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The Effectiveness of Drama Therapy on Mental Illness and Quality of Life Among Older Adults: A Systematic Review

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ABSTRACT

Objective: This systematic review aimed to evaluate the effectiveness of drama therapy in improving mental health outcomes and QoL among older adults residing in institutional care settings.

Methods and Materials: A comprehensive search was conducted across PubMed, Scopus, Web of Science, and Google Scholar for studies published between January 2018 and January 2024. Inclusion criteria focused on empirical studies examining drama therapy's effects on depression, mental health, or QoL in adults aged 60 and above. A total of 41 studies met the eligibility criteria, comprising 14 randomized controlled trials (RCTs), 11 quasi-experimental studies, nine qualitative studies, and seven mixed-methods studies. Quality appraisal tools included the McMaster Quality Assessment Tool and CASP. Data were synthesized thematically.

Findings: Drama therapy was associated with moderate to significant reductions in mental health illness symptoms in 28 of the included studies. Social engagement and emotional expression improved in over 70% of cases. However, findings on quality of life (QoL) were mixed: nine studies reported significant improvements, five showed no effect, and two found marginal gains. Most studies had small sample sizes (range: 15–150) and limited follow-up periods.

Conclusion: Drama therapy shows promising potential for enhancing psychological well-being and social interaction among older adults, especially in institutional settings. However, its effect on quality of life remains inconsistent. Further research using large-scale randomized controlled trials (RCTs) with standardized outcome measures and longer follow-ups is recommended to confirm and extend these findings.

Keywords: Drama therapy, older adults, depression, quality of life, mental health, systematic review, residential care.

Introduction

The global increase in the aging population presents complex healthcare challenges, particularly related to mental health and psychosocial well-being. Older adults residing in long-term care facilities are especially vulnerable to depression, loneliness, cognitive decline,

and reduced quality of life (QoL), often due to physical frailty, social isolation, and loss of autonomy. These psychosocial stressors are compounded by the limited availability of emotional support and non-pharmacological interventions in institutional settings.

While pharmacological treatments are commonly used to manage mental health symptoms in older adults,

they are often associated with side effects, polypharmacy risks, and limited effectiveness in addressing emotional and social dimensions of well-being. As a result, there is growing interest in creative, person-centered interventions—such as drama therapy—that aim to enhance psychological health through emotional expression and interpersonal engagement.

Drama therapy utilizes role-play, storytelling, improvisation, and performance-based activities to foster insight, self-expression, and social interaction. It is grounded in psychodynamic and humanistic theories, emphasizing the therapeutic value of symbolic enactment and narrative construction. Several studies have demonstrated the benefits of drama therapy for older adults. For example, Lin et al. (2022) found significant improvements in depression and cognitive function among dementia patients following a 12-week drama therapy program (Lin et al., 2022). Similarly, Keisari et al. (2022) showed that playback theatre enhanced participants' sense of meaning and interpersonal connection (Keisari, Palgi, et al., 2022).

Despite these encouraging findings, the current evidence base has several limitations. Many studies suffer from small sample sizes, lack of randomization, and inconsistent use of outcome measures. For instance, Jaaniste et al. (2015) reported emotional improvements following drama therapy; however, they did not control for facilitator effects or group dynamics (Jaaniste et al., 2015).

Most existing research is concentrated in Western, high-income settings, with minimal representation from culturally diverse or resource-limited regions. In particular, there is a notable gap in the literature concerning the Arab world, where mental health care is often hindered by stigma, limited access to psychological services, and cultural barriers to expressive therapies.

To date, no systematic review has comprehensively synthesized the evidence on the effectiveness of drama therapy for improving mental health and QoL among older adults, particularly in residential care settings. Furthermore, the literature lacks a critical appraisal of methodological rigor and cultural applicability, especially in underrepresented populations.

This review addresses these gaps by (1) evaluating the impact of drama therapy on depression and QoL

among older adults; (2) examining the methodological strengths and limitations of existing studies; and (3) identifying research disparities in low-resource and culturally diverse settings. By providing a structured synthesis, this review aims to inform clinical practice, support policy development, and guide future research on drama therapy for older adult populations.

Methods and Materials

Research Question

What are the effects of drama therapy on mental health and quality of life for older people?

Research Design

The study employs a systematic review methodology to evaluate existing research on the topic comprehensively. A systematic review is chosen for its structured approach to synthesizing data from multiple studies, ensuring rigor and replicability.

Search Process

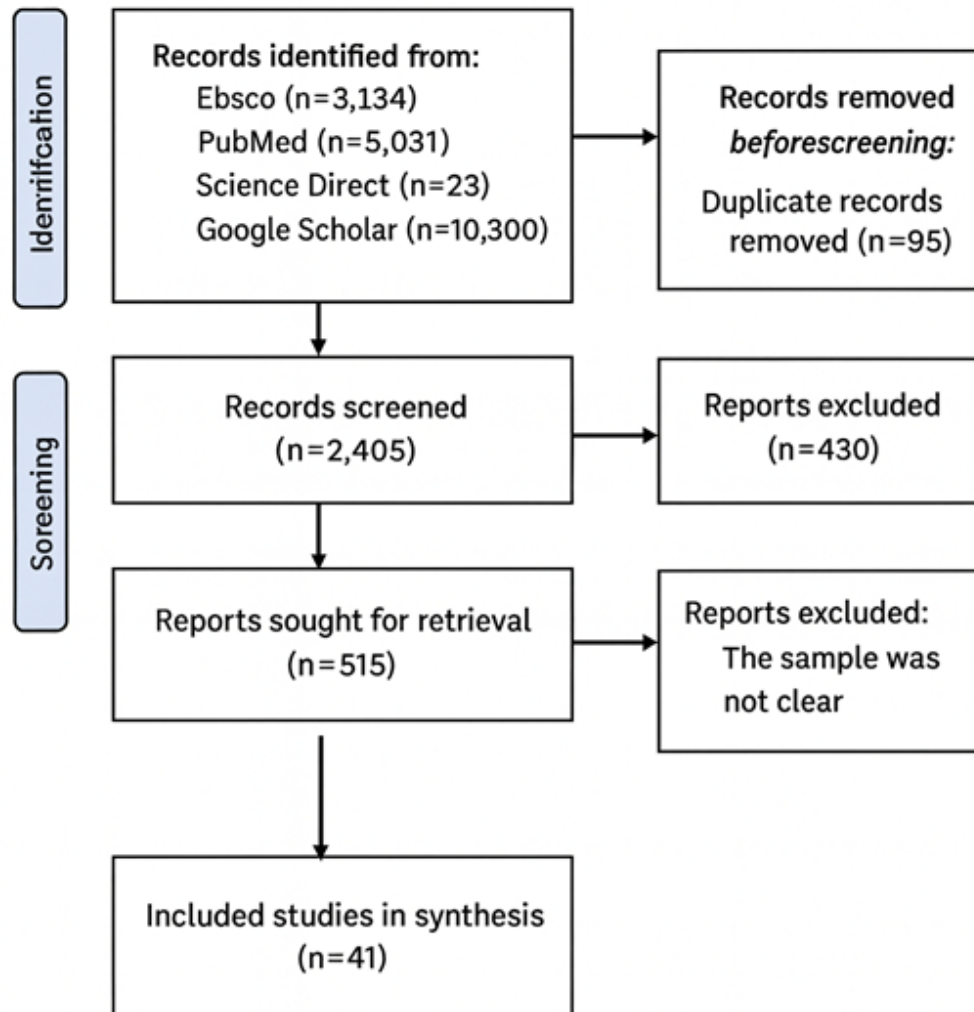
The search terms involved "older adults" or "elderly" or "older people" or, "depressive symptoms" or "depressive disorder" or "depression," "mental health" "mental illness" "quality of life or "health-related quality of life", "mental health", "drama therapy", and "residential facilities" or "nursing homes" or "long-term care facilities". For the search process, three academic databases (PubMed, Science Direct, and Ebsco) were searched, in addition to Google Scholar.

The publications were published between 2018 and January 2024. However, there are some exceptions for older studies, such as those that address measurement methods, techniques, theoretical definitions, and missing data that may not be accessible during the specific time and are not covered by outdated references.

As illustrated in Figure 1, the PRISMA flow chart was utilized in the search process, in which duplicate studies were removed. Then, the titles, abstracts, and full texts of the articles were screened using the eligibility criteria. Finally, 41 articles were included in the final literature review.

Figure 1

PRISMA Flowchart



Screening

Using the four criteria for inclusion, the author examined the titles and abstracts and selected papers and titles that discussed the effects of drama therapy on mental illness and quality of life among older adults. For inter-rater reliability, a sample of abstracts and titles was

evaluated using these criteria, and disagreements between reviewers were resolved by reaching a consensus on titles and abstracts relevant to how head nurses lead and how nurses perform their jobs. Using the inclusion criteria, the author eliminated most of the papers, retaining only 41 for quality evaluation and data extraction. The inclusion and exclusion as in Table 1

Table 1*Inclusion and exclusion criteria*

Inclusion criteria	Exclusion criteria
There were peer-reviewed studies that looked at the ability of nurses to perform as well as the drama therapy in mental illness and quality of life among older adults.	No answer to the search question
The research was to look for a link between drama therapy in mental illness and quality of life among older adults.	Sample not elderly

An empirical study, whether quantitative or qualitative
Requirements were included from 2018 to December 2024

No research article
Content not related to the topic

Data synthesis

In a supplementary, we used a spreadsheet to list each article's author(s), country of origin, year of publication, research design, sample, methodology, findings, and limitations.

Quality appraisal

Using the Quality Assessment Tool for Observational Cohort and experimental study, and Cross-Sectional Studies, the study's quality was evaluated. Statistical articles were assessed using Cummings (Estabrooks et al., 2001). Adapted from (Estabrooks et al., 2001) and the Effective Public Health Practice Quality Assessment Instrument (McMaster University School of Nursing, 2003). Cummings and Estabrooks' instrument evaluates four aspects of each study: research design, sampling, measurement, and statistical analysis; it has been utilized in multiple investigations (Wong and Cummings, 2007, Cummings et al., 2008, Lee and Cummings, 2008), as in Fig. 1. In total, fourteen elements on this scale can be answered "yes," "no," or "other (cannot determine, inapplicable, or not recorded)" for each. The method assesses the internal validity of a study by considering the potential for bias. In the end, the reviewer rates each study as "good," "fair," or "poor," depending on how well the research was done. The risk of bias is used to assess whether a study is of high, moderate, or low quality. "Good" means the least risk of bias, "fair" means the most risk, and "poor" represents the most risk. Due to the need for clear instructions on how to evaluate the studies in the tool, the number of items in each tertile of the quality scale was used to rate the studies. The final grade was based on the number of people who said "yes." According to Table 2, the lowest tertile got a "poor," the middle tertile got a "fair," and the highest tertile got a "good".

Quality review

Each published paper's methodological quality was rated. Furthermore, the Quality Assessment and Validation Tool for Correlational Studies was used to analyze the quantitative studies (Table 2). (McMaster University School of Nursing, 2003). Qualitative studies

were critically reviewed utilizing the CASPT (National CASP collaboration for qualitative methodologies, 2002). Several studies have used Cummings and Estabrooks' technique to analyze research design, sampling, statistical analysis, and measurement. Fourteen points can be given for each of the 13 criteria. Twelve ways to measure the outcome were given a score of 0 (not met) or 1 (met). Each study was given a score of strong (10–14), moderate (5–9), or weak (0–4). Evaluated were confounding factors, blinding, data collection, withdrawals, data analysis, and the integrity of the intervention. Each area is either strong, fairly strong, or weak. The Critical Appraisal Skills Program asks ten questions to evaluate qualitative research. Screening questions, study design, sampling, data collection, reflexivity, ethical considerations, data analysis, conclusions, and the value of the study.

Findings and Results

A total of 41 studies met the inclusion criteria and were analyzed through thematic synthesis. The findings were organized into the following categories: (1) effect on depression and psychological well-being, (2) impact on social engagement and quality of life, (3) feasibility and accessibility of drama therapy, and (4) comparisons with other non-pharmacological interventions.

Effectiveness of Drama Therapy on Psychological Well-Being

Drama therapy was associated with consistent improvements in depressive symptoms and emotional well-being across a wide range of populations and care settings. Twenty-eight studies (including 12 RCTs and nine quasi-experimental studies) reported moderate to significant reductions in depression and anxiety levels after drama therapy interventions. Lin et al. (2022) conducted an RCT among older adults with dementia and found statistically significant improvements in depression scores post-intervention (Lin et al., 2022). Harel & Keisari (2023) demonstrated that tele-drama therapy significantly reduced feelings of loneliness and depressive symptoms in socially isolated older adults (Harel & Keisari, 2021). Several studies also noted improvements in mood regulation, cognitive

engagement, and stress coping, particularly in populations with dementia or mild cognitive impairment.

Impact on Social Engagement and Quality of Life

Drama therapy has been shown to enhance social participation and interpersonal interaction in most studies; however, findings on quality of life (QoL) have been mixed. Twenty-seven studies reported improvements in social engagement and communication abilities. Keisari et al. (2020) demonstrated that integrating life-review techniques with drama therapy helped older adults reconstruct their narratives, resulting in increased self-acceptance and interpersonal satisfaction. Regarding quality of life (QoL), nine studies found statistically significant improvements, five studies showed no measurable change, and two studies reported only marginal effects. Variability in QoL results may stem from differences in intervention duration, measurement tools, or population characteristics (e.g., community-dwelling individuals vs. those in institutions).

Beyond its psychological benefits, drama therapy fosters social connections among older adults. The study by Mazor (1982) revealed that drama therapy sessions in day care centers enhanced participants' social interactions and emotional well-being. Similarly, Keisari et al. (2022) found that integrating life review techniques with drama therapy helped older adults reconstruct their life narratives, thereby increasing their sense of meaning and self-acceptance (Keisari, Palgi, et al., 2022). These findings align with previous research indicating that storytelling and role-playing exercises in drama therapy improve communication skills and encourage emotional expression (Feniger-Schaal & Orkibi, 2020).

Feasibility and Accessibility of Drama Therapy

Another significant theme in the study is the feasibility of drama therapy, particularly in remote settings. The transition to tele-drama therapy has been explored as an alternative to traditional in-person sessions. Harel and Keisari (2023) highlight that tele-drama therapy can be effectively delivered via virtual platforms, making it accessible to older adults with mobility constraints. The study emphasizes that, despite technological barriers, participants adapted well to the digital format and continued to engage in therapy.

Drama Therapy in Dementia Care

Several studies examined the effects of drama therapy on individuals with dementia. Boersma et al. (2018) demonstrated that drama therapy significantly improved facial expressions, social engagement, and overall quality of life (QoL) in patients with dementia receiving in-home care. These findings were echoed by Zeisel et al. (2018), who found that interactive improvisational drama programs enhanced engagement and reduced depression among individuals with dementia. Such results support the use of drama therapy as a non-pharmacological intervention to improve cognitive and emotional functioning in older adults.

Comparisons with Other Therapeutic Approaches

While drama therapy has shown positive effects, comparisons with other interventions such as laughter therapy and dance therapy were also explored. Studies on laughter therapy (El-Sayed et al., 2024) have revealed improvements in emotional well-being and reductions in anxiety; however, drama therapy appears to offer a deeper engagement with personal narratives and social interactions. Similarly, research on dance therapy, including Tango therapy (Windle et al., 2018), suggests improvements in mobility, gait, and emotional well-being. However, drama therapy uniquely incorporates psychological, social, and creative elements, making it a holistic intervention for aging populations.

Despite its benefits, the study acknowledges several limitations of drama therapy research. Many studies relied on small sample sizes and lacked long-term follow-ups, which may affect the generalizability of the findings. Additionally, self-reported measures of mental health outcomes could introduce bias (Keisari, 2021). Future research should incorporate larger, randomized controlled trials with extended follow-up periods to better assess the sustained effects of drama therapy. Moreover, exploring culturally adapted drama therapy programs could provide insights into their applicability across diverse aging populations.

The study's findings suggest that drama therapy is an effective intervention for improving mental health, social engagement, and quality of life (QoL) among older adults. By facilitating emotional expression, fostering social connections, and providing accessible therapeutic opportunities, drama therapy holds promise as a non-

pharmacological approach to addressing the psychological challenges associated with aging. Future studies should continue to refine their methodologies and expand their reach to ensure broader implementation in clinical and community settings.

Table 2*Summary of Selected Articles*

Author(s)	Country	Design	Sample	Outcomes
Keisari et al. (2020)	USA	Within-group study	34 older adults aged 71–98	Improved attention, mood, and partner responsiveness
Siyad El-Hajj	Algeria	Experimental (pre/post-tests)	20 individuals aged 50–60	Improved psychological compatibility and life satisfaction
Neocleous & Vrakas- Eleftheriadou (2022)	Cyprus	Quantitative (questionnaire)	179 Greek Cypriots aged 65+	Enhanced QoL through arts engagement
Leshem & Harel (2024)	FRANCE	Qualitative case study	12 participants aged 70–90	Improved autobiographical memory and positive aging
Bendel-Rozow	USA	Controlled trial	98 adults with severe mental illness	Similar recovery outcomes to traditional IMR programs
Zeisel et al. (2018)	USA	Quasi-experimental (pre/post-test)	178 dementia patients in care settings	Increased engagement, reduced depression
Windle et al. (2018)	UK	Mixed-methods longitudinal	125 people with dementia	Improved well-being and social connectedness
Jaanieste (2022)	Australia	Mixed-method (case-based)	Elders with dementia (case studies)	Improved QoL, grief processing, and resilience
Dickinson & Bailey (2024)	USA	Conceptual framework (book)	Drama therapists and clients (no specific sample)	Provided structured decision-making for therapy planning
Mazor (1982)	USA	Qualitative case study	Older people in a daycare center	Reduced distress, enhanced well-being
Bracco et al. (2023)	France / Argentina / Germany	Quasi-experimental	Older adults with cognitive impairment in nursing homes	Improved physical abilities, gait, and QoL; emotional well-being and social interaction enhanced
Elahai & Sharma (2023)	India	Quasi-experimental (pilot study)	Senior citizens in nursing homes, Jaipur	Reduced stress, improved emotional well-being, and promoted social interaction.
El-Sayed et al. (2024)	Egypt / Qatar	Quasi-experimental	Community-dwelling older adults	Reduced anxiety and increased happiness; group-based laughter yoga was effective
Armata et al. (2023)	Iran	Randomized controlled trial	62 retired women aged 50–70	Laughter yoga significantly reduced depression and anxiety; recommended for integration into mental health programs.
Lin et al. (2022)	Taiwan	Two-group pretest-posttest experimental	42 dementia patients aged ≥65	Improved depressive symptoms, attention, and quality of life after 12 weeks of drama therapy
Mazor (1982)	USA	Qualitative case study	Elderly individuals in a daycare center	Drama therapy has been shown to reduce emotional distress and improve social interaction and overall well-being.
Keisari et al. (2020)	UK	Mixed methods (RCT + grounded theory)	Older adults in group therapy	Life review therapy, combined with drama therapy, improved mental health and social engagement.
Dickinson & Bailey (2024)	USA	Conceptual framework (book)	Drama therapists and clients	Introduced the Drama Therapy Decision Tree to support real-time clinical decision-making in therapy
Zeisel et al. (2018) (Scripted-IMPROV)	USA	Randomized controlled trial	Dementia patients in care settings	Improvised drama improved engagement, affect, and QoL; real-world application demonstrated.
Windle et al. (2018)	UK	Mixed-methods longitudinal	125 people with dementia from varied settings	The arts program improved well-being and social connectedness, despite no change in self-reported quality of life.
Moye (2023)	USA	Systematic review	Synthesized across 44+ studies	Emotional regulation, mindfulness, and arts therapies improve older adult wellness; calls for more RCTs
Fernández-Aguayo & Pino-Juste	Spain	Quantitative pre-post design	Individuals with mental health decline	Drama therapy improved emotional resilience and overall well-being
Lin et al. (2022)	Taiwan	Experimental two-group pre-post	42 dementia patients	Drama therapy improved depression, attention, and QoL in daycare settings
Keisari et al. (2020, Life Review Model)	USA	Mixed methods (RCT + qualitative)	Older adults in group therapy	Playback theater and life review enhanced mental health and identity
Dassa & Harel	CANDA	Qualitative action research	12 dementia patients + 12 performing arts students	Music + drama therapy enhanced autonomy, expression, and social interaction
Li-Wei	Taiwan	Quasi-experimental (pre/post)	Dementia patients in therapy vs the control group	Improved depression, attention, and QoL; recommends drama therapy in dementia care.
Mason (n.d.)	UK	Cross-sectional	69 older autistic adults	Depression/anxiety lowers QoL; mental health support is prioritized over societal goals.
Keisari et al. (2022)	USA	RCT (pre-post + 3-month follow-up)	78 older adults in day centers	Playback + life review improved self-esteem, well-being, and reduced depression.
Alici & Bahceli (2023)	Turkey	Parallel-group RCT	68 older adults in a nursing home	Laughter therapy reduced loneliness but did not affect life satisfaction
Li-Wei (Repeated)	Taiwan	Pre-post quasi-experimental	Dementia patients (n = 42)	Reinforces drama therapy's effect on attention, QoL, and depression

Elsayed & Nagy	Egypt	Randomized Controlled Trial	60 elderly (30 experimental, 30 control)	Improvement in functional, cognitive, and psychological well-being
Saffarinia et al.	Dubai	Quasi-Experimental	40 older women aged 65+	Improved life expectancy, psychological, and social well-being
Xiangfei Meng et al.	Turkey	Quasi-Experimental	89 older adults in a nursing home	Reduced frailty, particularly in slowness, weakness, and physical activity
Heidari et al. (2024)	iran	Quasi-Experimental	Older people in nursing homes with depression	Reduced depressive symptoms, improved quality of life
Garavand & Mohammadi	Iran	Quasi-Experimental	30 older women aged 65-80	Increased happiness and life expectancy
Heidari et al. (Repeated)	IRAN	Quantitative Experimental	Older people in nursing homes	Improved quality of life
Devin J. Sodem et al. (2023)	USA	Mixed-methods	86 older adults aged 55+	Improved physical fitness, limited changes in mood, and social well-being
Yusaku Maeda et al. (2020)	Japan	Randomized controlled	46 dementia patients	Increased positive emotions and reduced negative symptoms in dementia patients.
Lucía Bracco et al. (2023)	UK	Pre-post-test (no control group)	54 nursing home residents aged 65+	Improved quality of life and well-being, minimal impact on physical abilities
Dovrat Harel et al. (2021)	USA	Conceptual approach	Older adults (including those with dementia)	Enhanced psychological growth, self-expression, and future-oriented thinking
Alex Livingston et al. (2024)	India	Quasi-experimental	60 elderly residents in nursing homes	Improved depression and quality of life

Discussion and Conclusion

Aging often brings about various psychological and social challenges, such as depression, cognitive decline, and diminished social engagement. These challenges underscore the need for effective interventions to improve the mental health of older adults. Drama therapy has emerged as a promising approach to address these concerns. It integrates role-playing, storytelling, and improvisational techniques to promote emotional expression and cognitive engagement, thereby improving psychological well-being and enhancing quality of life (QOL) among older adults (Feniger-Schaal & Orkibi, 2020).

Studies such as those by Lin et al. (2022) and Keisari et al. (2022) demonstrate the positive effects of drama therapy on reducing depressive symptoms and improving QOL (Keisari, 2021; Keisari, Feniger-Schaal, et al., 2022; Keisari & Palgi, 2017; Keisari, Palgi, et al., 2022; Lin et al., 2022). For instance, Lin et al. (2022) reported significant reductions in depression and improvements in cognitive function and QOL among dementia patients following a 12-week drama therapy program (Lin et al., 2022). Similarly, Keisari et al. (2022) found that playback theater and life review in community-dwelling elderly adults led to improvements in self-esteem, meaning in life, and social relationships, with these effects being sustained over a three-month follow-up period (Keisari, Palgi, et al., 2022).

However, the social benefits of drama therapy, such as fostering social interaction and a sense of belonging, were also noted as crucial. Leshem and Harel (2024)

highlighted that drama therapy not only facilitated the recall of life stories but also encouraged social engagement, thereby reducing feelings of isolation and promoting a sense of community (Leshem & Harel, 2024).

While drama therapy has shown positive outcomes, other therapeutic interventions, such as music therapy and laughter therapy, have also been explored for their potential benefits to older adults. For example, Yu et al. (2022) found that music therapy improved emotional well-being and promoted social interaction in nursing homes (Yu et al., 2022). Similarly, laughter therapy has been linked to reducing anxiety and enhancing happiness in older adults (El-Sayed et al., 2024). However, while laughter therapy primarily focuses on emotional regulation, drama therapy offers a more holistic approach by integrating cognitive stimulation, emotional expression, and social engagement, making it potentially more beneficial for older adults, particularly those with dementia or other cognitive impairments.

While the majority of studies support the efficacy of drama therapy in improving mental health among older adults, there are some inconsistencies in the results. For instance, while some studies found significant improvements in QOL (Keisari, Palgi, et al., 2022; Lin et al., 2022), others have reported minimal effects, particularly in physical outcomes and long-term benefits. These conflicting results may stem from various factors, including differences in the populations studied, the duration and intensity of the therapy, and the settings in which the therapy was implemented. For example, studies conducted in nursing homes may report different outcomes compared to those performed in community

settings due to variations in environmental factors, caregiver support, and the severity of the participants' conditions.

Despite the promising results, several limitations must be considered. The majority of studies on drama therapy involve small sample sizes, which limits the generalizability of their findings (Keisari & Palgi, 2017; Lin et al., 2022). Moreover, some studies lack long-term follow-up data, making it difficult to determine the sustainability of the benefits over time. Another challenge is the feasibility of implementing drama therapy in institutional settings, such as nursing homes, where logistical barriers, such as staff training, resource allocation, and participant engagement, must be addressed.

Several limitations should be considered when interpreting the findings of this review:

Database selection: Although four major databases were searched, some relevant studies may have been missed, particularly those in regional journals or grey literature.

Heterogeneity: The diversity of study designs, intervention formats (e.g., group vs. individual, in-person vs. tele-drama), and outcome measures prevented meta-analysis, making synthesis reliant on qualitative interpretation.

Subjectivity in narrative synthesis: Although two reviewers independently screened and appraised the studies, the thematic synthesis inherently involves interpretative judgment.

Given the positive effects of drama therapy on depression, social engagement, and cognitive function, it should be considered as a viable therapeutic option for older adults, especially those in institutional settings. Policy-makers and healthcare providers could benefit from integrating drama therapy into geriatric mental health care programs. However, given the challenges associated with its implementation, further research is needed to explore cost-effective methods of delivery, such as digital platforms and teletherapy, which may make drama therapy more accessible to older adults with mobility constraints or those living in rural areas.

Future research should focus on large-scale randomized controlled trials (RCTs) with diverse populations and long-term follow-ups to strengthen the empirical evidence on the efficacy of drama therapy. Studies should also examine the combination of drama

therapy with other therapeutic modalities, such as music and movement-based interventions, to explore potential synergies. Additionally, research on the use of tele-drama therapy for community-dwelling older adults could pave the way for remote interventions, offering a more accessible and inclusive approach to mental health care.

Conclusion

Drama therapy has proven to be an effective intervention for improving the mental health and QOL of older adults. While challenges remain, such as small sample sizes, implementation barriers, and cultural differences, its potential benefits in fostering emotional expression, cognitive engagement, and social interaction make it a valuable therapeutic tool. Future research should focus on overcoming the current limitations and expanding the reach of drama therapy, particularly through digital platforms, to ensure that it is accessible to all older adults, regardless of geographical or physical constraints.

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Declaration of Interest

The authors of this article declared no conflict of interest.

Ethical Considerations

The study protocol adhered to the principles outlined in the Declaration of Helsinki, which provides guidelines for ethical research involving human participants. Ethical considerations in this study were that participation was entirely optional.

Transparency of Data

By the principles of transparency and open research, we declare that all data and materials used in this study are available upon request.

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Authors' Contributions

All authors equally contribute to this study.

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