A Literature Review of Common Outcome in Cognitive Remediation for Schizophrenia

Abstract

Background: People with schizophrenia experience a change especially in the cognitive aspect, and therefore require immediate intervention to improve their cognitive and other aspects. Cognitive remediation is a program that has been developed with promising results. Objective: to review the literature on outcomes in general from the provision of cognitive remediation in people with schizophrenia.

Method: Searching relevant literature on relevant databases, i.e., Pubmed, Ebsco, Cochrane, JSTOR, and the Google Scholar search engine, using keywords: cognitive remediation, schizophrenia, therapy.

Result: Taken from reviewing 21 relevant articles. Cognitive remediation affects cognitive function, functional ability and problem-solving, social skill and cognition, clinical symptoms, neural outcome, quality of life, self-esteem, and cost-utility analysis.

Conclusions: Common outcomes in CRT (Cognitive Remediation Therapy) administration in people with schizophrenia have been identified. Improvement of cognitive function was defined to be the most commonly measured outcome in the study.

Keywords: Cognitive Remediation, Schizophrenia, outcome, literature review

INTRODUCTION

The American Psychiatric Association (APA) defines mental disorders as "clinically significant behavioral or psychological syndromes or patterns that occur individually and is associated with current pressure (e.g., pain symptoms) or disability (e.g., decrease in one or more important function areas) or with significantly increased risk of death, pain, disability, or significant loss of freedom." APA also mentions general criteria for diagnosing mental disorders, including dissatisfaction with one's characteristics, abilities, and achievements; unsatisfactory relationship; dissatisfaction with one's place in the world; not effectively overcome life events; and lack of personal growth. In addition, the person's behavior should not be culturally or sanctioned (Videbeck, 2011).

The schizophrenia spectrum and other psychotic disorders include schizophrenia, other psychotic disorders, and schizotypal (personality) disorder. They are defined by abnormalities in one or more of the following five domains: delusions, hallucinations, disorganized thinking (speech), grossly disorganized or abnormal motor behavior (including catatonia), and negative symptoms (Birx et al., 2011). Schizophrenia is a major and complex mental disorder, or disorder group, whose cause is still unknown and involves a complex set of disorders of thought, perception, influence,
Social behavior (Essali, 2017). Schizophrenia research has shown that genetic factors have an important role in aetiology. The main conclusion is that schizophrenia is a polygenic mess. Some convergent biological themes emerge. Current research efforts seek to link genetic findings to clinical and biological phenotypes. Understanding gene-related disease genes will help identify new targets for the detection, prevention, and treatment of schizophrenia (Essali, 2017).

The burden of mental illness continues to increase, resulting in a significant impact on health and social life, human rights, and the enormous economic impacts in all countries of the world (WHO, 2017). The provision of inadequate health care services for schizophrenic patients with suggestions is a huge economic burden (Chong et al., 2016).

The impact of schizophrenia is associated with predicted cognitive deficits in almost all functional domains. The literature on self-care and social function indicate that the nature of cognitive deficits depends on the level of initial cognitive deficits and the phases/stage of certain diseases (Rajji et al., 2014). Groups of schizophrenic patients still have a very short life expectancy because the mortality rate is very high in all age groups. The risk of suicide contributes to a shorter life expectancy (Laursen et al., 2014).

Patients with schizophrenia have difficulty succeeding in school, obtaining or maintaining a job, having a social relationship, independent living, and even for some, taking care of their basic daily needs (Rajji et al., 2014). In the world and including Indonesia, mental health is still one of the most significant issues. About 35 million people worldwide are affected by depression, 60 million people are affected by bipolar disorder, 21 million are exposed to schizophrenia, and 47.5 million people have dementia (WHO, 2017).

Anti-psychotic drugs, especially new-generation anti-psychotics, have been shown to effectively reduce positive symptoms and have moderate outcomes against negative symptoms with limited outcomes for cognitive impairment and psychosocial function. In most patients, medications help control symptoms but do not restore pre-morbid function levels nor result in a good performance. Drugs alone cannot be expected to improve the consequences of learning disabilities, inability to perform tasks, and social withdrawal (Drake & Bellack, 2005).

The latest therapeutic approaches to schizophrenia include multidimensional interventions to reduce multiple power in various domains (Drake & Bellack, 2005). One such approach is psychiatric rehabilitation. Rehabilitation is a process of refunctionalize and development to enable sufferers with disabilities capable of performing their social functions fairly in community life. Psychiatric rehabilitation is aimed at improving psychological function, social function, and occupational function (Drake & Bellack, 2005). Cognitive remediation is one form of psychiatric rehabilitation. In general, cognitive remediation or cognitive rehabilitation is a form of rehabilitation therapy used to treat individuals with brain disorders with various diagnoses, such as traumatic brain injury, stroke, and dementia. Cognitive remediation aims to help people with schizophrenia develop new skills that they can apply in social, vocational, or academic situations. Cognitive remediation is distinguished from cognitive behavioral therapy and cognitive therapy, which focuses on efforts to reduce psychotic symptoms (American Medical Association, 2006; Drake & Bellack, 2005).

The use of remediation cognition in health services, especially in Psychiatric hospitals in Indonesia, is still not widely used. This is probably due to the hospital has not been exposed to cognitive remediation methods that can be applied in mental hospitals. From the above problems, the authors intend to identify outcomes that appear after cognitive remediation therapy in people with schizophrenia.

**METHOD**

The method of the study used PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses).

**Search strategy**

The relevant literature searches on the relevant databases are Pubmed, Ebsco, Cochrane, JSTOR, and the Google Scholar search engine, using
keywords: cognitive remediation, cognitive remediation, schizophrenia, therapy, outcome.

**Inclusion and exclusion criteria**
A comprehensive and thorough search for a systematic search includes the gray literature. The searching period from 2013-2017. The author limits searches to English-language articles. Each article is identical after cognitive remediation is performed on all people with schizophrenia.

**RESULTS**
This review identified some outcomes posed by the provision of cognitive remediation in people with schizophrenia. A total of 21 articles are found in accordance with the topic of discussion specified by the author. Most of the studies found the effect of cognitive remediation on functional outcomes, and two studies show an influence on neural outcome in people with schizophrenia after cognitive remediation. A study did not identify the outcomes of cognitive remediation because it was a study protocol for the study to be performed (see table 1). The proposed protocol will help answer whether cognitive remediation improves the functional outcomes in forensic mental health in people with schizophrenia or schizoaffective disorder (O'Reilly et al., 2016). The key strength of the O'Reilly protocol (2016) is offered to a group of people with nationally representative mental health forensic schizophrenia. From studying a randomized control trial, 1 study using a mixed-method and 1 study is a systematic review.

**Target treatment outcome - major findings**
The findings of this review are found in cognitive remediation in people with schizophrenia are primary aspects of cognitive functions, social skills, problem-solving, social cognition, or metacognition. Other findings are on the aspects of Self-esteem, physical aspects, and clinical symptoms. The findings will be further explained in the discussion below.

**Cognitive function**
Cognitive improvement increased significantly due to cognitive remediation (Tan et al., 2016), particularly in the size of processing speed, executive function and in adaptive competence as well as work skills, and verbal memory (Bowie et al., 2014; Puig et al., 2014; Malchow et al., 2015). Improved cognitive functioning occurs in the poor community function group with intrinsic motivation after cognitive remediation (Bell et al., 2014). Another study found that there was no difference in cognitive function after cognitive remediation (Gomar et al., 2015; Tan & King, 2013) (Kurtz et al., 2015).

Acceptance and perception that cognitive improvement is due to cognitive remediation have also been found (Reeder et al., 2016). Cognitive remediation therapy demonstrates increased neurocognitive and cognitive functioning in processing rates, working memory, visual-spatial memory, reasoning, and overcoming cognitive domain problems (Garrido et al., 2013; Sánchez et al., 2014; Fiszdon et al., 2016; Rodewald et al., 2014; Fan et al., 2016).

A systematic review mentions that cognitive deficits in people with schizophrenia vary. Not everyone with schizophrenia exhibits a similar cognitive deficit, and they may be different in this disorder (Pentaraki et al., 2017). Premorbid IQ was significantly the result of post-treatment CRT, and the working memory performance was significant at younger ages (17-39 years) than the older age of 40-66 years (Kontis et al., 2012).

**Social cognition and social skills**
People with schizophrenia who participated in cognitive remediation showed greater improvement in social skill ability than in physical exercise (Tan & King, 2013), improvement in social cognition (Peña et al., 2016), and significantly increased in social adjustment activities (Malchow et al., 2015; Fiszdon et al., 2016). But other studies have found that social skills do not improve significantly from pre and post-training (Kurtz et al., 2015; Bowie et al., 2014).

**Problem-solving**
This study shows that the improvement of problem-solving abilities is predicted differently depending on the training program used. In the problem-solving group, people with the most disturbing schizophrenia in this domain show the strongest benefits. In contrast, in the success of basic cognition group training, improvements are
predicted with antipsychotic administration (Rodewald et al., 2014). The results of the study found that CCRT did not result in significant improvement in problem-solving with the labyrinth test (Fan et al., 2017).

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Metacognitive
Four people with schizophrenia who received CRT experienced a significant increase in the theory of mind (ToM), cognition, and metacognition after three months and one year later (Thibaudeau et al., 2017), but this study determined that the CRT program did not explicitly target capability social can improve ToM.

Quality of life
Schizophrenic groups who received CACR (Computer-assisted cognitive remediation therapy) showed significant results in their quality of life (Garrido et al., 2013). Participants who received CR showed that there was an outcome on the measurement of the quality of life scale (Fiszdon et al., 2016).

Functional Ability
Independent living scale in cognitive remediation participants increased significantly compared to physical exercise participants (Tan & King, 2013), and the poor community function group who received cognitive remediation showed their results worked significantly more significantly over the number of hours worked within two years than those in the only get support workers only. But other studies have found that people with schizophrenia, after receiving cognitive remediation, do not improve in level of function and work skill (Bowie et al., 2014). Assessment of performance-based skills, Disability Assessment Schedule scale of the World Health Organization, and global functional assessment have increased significantly after REHACOP therapy (Peña et al., 2016; Sánchez et al., 2014; Fiszdon et al., 2016). After CRT is administered at the early onset of schizophrenia, the results show that participants experience improvement in everyday life and adaptive function (Puig et al., 2014).

Physical aspects
Physical exercise participants experienced better physical fitness compared to participants who received cognitive remediation (Tan & King, 2013).

Self-esteem
Participants of CIRCuiTS reported that none experienced a decrease in self-esteem, although their cognitive feelings did not improve after therapy (Reeder et al., 2016). Other studies have shown participants experiencing a rise in self.

Neural outcome
Post-hoc tests show that there is a significant increase in activity in mPFC / ACC in CCRT but not in the TAU group. In this small sample study, computer cognitive remediation therapy was shown to increase the ACC morpho (anterior cingulate cortex) activity even in resting conditions and improve cognitive function in people with schizophrenia (Fan et al., 2017).

One study found that CRT responsiveness was associated with a baseline measure of cortical thickness in the frontal and temporal lobes. Positive changes in nonverbal memory were are associated with greater initial thickness in the cortical area involving the right frontal left
superior, left caudal frontal, left and paracentral precuneus; frontal superior, caudal middle right frontal gyrus, and pars opercularis. In addition, unconfirmed data also suggest that verbal memory improvements may be associated with CTh in some regions of the frontal and temporal lobes (Penadés et al., 2016).

Cost analysis
The CACR group showed a clear reduction in overcoming the period of acute psychiatric conditions and may help reduce the cost of health care for people with schizophrenia (Garrido et al., 2017).

DISCUSSION
The studies showed significant improvements in cognitive performance after CRT treatment. Although performance on several social tests also improved in the CRT, the benefits conveyed by CRT were considerably greater in these instances. CRT was implemented here as an alternative non-pharmacological therapy to prevent the decline in the cognitive and social function of schizophrenia patients. This indicates that these non-specific factors have a relatively significant effect on neurocognition in schizophrenia.

In this review, it can be seen that most outcomes are generated by cognitive remediation on the cognitive aspect, be it the structure and function. The change in cognitive function in a study determined that there was a change in activity in the cortex even in the resting state (Fan et al., 2017), as well as improvements in the verbal memory of people with schizophrenia after CRT due to changes in thickness in the cortical region (Penadés et al., 2016).

Besides the CRT, cognitive outcomes also affect other aspects in people with schizophrenia, such as social function. In general, cognitive improvement is experienced after obtaining CRT, but there are some studies that suggest otherwise. The result of the correlation analysis and the contradictory regression obtain the complex between cognitive and social function (Tan et al., 2016). Another review also determined that not everyone with schizophrenia exhibited similar cognitive deficits. Younger age experienced better cognitive enhancement than older age (Pentaraki et al., 2017; Kontis et al., 2012).

Self-esteem assessment was also performed by two studies among 21 studies. The study by Reeder et al. (2016) found no decrease in self-esteem, and the study by Garrido et al. (2013) found increased self-esteem after therapy. Not many studies have examined the outcomes of cognitive remediation of the patient’s self-esteem and the duration of the outcomes after therapy (Tan et al., 2016).

Four studies determined that both positive and negative symptoms did not differ significantly after cognitive remediation. However, three studies were suggesting that there was an improvement of negative symptoms in people with schizophrenia after CR. It was from 3 studies that had improved outcomes of negative symptoms, and two studies provided cognitive remediation combined with other therapies, i.e., social cognitive treatment, RC, and functional skill training and REHACOP (Peña et al., 2016; Sánchez et al., 2014).

Improving the condition of people with schizophrenia after being given RCT indirectly reduces the maintenance period of people with schizophrenia, especially when people with schizophrenia in crisis conditions can be traversed with a shorter time. The implication of this is to affect the cost or cost incurred for patient care and treatment, as determined by Garrido et al. (2017).

Limitations to this review are newly analyzed outcomes generated after CRT administration in people with schizophrenia. Not yet analyzed in depth against each of the more specific outcomes. However, it is expected to provide an overview of outcomes generated by CRT in people with schizophrenia. For further study, it is advisable to analyze the specific outcomes in CRT administration on each characteristic of people with more homogeneous schizophrenia and further meta-analysis.

CONCLUSION
The conclusion of this review is a general outcome for CRT administration in people with schizophrenia has been identified. Improvement of cognitive function was defined to be the most
commonly measured outcome in the study. Then a functional assessment and its effect on clinical symptoms have also been identified. Several things cause differentiation of study results with assessment on the same aspect. The condition of people with schizophrenia who are not always the same to be one cause and age factor apparently affect the improvement of the condition of people with schizophrenia given CRT. A combination of CRT with therapy or other programs is recommended to be performed because it proves to generate a more significant outcome on the aspects assessed. Self-esteem has not been much measured after being given CRT, while the results in some studies are substantial.

AUTHOR CONTRIBUTION
Sadarwati and Puspitosari contributed to the design and implementation of the research, to the analysis of the results, and to the writing of the manuscript.

CONFLICT OF INTEREST
The authors declare that there is no conflict of interest.

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Records identified through database searching (n=175)

Records after duplicates removed (n=161)

Records screened in title and abstract stage (n=161) → Records excluded (n=116)

Full text articles assessed for eligibility (n=45) → Full text articles excluded (n=24)
Unavailable in English (n=3)
Conference abstract or summary report only (n=16)
No primary outcome data (n=1)
Wrong population (n=4)

Studies included in review (n=21)

Figure 1. PRISMA Flow Diagram
| No | Author                  | Year | Participants       | Treatment(s) | Setting (individual/group) | Study design                  | Neural treatment outcome(s)                           | Functional treatment outcome(s)                      |
|----|-------------------------|------|---------------------|--------------|-----------------------------|-------------------------------|-------------------------------------------------------|-------------------------------------------------------|
| 1  | Jesús J. Gomar et al    | 2015 | CRT: 43 Participants | CRT          | Group                       | RCT                           | -                                                     | Improvements to cognitive functions are not significant compared to the control group. |
|    |                         |      | CC: 44 Participants  |              |                             |                               | -                                                    | outcome on physical fitness in PE is more significant |
|    |                         |      |                     |              |                             |                               | -                                                    | Social skills on CR are more significant              |
|    |                         |      |                     |              |                             |                               | -                                                    | Recovery of symptoms is better than PE.              |
| 2  | Bhing-Leet Tan and Robert King | 2013 | CR: 36 Participants  | CR           | Group                       | RCT                           | -                                                     | -                                                     |
|    |                         |      | PE: 34 Participants  |              |                             |                               | -                                                    | -                                                     |
| 3  | Tan S, et al            | 2015 | CRT: 52 MDT: 46     | CRT          | Individual                  | RCT                           | -                                                     | -                                                     |
| 4  | Bowie C.R, et al        | 2014 | CRT on early term course of illness: 12 | CR          | Group                       | Non Randomized Intervention Study | -                                                    | -                                                     |
|    |                         |      | CRT on long term course of illness: 27 |              |                             |                               | -                                                    | -                                                     |
| 5  | Bell M.D, et al         | 2014 | SE & CR: 86 SE: 65  | RCT          | Group                       | RCT                           | -                                                     | -                                                     |
| 6  | Kurtz M.M, et al        | 2015 | CR: 32 Control: 32  | CR           | Individual                  | RCT                           | -                                                     | -                                                     |
| 7  | Thibaudeau E, et al     | 2017 | 4 participants      | CRT          | Individual                  | A Multiple Case Study          | -                                                     | -                                                     |
|    |                         |      | CIRCuiTS            |              |                             | Mixed Methods                 | -                                                    | -                                                     |
| 8  | Reeder C, et al         | 2016 | 34 nonclinical participants | CIRCuiTS    | Individual                  |                               | -                                                    | -                                                     |
|    |                         |      | di study 1. 5       |              |                             |                               | -                                                    | -                                                     |
|    |                         |      | participants in study 1 dan 2. 20 participants in study 4. | || | | | |
| 9  | Fan F, et al            | 2017 | CCRT: 14 TAU: 13    | CCRT         | Group                       | RCT                           | Significant increase in activity in the medial prefrontal cortex | -                                                     | Improved cognitive function. Problem-solving increased significantly. |
| No. | Authors | Year | Intervention | Control | Design | Results |
|-----|---------|------|--------------|---------|--------|---------|
| 10  | Pena J, et al | 2016 | REHACOP: 52 | TAU: 52 | Group RCT | Significant reductions in neurocognitive, social cognitive, negative symptoms, functional disability, GAF, performance-based skills |
| 11  | Penades R, et al | 2016 | CRT: 17 | SST: 18 | Individual RCT | The basic size of cortical thickness in the frontal and temporal lobes changes significantly |
| 12  | Garrido, G., et al | 2013 | CACR: 38 | Active control group: 29 | Individual RCT | Significant improvements in neurocognitive, quality of life, and self-esteem |
| 13  | Puig O, et al | 2014 | CRT: 25 | TAU: 25 | Individual RCT | Improved executive / cognitive function, adaptive function, and daily life. |
| 14  | Sanchez P, et al | 2013 | REHACOP: 38 | Control Group: 54 | Group RCT | Improved executive / cognitive function, adaptive function, and daily life. |
| 15  | Fiszdon J.M, et al | 2016 | CR: 50 | TAU: 25 | Individual RCT | Significant changes in cognitive and functional function. |
| 16  | Malchow B, et al | 2015 | Schizophrenia Endurance Training: 25 | Healthy Controls Endurance Training: 27 | Group Non Randomized Intervention Study | Significant changes in GAF, social cognition, and cognitive function |
| 17  | O’Reilly K, et al | 2016 | CRT | TAU | Individual and group | The trial is currently enrolling by invitation |
| No. | Authors         | Year | Study Design | Type of Intervention | Comparison | Outcome Measures | Findings |
|-----|-----------------|------|--------------|----------------------|------------|------------------|----------|
| 18  | Pentaraki A, et al | 2017 | CRT & TAU TAU | CRT                  | Individual | Systematic Reviews | Cognitive deficits in people with schizophrenia are heterogeneous. Not all people with schizophrenia show the same cognitive deficits, and they may vary through the course of the disorder. |
| 19  | Garrido G, et al | 2017 | CACR:38      | CACR                 | Group      | RCT              | The cost of treating people with schizophrenia declines globally. |
| 20  | Rodewald K, et al | 2014 | CR           | CR                   | Group dan individual | RCT       | Changes in working memory and manipulation decreased negative symptoms and disorganization. Premorbid IQ results are significant after treatment in younger, not on older patients. |
| 21  | Dimitris K, et al | 2013 | COuSE TAU:42 CRT:92 | COuSE         | Group      | RCT              | Working memory performance and premorbid IQ results are significant after treatment in younger, not on older patients. |

Abbreviations: CRT: cognitive remediation therapy, CC: control condition, PE: physical exercise, TAU: treatment as usual, CCRT: computerized cognitive remediation training, CIRCuiTS (Computerized Interactive Remediation of Cognition – a Training for Schizophrenia), REHACOP: the efficacy of an integrative cognitive remediation program, CACR: computer-assisted cognitive remediation, COuSE: Cognitive remediation in Supported Employment, MDT: Music and dance therapy.