying Zheng.

**Validation:** Xiaoying Zheng.

**Visualization:** Xiaoying Zheng.

**Writing – original draft:** Jiaqi Huang, Xiaomei Chen, and Haiying Li.

**Writing – review & editing:** Jiaqi Huang, Xiaomei Chen, and Haiying Li.

**References**

[1] Monroy-Fraustro D, Maldonado-Castellanos I, Aboites-Molina M, et al. Bibliotherapy as a non-pharmaceutical intervention to enhance mental

---

*Figure 1. Flow diagram of the literature retrieval.*
health in response to the COVID-19 pandemic: a mixed-methods systematic review and bioethical meta-analysis. Front Public Health 2021;9:629872–1629872.

[2] Zhao YH, Zhao L, Yang XC, Wang P. Cardiovascular complications of SARS-CoV-2 infection (COVID-19): a systematic review and meta-analysis. Rev Cardiovasc Med 2021;22:159–65.

[3] Zhang X, Lewis AM, Moley JR, Brestoff JR. A systematic review and meta-analysis of obesity and COVID-19 outcomes. Sci Rep 2021;11:7193.

[4] Papoutsi E, Giannakoulis VG, Xourgia E, Routsi C, Kotanidou A, Siempos II. Effect of timing of intubation on clinical outcomes of critically ill patients with COVID-19: a systematic review and meta-analysis of non-randomized cohort studies. Crit Care (London, England) 2021;25:121.

[5] Hayashi Y, Wagatsuma K, Nojima M, et al. The characteristics of gastrointestinal symptoms in patients with severe COVID-19: a systematic review and meta-analysis. J Gastroenterol 2021;56:409–20.

[6] Song LG, Xie QX, Lao HL, Lv ZY. Human coronaviruses and therapeutic drug discovery. Infect Dis Poverty 2021;10:28.

[7] Mojtahab H, Javidi N, Naviaux AF, et al. Exploration of the epidemiological and emotional impact of quarantine and isolation during the COVID-19 pandemic. Adv Exp Med Biol 2021;1318:687–703.

[8] Nussbaumer-Streit B, Mayr V, Dobrescu AI, et al. Quarantine alone or in combination with other public health measures to control COVID-19: a rapid review. Cochrane Database Syst Rev 2020;9:CD013574.

[9] Sun P, Fan DJ, Li HZ, et al. The impact of age on anxiety in Covid-19 patients in quarantine wards. Psychol Health Med 2021;1–6.

[10] El Keshky MES, Alsabban AM, Basyouni SS. The psychological and social impacts on personal stress for residents quarantined for COVID-19 in Saudi Arabia. Arch Psychiatr Nurs 2021;35:311–6.

[11] Zhu K, Niu Z, Freudenheim JL, et al. COVID-19 related symptoms of anxiety, depression, and PTSD among US adults. Psychiatry Res 2021;301:113959.

[12] Shaygan M, Yazdani Z, Valibeygi A. The effect of online multimedia psychoeducational interventions on the resilience and perceived stress of hospitalized patients with COVID-19: a pilot cluster randomized parallel-controlled trial. BMC Psychiatry 2021;21:93.

[13] Liu ML, Liu M, Zhong H, et al. Significance and operation mode of moxibustion intervention for the group under quarantine after close contact with COVID-19. Zhongguo Zhen Jiu 2020;40:457–61.

[14] Tang Q, Huang Z, Zhou H, Ye P. Effects of music therapy on depression: a meta-analysis of randomized controlled trials. PloS One 2020;15:e0240862.

[15] Huang J, Yuan X, Zhang N, Qiu H, Chen X. Music therapy in adults with COPD. Respir Care 2021;66:501–9.

[16] Santiváñez-Acosta R, Tapia-López ELN, Santero M. Music therapy in pain and anxiety management during labor: a systematic review and meta-analysis. Medicina (Kaunas) 2020;56;.

[17] Li Y, Xing X, Shi X, et al. The effectiveness of music therapy for patients with cancer: a systematic review and meta-analysis. J Adv Nurs 2020;76:1111–23.

[18] Shamseer L, Moher D, Clarke M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647.

[19] Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:455–63.

[20] Zhong Z, Li H, Zhu J, et al. Clinical characteristics of 2,459 severe or critically ill COVID-19 patients: a meta-analysis. Medicine 2021;100:e23781.

[21] He X, Cheng X, Feng X, Wan H, Chen S, Xiong M. Clinical symptom differences between mild and severe COVID-19 patients in China: a meta-analysis. Front Public Health 2020;8:561264.