



Non-pharmacological interventions for caregivers of patients with schizophrenia: A meta-analysis

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ABSTRACT

It has been estimated that about 50–80% of patients with schizophrenia live with or closely contact with their caregivers, and rely on them for housing, and emotional and financial supports. Caregiving experience is usually described as stressful for their caregivers. Non-pharmacological interventions seem to be beneficial to improving life quality. However, there is still no meta-analysis focused on this topic to give an overview. We searched the electronic databases including PubMed, EMBASE, CINAHL, Cochrane Library and China National Knowledge Infrastructure, respectively from the beginning of database to July 2015 for all the randomized controlled trials evaluating the caregiver interventions. Continuous data were expressed mean differences (MD) with 95% confidential intervals (CIs). Standardized mean difference was planned to express, if different scales were used to measure the same outcome. We pooled the results using a random-effect model. As a result, nine studies met the inclusion criteria, comprising 608 randomized participants. In which, 321 participants were in interventional group, while 287 participants were in control group. Concerning the care burden, there was significant difference found between non-pharmacological interventions and control groups ($n=290$, MD -2.10 , 95% CI -3.46 to -0.74 , $P=0.002$; level of heterogeneity $\tau^2=1.81$, $\chi^2=62.13$, $df=3$, $P<0.00001$, $I^2=95\%$). However, no differences were found in family support, family functioning and satisfaction. Of note, our meta-analysis demonstrated the efficacy of non-pharmacological interventions for caregivers of schizophrenia, and supported the application in the clinical practice. However, all the conclusions should be explained cautiously and further confirmation is required by well-designed trials with large sample.

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1. Introduction

Schizophrenia is a severe mental illness, mainly characterized by the abnormal social behaviors, such as false beliefs, unclear or confused thinking, auditory hallucinations, reduced social engagement and emotional expression (Howes and Murray, 2014). The lack of insight is the crucial point for the diagnosis (Palanisappan et al., 2011). According to ICD-10 criteria, the diagnosis of schizophrenia is mainly based on the self-reported experiences of the patients and observed behavior reported by others like their caregivers (Jakobsen et al., 2005). Moreover, caregivers also play an important role in the clinical rehabilitation of patients with schizophrenia. Therefore, the issue of caregivers should not be neglected in the field of schizophrenia.

Actually, the caregiving experience is generally described as

stressful for their caregivers (Chan, 2011). It has been estimated that about 50–80% of patients with schizophrenia live with or closely contact with their caregivers, and rely on them for housing, and emotional and financial supports (Saunders, 2003). It has been estimated the quality of caregiving greatly influences the outcomes of patients with schizophrenia, as well as the burden, coping, satisfaction, social support, expressed emotions and psychological morbidity of their caregivers (Kulhara et al., 2012). Moreover, some studies have found a positive correlation between the severity of disease and the burden of caregivers (Awad and Voruganti, 2008). Moreover, stigma around mental illness also contributed to caregiver burden (Tan et al., 2012).

Some pharmacological interventions on the patients with schizophrenia have been suggested to be beneficial to improving the care burden (Tardy et al., 2014). On the other hand, non-pharmacological interventions for caregivers have been regarded as the potential methods for relieving the burden of caregivers in the other diseases like stroke (Legg et al., 2011). The contents of non-pharmacological interventions mainly include

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psychoeducation (Sin and Norman, 2013), mutual support (Chien and Norman, 2009), counseling intervention (Shuler, 2014), telephone intervention (Wessling et al., 2006) and internet intervention (Haker et al., 2005). However, there is still no meta-analysis focused on this topic to systematically focus on these interventions.

The possible mechanisms of non-pharmacological interventions are summarized as mental health, emotional interaction and providing information for the caregivers. Our work aims to determine the efficacy of non-pharmacological interventions on caregivers of patients with schizophrenia, via measuring the burden, coping, social support, satisfaction of their caregivers. Because they are the common outcomes measured in the current clinical trials for caregivers.

2. Methods

2.1. Data sources

We searched the electronic databases including PubMed, EMBASE, CINAHL, Cochrane Library and China National Knowledge Infrastructure, respectively from the beginning of database to July 2015 for all the randomized controlled trials. The search terms in English and their Chinese equivalents were schizophrenia, caregiver(s), carer(s), non-pharmacological intervention, cognitive-behavioral support, mutual support, counseling, psychoeducation and psychosocial support. Concerning the other sources, we looked through trial protocols in order to identify unpublished data. Conference abstracts and reference lists of related reviews were screened to identify additional trials.

2.2. Study selection and data extraction

We would include the randomized controlled trials (RCTs) with either parallel or cross-over design. The participants must be the caregivers of patients with schizophrenia. The interventions for caregivers must be non-pharmacological interventions, e.g. psychoeducation, counseling and mutual support, in comparison with non-intervention. The trials, in which the interventions were given to both of schizophrenia patients and their caregivers, were excluded in our study. The primary outcomes were the changes in care burden score. The secondary outcomes included coping, satisfaction, family functioning and depression. All the outcomes were measured at the endpoint. Two review authors (LC and JL) independently evaluated the possible studies. Another author (JZ) would be consulted, when any disagreement was found. Thereafter, we used the checklists to independently extract details including study design, characters of study population, number of randomized participants, intervention and main outcomes. The risk of bias (random sequence generation, allocation concealment, patient blind, assessor blind, drop-out or withdraw, selective report) was evaluated as low risk, unclear risk, or high risk.

2.3. Data synthesis

Continuous data were expressed mean differences (MD) with 95% confidential intervals (CIs). Standardized mean difference was planned to express, if different scales were used to measure the same outcome. When there were multiple parallel interventional groups, we combined all relevant experimental groups of the study into a single group to compare with control group. Concerning the missing standard deviations for changes from baseline, we calculated them with CIs, standard errors, t or P values for differences in means. When the levels of significance were reported (such as $P < 0.05$) rather than exact P values, we would use a conservative approach to take the P value at the upper limit (e.g. for $P < 0.05$ take $P = 0.05$, for $P < 0.01$ take $P = 0.01$), according to the principles provided in Cochrane handbook (Higgins and Green, 2011). We pooled the results using a random-effect model. When there was significant clinical heterogeneity, we gave a descriptive summary of the results. The publication bias was to be analyzed with a funnel plot if more than 10 studies were found. Subgroup analysis was carried out based on the different interventions on caregivers.

3. Results

3.1. Description of study

A total of 1631 references were found through database

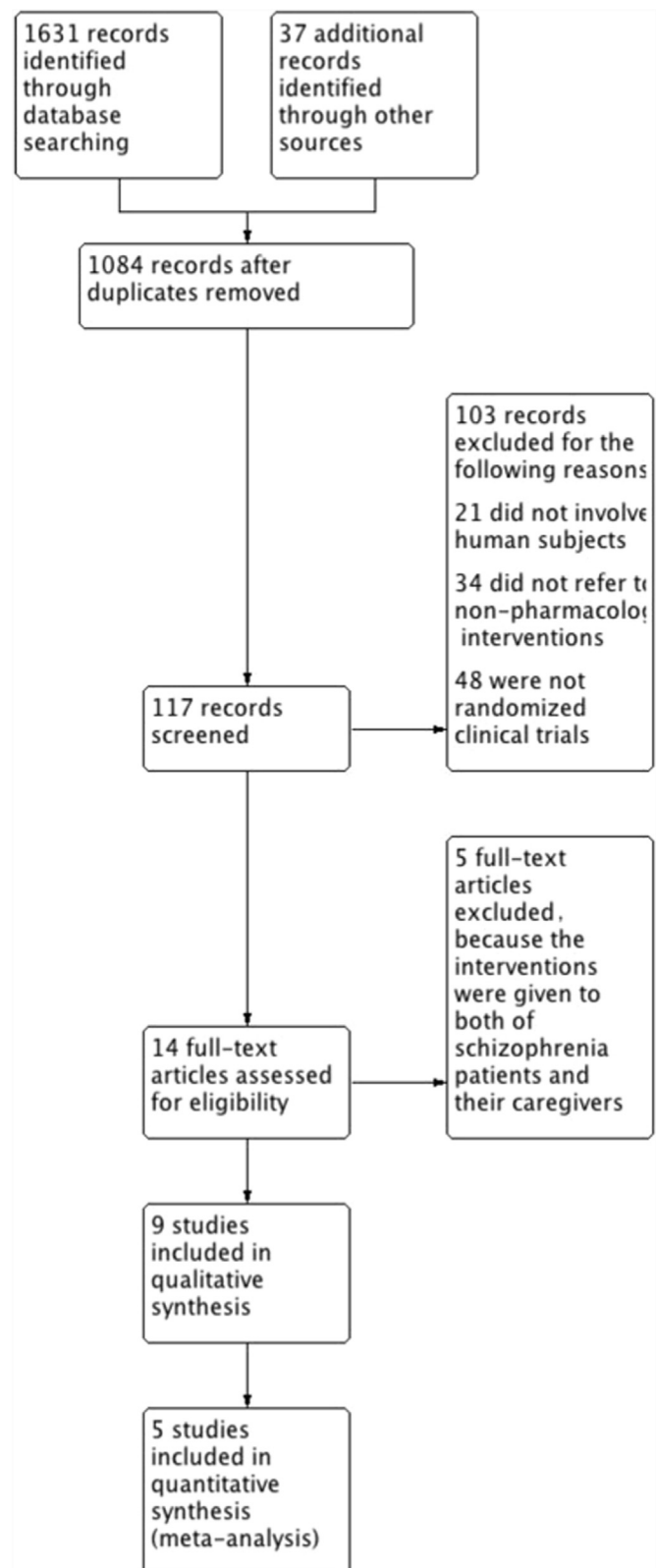


Fig. 1. Flow diagram of the selection process.

searching, while 37 records were detected in the other sources. After excluding duplicates, there were 1084 references identified (Fig. 1). By screening of titles and abstracts, the full-text of 14 studies were obtained and assessed for eligibility. As a result, nine studies met the inclusion criteria, comprising 608 randomized participants (Szmukler et al., 1996; Chou et al., 2002; Chien et al.,

Table 1
Baseline characteristics of included studies.

Study	Design	Population	No. Rand.	Intervention	Risk of bias	Measurements	Results	Conclusion
Szmukler 1996	Parallel RCT	Australia Sch. caregivers	63	Counseling intervention vs. control	UUUUU	Coping, Caregivers' satisfaction	Difference was not found in coping style, but found in caregivers' satisfaction	Counseling intervention is of benefit to caregivers
Chou 2002	Parallel RCT	Taiwan Sch. caregivers	70	Mutual support vs. control	UUUUU	Care burden, Depression, Satisfaction	Caregivers' burden and depression was improved by mutual support	Mutual support provides more effective assistance to caregivers
Chien 2004	Parallel RCT	HK Sch. caregivers	48	Mutual support vs. usual care	LUUUU	Care burden, Family functioning, Social support	Improvement of family burden and functioning was found by mutual support	Support can benefit family caregivers
Chien 2005	Parallel RCT	HK Sch. caregivers	96	Mutual support, psychoeducation, standard care	LUUUU	Care burden, Family functioning, Social support	Family functioning and care burden was improved by mutual support	Mutual support can benefit family and care burden
Cheng 2005	Parallel RCT	HK Sch. caregivers	64	Psychoeducation vs. control	UUUUU	Care burden, Social support	Improvement of care burden was found by psychoeducation	Psychoeducation is an effective nursing intervention
Chien 2008	Parallel RCT	HK Sch. caregivers	76	Mutual support vs. standard care	UUUUU	Care burden, Satisfaction, Family functioning	Significant improvements in families' burden and number of support persons were improved	Mutual support can be an effective family-initiated intervention
Kulhara 2008	Parallel RCT	India Sch. caregivers	76	Psychoeducation vs. routine care	UUUUH	PANSS, Care burden, Coping, Social support, Satisfaction	Support and satisfaction of caregivers were improved	Psychoeducational intervention is a viable option
Gutiérrez 2009	Parallel RCT	Chile Sch. caregivers	45	Psychoeducation vs. control	UUUUU	Family Attitude Scale, Family Opinions, Family Coping	Psychoeducational was effective in modifying caregivers' attitudes	Psychoeducation modifies the negative attitudes of caregivers towards sch.
Sharif 2012	Parallel RCT	Iran Sch. caregivers	70	Psychoeducation vs. control	UUUUU	Care burden	Caregiver burden was significantly reduced	Psychoeducation may improve the outcomes of their families

Risk of bias (random sequence generation, allocation concealment, patient-blind, assessor-blind, dropout or withdrawal, selective report), L low risk, U unclear risk, H high risk, HK, Hongkong; No. Rand., Number of randomization; PANSS, Positive and negative syndrome scale; RCT, Randomized controlled trial; Sch., Schizophrenia

2004, 2005, 2008; Cheng and Chan, 2005; Kulhara et al., 2009; Gutiérrez-Maldonado et al., 2009; Sharif et al., 2012). In which, 321 participants were in interventional group, while 287 participants were in control group. All included studies were parallel design and focused on caregivers of patients with schizophrenia. The details of baseline information are listed in Table 1. Five studies were originated from Hongkong and Taiwan (Chou et al., 2002; Chien et al., 2004, 2005, 2008; Cheng and Chan, 2005), while other four studies were carried out respectively in India, Iran, Australia and Chile (Szmukler et al., 1996; Kulhara et al., 2009; Gutiérrez-Maldonado et al., 2009; Sharif et al., 2012). Concerning the interventions, one study focused on counseling intervention (Szmukler et al., 1996), four studies focused on mutual support (Chou et al., 2002; Chien et al., 2004, 2005, 2008), and four studies focused on psychoeducation (Cheng and Chan, 2005; Kulhara et al., 2009; Gutiérrez-Maldonado et al., 2009; Sharif et al., 2012). The quality of studies was evaluated by the risk of bias with six items (Table 1). Seven studies did not provide details on random sequence generation; none of studies reported the concrete methods of allocation concealment, as well as the methods of patient blind or assessor blind; only one study had more than 10% withdrawals; and no study was with a selective report. Agreement between the two review authors on study selection and quality assessment was 100%.

3.2. Care burden

As far as care burden in caregivers of schizophrenia, six studies provided the relevant data (Chou et al., 2002; Chien et al., 2004, 2005, 2008; Cheng and Chan, 2005; Sharif et al., 2012). The scales used for burden measurement included family burden interview schedule (Perlick et al., 2006), family burden questionnaire (Quinn et al., 2003) and caregiver's burden inventory (Marvardi et al., 2005). However, only four of them were available for meta-analysis. There was significant difference found between non-pharmacological interventions and control groups ($n=290$, MD -2.10 , 95% CI -3.46 to -0.74 , $P=0.002$; level of heterogeneity $\tau^2=1.81$, $\chi^2=62.13$, $df=3$, $P<0.00001$, $I^2=95\%$) (Fig. 2A).

3.3. Family support

There were four studies discussing the family support changes of caregivers by non-pharmacological interventions in comparison with control (Chien et al., 2004, 2005, 2008; Cheng and Chan, 2005). The tools for assessment were six-item social support questionnaire and family support services index. Three studies were included in meta-analysis without significant difference ($n=242$, MD -1.01 , 95% CI -2.18 to 0.15 , $P=0.09$; level of heterogeneity $\tau^2=0.80$, $\chi^2=28.19$, $df=2$, $P<0.00001$, $I^2=93\%$) (Fig. 2B).

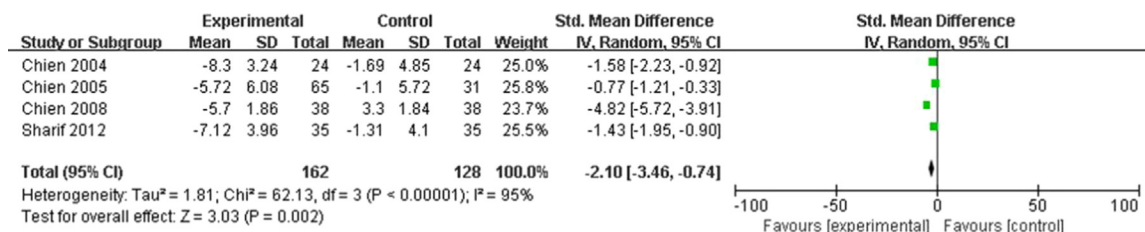
3.4. Family functioning

Concerning family functioning of caregivers, a total of four studies were involved and combined by meta-analysis (Chien et al., 2004, 2005, 2008; Gutiérrez-Maldonado et al., 2009). The scales for assessing the family functioning were family assessment device and general health questionnaire SF-36. No significant difference was found between non-pharmacological interventions and control groups ($n=287$, MD 2.11 , 95% CI -0.25 to 4.48 , $P=0.08$; level of heterogeneity $\tau^2=5.60$, $\chi^2=173.20$, $df=3$, $P<0.00001$, $I^2=98\%$) (Fig. 2C).

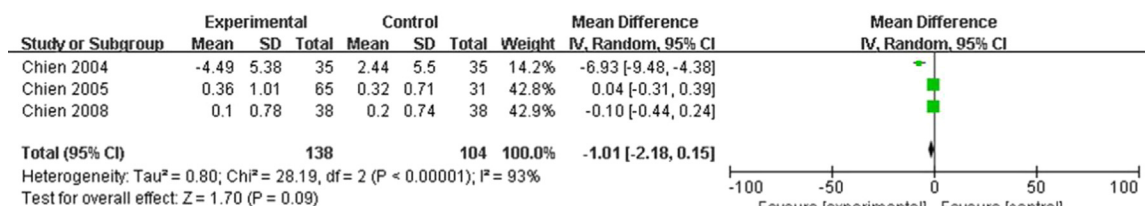
3.5. Satisfaction

Three studies reported caregiver's satisfaction after non-

A Changes of care burden score. There was significant difference in non-pharmacological interventions vs. control. Chien 2004, Chien 2005 and Chien 2008 were assessed by family burden interview schedule. Sharif 2012 was assessed by family burden questionnaire.



B Changes of family support services index. No significant difference was found in non-pharmacological interventions vs. control.



C Changes of family functioning score. No significant difference was found in non-pharmacological interventions vs. control. Chien 2004, Chien 2005 and Chien 2008 were measured by family assessment device. Gutierrez 2009 was measured by general health questionnaire SF-36.

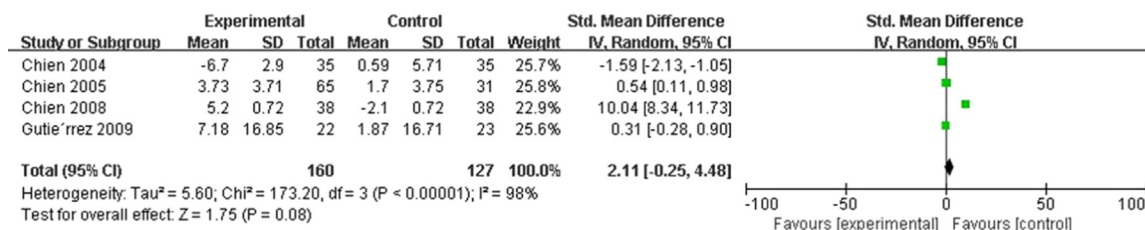


Fig. 2. Efficacy.

pharmacological interventions versus control (Szmukler et al., 1996; Chou et al., 2002; Kulhara et al., 2009). The scales for evaluation of satisfaction were different self-questionnaire. All the studies suggested that the non-pharmacological was highly satisfactory to caregivers (Szmukler et al., 1996; Chou et al., 2002; Kulhara et al., 2009). Meta-analysis could not be performed due to substantial heterogeneity.

4. Discussion

Recently, a systematic literature review evaluated the worldwide schizophrenia prevalence from all the published data during 1990–2013. As a result, the overall median lifetime prevalence was 0.48% (Simeone et al., 2015). While the prevalence of schizophrenia in Chinese mainland was 1.64% in the population aged 18–29 years and 1.51% in the population aged 30–39 years, respectively (Liu et al., 2013). The data is higher than the prevalence for the Chinese population of similar age reported by the previous study (Phillips et al., 2004). Considering the large population of schizophrenia patients, it is definitely a huge burden for Chinese public health system, including the needs of pharmacological treatment, psychological intervention, physical rehabilitation and caregiving. Usually, the caregiving of schizophrenia patients is a challenge for the caregivers, because of the disorders in behavior and emotion. Moreover, suicide can be commonly seen in schizophrenia, and is highly related to the care burden (Whiteford et al., 2013).

Therefore, the effective interventions to relieving the burden are urgently required.

Non-pharmacological interventions as the potential interventions have been paid more attentions in the recent years. In the research of caregivers of patients with dementia, it has been suggested that non-pharmacological interventions such as multimedia education and mutual support, might be beneficial to decreasing the care burden (Liu and Wang, 2013; Liu et al., 2012). Of note, our meta-analysis demonstrated the efficacy of non-pharmacological interventions for caregivers of schizophrenia, and supported the application in the clinical practice. However, these interventions seemed to have no benefits in family support, functioning and caregiver's satisfaction. Five of nine studies were originated from Hongkong and Taiwan, and eight of nine studies came from developing countries, which suggested the findings could be probably convincing for Chinese people.

It is worth to note that family intervention as a potential intervention has also been involved in the included trials, considering the background of family care. Actually, family interventions have been shown to improve outcomes for people with schizophrenia and are now widely used. There was a Cochrane systematic review focusing on brief family intervention for schizophrenia (Okpokoro et al., 2014). Brief family intervention was defined that a mental health professional educates the person with schizophrenia and their family members about the illness over a limited number of sessions. In which, the objective was both of the patients with schizophrenia and their caregivers. While the

interventions in our included trials were just for the caregivers alone. The authors believed that the importance of family intervention should not be dismissed outright, and could be further confirmed by larger studies with enough power to inform clinical practice.

We must also consider the limitations of this meta-analysis. First of all, the search strategy was strict, but we could not assert if there are still other unpublished studies. Secondly, some included trials did not directly provide the concrete data in the text, e.g. the changes of mean value and standard deviation from baseline. Only the studies with clear data were included in meta-analysis. The baseline information, such as the definition of main caregivers, mental health of caregivers and the caregivers receiving only non-pharmacological interventions or not, was unclear. Thirdly, there were less than 10 studies available in any of the outcomes, so that publication bias could not be assessed by funnel plots (Egger et al., 1997). Finally, the sample size of meta-analysis was too small and the quality of included trials was not very high (Table 1), which could cause potential bias for the final results. The heterogeneity of data synthesis was obvious ($I^2 > 50\%$). Therefore, all the conclusions should be explained cautiously and further confirmation is required by well-designed trials with large sample.

Competing interests

The authors declare that they have no competing interests.

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