Taipei Medical University

Ph.D. Program in School of Nursing

Doctoral Dissertation

Advisor: Kuei-Ru Chou, PhD., FAAN

Global Prevalence of Post-Traumatic Stress Disorder During COVID-19 Pandemic and the Effectiveness of Psychotherapies for People with PTSD

Student's Name: Ninik Yunitri

July 2022

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This thesis is the doctoral dissertation of NINIK YUNITRI in the Ph.D. Program in School of Nursing at Taipei Medical University. This work has been judged satisfactory by the committee members after the degree candidate passed an oral examination.

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"*How wonderful is the case of a Believer! There is good for him in whatever happens to him - and none, apart from him, enjoys this blessing*"

The Prophet Muhammad SAW

(Muslim)

My life has been a series of great adventures that taught me the meaning of life and love. Grateful might be the most appropriate word I can choose to explain how I feel for everything happened in the past, now, and the day after. Surrounded by lovely people that support me to escalate and acquire into a better version of me. I am certainly aware that they provide me such a great support so I able to get through all the process.

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Abstract

Title of Dissertation: Global Prevalence of Post-Traumatic Stress Disorder During COVID-19 Pandemic and the Effectiveness of Psychotherapies for People with PTSD

Institution: Ph.D. Program in School of Nursing Taipei Medical University

Author: Ninik Yunitri

Dissertation directed by: Kuei-Ru Chou, PhD., FAAN, Professor

Background: More than 70% people in the world exposed to one or more traumatic event during their lifetime. Posttraumatic stress disorder (PTSD) is a common disorder in populations that have been exposed to severe trauma. PTSD was one of the most common mental health problems and long-term consequences of coronavirus outbreaks. COVID-19 affected our mental health in many ways. High numbers of infection and deaths along with social interaction restrictions have negatively impacted the psychological well-being of individual and society. It increases the vulnerability to develop PTSD. Numerous psychotherapies have been developed for people with PTSD. Different approaches applied in facilitating the person to process their traumatic memories. Therefore, there is a need to evaluate the prevalence of PTSD during COVID-19 pandemic and compared the effectiveness of different type of psychotherapies for people with PTSD.

Objectives: The purposes of this study were to (1) determine the prevalence of PTSD during the COVID-19 pandemic among patients/survivors of COVID-19, health professionals, and the population at large, along with the associated risk factors; and (2) explore the comparative

effectiveness of psychotherapies for PTSD on immediate, short-and-long-term follow-up measurements retrieved from RCTs studies in all age groups.

Methods:

Study 1: A comprehensive literature review on the prevalence of PTSD was conducted in Cochrane library, CINAHL, Embase, Medline-Ovid, PubMed, Scopus, and Web of Science without language restriction. We included studies evaluating the prevalence of PTSD during the COVID-19 pandemic either in patient/survivors of COVID-19, health professionals, and the population at large. The data were analyzed using *logit transformation* with random-effects mode using *metaprop* module in R software version 4.0.2. The quality of studies included were assessed using Hoy and colleagues. While potential publication bias was determined using Peter's method.

Study 2: Literature search was directed in Cochrane library, Embase, Medline-OVID, PsycInfo, PubMed, and Scopus up to March 2021. Studies focused on determining the clinical effectiveness of cognitive processing therapy (CPT), cognitive therapy (CT), eye movement desensitization reprocessing (EMDR), narrative exposure therapy (NET), prolonged exposure (PE), cognitive behaviour therapy (CBT), present-centered therapy (PCT), brief eclectic psychotherapies (BEP), psychodynamic therapy (PDT) or combination among them compared to no treatment (NT) or treatment as usual (TAU) on people with PTSD were included. Frequentist and Bayesian approach were used for analysis using *netmeta* modul in R software version 4.0.2. The study quality was determine using GRADE analysis.

Results:

Study 1: A total of 63 studies (n=124,952) from 24 different countries were analyzed. The overall pooled estimate of PTSD prevalence was 17.52% (95% CI 13.89 to 21.86), with no

evidence of publication bias (t=-0.22, p-value=0.83). This study found a high prevalence of PTSD among patients with COVID-19 (15.45%; 95% CI 10.59 to 21.99), health professionals (17.23%; 95% CI 11.78 to 24.50), and the population at large (17.34%; 95% CI 12.21 to 24.03). Subgroup analyses showed that those working in COVID-19 units (30.98%; 95% CI, 16.85 to 49.86), nurses (28.22%; 95% CI, 15.83 to 45.10), those living in European countries (25.05 %; 95% CI 19.14 to 32.06), and studies that used Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) (30.18 %, 95% CI 25.78 to 34.98) demonstrated to have the highest PTSD prevalence compared to other groups. Meta-regression analyses revealed that the elderly (above age 65) had lower PTSD prevalence (-1.75, 95% CI -3.16 to -0.34) than the adult population.

Study 2: A total of 141 studies with 8,820 participants. Compared to NT, CPT, CT, NET, EMDR+PE, EMDR, PE, CBT, and PCT were significant to reduce PTSD symptom (SMD range: -1.57 to -0.84) at posttreatment and ranked accordingly. CPT was the only therapy with large effect size (SMD: -1.12) in short-term follow-up, while CPT and NET both did (SMD range: -0.91 to -0.89) in long-term follow-up. For secondary outcomes, all psychotherapies were effective (RR range: 3.18 to 1.98) in remitting the patients.

Conclusions: This study found considerable PTSD prevalence rates in patients/survivors of COVID-19, health professionals, and the population at large. Moderator analysis found age, unit of work, health profession, continent, and PTSD assessment tool as significant moderators. In term of PTSD treatments, CPT, CT, NET, EMDR+PE, EMDR, PE, CBT, PCT showed as effective therapies on PTSD with moderate to large effect in immediate measurement. The remission rates showed all specific psychological treatments tend to decrease the number of people who meet PTSD diagnosis at the treatment endpoint. Moderator analyses different rank of psychotherapies between children-adolescent and adults.

Keywords: PTSD, prevalence, COVID-19, psychotherapy, meta-analysis, network meta-analysis

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CHAPTER 1 – Introduction

1.1. Background

Trauma is presented as "Exposure to a stressful event or situation of exceptionally threatening or horrific nature likely to cause pervasive distress in almost anyone" according to the *International Classification of Disease* version 11's (ICD-11), Meanwhile, the *Diagnostic and Statistical Manual of Mental Disorders* version 5's (DSM-5) definition of trauma is "exposure to death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence" (American Psychiatric Association, 2013).

More than 70% people in the world exposed to one or more traumatic event during their lifetime with unexpected death of loved one (31.4%) found as the most common trauma types. (Kessler et al., 2017). Experiencing traumatic event could increase the vulnerability to having PTSD up to 19% depend on the trauma type (Kessler et al., 2017; Liu et al., 2017). Among people exposed to traumatic event, the average global PTSD prevalence was 5.6%. This number was 1.5 times higher than the lifetime prevalence of PTSD (Koenen et al., 2017).

An event can be considered as traumatic if it is a shocking, scary, or dangerous experience that can affect someone emotionally and physically (National Institute of Mental Health). In general, natural disaster, violence, accident, death of loved one can be classify as traumatic event. But traumatic experience is subjective to everyone depend on their personality, belief, value, and previous experience (Adams, 2018). Currently, the pandemic of COVID-19, classify as a disaster by red cross, also become a traumatic event because of its damages to the people and society.

COVID-19 is the latest coronavirus outbreak after severe acute respiratory syndrome (SARS) in 2003 and Middle East Respiratory Syndrome (MERS) in 2012. SARS, the first generation of coronavirus, originated found in China and eventually spread to 30 countries. While MERS as the second coronavirus pandemic, was found in Middle East countries with the highest number of cases in Saudi Arabia. COVID-19 pandemic was spread globally to all countries after discovered in a Wuhan China in the late of 2019. Compared to COVID-19, SARS and MERS showed lower total case with 8,096 (WHO, 2015a) and 2,589 (WHO, 2022) respectively. To date, the total case of COVID-19 in the world almost hits 500 million with over six million death cases (Worldometer, 2022). As May 31, 2022, more than 6 million deaths among 530 million confirmed cases have been reported to WHO. Although the mortality rate COVID-19 was lower than SARS and MERS (Abdelghany et al., 2021), yet the reproductive number showed the highest (1.8 to 3.6) (Petersen et al., 2020).

The "Population Exposure Model" espouses that different segments of the population may be more or less affected based on exposure to the traumatic event (DeWolfe, 2004). It is believed that the individuals who are most personally, physically, and psychologically exposed to a traumatic event are likely to be affected the most. This model further observed the macro-view of the entire community and the gradation of trauma effect across population groups (U.S Department of Health and Human Services, 2004). Based on the population exposure model, we proposed that three population groups should be analyzed to assess the PTSD associated effects of the COVID-19 pandemic into those directly exposed or affected (patients/survivors), those who witness the suffering of those affected (health professionals), and everyone else not in the previous categories as the population at large.

COVID-19 affected the people mental health in many ways. Children, adolescence, older adults, and diffable people are considered as vulnerable population. High numbers of cases and deaths along with social interaction restrictions negatively impacted the individual and society's psychological well-being (Asim et al., 2020). Uncertainty about the disease, being isolated from friends, family, and colleagues, and staying at home for a long period could result in unstable mental health status (Javed et al., 2020; Vahia et al., 2020). People infected by COVID-19 not only experienced feelings of trauma due to the disease and hospitalization, the stigmatization from others after recovery or release from quarantine may weighted the burden and mental instability. Health professionals, who work on the frontline, are also seen as a vulnerable group during the pandemic (Javed et al., 2020). Lack of knowledge, fear, work overload, shortage of self-protection gear and medication, deaths of colleagues, and isolation from family and friends can increase the risk for mental health problems in this population (Marshall, 2020). Thus, more nuanced analyses with these groups could provide better information for further management and treatment of mental health problems.

Thus, long-term psychological consequences of COVID-19 to all populations should be considered as a major problem (Chirico et al., 2021). Studies conducted after previous coronavirus outbreaks, SARS and MERS, found that PTSD (Fan et al., 2021), depression, anxiety (Rogers et al., 2020), and burnout (Magnavita, Chirico, et al., 2021) were the most common mental health problems occurred after the outbreaks. The prevalence of PTSD during SARS was up to 18% (Salehi et al., 2021; Wu et al., 2005; Wu et al., 2009) while in MERS pandemic showed higher rate up to 42.9% (Park et al., 2020; Salehi et al., 2021).

Posttraumatic stress disorder defined as a disorder that develops in people who have experienced a shocking, scary, and dangerous or event (National Institute of Mental Health,

2020). Early identification of PTSD among people exposed to COVID-19 pandemic might give the opportunity to provide mental support needed, because untreated PTSD will lead to others mental health problems. People with untreated PTSD are more likely to conduct suicidal attempted, substance used, developed complex PTSD, having physical and mental health complication (Armenta et al., 2018; Flannery, 2001; Fox et al., 2021), and tend to show poor prognosis once they paced to receive treatment (Priebe et al., 2009). As consequence, Prolonged morbidity, low quality of life, and higher cost of care are some problems that emerged (Priebe et al., 2009).

A variety of approaches have been recommended for treating people with PTSD including pharmacotherapies and psychotherapies. Astonishingly, previous meta-analyses found psychotherapies superior to pharmacological interventions in in decreasing PTSD symptoms (Coventry et al., 2020; Merz et al., 2019). To date, a large number of psychotherapies with different approach have been developed to treat people with PTSD including cognitive processing therapy (CPT), cognitive therapy (CT), prolonged exposure (PE), cognitive behavioral therapy (CBT) eye movement desensitization and reprocessing (EMDR), narrative exposure therapy (NET), and brief eclectic psychotherapies (BEP) (APA, 2017).

Those psychotherapies are differed in the intervention, number of sessions, duration, and format. However, they commonly facilitate the person with PTSD to 'process' their traumatic memories. Briefly, of the recommended therapeutic approaches, most of the psychotherapies, CPT, CT, CBT, BEP, PCT, and PDT, focus on cognitive restructuring skills by challenging the maladaptive cognitions through the use of cognitive restructuring techniques. As results, patients will improve the understanding about their negative patterns in thoughts and feelings are in order to have a more realistic idea and behavioral pattern (Adams, 2018). On the other

side, PE and NET, used gradual exposures (McLean & Foa, 2011) of stimuli using writing, imagery, or event direct contact to the related place through a hierarchical of fearful event, one at a time. After through repeated exposure, it is believed will increase the ability people with PTSD to confront without feeling traumatized and anxiety. Meanwhile, EMDR, works by extracted all the anxious feelings and leads to a decrease in vividness and emotionality in regard to memory to reconstructs patients' cognitive thinking, along with their emotional status which in turn helps the patient to process the memory and emotions correctly.

A huge number of trials have been conducted to evaluate the effectiveness of psychotherapies to treat people with PTSD (Brown et al., 2019; Maieritsch et al., 2016; Meentken et al., 2020; R. Meiser-Stedman et al., 2017; Niemeyer et al., 2020; Nijdam et al., 2012; Peltonen & Kangaslampi, 2019a; Peterson et al., 2020; Resick, Wachen, et al., 2017; Shapiro et al., 2018; Stecker et al., 2014) and meta-analyses that have been conducted to evaluate the efficacy of psychotherapies for PTSD (Chen et al., 2015; Kayrouz et al., 2018; Lenz & Hollenbaugh, 2017; Moreno-Alcazar et al., 2017; Powers et al., 2010). Yet conventional study or meta-analysis can only compare two different treatments or formats on direct effects.

Moreover, some inconsistencies regarding recommended psychotherapies were found among PTSD guidelines developed either by global or national scale organizations (Departments of Veterans Affairs and Defense, 2017; International Society of Traumatic Stress Studies, 2018; National Institute for Clinical Excellence, 2018; Phoenix Australia Centre for Posttraumatic Mental Health, 2013). According to APA's PTSD guideline, CBT, CPT, CT, and PE strongly recommended as psychotherapies for treating people with PTSD while BEP, EMDR, and NET were suggested (APA, 2017). On the other side, the Veteran Affairs/DoD clinical

practice PTSD guidelines recommended PE, CPT, EMDR, BEP, and NET as trauma-focused psychotherapies for full PTSD (Departement of Veterans Affairs, 2017).

1.2. Research Objectives and Hypothesis

Given the serious consequence of COVID-19 to the population and diverse psychotherapies have been developed to treat people with PTSD, therefore, the present study endeavors to determine what is the prevalence of PTSD among people during the pandemic including among patients or COVID-19 survivors, health professionals, and population at large and which psychotherapies work better and give optimum results to people with PTSD?

Objective 1. To examine the prevalence of PTSD during the COVID-19 pandemic among patients/survivors of COVID-19, health professionals, and the population at large along with the associated risk factors.

Hypothesis 1.1 This study hypotheses there is a significant PTSD prevalence among patients or COVID-19 survivors during the pandemic

Hypothesis 1.2 This study hypotheses that age, gender, educational level, marital status, continent, units of work, type of health professional, total cases, total death cases are not significant moderator to PTSD prevalence during COVID-19 pandemic

Objective 2. To determine the effectiveness of nine psychotherapies in treating people diagnosed with PTSD on immediate, short-and-long-term follow-up measurements in RCTs studies for all age groups

Hypothesis 2.1 This study hypothesis CBT to be more effective compared to other psychotherapies (CT, CPT, EMDR, PE, NET, BEP, PCT, PDT) in decreasing PTSD symptoms for people with PTSD

Hypothesis 2.2 This study hypotheses higher PTSD remission rate after CBT compared to other psychotherapies (CT, CPT, EMDR, PE, NET, BEP, PCT, PDT) in term of PTSD remission rate.

CHAPTER 2 – Literature Review

2.1. Definition of PTSD

PTSD has been existing as diagnosis for more than four decades since it was officially included in the Diagnostic and Statistical Manual of Mental Disorders third edition (DSM-III) (Adams, 2018; Brewin, 2003; Bromet et al., 2018). During that period, PTSD defined as a set of symptoms occurs after experiencing trauma that "beyond the normal range of human experience" (Adams, 2018; Brewin, 2003; Friedman, 2013). Furthermore, DMS-IV was included experiencing or witnessing event that involved actual or threatened event as part of PTSD definition (Bromet et al., 2018).

Finally, PTSD has comprehensive criteria and classified as part of trauma-and-stressor-related disorders in DSM-5. It comprised a clear the controversy regarding Criterion A, the traumatic exposure stressor. In DSM-5, PTSD refers to a condition that developed in some people following exposure to one or more traumatic events (APA, 2013). While Torres (2020) define PTSD as a psychiatric disorder that can occur in people who experience or witnessed traumatic event.

Traumatic event is subjective and personal, because an event can be traumatized to one person while other sees as less significant (Adams, 2018). The traumatic event bowled as a watershed to the person and as consequence the person no longer able to feel the same about themselves, the world, and the future. Unlike anxiety disorders that feeling fear or worry to impending threat, people with PTSD suffer persistent, intrusive, and reminiscing instead of adapting to life after experienced trauma.

2.2. Theory of PTSD

Several psychological theories were developed to help better understanding about process symptoms of PTSD including dual representation theory (Brewin et al., 1996) and emotional processing theory (Foa & Kozak, 1986). Recently, cognitive theory was developed by grounding previous theories (Ehlers & Clark, 2000). It was designed to explain the persistence of PTSD as well as provide the framework for cognitive behavior treatment. Although seeing the PTSD process from different perspective, the fundamental approach on treatments remain the same.

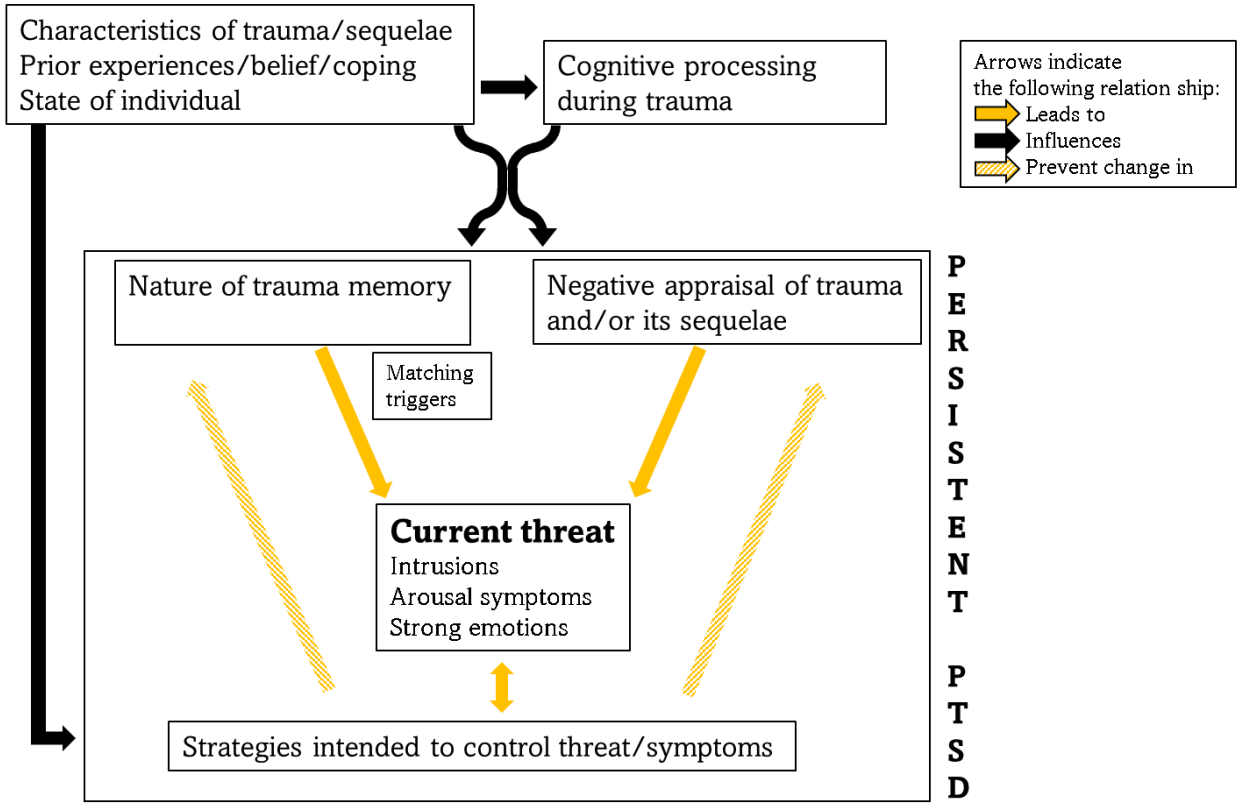

Figure 1. Cognitive theory model of PTSD by Ehlers & Clark (2000)

Cognitive model conceptualized PTSD from cognitive perspective and believe that individual are differences in the way they appraised the trauma and the nature of memory for an event. People with PTSD appraised the trauma negatively. They tend to exaggerate and overgeneralize the traumatic event as more dangerous than they really are. Traumatic experience may disrupt cognition that not only evoking overwhelming emotions, but also failing to integrate into general cognitive schemata. Any activation of trauma schemata can prompt patients to slip into traumatic awareness, a condition that people with PTSD more likely to interpret current experiences in relation to their trauma.

PTSD occur as consequence of impaired information processing causing the memory to be stored in a raw, unprocessed, and maladaptive form (Bomyea et al., 2016; Shapiro, 1989b; Weber, 2008). People with PTSD perceive external events as negative and uncontrolled experiences. They tend to believe that positive experiences do not result from their own actions. In PTSD, distortions in information processing may lead to a disproportionate processing of trauma-related or generally threatening cues, such that this type of information becomes over-represented in cognition (Bomyea et al., 2016). Therefore, people with PTSD tend to have negative appraisal of the sequelae that can contribute to persistent symptoms including intrusive recollections, flashback, irritability, mood swings, lack of concentration and numbing (Ehlers & Clark, 2000). Those symptoms may misinterpret as threat to their physical and mental well-being. Pathological symptoms would occur when new information is inadequately processed and then stored in the memory network along with distorted thoughts, sensations, and negative emotions.

Furthermore, the intensity of experience leaves a strong sensory, affective, and action memory traces that particular to the traumatic experience. The external stimulation can trigger

sensation and image from past traumatic experiences and leave the person at a high risk of re-experiencing certain feelings and body sensations. Inability to process the traumatic information leaves people with PTSD with unstable emotional status that could affect their behavior such as avoidance, withdrawal, apathy, and emotional numbing (Weber, 2008).

People with PTSD tend to use passive coping such as substance use and religious coping (Adhikari Baral & K, 2019), avoidant coping (social withdrawal) (Thompson et al., 2018) compared to those without PTSD symptoms. Rather than take action to remedy the situation, they tend to withdraw into their feelings of distress and helplessness. The coping mechanism selected relatively linked to how the individual's appraisals of the trauma and its sequelae. Instead of solving the problems, the strategy intended to control the threat maintained the PTSD symptoms instead. These states of intrusion and avoidance as a necessary cyclical pattern of gradual adaptation to trauma, wherein extreme tension between these states may prolong the process of resolution. In PTSD, extreme avoidance can hinder adaptive interactions with new circumstances, leaving a person stuck in a trauma response pattern. In general, by avoiding the stressor, people with PTSD loss their chance to correct the appraisal and memory about traumatic event.

2.3. PTSD Signs and Symptoms

According to DSM-5, PTSD consists of five major symptom clusters including (A) exposure to actual or threatened death, serious injury, sexual violence, (B) intrusion, (C) persistent avoidance, (D) negative alteration in cognitions and mood associated with traumatic events, and (E) Alteration in arousal and reactivity. The disturbances (criteria A, B, c, and D) should be more than one month, caused clinical distress or impairment, and did not attribute to

the psychological effects from substance abuse, medication, alcohol, or other medical conditions (American Psychiatric Association, 2013). Although the onset develops within one to six months, about 24.5% cases showed delayed onset of PTSD (Utzon-Frank et al., 2014).

Traumatic experience is believed as the core of PTSD. However, there is no clear definition to line between traumatic and nontraumatic event. Every trauma raises similar issue, and each person might experience the same event yet impacted the person in different way. It can be considered as traumatic to some person while others seen it as less traumatic. There are huge range of possible traumatic events, and it is subjective to each person. But at the end of the day, experts agree that the event rolled as watershed in the people lives. There is a major discontinuity between pre and post traumatic event (Friedman, 2013).

People with PTSD experience *intrusion* associated with the traumatic event. Intrusions mostly involving sensory impressions such as visual, auditory, smell, and bodily sensation from the traumatic event. Reexperiencing may involves one or more intrusion symptoms includes flashbacks, spontaneous memories, or recurrent dreams related to the traumatic event. A study to 44 participants with motor vehicle accident history showed 96% of them experienced 294 intrusions within a week. Similar event was the most common triggers to the intrusion (48%) (Kleim et al., 2013).

Avoidance refers to the patients' active effort in avoiding reminders of the traumatic event and any associations that may trigger distressing memories. Avoidance or effort to avoid traumatic reminder could include memory, thoughts, feelings, people, places, objects, activity, situation even conversation (American Psychiatric Association, 2013). People with PTSD showed greater effort to avoid reminder object compared to people with no PTSD (Sheynin et al., 2017).

Negative alteration cognitions and mood are marked by inability to remember important aspect of traumatic event(s), distorted beliefs or thoughts about self and others, persistent negative emotional state, wrongly blaming self, diminished interests in activities previously enjoyed, estrangement from others, feeling of detachment from others, and persistent inability to experience positive emotions (American Psychiatric Association, 2013).

Finally, the last PTSD symptom is *hyperarousal*. This symptom begins to rise or worsening after the traumatic exposure. It rises as the fight or flight reaction as a result of thinking about the trauma. Being aggressive, irritable, reckless, self-destructive, hypervigilant, problem with concentration or having sleep problems are the most common symptom found related to hyperarousal (American Psychiatric Association, 2013).

2.4. PTSD Diagnosis

Numerous instruments have been developed to assess PTSD either instrument based or self-reported including the Clinician-Administered PTSD Scale (CAPS/CAPS-5), PTSD Symptom Scale Interview (PSS-I/PSSI-5), Structures Clinical Interview PTSD module (SCID PTSD module), Structured Interview for PTSD (SIP or SI-PTSD), Treatment-Outcome PTSD Scale (TOP-8), Davidson Trauma Scale (DTS), Impact of Event Scale-Revised (IES-R), Mississippi Scale for Combat-Related PTSD (MISS or M-PTSD), Modified PTSD Symptom Scale (MPSS-SR), PTSD Checklist (PCL/PCL-5), PTSD Symptom Scale Self-report version (PSS-SR), Short PTSD Rating Interview (SPRINT) (American Psychological Association, 2017). The detail information about all instruments is provided in Table 1.

Table 1. PTSD diagnostic and screening tools

Instrument	type	Detail information
Interview		
Clinician-administered PTSD scale for DSM-5 (CAPS)	Diagnosis and assessment	• 30 items • Deliver by clinicians and clinical researchers with knowledge of PTSD • Administration time: 45-60 minutes
PTSD symptom scale interview (PSS-I and PSS-I-5)	Assessment and diagnosis	• 17 items • Correspond to DSM-IV PTSD criteria • Administration time: 20 minutes
PTSD symptom scale interview (PSS-I-5)	Assessment	• 20 items and additional 4 items • Correspond to DSM-5 PTSD criteria
Structured clinical interview; PTSD module (SCID PTSD module)	Diagnosis	• Administered by trained mental health professionals • Correspond to DSM-5 PTSD criteria • Administration time: 15 minutes to several hours
Structured interview for PTSD (SIP or SI-PTSD)	Assessment	• Correspond to DSM-IV PTSD criteria • Administration time: 20-30 minutes
Treatment-Outcome Posttraumatic Stress Disorder (TOP 8)	Assessment	• 8 items • Brief version of SI-PTSD • Correspond to DSM-IV PTSD criteria
Self-reports		
Davidson Trauma Scale (DTS)	Assessment	• 17 items, Likert scale • Correspond to DSM-IV PTSD criteria
Impact Event Scale (IES)	Assessment	• 22 items, Likert scale • Determined subjective distress or PTSD symptoms based on past seven days • Able to use to make preliminary PTSD diagnosis • Correspond to DSM-IV PTSD criteria
Mississippi Scale for Combat-related PTSD (MISS or M-PTSD)	Assessment	• 35 items • Specifically for combat-related PTSD in veteran populations • Correspond to DSM-III PTSD criteria
Modified PTSD symptom scale (MPSS-SR)	Assessment	• 17 items • Correspond to DSM-III-R PTSD criteria • Able to use to make preliminary PTSD diagnosis
PTSD checklist for DSM-5 (PCL-5)	Assessment	• 20 items • Correspond to DSM-5 PTSD criteria • Able to use to make preliminary PTSD diagnosis
PTSD symptom scale self-report version (PSS-SR)	Assessment	• 17 items, Likert scale • Correspond to DSM-IV PTSD criteria
Short PTSD rating interview (SPRINT)	Assessment	• 8 items, liker scale • Do not correspond to any specific DSM criteria

CAPS or CAPS-5 are considered as the gold standard instrument to diagnosed PTSD. There are slights change from CAPS based on DSM IV and CAPS-5 based on DSM-5. The instrument is an interview-based assessment, CAPS took 45 to 60 minutes to administer by a

mental health professional. CAPS-5 items and scoring system correspond to the criterions in DSM-5. In order to have PTSD diagnosis, the person should show at least one symptom in criterion B and C, two symptoms in criterion D and E, meet the criterion F and G. The PTSD severity is calculated by summing the individual item severity score that covers all criterions. The scoring system ranged between 0 (absent) to four (extreme or incapacitating) (Weathers et al., 2013). CAPS-5 showed high internal consistency (α=0.88) and interrater reliability (ICC= 0.91) (Weathers et al., 2018).

Although CAPS or CAPS-5 is the gold standard instrument used to diagnosed people with PTSD, many clinicians and researchers also rely on other type of instruments. According to Elhai et al. (2005), PCL was found as the most used both in clinical or for research purposes followed by IES, Harvard trauma questionnaire, Conflict tactics scale, CAPS, Standford acute stress reaction questionnaire, and Deployment risk and resilience inventory.

2.5. PTSD Prevalence

The prevalence of PTSD remained increasing as more patient are surviving from traumatic experience. A study by Kessler et al. (2017) in 24 countries (n = 50,855) found the lifetime exposure to one or more trauma was about 70.4% with at least 3.2 percapita. Of those who had traumatic experience, up to16% will develop PTSD symptoms (Kolaitis, 2017). The prevalence of PTSD among children and adolescents were 15.9% (Alisic et al., 2014) while the lifetime PTSD prevalence among adult was 6.1% (Goldstein et al., 2016).

People that either direct or indirect exposed to traumatic event have higher risk to develop PTSD. Kessler et al. (2017) categorized the trauma event into seven types including war related trauma, physical violence, intimate partner or sexual violence, accident, unexpected death of

loved one, and other trauma. Rape, physical abuse, being kidnapped, and sexually assaults showed as event with higher risk in developing PTSD compared to other type of traumatic event. However, the highest number of PTSD was associated with unexpected death of loved one (2.9 episode of PTSD/100 population) (Kessler et al., 2017). PTSD also happened to whose being involved in rescue and reconstruction duties such as police, firefighters, or military personnel. They tend to feel nothing, yet further analysis found this population are at greater risk in developing PTSD (Friedman, 2013). About 6.6%, 1.6% and 6.6% municipality, firefighter and medical staff experienced PTSD 14 months after exposed to disaster respectively (Sakuma et al., 2015).

Several factors also play an important role in increasing the risk for having PTSD. A meta-analysis of 77 studies found 14 risk factors that predicted the prevalence of PTSD including trauma severity, lack of education, younger age, female sex, race (minority status), psychiatric history, low socioeconomic status, adverse childhood factors, previous trauma, family psychiatric history, lack of social support, childhood abuse, life stress, and low intelligence (Brewin et al., 2000).

2.6. PTSD Treatments

The main treatment for people with PTSD consists of medications, psychotherapies, or both. Although the combination of pharmacological and non-pharmacological treatments found to bring the most optimum results, previous meta-analyses suggest that psychotherapies are superior to pharmacological treatments in treating people with PTSD (Coventry et al., 2020; Merz et al., 2019). However, each of people with PTSD have unique experience, demographical background as well as influencing factors. Therefore, different treatments work differently for

each person. There is no 'the best' treatment of PTSD that applied to everyone. Ideally, each people with PTSD should be treated individually.

Numerous PTSD practice guidelines were developed either by global or national scale organizations such as American psychology association, Departments of Veterans Affairs and Defense, International Society of Traumatic Stress Studies, National Institute for Clinical Excellence, and Phoenix Australia Centre for Posttraumatic Mental Health. Among various psychotherapies developed and recommend for treating people with PTSD, The American psychological Association found cognitive processing therapy (CPT), cognitive therapy (CT), prolonged exposure (PE), cognitive behavioral therapy (CBT) as strongly recommend therapies, while eye movement desensitization and reprocessing (EMDR), narrative exposure therapy (NET), and brief eclectic psychotherapies (BEP), were suggested or conditionally recommended (APA, 2017). While Department of veteran affairs suggested manualized trauma-focused psychotherapies including PE, CPT, EMDR, BEP, NET, and written narrative exposure to treat people with PTSD (Departement of Veterans Affairs, 2017).

Briefly, of the recommended therapeutic approaches, the explanation of most common recommended therapies will be explained below:

a. Cognitive processing therapy (CPT)

CPT was developed by Dr. Resick and Dr. Schnicke specifically for people who had traumatic experiences. CPT focus on trauma memories and reducing distress via written exposures and cognitive restructuring around themes of safety, trust, power/control, esteem, and intimacy. It is focused on teaching cognitive restructuring skills by repeatedly challenging the maladaptive cognitions through the use of cognitive restructuring techniques, individuals are able to develop more balanced and healthy appraisals of the traumatic event,

themselves, and the world. In this line of reasoning, changing negative cognition plays a vital role in improving PTSD symptoms (Resick, Monson, et al., 2017). The comprehensive 12 sessions in CPT help mediate the change of cognition, especially assimilation, accommodation, overaccommodation, and information. CPT was superior to waitlist group (Galovski et al., 2012; Rosner et al., 2019).

Compared to other psychotherapies, CPT showed more effectiveness in decreasing PTSD symptoms (Butollo et al., 2016; Holliday et al., 2014; Nixon, 2012; Resick et al., 2015; Sloan et al., 2018).

b. Cognitive therapy (CT)

CT is a brief and goal-oriented therapy to modify pessimistic evaluations and memories of traumas to interrupt problematic behaviors. CT is based mainly on the cognitive model, and its main principle holds that cognitions cause an emotional and behavioral state change (Anke Ehlers et al., 2003). Although CT also known as CBT, some studies use different terminology to describe the therapy. Therefore, we differentiate the treatment into separate part. CT showed more effective in decreasing PTSD symptoms compared to control group (Ehlers et al., 2005; A. Ehlers et al., 2003; Ehlers et al., 2014; Kubany et al., 2003; Richard Meiser-Stedman et al., 2017) and compared to other PTSD therapies (Ehlers et al., 2014; Tarrier et al., 1999).

c. Cognitive behavior therapy (CBT)

CBT refers to the original format of CBT pioneered in the 1960s by Dr. Beck, which targets current problematic symptoms by focusing on the relationships among and between thoughts, feelings, and behaviors (Beck, 1997). Although CBT originally developed for people with depression, the trauma focused CBT (TF-CBT) is one of helpful treatment

during the acute aftermath of trauma exposure. TF-CBT works by improve patients understanding about their negative patterns in thoughts and feelings are in order to have a more realistic idea and behavioral pattern (Adams, 2018). The duration of TF-CBT is ranged from eight to 12 sessions. But in fact, fewer sessions, five, is considered give clinical impact to people with PTSD. Previous trials found TF-CBT more effective to reduce PTSD symptoms compared to control group (Bryant et al., 2018; Castillo et al., 2016; Goldbeck et al., 2016; Jaberghaderi et al., 2019)

d. *Prolonged exposure (PE)*

PE is one of TF-CBT for people with PTSD. PE, developed by Foa (Foa et al., 1991), is based on emotional processing theory and works by assisting the patient to process the traumatic experience by altering the fear structure through gradual imaginal and *in vivo* exposure (McLean & Foa, 2011). In PE, those who are traumatized usually exposed to the stimuli using writing, imagery, or event direct contact to the related place through a hierarchical of fearful event, one at a time. After through repeated exposure, it is believed will increase the ability people with PTSD to confront without feeling traumatized and anxiety. The duration of the treatment is between 9-12 weekly session. PE produced a superior impact to decreasing PTSD symptom compared to control group (Cigrang et al., 2017; Franklin et al., 2016; van den Berg et al., 2015) and other therapy (Foa et al., 2018; Rossouw et al., 2016).

e. *Eye movement desensitization and reprocessing (EMDR)*

EMDR was developed based on the Adaptive Information Processing (AIP) model to assist the processing of traumatic memories with bilateral eye stimulations (Hase et al., 2017; Landin-Romero et al., 2018). EMDR extracts all the anxious feelings and leads to a

decrease in vividness and emotionality in regard to memory; this approach reconstructs patients' cognitive thinking, along with their emotional status which in turn helps the patient to process the memory and emotions correctly. Thus, the eight sessions of EMDR is targeted to access the dysfunctional memory, such that the appropriate connections can be made to the adaptive networks. As the ability to process new information improves, or reprocessing occurs, people tend to have a positive perspective toward new information and to proceed it as non-threatening (Hase et al., 2017; Shapiro, 1989a). Previous studies showed that EMDR was superior over waitlist groups. In addition, compared to other psychotherapies, EMDR showed more effectiveness in decreasing PTSD symptoms (Capezzani et al., 2013; Jarero et al., 2018).

f. Narrative exposure therapy (NET)

NET refers to a guided autobiographical exposure therapy that focuses on expressing the traumatic experience in a narrative way. NET works on the premise that people who suffer from PTSD have a significant distortion in their autobiographical memory, and thus NET aims to give the person a chance to internalize and organize all traumatic memories, with the purpose to facilitate the integration of thoughts and behaviors (Neuner et al., 2008). Although limited study was conducted to determine its effectiveness, but NET showed superior effect in decreasing PTSd symptoms compared to control group (Orang et al., 2018; Peltonen & Kangaslampi, 2019b).

g. Brief eclectic psychotherapy (BEP)

BEP focuses on combatting the emotions of shame and guilt and combines aspects of CBT with a psychodynamic approach. As such, BEP combines and integrates elements

from psychodynamic, cognitive-behavioral, and directive psychotherapy (Gersons & Schnyder, 2013).

h. Present centered therapy (PCT)

PCT was developed as comparisons for trauma studies, focusing on adaptive responses for current life stressors that may be directly or indirectly related to PTSD symptoms. It usually utilizes a structured approach and was initially developed as a comparison condition for CBT treatment. Components of PCT include supportive therapeutic relationships to build interpersonal connections, normalize symptoms, encourage the expression of feelings, and increase mastery in dealing with stressors (Belsher et al., 2019).

i. Psychodynamic therapy (PDT)

PDT coming from a long history of depth psychology, focuses on present behaviors and emotions that manifest from unconscious processes. This therapy facilitates self-reflection and self-examination; and the use of the relationship between therapist and patient is integral to the reduction of symptoms (Krupnick, 2002). By facilitating self-awareness, PDT can increase the understanding of one's past and present behavior.

CHAPTER 3 – Methodology

This dissertation elaborates two studies related to PTSD. The first study was a meta-analysis of global prevalence of PTSD during COVID-19 pandemic. The second study was a network meta-analysis to compare the effectiveness of psychotherapies for people with PTSD.

Study 1: Global Prevalence of Posttraumatic Stress Disorder and Associate Risk Factors during COVID-19 Pandemic: A Meta-Analysis

3.1.1. Study Design

This was a prevalence meta-analysis to identify the prevalence of PTSD during COVID-19 pandemic and the associated factors. This study was registered to the international database of prospective registered systematic reviews (PROSPERO) with registration number: CRD42020218762

3.1.2. Search Method

A comprehensive literature search was conducted in seven databases, including CINAHL, Embase, Medline-OVID, PsycInfo, PubMed, Scopus, and Web of Science without language restriction up to June 2021. Further manual search from Google Scholar and included studies or references list of previously published review articles was also done to identify potential studies. The search was conducted following Population Exposure and Outcome (PEO) principle using combination keywords ‘prevalence’ AND ‘posttraumatic stress disorder’ AND 'Covid-19'.

3.1.3. Study Selection and Data Extraction

All articles from databases and manual search were then screened using EndNote version 9.3 software. After removal of duplicates, articles were screened by title and abstract and then eligible studies were screened by full text. More specifically we screening the data based on P (population), E (exposure), and O (outcome), S (study design) principal.

Population. This meta-analysis only included studies that recruited either patient/survivor of COVID-19, health professionals (including medical doctor, nurse, nutritionist, pharmacist, health assistant, and auxiliary workers) and population at large,

Exposure. This study we only focus on all population that exposed to COVID-19 pandemic happened from December of 2019. Therefore, studies published before the pandemic will be excluded.

Outcome. Studies that measured PTSD prevalence as the outcome were included. PTSD condition can be diagnosed either using a standardized mental health diagnostic manual (DSM-III, DSM III-R, DSM-IV, DSM-IV-R, DSM-5, ICD-10) or those using validated PTSD assessment tools.

Study design. Observational studies either cohort or cross-sectional were included. Cohort study refers to an approach to follow study participants over a period of time after being exposed to certain risk factors (Barrett & Noble, 2019). While cross-sectional was defined a study that measures the outcome as well as the exposures in study participants at the same time (Setia, 2016). Articles were excluded if they were (1) irrelevant to the topic, (2) PTSD not related to COVID-19 pandemic, (3) irrelevant population, (4) review/meta-analysis, (5) irrelevant study designs, (6) study protocol, (7) studies with insufficient data and (7) studies using similar dataset with other included study.

All the data from the eligible studies in the analysis were extracted using standard pre-designed tables. According to study characteristics, studies included were extracted based on study ID, setting, time, design, PTSD prevalence, PTSD assessment tools, and risk of bias. While according to studies' participants, the data of mean age, range age, gender, marital status, educational level, unit of work, health profession type, continent, countries' gross domextic product (GDP), countries' total case and death case were extracted.

3.1.4. Quality Assessment

This study using Hoy criteria to evaluate the risk of bias assessment which determines the internal and external validity for prevalence studies design (Hoy et al., 2012). This is a 10-item assessment tool with score ranging from 0 to 10. The overall quality of the included eligible studies was categorized into as low (9-10), moderate (7-8), and high (0-6) risk of bias. Two reviewers independently appraised the included studies. The two reviewers met to discuss their results and come to a consensus for each item on the checklist for each study. A third reviewer was consulted if there was a discrepancy in data extraction between the two primary reviewers and a consensus regarding the information was needed.

3.1.5. Statistical Analysis

The pooled prevalence of PTSD was analyzed based on *Logit transformation* random-effects model using *metaprop* package in R software version 4.0.2. Compared to other type of analysis, the *Logit transformation* showed high performance in account for the variability and heterogeneity of prevalence rates among the included studies (Lin & Xu, 2020). The prevalence of PTSD was pooled for the overall population and then to be divided into three groups

according to the population exposure model: patients/survivors of COVID-19, health professionals, and the population at large. The main outcomes were presented in proportion format with corresponding 95% confidence interval (95%CI) and 95% prediction interval (95%PrI) along with the heterogeneity (Tau^2, I^2, Q-*statistic*, and p-value). Random effect model was used based on the existence of significant heterogeneity. I^2 value of 25% indicated low heterogeneity, 50% indicated moderate heterogeneity, and 75% indicated high heterogeneity (Higgins et al., 2003). Publication bias among the included studies was analyzed using Peter's regression test (Peters et al., 2006). This method is based on weighted linear regression on the inverse of total sample single proportion where a p-value <0.1 indicates a significant publication bias.

In term of significant high heterogeneity is observed among the included studies, moderator analysis with sub-group and meta-regression were conducted to find potential moderator variables. A p-value <0.05 indicates a significant moderator effect to PTSD prevalence during COVID-19 pandemic. Furthermore, to evaluate the robustness of this study findings, sensitivity analyses was conducted based on risk of bias and assessment tools. First, we excluded studies with moderate and high risk of bias. Second, we excluded studies using non-recommended assessment tools according to PTSD guidelines by the APA (American Psychological Association, 2020). We evaluate the change in PTSD prevalence before and after sensitivity analysis was conducted.

Study 2: The Comparative Effectiveness of Psychotherapies in Posttraumatic Stress Disorder: A Network Meta-Analysis of Randomized Controlled Trials

3.2.1. Study Design

This was a network meta-analysis to evaluate and compared the effectiveness of psychotherapies toward PTSD

3.2.2. Search Method

The literature was identified in Cochrane library, Embase, Medline-OVID, PsycInfo, PubMed, and Scopus. The search was conducted using medical subject heading terms (MeSH) for all experimental RCT that focused on determining the effectiveness of psychotherapies toward people diagnosed with PTSD in the title, abstract, and keywords without date and language restrictions up to January 2021. In addition, we conducted a manual search through Google Scholar and references from previously published meta-analysis and/or systematic reviews. Meta-analysis of CPT (Asmundson et al., 2019), CT, EMDR (Chen et al., 2015), NET (Lely et al., 2019), PE (Zhou et al., 2020), CBT (Lenz & Hollenbaugh, 2017), and Network meta-analysis (Forman-Hoffman et al., 2018; Mavranezouli, Megnin-viggars, Dally, & Dias, 2020; Mavranezouli, Megnin-viggars, Dally, Dias, et al., 2020) were checked to find potential articles to be included in this study. Relevant literature was also retrieved from ClinicalTrials.gov and The International Clinical Trials Registry Platform to ensure completeness.

3.2.3. Study Selection and Data Extraction

A systematic screening was carried out by two independent reviewers to identified relevant studies. A study was selected and included in network meta-analysis if it is meet the PICOS criteria:

Population. Participants of studies experienced PTSD as the primary diagnosis. PTSD was defined either according to DSM by APA, ICD by WHO, or validated by PTSD assessment tools with established thresholds for measurement of symptoms. Study subjects could have a comorbid mental disorder or condition as long as PTSD was the primary diagnosis. Participants were not restricted to specific demographic characteristics (age, sex, educational background, marital status, traumatic background).

Intervention. This study focused on determining the clinical importance of included therapies, CPT, CT, EMDR, NET, PE, CBT, PCT, BEP, PDT, or combination among them. The psychotherapies included in this study were chosen based on the APA and DoD's PTSD guidelines (APA, 2017; Departement of Veterans Affairs, 2017).

Studies that compared psychotherapies with non-included therapies, compared different formats of the same therapy, insufficient data for analysis were excluded. In terms of psychopharmacotherapy, a study was included only if the participant maintained stable medication types and dosages before and during the study. Any difference in opinion about the eligibility of study was resolved by discussion with a more expert reviewer to reach a general consensus.

Comparison. Studies that determined psychotherapies' effectiveness were included in the analysis when comparisons use control conditions, including waitlist/no treatment (NT), standard care/treatment as usual (TAU), or other guideline-recommended interventions (CPT,

CT, EMDR, NET, PE, CBT, PCT, BEP, PDT). Studies are excluded when comparison therapies are beyond the scope of this study.

Outcome. The primary outcome for this study was PTSD symptoms. The outcome at immediate posttreatment and longitudinal measurement (short-term (< 6 months) and long-term (≥ 6 months)) follow-up measurements were retrieved. PTSD symptoms changes from observer-rated measurements were prioritized over self-reported. Intention to treat (ITT) was prioritized over per-protocol (PP) if both were available in a study. Data from the latest observation were preferred if there were more than one observation in short-term or long-term follow-up measurements. Previous research has shown both self-reported assessments and ITT provided more conservative effect estimates (Cuijpers et al., 2010).

Secondary outcome, the remission rate, refers to the number of participants that no longer meet PTSD diagnosis criteria at posttreatment (Morina et al., 2014). A higher remission rate represents more effectiveness of psychotherapies to achieve better end-state functioning.

Study design. We only included experimental study that using randomized controlled trials (RCT) design. All type of RCT will be included as long as provide a clear data that differentiate the outcome of each group.

All eligible studies data were extracted into study's identifiers (author and year of publication), study's characteristics (risk of bias, country/region), participant's characteristics (standard diagnosis manual used, number of samples in all groups, mean age, sex), therapy's characteristics (therapy, number of sessions, frequency, duration, format, comparison therapy), and outcome's characteristics (assessment tools, follow up time). For analysis purposes, the summary of outcomes, including sample size, pre-post mean difference, standard deviations, and number of remitted participants were extracted and documented into a separate excel file.

For follow-up measurements, the latest measurement was prioritized if there were more than one data in one follow-up category. Remission rate data were retrieved based on treatment endpoint measurement.

3.2.4. Quality Assessment

In order to evaluate the true effect of therapies included in the network meta-analysis, Grading of Recommendation Assessment Development and Evaluation (GRADE) NMA was used to assess the certainty in each comparison. The quality of evidence was assessed for the main outcome and divided into four levels of quality which were high quality of evidence (⊕⊕⊕⊕), moderate quality of evidence (⊕⊕⊕), low quality of evidence (⊕⊕), and very low quality of evidence (⊕). Five domains, including the risk of bias (also known as study limitation), inconsistency, indirectness, imprecision, and other considerations (publication bias) were assessed to rate the certainty.

(1) *Risk of bias* was measured based on the Cochrane RoB 2.0. Two independent researchers analyzed the risk of bias to cover the five domains that are known to affect the results of randomized trials (randomization process, deviation from intended intervention, missing outcome data, measurement of the outcome, and selection of the reported results) to categorize the article as low risk, some concern, or high risk of bias.

(2) *Inconsistency* refers to the variability seen in the magnitude of the effects across studies for a specific comparison after accounting for differences between subgroups. The node-splitting method provides a more specific assessment by splitting the information of direct and indirect and assessing the conflict between each node (Dias et al., 2010).

(3) *Indirectness* refers to the variance of the subjects, intervention-and-comparator, outcome-and-measurement of the study. According to GRADE guidelines, there were four types of indirectness in NMA which were population, intervention, outcome, and indirect comparison or lack of direct comparison. The quality of evidence may be decreased when there are substantial differences in population, intervention, outcome or if there are no direct comparisons (Jansen & Naci, 2013).

(4) *Imprecision* evaluation is based on 95% confidence interval effect size (Puhan et al., 2014). The certainty of each comparison was divided into four levels - very low, low, moderate, and high - by presenting direct, indirect, and network estimates of effect and rating the certainty (Bonner et al., 2018; Brignardello-Petersen et al., 2018; Guyatt et al., 2011; Puhan et al., 2014; Salanti et al., 2014).

(5) *Other consideration* consists of publication bias and therapy's effect. Publication bias was determined based on bias in each comparison. Low risk of bias represents undetected publication bias while some concern and high risk of bias represent strongly detected. While therapy's effect was determined according to treatment effect size. Effect size >80% considered as having large effect.

3.2.5. Statistical Analysis

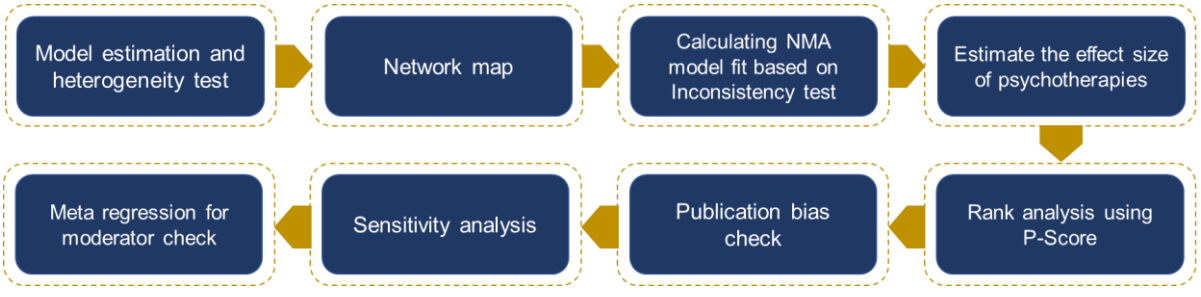

Figure 2. The analysis flow chart of network meta-analysis

This study calculated network evidence based on direct and indirect evidence from all studies included. In NMA, direct evidence refers to the relative effect of two comparisons that are directly determined in a study. In contrast, indirect comparison refers to the relative effects of two interventions that have not been compared directly within study. For example, the comparisons of A versus B and B versus C are direct comparisons, so A versus C represent the indirect comparison. In this study, we used frequentist approach for NMA by utilizing *netmeta* package in R (version x64 4.0.2). Bayesian approach of NMA using *gemtc* package was used for the moderator and sensitivity analyses. Past studies had concluded that Bayesian and frequentist report similar results (Rucker & Schwarzer, 2015; Seide et al., 2020).

For the main analysis, several steps were used to produce all of the NMA results (**Figure 2).** (1) The network meta-analysis model was estimated using a fixed or random-effect model. (2) A network map was created to determine the network relationship between studies. (3) NMA model fit was calculated using inconsistency tests to check for inconsistency between direct and indirect effects in this study. Inconsistency was analyzed using two methods, node splitting and design by treatment interaction model. P-value less than 0.05 was considered as significant inconsistency. (4) The effect sizes of treatments were compared with NT by using standardized mean difference (SMD), 95% confidence intervals (CI), and with mean rank analysis (P-scores). SMDs of 0.2, 0.5, and 0.8 were considered as small, medium, and large effect sizes (Cohen, 1988; Faraone, 2008; Lakens, 2013). In addition, the 95% prediction intervals (PrI) are also provided (Lin, 2019). (5) The P-scores are used to estimate the best treatment rank and categorized into four-levels: (a) ≥75% as *upper quartile*; (b) >50%-75% as the *second quartile*; (c) >25%-50% as the *third quartile*; and (d) ≤25% as *lower quartile*.

(6) The funnel command from *netmeta* package was utilized to produce the comparison-adjusted funnel plot. An Egger's regression test method was also used to test for publication bias along with the funnel plot. The presence of publication bias is considered if there are more studies on the outside than inside the comparison-adjusted funnel plot. The p-value of less than 0.05 in Egger's regression test could indicate that there is publication bias.

3.2.6. Sensitivity Analysis

To check the robustness of the study's findings, sensitivity analyses was conducted based on different combinations of CBT treatment groupings were compared, these were CBT only, CBT+CT, CBT+CT+CPT, and CB+CT+CPT+PE. The significant changes between unadjusted and adjusted models were evaluated with the DIC. In addition, we also evaluate the effectiveness of psychotherapies alone without additional therapy. We include studies that the participants did not take any mental-related medication or maintain stable dose of medication before and during the study.

3.2.7. Moderator Analysis

Moderator analysis was conducted by utilizing *gemtc* package from *Bayesian* approach to calculate moderator effects of age. Studies were categorized into children to adolescents and adult groups. The moderator effect's occurrence is based on a significant change DIC. The NMA Model with lower scores of DIC suggests a better model fit compared with the other NMA model (Chaimani & DSalanti, 2012). A 10-point lower DIC from the initial model indicates significantly different results or moderator effect.(Spiegelhalter et al., 2002).

CHAPTER 4 – Results

Study 1: Global prevalence of posttraumatic stress disorder and associate risk factors during COVID-19 pandemic: A meta-analysis

4.1.1. Search Results

A total of 4,045 studies were retrieved from the databases of Cochrane library, CINAHL, Embase, Medline-OVID, PubMed, Scopus, and Web of Science. Another 15 articles were found through manual search in Google Scholar and previously published meta-analyses (Arora et al., 2020; Li et al., 2021; Yuan et al., 2021). About 79 full-text articles were eligible for further consideration. After evaluated the full-text, only 63 studies were included in the final analysis (**Figure 3)**

4.1.2. Study Characteristics

A total of 72 proportion estimates from 63 studies were included with 124,952 participants from 24 countries. Eleven (15.3%) proportion estimates PTSD prevalence among patients/survivors of COVID-19, 24 (33.3%) proportions represented health professionals, 36 (50%) proportions of population at large, and 1 (1.4%) study with mixed population. Most of the studies were conducted in mainland China (47.6%), around February to April (65%), published in 2020 (100%), and used PTSD checklist as diagnostic assessment tools (47.6%) (**Table 2**).

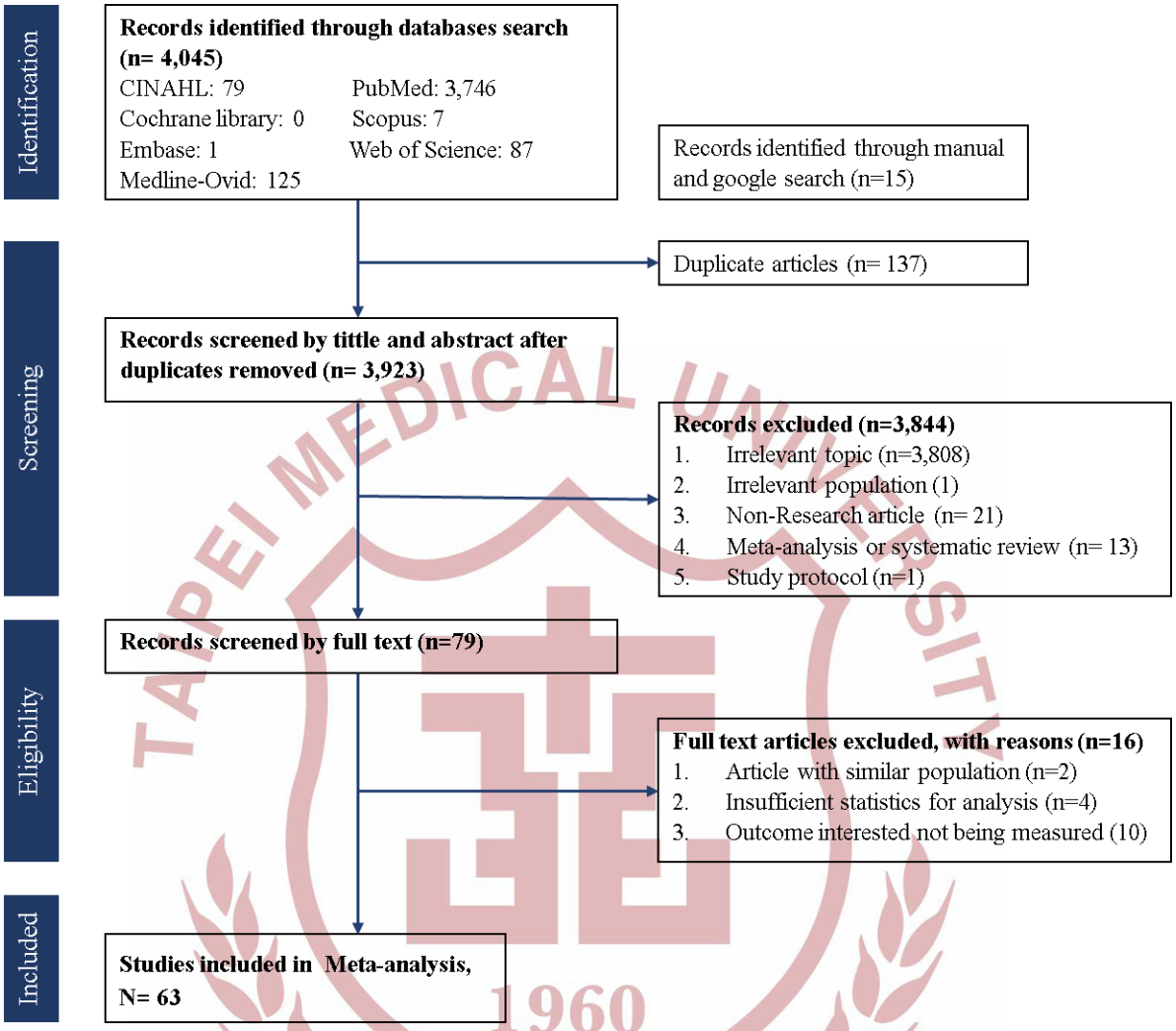

Figure 3. PRISMA flow chart of PTSD prevalence meta-analysis

4.1.3. Quality of Study

All included studies were evaluated using the 10 items risk of bias tool developed specifically for prevalence meta-analysis by Hoy and colleagues. Two independent raters conducted the evaluation, and there was no disagreement between raters for each article included

in this study. Overall results showed 41 (65.1%) and 22 (34.49%) studies were classified as low and moderate risk of bias (**Table 2**).

Table 2. Data extraction of included studies of PTSD prevalence during COVID-19 pandemic

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
1	Alshehri et al, 2020	Saudi Arabia	Cross-sectional	PCL-S	Population at large	1,374	22.63%	Mean age: NA Range age: 18->55 Gender Male: 674 (49.05%) Female: 700 (50.95%)	June 2020	9 – L
2	Berthelot et al, 2020	Canada	Cohort	PCL-5	Population at large	1,258	1.19%	Mean age: 29.27 Range age: 18-46 Gender Male: - Female: 1258(100%)	April 2020	9 – L
3	Blekas et al, 2020	Greece	Cross-sectional	PTSD-8	Health professionals	270	16.67%	Mean age: 37.61 Range age: NA Gender Male: 71 (22.9%) Female: 199 (77.1%)	April 2020	9 – L
4	Cai et al, 2020	China	Cross-sectional	PTSD-SS	Patients/survivor	126	30.95%	Mean age:45.7 Range age: 11-72 Gender Male: 60 (47.6%) Female: 66 (52.4%)	February-March 2020	8 – M
5	Caillet et al, 2020	France	Cross-sectional	IES-R	Health professionals	208	25%	Mean age: 35 Range age: NA Gender Male: 52 (25%) Female: 156 (75%)	April 2020	7 – M
6	Castelli et al, 2020	Italy	Cross-sectional	PCL-5	Population at large	1,321	20%	Mean age: 35.1 Range age: NA Gender Male: 399 (31%) Female: 922(69%)	March-April 2020	8 – M
7	Chang et al, 2020	South Korea	Cross-sectional	PCL-5	Patients/survivor	64	20.31%	Mean age:54.7 Range age: NA Gender Male: 28 (43.7%)	February-April 2020	8 – M

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Female: 36 (56.3%)		
8	Chew et al, 2020 (a)	Singapore	Cross-sectional	IES-R	Health professionals	277	12.27%	Mean age: 35 Range age: NA Gender Male: 84 (30.3%) Female: 193 (69.7%)	April-June 2020	9 – L
	Chew et al, 2020 (b)	India	Cross-sectional	IES-R	Health professionals	384	2.08	Mean age: 27.7 Range age: NA Gender Male: 133 (34.5%) Female: 251 (65.4%)	April-June 2020	9 – L
	Chew et al, 2020 (c)	Malaysia	Cross-sectional	IES-R	Health professionals	175	6.29%	Mean age: 32.4 Range age: NA Gender Male: 57 (32.6%) Female: 118 (67.4%)	April-June 2020	9 – L
	Chew et al, 2020 (d)	Vietnam	Cross-sectional	IES-R	Health professionals	60	15%	Mean age: 34.7 Range age: NA Gender Male: 16 (26.7%) Female: 44 (73.3%)	April-June 2020	9 – L
	Chew et al, 2020 (e)	Indonesia	Cross-sectional	IES-R	Health professionals	250	11.60%	Mean age: 33.2 Range age: NA Gender Male: 110 (44%) Female: 140 (56%)	April-June 2020	9 – L
9	Chew, Nicolas et al, 2020 (a)	Singapore	Cross-sectional	IES-R	Health professionals	480	7.5%	Mean age: 29 Range age: 25-35 Gender Male: NA Female: NA	February-April 2020	9 – L
	Chew, Nicolas et al, 2020 (b)	India	Cross-sectional	IES-R	Health professionals	426	7.28%	Mean age: 29 Range age: 25-35 Gender Male: NA	February-April 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Female: NA		
10	Chi et al, 2020	China	Cross-sectional	PCL	Population at large	2,038	30.81%	Mean age: 20.56 Range age: NA Gender Male: 755 (37%) Female: 1,283 (63%)	February 2020	9 – L
11	Czeisler et al, 2020	United States	Cross-sectional	IES-6	Population at large	5,470	4.59%	Mean age: NA Range age: 18-44 Gender Male: 2,676 (48.9%) Female: 2,784 (50.9%) Others: 10 (0.2%)	April-June 2020	9 – L
12	DiCrosta et al, 2020	Italy	Cross-sectional	IES-R	Population at large	1,253	35.59%	Mean age: 39.48 Range age: 18-65 Gender Male: 445 (35.5%) Female: 808 (64.5%)	April 2020	9 – L
13	Einvik et al, 2021(a)	Norway	Cross sectional	PCL-5	Patients/survivor (hospitalised)	125	9.5%	Mean age: NA Range age: NA Gender Male: NA Female: NA	June 2020	7 – M
	Einvik et al, 2021(b)	Norway	Cross sectional	PCL-5	Patients/survivor (non-hospitalised)	458	7.0%	Mean age: NA Range age: NA Gender Male: NA Female: NA	June 2020	7 – M
14	Fekih-Romdhane et al, 2020	Tunisia	Cross sectional	IES-R	Population at large	603	33.0%	Mean age: 29.2 Range age: >18 Gender Male: 157 (26%) Female: 446 (74%)	April 2020	8 – M
15	Forte et al, 2020	Italy	Cross sectional	IES-R	Population at large	2,291	27.72%	Mean age: 30.0 Range age: 18-89 Gender	March 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Male: 580 (25.2%) Female: 1708 (74.6%) Other: 3 (0.2%)		
16	Giusti et al, 2020	Italy	Cross sectional	IES-6	Health professionals	330	36.67%	Mean age: 44.6 Range age: 18-89 Gender Male: 124 (37.4%) Female: 206 (62.6%)	May 2020	8 – M
17	Gonzaler-Sanguino et al, 2020	Spain	Cross sectional	PCL-C-2	Population at large	3,480	13.97%	Mean age: 37.92 Range age: 18-80 Gender Male: 870 (25%) Female: 2,610 (75%)	March 2020	9 – L
18	Goularte et al, 2021	Brazil	Cross-sectional	IES-R	Population at large	1,996	34.22%	Mean age: 34.22 Range age: NA Gender Male: 320 (15.5%) Female: 1,676 (84.5%)	May-July 2020	9 – L
19	Gu et al, 2020	China	Cross-sectional	IES-R	Covid-19 patients	461	24.95%	Mean age: NA Range age: 18->50 Gender Male:162 (35.1%) Female: 299 (64.9%)	February 2020	8 – M
20	Guo, Qian et al, 2020	China	Cross-sectional	PCL-5	Patients/survivors	103	7.8%	Mean age: 42.50 Range age: 18-75 Gender Male:59 (57.3%) Female: 44 (42.7%)	February 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
21	Guo, Jing et al, 2020	China	Cross-sectional	PCL-5	Mixed population	2,441	72.6%	Mean age: NA Range age: 18->51 Gender Male:1172 (48%) Female: 1296 (52%)	February 2020	9 – L
22	Hao et al, 2020 (a)	China	Cross-sectional	IES-R	Population at large	76	31.58%	Mean age: 32.8 Range age: NA Gender Male: 25 (32.9%) Female: 51 (37.1%)	February 2020	8 – M
	Hao et al, 2020 (b)	China	Cross-sectional	IES-R	Population at large	109	13.76%	Mean age: 33.1 Range age: NA Gender Male: 41 (37.6%) Female: 68 (62.4%)	February 2020	8 – M
23	Huang, et al, 2020	China	Cross-sectional	PTSD-SS	Health professionals	230	27.39%	Mean age: 32.6 Range age: - Gender Male: 43 (18.7%) Female: 187 (61.3%)	February 2020	8 – M
24	Janiri et al, 2021	Italy	Cross-sectional	CAPS-5	Patients/survivors	381	30.2%	Mean age: 53.1 Range age: NA Gender Male: 51 (44.3%) Female: 64 (55.7%	April-October 2020	8 – M
25	Johnson et al, 2020	Norway	Cross-sectional	PCL-5	Health professionals & public service providers	1,773	11.68%	Mean age: NA Range age: 18->60 Gender Male: 166 (15.3%) Female: 1507 (84.7%)	March-April 2020	10 – L
26	Joseph et al, 2020	Saudi Arabia	Cross-sectional	IES-6	Population at large	584	59.93	Mean age: NA Range age: 15-44 Gender Male: 361 (61.8%)	April-May 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Female: 223 (38.2%)		
27	Karatzias et al, 2020	Ireland	Cross-sectional	ITQ	Population at large	1,041	17.68%	Mean age: NA Range age: 15->65 Gender Male: 505 (48.5%) Female: 536 (51.5%)	March 2020	9 – L
28	Lahav, 2020	Israel	Cross-sectional	PCL-5	Population at large	976	5.53%	Mean age: 33.1 Range age: NA Gender Male: 180 (18.4%) Female: 796 (81.6%)	April 2020	9 – L
29	Leng et al, 2020	China	Cross-sectional	PLC-C	Health professionals	90	5.6%	Mean age: NA Range age: 20-40 Gender Male: 25 (17.8%) Female: 65 (72.2%)	March 2020	9 – L
30	Liang et al, 2020 (a)	China	Cross-sectional	PCL-C	Population at large	570	12.81%	Mean age: NA Range age: 14-35 Gender Male: 205 (36%) Female: 365 (64%)	January 2020	9 – L
31	Liang et al, 2020 (b)	China	Cross-sectional	PCL-C	Population at large	584	14.38%	Mean age: NA Range age: 14-35 Gender Male: 223 (38.2%) Female: 361 (61.8%)	January 2020	9 – L
32	Li, Q, 2020	China	Cross-sectional	IES-R	Population at large	1,109	67.09%	Mean age: NA Range age: 18->60 Gender Male: 622 (56.1%) Female: 487 (43.9%)	March 2020	9 – L
33	Li-Xuenyuan et al, 2020	China	Cross-sectional	IES-R	Health professionals	225	31.56%	Mean age: NA Range age: 21-60 Gender Male: 63 (28%)	January-March 2020	8 – M

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Female: 162 (72%)		
34	Li Xiuchuan et al, 2020	China	Cohort	PCL-5	Health professionals	356	61.80%	Mean age: 31.3 Range age: NA Gender Male: 49 (13.8%) Female: 307 (86.2%)	January-March 2020	8 – M
35	Liu CH et al, 2020	United States	Cross-sectional	PCL-C	Population at large	898	4.34%	Mean age: 24.5 Range age: 18-30 Gender Male: 127 (14.1%) Female: 730 (81.3%) Other: 41 (4.6%)	April-May 2020	9 – L
36	Liu, Dong et al, 2020	China	Cross-sectional	PCL-5	Patients/ survivors	675	12.44%	Mean age: 53.58 Range age: NA Gender Male: 317 (47%) Female: 358 (53%)	April 2020	8 – M
37	Liu, Nianqi et al, 2020	China	Cross-sectional	PCL-5	Population at large	285	7%	Mean age: NA Range age: NA Gender Male: 130 (45.6%) Female: 155 (54.4%)	January 2020	9 – L
38	Luceno-Moreno et al, 2020	Spain	Cross-sectional	IES-R	Health professionals	1,422	56.6	Mean age: 43.88 Range age: 19-68 Gender Male: 194 (13.6%) Female: 1228 (86.4%)	April 2020	9 – L
39	Mazza et al, 2020	Italy	Cross-sectional	PCL-5	Patients/survivors	402	28%	Mean age: 57.8 Range age: 18-87 Gender Male: 256 (63.7%) Female: 146 (36.3%)	April-June 2020	9 – L
40	Qi et al, 2020	China	Cross-sectional	PCL-C	Covid-19 patients	43	12.20%	Mean age: 40.01 Range age: NA Gender	February 2020	7 – M

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Male: 18 (41.9%) Female: 25 (58.1%)		
41	Ramirez et al, 2020	Mexico	Cross-sectional	IES-R	Population at large	3,932	27.21%	Mean age: 33 Range age: 18-77 Gender Male: 1004 (25.5%) Female: 2928 (74.5%)	March-April 2020	9 – L
42	Ren et al, 2020	China	Cross-sectional	PCL-5	Population at large	1,172	6.99%	Mean age: 22 Range age: NA Gender Male: 360 (30.7%) Female: 812 (69.3%)	March 2020	9 – L
43	Romito et al, 2020	Italy	Cross-sectional	IES-R	Population at large	77	36.36%	Mean age: 56.6 Range age: 22-85 Gender Male: 39 (50.6%) Female: 38 (49.4%)	April 2020	9 – L
44	Rossi et al, 2020(a)	Italy	Cross-sectional	GPS-PTSS	Population at large	1,379	49.38%	Mean age: 39 Range age: NA Gender Male: 315 (22.8%) Female: 1064 (77.2%)	March 2020	9 – L
	Rossi et al, 2020(b)	Italy	Cross-sectional	GPS-PTSS	Health professionals	18,147	36.73%	Mean age: 38 Range age: NA Gender Male: 3700 (20.4%) Female: 14447 (79.6%)	March 2020	9 – L
45	Seyahi et al, 2020 (a)	Turkey	Cross-sectional	IES-R	Health professionals	535	40.93%	Mean age: 31 Range age: 19-58 Gender Male: 181 (33.8%) Female: 354 (66.2%)	April 2020	9 – L
	Seyahi et al, 2020 (b)	Turkey	Cross-sectional	IES-R	Population at large	1,688	26.18%	Mean age: 38.2 Range age: 16-81 Gender	April 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Male: 503 (29.8%) Female: 1,185 (70.2%)		
46	Shevlin et al, 2020	United Kingdom	Cross-sectional	ITQ	Population at large	2,025	16.79%	Mean age: 45.44 Range age: 18-83 Gender Male: 978 (48.3%) Female: 1047(51.7%)	March 2020	9 – L
47	Si et al, 2020	China	Cross-sectional	IES-6	Health professionals	863	40.21%	Mean age: NA Range age: NA Gender Male: 253 (29.3%) Female: 610 (70.7%)	February-March 2020	9 – L
48	Song et al, 2020	China	Cross-sectional	PCL-5	Health professionals	14,825	9.13%	Mean age: 34 Range age: 18->40 Gender Male: 5,289 (35.7%) Female: 9,536 (64.3%)	February-March 2020	9 – L
49	Sun Luna et al, 2020	China	Cross-sectional	PCL-5	Population at large	2,091	4.6%	Mean age: NA Range age: 18->60 Gender Male: 819 (39.2%) Female: 1272 (60.8%)	January-February 2020	9 – L
50	Sun Shufang et al, 2020	China	Cross-sectional	IES	Population at large	1,912	67.05%	Mean age: 20.28 Range age: 18-49 Gender Male: 578 (30.23%) Female: 1334 (69.77%)	March-April 2020	9 - L
51	Tan et al, 2020	China	Cross-sectional	IES-R	Population at large	673	10.85%	Mean age: 30.8 Range age: 18-83 Gender Male: 501 (74.4%) Female: 172 (25.6%)	February 2020	8 – M
52	Tang et al, 2020	China	Cross-sectional	PCL-C	Population at large	2,485	2.70%	Mean age: 19.81 Range age: 16-27 Gender	February 2020	8 – M

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Male: 960 (39.2%) Female: 1525 (60.8%)		
53	Tarsitani et al, 2021	Italy	Cohort	PCL-5	Patients/survivors	115	10.4%	Mean age: 58 Range age: 48-67 Gender Male: 2 (17%) Female: 10 (83%)	April 2020	9 – L
54	Tomaszek et al, 2020	Poland	Cross-sectional	IES-R	Population at large	184	69.57%	Mean age: 21.92 Range age: 18-48 Gender Male: 29 (15.8%) Female: 155 (84.2%)	March-April 2020	9 – L
55	Wang, Ya-Xi et al, 2020	China	Cross-sectional	PCL-C	Health professionals	202	16.83%	Mean age: 32 Range age: 29-40 Gender Male: 25 (12.4%) Female: 177 (87.6%)	February-March 2020	8 – M
56	Wang Ying et al, 2020	China	Cross-sectional	IES-R	Health professionals	1,897	9.75%	Mean age: 34 Range age: 18->40 Gender Male: 332 (17.5%) Female: 1565 (82.5%)	January-February 2020	9 – L
57	Wang-yuan et al, 2020	China	Cross-sectional	IES-R	Population at large	6,213	9.30%	Mean age: 50.57 Range age: NA Gender Male: 3278 (52.8%) Female: 2935 (47.2%)	April 2020	8 – M
58	Wathelet et al, 2021	France	Cross-sectional	PCL-5	Population at large	22,883	19.5%	Mean age: 21.2 Range age: NA Gender Male: 925 (20.8%) Female: 3408 (76.5%) Others: 123 (2.8%)	June-July 2020	9 – L
59	Yin et al, 2020	China	Cross-sectional	PCL-5	Health professionals	371	3.8%	Mean age: 35.3 Range age: 18-60	February 2020	9 – L

No	Author (year)	Study setting	Study design	Diagnostic criteria	Study population	Sample size	PTSD prev	Study population characteristics	Time of study	Risk of bias
								Gender Male: 143 (38.5%) Female: 228 (61.5%)		
60	Zanghi et al, 2020	Italia	Cross-sectional	SSS-DSM-IV	Population at large	432	31.71%	Mean age: 40.4 Range age: NA Gender Male: 155 (35.9%) Female: 277 (64.1%)	May 2020	8 – M
61	Zhang et al, 2020	China	Cross-sectional	PCL-C	Health professionals	642	20.87%	Mean age: NA Range age: NA Gender Male: 96 (14.95%) Female: 546 (85.05%)	June 2020	8 – M
62	Zhao et al, 2020	China	Cross-sectional	PCL-5	Population at large	515	5.63%	Mean age: NA Range age: NA Gender Male: 173 (33.6%) Female: 342 (66.4%)	January-February 2020	9 – L
63	Zhou et al, 2020	China	Cross-sectional	PCL-5	Population at large	859	2.68%	Mean age: 32.68 Range age: 20-47 Gender Male: 0 Female: 859 (100%)	February-March 2020	8 – M

Abbreviations: Post-traumatic stress disorder checklist-survey (PCL-S); Post-traumatic stress disorder checklist-based DSM 5(PCL-5); Clinical-administered PTSD Scale for DSM-5 (CAPS-5); Posttraumatic stress disorder-8 inventory (PTSD-8); Post-traumatic stress disorder self-rating scale (PTSD-SS); Impact Event Scale-Revision (IES-R); The abbreviated PTSD checklist (PCL); Six items Impact Event Scale (IES-6); Post-traumatic stress disorder checklist-reduced version (PCL-C-2); International Trauma Questionnaire (ITQ); The PTSD checklist-civilian (PCL-C); The global psychotrauma screen, post-traumatic stress symptoms subscale (GPS-PTSS); Impact Event Scale (IES); The short screening scale Diagnostic and Statistical Manual for Mental Disorders 4th Edition (SSS-DSM-IV); Not available (NA).

4.1.4. Prevalence of PTSD

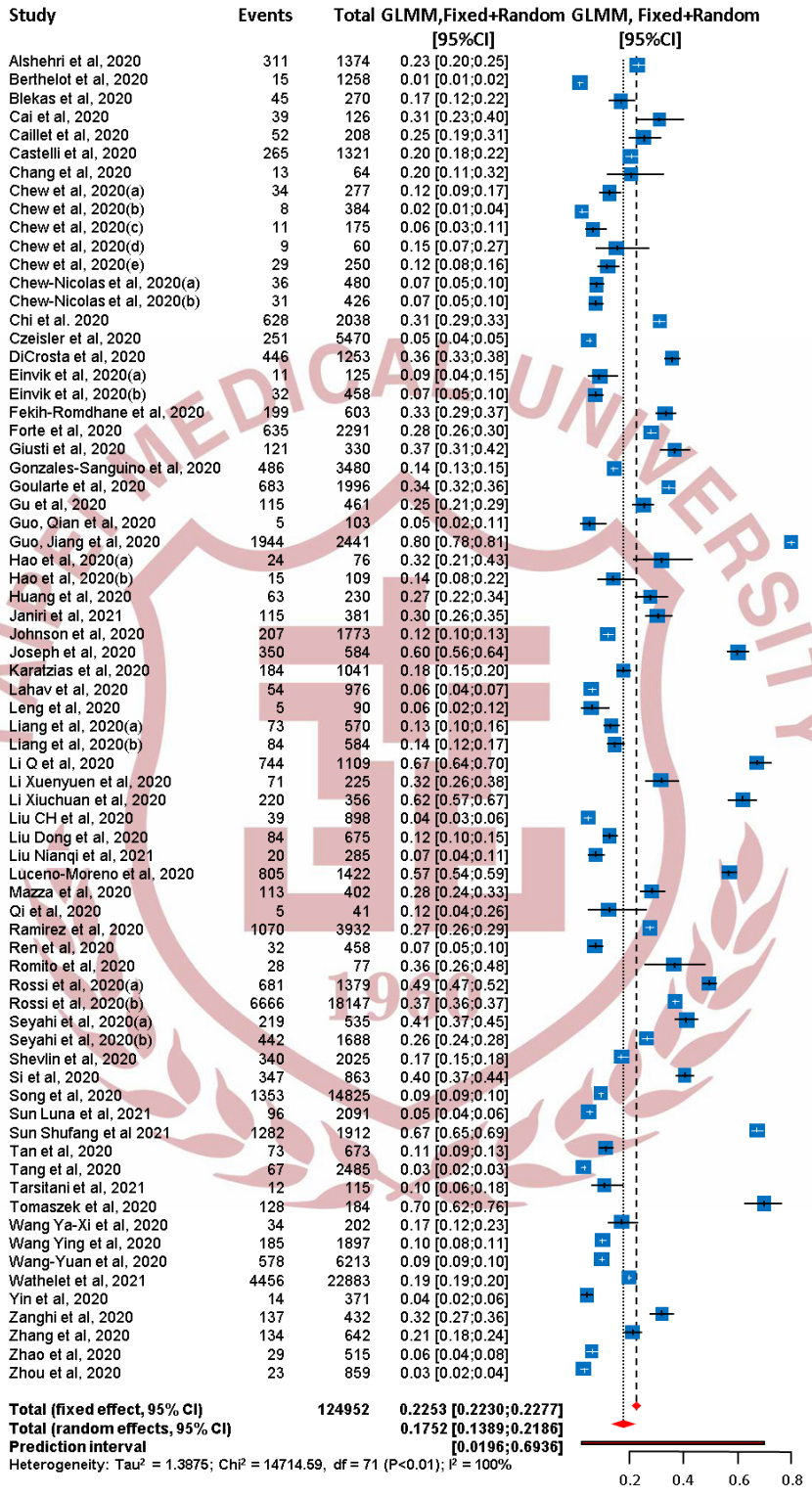

Figure 4. Forest plot overall prevalence of PTSD during COVID-19 pandemic

According to random effect model, the overall prevalence of PTSD during the COVID-19 pandemic was 17.52% (95%CI 13.89% to 21.86%) with high heterogeneity (I^2=99.7% and τ^2=1.39). The analysis found future similar studies would have PTSD prevalence ranged between 1.96% to 69.36% (**Figure 4**). Although the number of studies distributed in left and right side of funnel plot did not equal in number (**Figure 5**), yet further regression test using Peters indicated no evidence of significant publication bias with t=0.22, p-value=0.83.

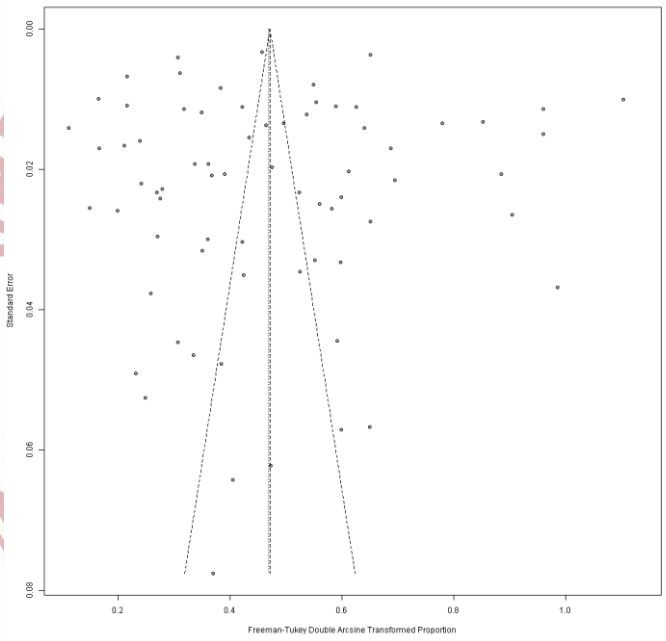

Figure 5. Funnel plot PTSD prevalence meta-analysis

One study was not included in the analysis based on populations because the prevalence represents mixed population. The analysis found there were no statistically significant difference in PTSD prevalence among the three different population groups according to the population exposure model (patients/survivors of COVID-19, health professionals, and the population at large). Those with direct exposure, patients/survivors of COVID-19, had the

lowest proportion of PTSD at 15.45% (95%CI 10.59 to 21.99; 95%PrI 3.46% to 48.23%) with high heterogeneity (I^2=94.3%, τ^2=0.47) compared to health professionals, and population at large.

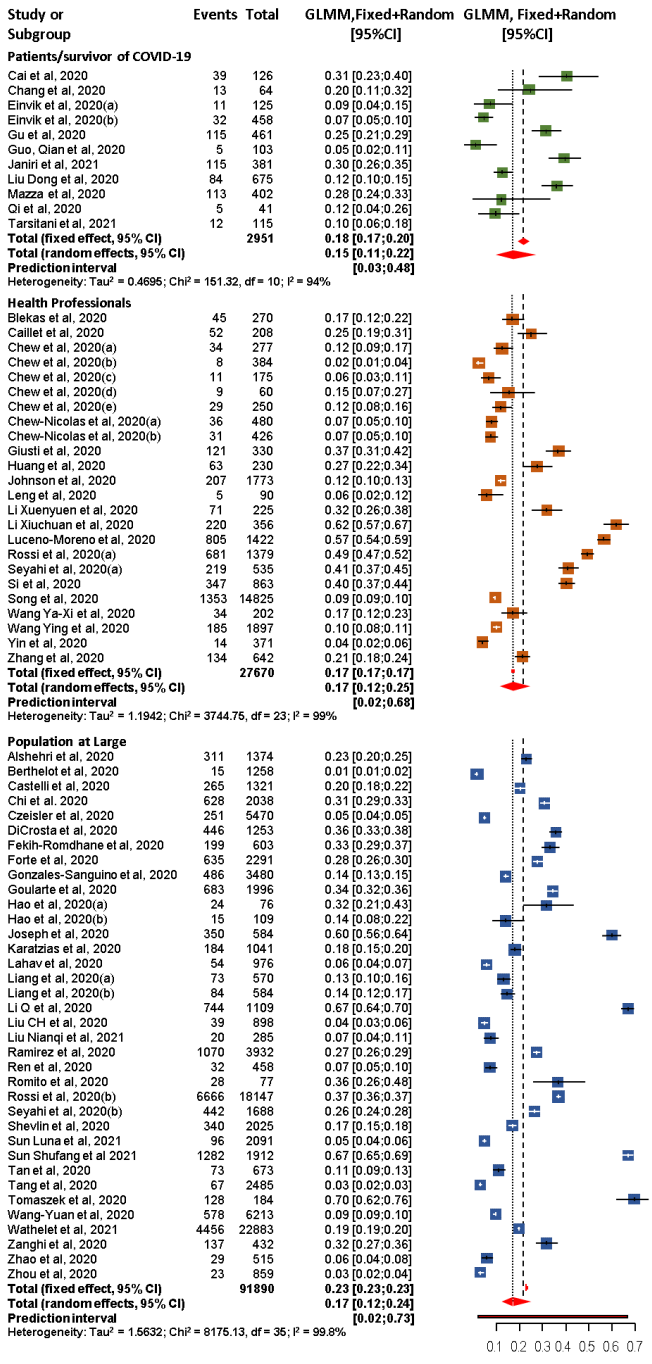

Figure 6. Forest plot prevalence PTSD of three populations during COVID-19 pandemic

Among the witness to exposure group, the PTSD prevalence of health professionals was 17.23% (95%CI 11.78 to 24.50; 95%PrI 2.02% to 67.81%) with high heterogeneity (I^2=99.3%, and τ^2=1.19). While in population at large was of 17.34% (95%CI 12.21 to 24.03; 95%PrI 1.57% to 73.40%) with high heterogeneity (I^2=99.8% and τ^2=1.56) (**Figure 6)**.

4.1.5. Moderator Analysis

Subgroup analyses and meta-regression were conducted based on studies' characteristics (geographic location by continent, gross domestic product, total case, and total death case), participants' characteristics (gender, age, marital status, educational level), and health professionals' characteristics (unit of work and profession).

According to studies' characteristics, subgroup analyses found the study's continent and assessment tools as significant moderators while countries' GDP, total case, and death case were not. The highest prevalence of PTSD found in people live in European (25.05%, 95%CI 19.14 to 32.06) compared to Asia (15.50%, 95%CI 11.29 to 20.92) and north and South American (8.08%, 95%CI 2.47 to 23.37). Studies that used CAPS-5 showed the highest PTSD prevalence (30.18%, 95% CI 25.78 to 34.98) compared to PCL-5/S/C/C2 (10.60%, 95%CI 6.39 to 17.09), and IES/R/6 (21.68%, 95%CI 15.49 to 29.47). Meta-regression analysis showed that female were eight times higher people who lived in European continent were 0.59 (95%CI 0.01 to 1.17) times higher more likely to had PTSD than those who lived in Asia continent (**Table 3**).

Regarding participants' characteristics, subgroup analyses found age, gender, marital status, and educational level were not statistically significant moderators. While meta-regression analysis found age as the only significant moderator with those in the elderly group (>65 years

old) had 1.75 (95%CI -3.16 to -0.34) times less likely to have PTSD because of COVID-19 pandemic compared to adults (**Table 3**).

According to health professionals' characteristics, subgroup analysis found the unit of work and health profession types as significant moderators. Health professionals who worked in COVID -19 units showed higher PTSD prevalence (30.98%, 95%CI 16.85 to 49.86) compared to those who did not work in COVID-19 units (13.16%, 95%CI 6.79 to 23.96). Among health professionals, nurses were found to have the highest PTSD prevalence with (28.22%, 95%CI 15.83 to 45.10), followed by medical doctors (10.80%, 95%CI 6.12 to18.38), and others (physiotherapists, care assistants, and admission staff) (7.69%, 95%CI 4.42 to 12.19). Meta-regression analysis also showed that nurses were 1.18 (95%CI 0.21 to 2.15) times more likely to have PTSD compared to medical doctors (**Table 3**).

Table 3. Moderator Analysis of PTSD Prevalence during COVID-19 Pandemic

Variable	**Subgroup analysis**				**Meta-regression analysis**	
	n of study (event sample size)	**Pooled estimate % (95% CI)**	I^2**(%)**	***p*-value**	**Pooled estimate (95% CI)**	***p*-value**
Participants' characteristics						
Mean Age	17	-	-	-	ref	
					-0.02 (-0.07 to 0.02)	0.269
Age						
Adult (18-65 years old)	12 (35,799)	25.67 (17.12 to 36.60)	99.6	0.089	ref	
Elderly (>65 years old)	5 (544)	5.68 (0.85 to 29.72)	89.7		-1.75 (-3.16 to -0.34)	**0.015**
Gender						
Male	22 (12,264)	21.86 (13.41 to 33.58)	99.2	0.519	ref.	
Female	22 (30,193)	26.21 (18.91 to 35.11)	99.4		0.23 (-0.49 to 0.95)	0.535
Marital Status						
Single/not married	11 (3,277)	22.90 (12.86 to 37.40)	98.4	0.423	ref	
Married	11 (6,455)	30.86 (17.99 to 47.60)	99.2		0.41 (-0.59 to 1.41)	0.421
Education level						
High school and below	8 (2,210)	37.37 (21.59 to 56.40)	98.2	0.889	ref	
Bachelor and over	8 (4,238)	35.73 (22.77 to 51.17)	99.3		-0.07 (-1.07 to 0.93)	0.888

Health worker						
Unit of work						
Not work in Covid-19 unit	3 (1,670)	13.16 (6.79 to 23.96)	93.8	**0.049**	ref	
Work in Covid-19 unit	4 (1,420)	30.98 (16.85 to 49.86)	97.3		1.08 (-0.05 to 2.20)	0.060
Health profession						
Medical doctor	4 (830)	10.80 (6.12 to 18.38)	84.3	**0.003**	ref	
Nurse	5 (2,422)	28.22 (15.83 to 45.10)	97.8		1.18 (0.21 to 2.15)	**0.017**
Others	1 (65)	7.69 (4.42 to 12.19)	-		-0.39 (-2.04 to 1.25)	0.637
Study Characteristics						
Countries' continent						
Asia	44 (50,798)	15.50 (11.29 to 20.92)	99.4	**0.017**	ref.	
Europe	22 (13, 554)	25.05 (19.14 to 32.06)	99.6		0.59 (0.01 to 1.17)	**0.046**
America	5 (59,997)	8.08 (2.47 to 23.37)	99.8		-0.73 (-1.78 to 0.32)	0.173
Countries GDP						
Low income	4 (1,473)	9.88 (3.37 to 25.61)	96.9	0.342	ref.	
Upper middle income	37 (51,851)	17.05 (12.15 to 23.41)	99.6		0.63 (-0.60 to 1.86)	0.313
High income	31 (71,378)	19.35 (13.93 to 26.23)	99.7		0.78 (-0.46 to 2.03)	0.217
Countries' total case						
Non top 10 country	49 (57,409)	15.73 (11.62 to 20.94)	99.5	0.142	ref.	
Top 10 country	23 (67,159)	21.84 (15.65 to 29.61)	99.8		0.09 (-0.13 to 0.28)	0.356
Countries' total death						
Non top 10 country	50 (55,316)	16.07 (11.92 to 21.31)	99.4	0.223	ref.	
Top 10 country	22 (69,252)	21.18 (15.00 to 29.03)	99.8		0.22 (-0.08 to 0.51)	0.158
Assessment tools						
CAPS-5	1 (381)	30.18 (25.78 to 34.98)	0.00	**<0.0001**	ref	
PCL (5/S/C/C2)	21 (64,758)	10.60 (6.39 to 17.09)	99.7		-1.29 (-3.60 to 1.03)	0.276
IES (R/6)	26 (36,163)	21.68 (15.49 to 29.47)	99.4		-0.43 (-2.75 to 1.86)	0.705

Abbreviation: Study size (n); Confident interval (CI); Gross domestic product (GDP); Reference (ref)
Significancy level <0.05

4.1.6. Quality of Studies

All included studies were evaluated using Hoy criteria, a ten items risk of bias tool, developed specifically for observational study. There was no disagreement between raters in term of risk of bias of all included studies. Overall results showed 41 (65.1%) and 22 (34.49%) studies were classified as low and moderate risk of bias.

4.1.7. Sensitivity Analysis

Sensitivity analyses was conducted according to the studies' quality and assessment tools used. According to study quality, the prevalence of PTSD during COVID-19 pandemic was 16.93% (95%CI, 12.46 to 22.60; 95%PrI, 1.55 to 72.53) after excluded 22 studies with moderate risk of bias. Furthermore, the analysis also found no significant difference in PTSD prevalence during COVID-19 pandemic (16.83%, 95% CI, 13.20 to 21.21: 95%PrI,1.82 to 68.82) after four studies using non suggested instrument (PTSD-8 inventory, the global psychotrauma screen, PTSS and the short screening scale DSM-IV) were excluded.

Study 2: The comparative effectiveness of psychotherapies in posttraumatic stress disorder: A network meta-analysis of randomized controlled trials

4.2.1. Search Results

After the removal of duplicate studies, 18,961 studies were found from Cochrane library, Embase, Medline-OVID, PubMed, PsycInfo, and Scopus. In addition, 4 articles were found through the Google Scholar and previously published meta-analysis. About 17,128 studies were screened after the exclusion of the duplicate articles. After screened by the title and abstract, 506 articles were eligible for full-text check. About 365 articles were excluded because irrelevant study design (252), secondary analysis of RCT (93), outcome intended not measured (8) and insufficient data for analysis (12). Finally, 141 RCT were included in the network meta-analysis (**Figure 7**).

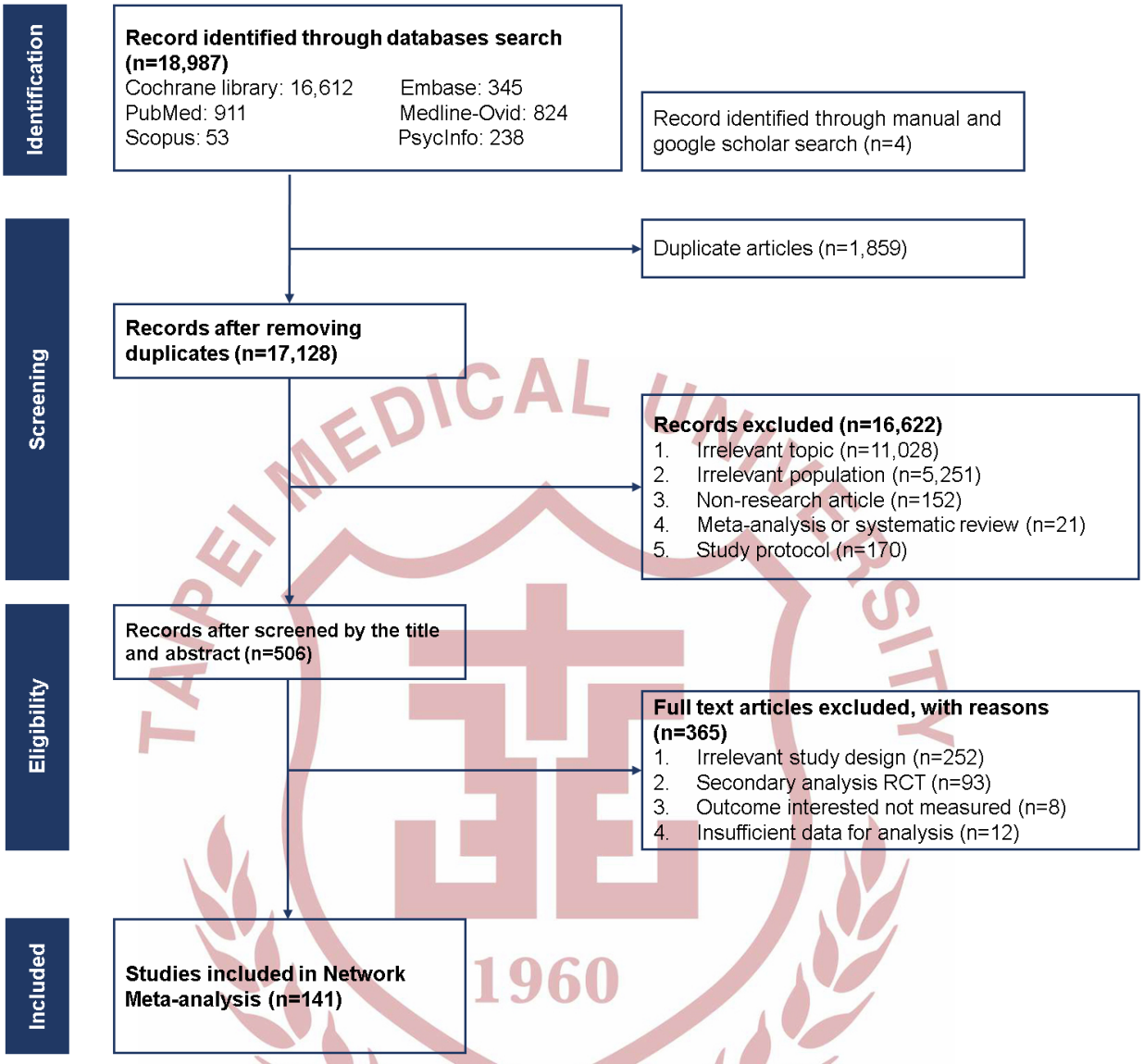

Figure 7. PRISMA flow chart of network meta-analysis

were eligible to for further full-text evaluation. One non-English language publication could not be used because the authors did not reply to email requests. Finally, 141 RCT's studies published ranged from 1990 to 2020, involving 8,820 participants, consist of eight therapies (CPT, CT, EMDR, NET, PE, CBT, PCT, BEP, PDT, PDT), one combination therapy (EMDR+PE), and two types of control (NT or TAU) were included in this network meta-analysis (**Figure 7**).

Table 4. Data Extraction of Included Studies in Network Meta-analysis

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
1.	Lindauer et al, 2005	Netherlands	DSM-IV SI-PTSD Mixed trauma	BEP	No treatment	Format: Individual Frequency: 16 sessions Duration: 45-60 minutes Days of week: 1 x/week Total times: 16 hours	Total: 24 E: 12 C: 12 Male: 11 Female: 13	Mean age: 38.95 Range age: NA	Baseline Posttreatment	Remission rate Retention rate Depression Anxiety
2.	Nidjam et al, 2012	Netherlands	DSM-IV IES-R Mixed trauma	BEP	EMDR	Format: Individual Frequency: 3-6 sessions Duration: 45-90 minutes Days of week: 1 x/week Total times: 2.25-9 hours	Total: 140 E: 70 C: 70 Male: 61 Female: 79	Mean age: 37.8 Range age: 18-65	Baseline Posttreatment 4 months (17 weeks)	Retention rate Depression Anxiety
3.	Schnyder et al, 2011	Switzerland	CAPS Mixed trauma	BEP	No treatment	Format: Individual Frequency: 16 sessions Duration: 50 minutes Days of week: 1 x/week Total times: 13.33 hours	Total: 30 E: 16 C: 14 Male: 16 Female: 14	Mean age: 39.9 Range age: 18-70	Baseline Posttreatment 6 months	Remission rate Depression Anxiety
4.	Akbarian et al, 2015	Switzerland	DSM-5 IES-R Mixed trauma	CBT	No treatment	Format: Group Frequency: 10 sessions Duration: 60-90 minutes Days of week: 1x/week Total times: 6-9 hours	Total: 28 E: 14 C: 14 Male: NA Female: NA	Mean age: 31.69 Range age: 18-45	Baseline Post treatment	Retention rate Depression Anxiety
5.	Beck et al, 2009	USA	DSM-IV CAPS Injury & threatening illness related trauma	CBT	No treatment	Format: Group Frequency: 14 sessions Duration: 120 minutes Days of week: 1x/week Total times: 28 hours	Total: 44 E: 26 C: 18 Male: 8 Female: 36	Mean age: 43.3 Range age: 22-69	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
6.	Blanchard et al, 2003	USA	DSM-IV CAPS Injury & threatening illness related trauma	CBT	No treatment	Format: Individual Frequency: 8-12 sessions Duration: - Days of week: 1x/week Total times: -	Total: 51 E: 27 C: 24 Male: 21 Female: 29	Mean age: 41.06 Range age: -	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
7.	Bryant et al, 2003	Australia	DSM-IV CAPS-2	CBT	PE	Format: Individual Frequency: 8 sessions	Total: 40 E: 20	Mean age: 34.7 Range age: NA	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Duration: 90 minutes Days of week: 1 x/week Total times: 12 hours	C: 20 Male: NA Female: NA		6 months	Depression Anxiety
8.	Bryant et al, 2011	Thailand	DSM-IV PSS War & terrorist related trauma	CBT	TAU	Format: Individual Frequency: 8 sessions Duration: 60 minutes Days of week: 1 x/week Total weeks: 8 weeks Total times: 8 hours	Total: 28 E: 16 C: 12 Male: 1 Female: 27	Mean age: 42.99 Range age: 18-69	Baseline Post treatment 3 months	Remission rate Retention rate Depression
9.	Bryant et al, 2018	Australia	DSM-IV CAPS Mixed trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1x/week Total times: 18 hours	Total: 77 E: 33 C2: 34 Male: - Female: -	Mean age: 37.96 Range age: 19-65	Baseline Post treatment	Retention rate Depression
10.	Capone et al, 2018	USA	DSM-IV SCID-I/P Mixed trauma	CBT	TAU	Format: Individual & Group Frequency: 12 sessions Duration: NA Days of week: NA Total times: NA	Total: 44 E: 21 C: 23 Male: 42 Female: 2	Mean age: 34.19 Range age: NA	Baseline Post treatment 3 months	Retention rate
11.	Castillo et al, 2016	USA	DSM-IV CAPS Mixed trauma	CBT	No treatment	Format: Group Frequency: 16 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 24 hours	Total: 86 E: 44 C: 42 Male: - Female: 86	Mean age: 35.92 Range age: NA	Baseline Post treatment 3 months 6 months	Retention rate
12.	Chen et al, 2014	China	CRIES-13 Injury & threatening illness related trauma	CBT	No treatment	Format: Group Frequency: 6 sessions Duration: minutes Days of week: 1 x/week Total times: 24 hours	Total: 22 E: 10 C: 12 Male: 6 Female: 16	Mean age: 14.41 Range age: 7 - 14	Baseline Post treatment 3 months	Retention rate Depression
13.	Cohen et al, 2011	USA	DSM-IV K-SADS-PL Assaults & Abuse	CBT	TAU	Format: Individual Frequency: 8 sessions Duration: 45 minutes Days of week: 1x/week Total times: 6 hours	Total: 124 E: 64 C: 60 Male: 61 Female: 63	Mean age: 9.64 Range age: -	Baseline Post treatment	Retention rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
14.	De Roos et al, 2011	Netherlands	DSM-IV PTSD-RI Injury & threatening illness related trauma	CBT	EMDR	Format: Individual Frequency: 4 sessions Duration: 60 minutes Days of week: 1x/week Total times: 4 hours	Total: 52 E: 26 C: 26 Male: 29 Female: 23	Mean age: 10.1 Range age: -	Baseline Post treatment 3 months	Remission rate Retention rate Depression Anxiety
15.	Diehle et al, 2014	Netherlands	DSM-IV-TR CAPS-CA Mixed trauma	CBT	EMDR	Format: Individual Frequency: 8 sessions Duration: 60 minutes Days of week: 1x/week Total times: 8 hours	Total: 48 E: 23 C: 25 Male: 18 Female: 30	Mean age: 13 Range age: 8-18	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
16.	Difede et al, 2007	USA	DSM-IV-TR CAPS War & terrorist related trauma	CBT	TAU	Format: Individual Frequency: 12 sessions Duration: 75 minutes Days of week: 1x/week Total times: 15 hours	Total: 31 E: 15 C: 16 Male: 1 Female: 30	Mean age: 45.77 Range age: 18-65	Baseline Post treatment	Retention rate Depression
17.	DuHamel et al, 2010	USA	PTSD Check list Injury & threatening illness related trauma	CBT	No treatment	Format: Individual Frequency: 10 sessions Duration: 60-90 minutes Days of week: 1x/week Total times: 10.5 hours	Total: 81 E: 47 C: 34 Male: 40 Female: 41	Mean age: 52.12 Range age: 19-74	Baseline Post treatment 3 months 6 months	Retention rate Depression
18.	Dunne et al, 2012	Australia	DSM-IV TR PDS Injury & threatening illness related trauma	CBT	No treatment	Format: Individual (telephone based) Frequency: 10 sessions Duration: 60 minutes Days of week: 1x/week Total times: 10 hours	Total: 26 E: 13 C: 13 Male: NA Female: NA	Mean age: 32.54 Range age: 20-49	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
19.	Fecteau et al, 1999	Canada	DSM-IV CAPS-2 Injury & threatening illness	CBT	No treatment	Format: Individual Frequency: 4 sessions Duration: 120 minutes Days of week: 1x/week Total times: 8 hours	Total: 20 E: 10 C: 10 Male: 6 Female: 14	Mean age: 41.3 Range age: 25-63	Baseline Post treatment	Remission rate Retention rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			related trauma							
20.	Foa et al, 2004	Canada	PSS-I	CBT	PE	Format: Individual Frequency: 9 sessions Duration: 90-120 minutes Days of week: 1x/week Total times: 13.5 hours	Total: 54 E: 27 C: 27 Male: - Female: 54	Mean age: 34.1 Range age: NA	Baseline Post treatment 12 months	-
21.	Foa et al, 2006	USA	DSM-IV PSS-I Assaults & Abuse	CBT	No treatment	Format: Individual Frequency: 4 sessions Duration: 120 minutes Days of week: 1x/week Total times: 8 hours	Total: 45 E: 22 C: 23 Male: NA Female: NA	Mean age: 33.7 Range age: 18-65	Baseline Post treatment 3 months 9 months	Remission rate Retention rate Depression Anxiety
22.	Gallegos et al, 2015a	USA	PTSD Checklist-military version War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 4 sessions Duration: 45-60 minutes Days of week: 1x/week Total times: 4 hours	Total: 238 E: 102 C: 136 Male: 238 Female: -	Mean age: 28.9 Range age: 18-65	Baseline Post treatment 3 months 6 months	Retention rate Depression
23.	Gallegos et al, 2015b	USA	PTSD Checklist-military version War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 4 sessions Duration: 45-60 minutes Days of week: 1x/week Total times: 4 hours	Total: 35 E: 21 C: 14 Male: - Female: 35	Mean age: 32 Range age: 18-65	Baseline Post treatment 3 months 6 months	Retention rate Depression
	Goldbeck et al, 2016	Germany	DSM-IV Mixed trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1x/week Total times: 18 hours	Total: 159 E: 76 C: 83 Male: 45 Female: 114	Mean age: 13.03 Range age: 7-17	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
24.	Hinton et al, 2004	USA	DSM-III-R HTQ War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 11 sessions Duration: NA Days of week: 1x/week Total times: NA	Total: 12 E: 6 C: 6 Male: 6 Female: 6	Mean age: NA Range age: NA	Baseline Post treatment 2 weeks	Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
25.	Hinton et al, 2005	USA	DSM-IV CAPS War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: NA Days of week: 1x/week Total times: NA	Total: 40 E: 20 C: 20 Male: 16 Female: 24	Mean age: 51.8 Range age: NA	Baseline Post treatment 2 weeks	-
26.	Hinton et al, 2009	USA	DSM-IV CAPS War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: NA Days of week: 1x/week Total times: NA	Total: 24 E: 12 C: 12 Male: 10 Female: 14	Mean age: 49.5 Range age: NA	Baseline Post treatment	Retention rate
27.	Hollifield et al, 2007	Mexico	DSM-IV PSS-SR Assaults & Abuse	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: 120 minutes Days of week: 1x/week Total times: 24 hours	Total: 49 E: 25 C: 24 Male: NA Female: NA	Mean age: NA Range age: NA	Baseline Post treatment 3 months	Remission rate Retention rate Depression Anxiety
28.	Ivarsson et al, 2014	Sweden	DSM-IV IES-R Mixed trauma	CBT	TAU	Format: Individual Frequency: 8 sessions Duration: NA Days of week: 1x/week Total weeks: 8 weeks Total times: - hours	Total:62 E: 31 C: 31 Male: 11 Female: 51	Mean age: 46 Range age: 21-67	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
29.	Jaberghaderi et al, 2004	Iran	DSM-IV CROPS Assaults & Abuse	CBT	EMDR	Format: Individual Frequency: 12 sessions Duration: 30-45 minutes Days of week: NA Total weeks: NA Total times: 10-15 hours	Total:14 E: 7 C: 7 Male: - Female: 14	Mean age: NA Range age: 12-13	Baseline Post treatment	Remission rate Retention rate
30.	Jaberghaderi, 2019	Iran	PROPS Assaults & Abuse	CBT	C1: EMDR C2: No treatment	Format: Individual Frequency: 12 sessions Duration: 45-60 minutes Days of week: NA Total times: 12 hours	Total:139 E: 40 C1: 40 C2: 59 Male: 70 Female: 69	Mean age: NA Range age: 8-12	Baseline Post treatment	Remission rate Retention rate
31.	Jensen et al, 2018	Norway	DSM-5 CPSS	CBT	TAU	Format: Individual Frequency: 12-15 sessions	Total: 116 E: 55	Mean age: NA Range age: NA	Baseline Post treatment	Retention rate Depression

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			Mixed trauma			Duration: NA Days of week: NA Total weeks: NA Total times: NA	C: 61 Male: NA Female: NA			
32.	Kameoka et al, 2020	Japan	DSM-IV K-SADS Mixed trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: 90-100 minutes Days of week: 1x/week Total times: 20 hours	Total: 30 E: 14 C: 16 Male: 8 Female: 22	Mean age: 13.9 Range age: 6-18	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
33.	Knaevelsrud et al, 2007	Germany	DSM-IV IES-R Mixed trauma	CBT	No treatment	Format: Individual Frequency: 10 sessions Duration: NA Days of week: 2x/week Total times: NA	Total: 96 E: 49 C: 47 Male: 10 Female: 86	Mean age: 35 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
34.	Knaevelsrud et al, 2015	Germany	DSM-IV PDS Mixed trauma	CBT	No treatment	Format: Individual (Internet Based) Frequency: 10 sessions Duration: NA Days of week: 2x/week Total times: 15 hours	Total: 159 E: 79 C: 80 Male: 45 Female: 114	Mean age: 28.1 Range age: 18-56	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
35.	King et al, 2000 –pindah atas	Australia	DSM-IV ADIS Assaults & Abuse	CBT	No treatment	Format: Individual Frequency: 20 sessions Duration: 50 minutes Days of week: 1 x/week Total times: 16.6 hours	Total: 24 E: 12 C: 12 Male: NA Female: NA	Mean age: 11.5 Range age: -	Baseline Post treatment 4 months	Retention rate Depression Anxiety
36.	Madigan et al, 2015	Canada	DSM-IV CPTSDI Injury & threatening illness related trauma	CBT	TAU	Format: Individual (Internet Based) Frequency: 12 sessions Duration: 60 minutes Days of week: 1x/week Total times: 12 hours	Total: 29 E: 14 C: 15 Male: - Female: 29	Mean age: 17.04 Range age: NA	Baseline Post treatment 6 months	Remission rate Retention rate Depression Anxiety
37.	Maercker et al, 2006	United Kingdom	DSM-IV-TR CAPS Injury & threatening illness	CBT	No treatment	Format: Individual Frequency: 8-12 sessions Duration: NA Days of week: 1 x/week Total times: NA	Total: 42 E: 21 C: 21 Male: 10 Female: 32	Mean age: 40.15 Range age: -	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			related trauma							
38.	Maguen et al, 2017	USA	DSM-IV SCID War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: 6-8 sessions Duration: 60-90 minutes Days of week: 1 x/week Total times: 6-12 hours	Total: 33 E: 17 C: 16 Male: 33 Female: -	Mean age: 61.2 Range age: -	Baseline Post treatment 3 months	Retention rate Depression Anxiety
39.	McDonagh et al, 2005	USA	DSM-IV SCID Assaults & Abuse	CBT	1: PCT 2: No treatment	Format: Individual Frequency: 14 sessions Duration: 90-120 minutes Days of week: 1x/week Total times: 24.5 hours	Total: 52 E: 29 C: 23 Male: - Female: 74	Mean age: 40.42 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
40.	McMullen et al, 2013	UK	UCLA-PTSD War & terrorist related trauma	CBT	No treatment	Format: Individual and group Frequency: 15 sessions Duration: NA Days of week: NA Total times: NA	Total: 48 E: 24 C: 24 Male: 48 Female: -	Mean age: 15.75 Range age: NA	Baseline Post treatment	Retention rate
41.	Monson et al, 2012	Canada	DSM-IV-TR SCID Mixed trauma	CBT	No treatment	Format: Individual Frequency: 15 sessions Duration: NA Days of week: 2x/week Total times: 15 hours	Total: 40 E: 20 C: 20 Male: 10 Female: 30	Mean age: 45.77 Range age: 18-70	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
42.	Murray et al, 2015	USA	UCLA-PTSD Mixed trauma	CBT	TAU	Format: Individual Frequency: 9 sessions Duration: 60-90 minutes Days of week: 1x/week Total times: 9-12 hours	Total: 257 E: 131 C: 126 Male: 129 Female: 128	Mean age: 13.66 Range age: 5-18	Baseline Post treatment	Retention rate
43.	Nieminen et al, 2016	Sweden	DSM-IV IES-R Injury & threatening illness related trauma	CBT	No treatment	Format: Individual Frequency: 8 sessions Duration: NA Days of week: 1x/week Total times: NA	Total: 56 E: 28 C: 28 Male: - Female: 56	Mean age: 34.6 Range age: 25-50	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
44.	Nixon et al, 2012	Australia	DSM-IV CAPS-CA	CBT	CT	Format: Individual Frequency: 9 sessions	Total: 33 E: 17	Mean age: 10.82 Range age: 7-17	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			Mixed trauma			Duration: 90 minutes Days of week: 1 x/week Total times: 13.5 hours	C: 16 Male: 21 Female: 12		6 months FU	Depression Anxiety
45.	O'Donnell et al, 2012	Australia	CAPS War & terrorist related trauma	CBT	TAU	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1x/week Total times: 15 hours	Total: 46 E: 24 C: 22 Male: - Female: 56	Mean age: 35.85 Range age: 25-50	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
46.	Ooi et al, 2016	Australia	DSM-IV CRIES-13 Mixed trauma	CBT	No treatment	Format: Group Frequency: 8 sessions Duration: 60 minutes Days of week: NA Total times: 8 hours	Total: 82 E: 45 C: 37 Male: 53 Female: 29	Mean age: 12.64 Range age: NA	Baseline Post treatment 3 months	Retention rate Depression
47.	Paunovic & Ost, 2001	Sweden	DSM-IV CAPS Mixed trauma	CBT	PE	Format: Individual Frequency: 16-20 sessions Duration: 60-120 minutes Days of week: 1x/week Total times: 16-40 hours	Total: 16 E: 8 C: 8 Male: NA Female: NA	Mean age: 37.9 Range age: 22-48	Baseline Post treatment 6 months	Retention rate Depression Anxiety
48.	Pityaratstian et al, 2015	Thailand	DSM-IV-TR PTSD-RI Injury & threatening illness related trauma	CBT	No treatment	Format: Group Frequency: 3 sessions Duration: 120 minutes Days of week: 3 days Total times: 6 hours	Total: 36 E: 18 C: 18 Male: 10 Female: 26	Mean age: 12.25 Range age: 10-15	Baseline Post treatment	Retention rate
49.	Pruiksma et al, 2020	USA	DSM-V CAPS-5 Mixed trauma	CBT	TAU	Format: Individual Frequency: 5 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 7.5 hours	Total: 40 E: 20 C: 20 Male: 34 Female: 6	Mean age: 33.03 Range age: NA	Baseline Post treatment	Retention rate Depression
50.	Scheeringa et al, 2011	USA	DSM-IV Mixed trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: NA Days of week: 1x/week Total times: NA	Total: 75 E: 51 C: 24 Male:49 Female: 26	Mean age: 5.3 Range age: 3-6	Baseline Post treatment	Retention rate Depression Anxiety
51.	Shein-Szydlo et al, 2016	Mexico	DISC-2.3 Mixed trauma	CBT	No treatment	Format: Individual Frequency: 12 sessions Duration: 60 minutes	Total: 99 E: 50 C: 49	Mean age: 14.9 Range age: NA	Baseline Post treatment	Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Days of week: 1 x/week Total times: 12 hours	Male: 36 Female: 63			
52.	Sijbrandij et al, 2007	Netherlands	DSM-IV Mixed trauma	CBT	No treatment	Format: Individual Frequency: 4 sessions Duration: 120 minutes Days of week: 1 x/week Total times: 8 hours	Total: 113 E: 98 C: 100 Male: 57 Female: 56	Mean age: 37.63 Range age: NA	Baseline Post treatment 4 months	Remission rate Retention rate Depression Anxiety
53.	Smith et al, 2007	United Kingdom	ADIS-CP	CBT	No treatment	Format: Individual Frequency: 10 sessions Duration: NA Days of week: 1 x/week Total times: 10 hours	Total: 24 E: 12 C: 12 Male: 12 Female: 12	Mean age: 13.69 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
54.	Spence et al, 2011	Australia	DSM-IV PCL-C Mixed trauma	CBT	No treatment	Format: Individual Frequency: 7 sessions Duration: NA Days of week: NA Total weeks: 8 weeks Total times: NA	Total: 42 E: 23 C: 19 Male: 8 Female: 34	Mean age: 42.6 Range age: 21-68	Baseline Post treatment	Retention rate Anxiety
55.	Stecker et al, 2014	Lebanon	MINI War & terrorist related trauma	CBT	No treatment	Format: Individual Frequency: Duration: 45-60 minutes Days of week: 1 x/week Total weeks: Total times:	Total: 274 E: 123 C: 151 Male: 238 Female: 35	Mean age: 29 Range age: -	Baseline Post treatment 3 months 6 months	Retention rate Depression
56.	Zoellner et al, 2011		DSM-IV	CBT	No treatment	Format: Individual Frequency: 8-12 sessions Duration: 90 minutes Days of week: 1 x/week Total weeks: 8-12 weeks Total times: 12-18 hours	Total:40 E: 20 C: 20 Male: 10 Female: 30	Mean age: 41.2 Range age: NA	Baseline Post treatment	
57.	Ahrens & Rexford, 2002	USA	DSM-IV Mixed trauma	CPT	No treatment	Format: Individual Frequency: 8 sessions Duration: 60 minutes Days of week: 1x/week Total times: 8 hours	Total: 38 E: 19 C: 19 Male: 38 Female: -	Mean age: 16.4 Range age: 15-18	Baseline Post treatment	Depression
58.	Bass et al, 2013	Congo	HTQ Assaults & Abuse	CPT	TAU	Format: Individual & Group Frequency: 12 sessions	Total: 405 E: 157 C: 248	Mean age: 35 Range age: NA	Baseline Post treatment 6 months FU	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Duration: 120 minutes Days of week: NA Total times: 24 hours	Male: - Female: 405			
59.	Chard, 2005	USA	DSM-IV CAPS Mixed trauma	CPT	No treatment	Format: Individual & Group Frequency: 17 sessions Duration: 60-90 minutes Days of week: 2x/week Total times: 21 hours	Total: 71 E: 36 C: 35 Male: - Female: 71	Mean age: 32.77 Range age: 18-56	Baseline Post treatment 3 months 12 months	Remission rate Retention rate Depression
60.	Forbes et al, 2012	Australia	DSM-IV CAPS War & terrorist related trauma	CPT	TAU	Format: Individual Frequency: 12 sessions Duration: 60 minutes Days of week: 2x/week Total times: 12 hours	Total: 59 E: 30 C: 29 Male: 57 Female: 2	Mean age: 53.36 Range age: NA	Baseline Post treatment 3 months	Remission rate Depression Anxiety
61.	Galovski et al, 2012	USA	CAPS Assaults & Abuse	CPT	No treatment	Format: Individual Frequency: 4-18 sessions Duration: NA Days of week: NA Total times: NA	Total: 55 E: 69 C: 47 Male: - Female: -	Mean age: 39.4 Range age: 18-65	Baseline Post treatment 6 months	Retention rate Depression
62.	Holliday et al, 2014	USA	PTCI Assaults & Abuse	CPT	PCT	Format: Individual Frequency: 12 sessions Duration: 60 minutes Days of week: 1 x/week Total times: 12 hours	Total: 45 E: 32 C: 13 Male: 11 Female: 34	Mean age: 44.91 Range age: NA	Baseline Post treatment 4 months 6 months	-
63.	Monson et al, 2006	USA	DSM-IV-TR CAPS Mixed trauma	CPT	No treatment	Format: Individual Frequency: 12 sessions Duration: NA Days of week: 2 x/week Total times: NA	Total: 60 E: 30 C: 30 Male: 54 Female: 6	Mean age: 54 Range age: -	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
64.	Pearson et al, 2019	USA	DSM-IV Injury & threatening illness related trauma	CPT	No treatment	Format: Individual Frequency: 13 sessions Duration: NA Days of week: NA Total times: NA	Total: 73 E: 37 C: 36 Male: - Female: 73	Mean age: NA Range age: 18-60	Baseline Post treatment 3 months FU	Retention rate
65.	Resick et al, 2002	USA	DSM-IV CAPS	CPT	C1: PE	Format: Individual Frequency: 12 sessions	Total: 171 E: 62	Mean age: 32 Range age: -	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			Mixed trauma		C2: No treatment	Duration: 60 minutes Days of week: 2 x/week Total times: 13 hours	C1: 62 C2: 47 Male: - Female: 171		3 months 9 months	Depression
66.	Resick et al, 2015	USA	DSM-IV-TR PCL-S War & terrorist related trauma	CPT	PCT	Format: Group Frequency: 12 sessions Duration: 90 minutes Days of week: 2 x/week Total times: 18 hours	Total: 108 E: 56 C: 52 Male: 100 Female: 8	Mean age: 32.09 Range age: -	Baseline Post treatment 12 months	Remission rate Retention rate Depression
67.	Rosner et al, 2019	Germany	DSM-IV CAPS-CA Mixed trauma	CPT	No treatment	Format: Individual Frequency: 30 sessions Duration: 50 minutes Days of week: 2 x/week Total times: 25 hours	Total: 65 E: 29 C: 36 Male: 9 Female: 56	Mean age: 18.1 Range age: -	Baseline Post treatment 3 months	Remission rate Retention rate Depression
68.	Suris et al, 2013	USA	CAPS Assaults & Abuse	CPT	PCT	Format: Individual Frequency: 12 sessions Duration: 60 minutes Days of week: 2 x/week Total times: 12 hours	Total: 86 E: 52 C: 34 Male: 13 Female: 73	Mean age: 46.1 Range age: -	Baseline Post treatment 2 months 6 months	Depression
69.	Duran et al, 2020	Brazil	DSM-IV-TR SCID Mixed trauma	CT	PE	Format: Individual Frequency: 13 sessions Duration: 60 minutes Days of week: 1x/week Total times: 13 hours	Total: 96 E: 44 C: 51 Male: 20 Female: 76	Mean age: 41.8 Range age: 18-65	Baseline Post treatment 3 months	Retention rate Depression Anxiety
70.	Ehlers et al, 2003	England	DSM-IV SCID Injury & threatening illness related trauma	CT	No treatment	Format: Individual Frequency: 12 sessions Duration: 60-90 minutes Days of week: 1x/week Total times: 12.5 hours	Total: 55 E: 28 C: 27 Male: - Female: -	Mean age: 39.4 Range age: 18-65	Baseline Post treatment 6 months	Retention rate Depression Anxiety
71.	Ehlers et al, 2005	England	DSM-IV SCID Mixed trauma	CT	No treatment	Format: Individual Frequency: 12 sessions Duration: 60-90 minutes Days of week: 1x/week Total times: 12.5 hours	Total: 28 E: 14 C: 14 Male: 13 Female: 15	Mean age: 36.6 Range age: 18-64	Baseline Post treatment	Retention rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
72.	Ehlers et al, 2014	England	DSM-IV CAPS Mixed trauma	CT	No treatment	Format: Individual Frequency: 12 sessions Duration: 90-120 minutes Days of week: 1x/week Total times: 18 hours	Total: 61 E: 31 C: 30 Male: 25 Female: 36	Mean age: 39.2 Range age: NA	Baseline Post treatment	Depression Anxiety
73.	Kubany et al, 2003	USA	DSM-IV CAPS Mixed trauma	CT	No treatment	Format: Individual Frequency: 8-11 sessions Duration: 90 minutes Days of week: 1x/week Total times: 12-16.5 hours	Total: 32 E: 18 C: 14 Male: - Female: 32	Mean age: 36.8 Range age: NA	Baseline Post treatment 3 months	Remission rate Retention rate Depression
74.	Meiser-Stedman et al, 2017	England	DSM-IV Mixed trauma	CT	No treatment	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1x/week Total times: 15 hours	Total: 29 E: 14 C: 15 Male: 8 Female: 21	Mean age: 13.3 Range age: 8-17	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
75.	Tarrier et al, 1999	UK	DSM-III-R CAPS Mixed trauma	CT	PE	Format: Individual Frequency: 16 sessions Duration: 60 minutes Days of week: 1x/week Total times: 16 hours	Total: 72 E: 37 C: 35 Male: 36 Female: 36	Mean age: 38.6 Range age: NA	Baseline Post treatment 6 months	Remission rate Retention rate Depression Anxiety
76.	Acarturk et al, 2015	Turkey	IES-R War & terrorist related trauma	EMDR	No treatment	Format: Individual Frequency: 7 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 10.5 hours	Total:29 E: 15 C: 14 Male: 7 Female: 22	Mean age: 36.5 Range age: 19-63	Baseline Post treatment	Remission rate Retention rate Depression
77.	Acarturk et al, 2016	Turkey	DSM-IV IES-R War & terrorist related trauma	EMDR	No treatment	Format: Individual Frequency: 8 sessions Duration: 90 minutes Days of week: 1 x/week Total weeks: 8 weeks Total times: 12 hours	Total: 98 E: 49 C: 49 Male: 25 Female: 73	Mean age: 33.68 Range age: 17-64	Baseline Post treatment 1 months	Remission rate Retention rate Depression
78.	Ahmad et al, 2007	Sweden	DSM-IV DICA Mixed trauma	EMDR	No treatment	Format: Individual Frequency: 8 sessions Duration: 45 minutes Days of week: 1 x/week Total times: 6 hours	Total: 33 E: 17 C: 16 Male:13 Female: 20	Mean age: 9.94 Range age: 6-16	Baseline Post treatment	Retention rate
79.	Arabia et al, 2011	Italy	DSM IV-TR IES-R	EMDR	PE	Format: Individual Frequency: 8 sessions	Total: 42 E: 21	Mean age: 63.48 Range age: 34-79	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			Injury & threatening illness related trauma			Duration: 45 minutes Days of week: 2 x/week Total times: 6 hours	C: 21 Male: 28 Female: 14		6 months	Depression Anxiety
80.	Capezzani et al, 2013	Italy	DSM IV CAPS Injury & threatening illness related trauma	EMDR	CBT	Format: Individual Frequency: 8 sessions Duration: NA Days of week: 1 x/week Total times: NA	Total: 21 E: 11 C: 10 Male: 2 Female: 19	Mean age: 51.72 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
81.	Carlson et al, 1998	USA	DSM-IV CAPS War & terrorist related trauma	EMDR	No treatment	Format: Individual Frequency: 12 sessions Duration: 60-75 minutes Days of week: 1 x/week Total times: 12-15 hours	Total: 22 E: 10 C: 12 Male: 23 Female: -	Mean age: 49.42 Range age: 41-70	Baseline Post treatment	Depression Retention rate Anxiety
82.	Chemtob et al, 2002	USA	DSM-IV Injury & threatening illness related trauma	EMDR	No treatment	Format: Individual Frequency: 3 sessions Duration: NA Days of week: 1 x/week Total times: NA	Total: 32 E: 18 C: 18 Male: 10 Female: 22	Mean age: 8.4 Range age: 6-12	Baseline Post treatment 6 months	Retention rate Depression Anxiety
83.	De Roos et al, 2017	Netherlands	DSM-IV Mixed trauma	EMDR	C1: CBT C2: No treatment	Format: Individual Frequency: 6 sessions Duration: 45 minutes Days of week: 1 x/week Total times: 4.5 hours	Total: 85 E: 43 C1: 42 C2: 18 Male: 44 Female: 59	Mean age: 13.06 Range age: 8-18	Baseline Post treatment 3 months 12 months	Remission rate Retention rate
84.	Devilly et al, 1998	Australia	DSM-III-R War & terrorist related trauma	EMDR	TAU	Format: Individual Frequency: 8 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 12 hours	Total: 22 E: 12 C: 10 Male: 22 Female: -	Mean age: 50.1 Range age: NA	Baseline Post treatment 6 months	Retention rate Depression Anxiety
85.	Devilly et al, 1999	Australia	DSM-IV Mixed trauma	EMDR	CBT	Format: Individual Frequency: 8 sessions Duration: 90 minutes Days of week: 1 x/week	Total: 23 E: 11 C: 12 Male: 8	Mean age: 37.96 Range age: NA	Baseline Post treatment 3 months	Remission rate Retention rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Total times: 12 hours	Female: 15			
86.	Hogberg et al, 2007	Sweden	DSM-IV SCID-1 Injury & threatening illness related trauma	EMDR	No treatment	Format: Individual Frequency: 5 sessions Duration: 90 minutes Days of week: 1 x/week Total weeks: 8 weeks Total times: 7.5 hours	Total: 24 E: 13 C: 11 Male: 19 Female: 5	Mean age: 43 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
87.	Ironson et al, 2002	USA	DSM-III-R PSS-SR Mixed trauma	EMDR	PE	Format: Individual Frequency: 6 sessions Duration: 90 minutes Days of week: NA Total times: 9 hours	Total: 19 E: 10 C: 9 Male: - Female: -	Mean age: NA Range age: 16-32	Baseline Post treatment 3 months	Remission rate Retention rate Depression
88.	Jarero et al, 2015	Mexico	SPRINT Injury & threatening illness related trauma	EMDR	No treatment	Format: Individual Frequency: 8 sessions Duration: 60 minutes Days of week: 1 x/week Total times: 8 hours	Total: 25 E: 13 C: 12 Male: 4 Female: 21	Mean age: 38.56 Range age: 23-56	Baseline Post treatment	Retention rate
89.	Jarero et al, 2018	Mexico	DSM-5 PCL-5 Injury & threatening illness related trauma	EMDR	No treatment	Format: Group Frequency: 6 sessions Duration: 50-100 minutes Days of week: 2 days Total times: 6 hours	Total: 61 E: 35 C: 26 Male:- Female: 61	Mean age: 47.02 Range age: 26-79	Baseline Post treatment	Retention rate
90.	Jensen, 1994	USA	DSM-III SI-PTSD War & terrorist related trauma	EMDR	No treatment	Format: Individual Frequency: 3 sessions Duration: NA Days of week: 10 days Total times: NA	Total: 25 E: 13 C: 12 Male: 25 Female: -	Mean age: 43.1 Range age: 40-55	Baseline Post treatment	Retention rate
91.	Kemp et al, 2010	Australia	DSM-IV PTS-RI Mixed trauma	EMDR	No treatment	Format: Individual Frequency: 4 sessions Duration: 60 minutes Days of week: 1 x/week Total times: 4 hours	Total: 27 E: 14 C: 13 Male: 15 Female: 12	Mean age: 8.93 Range age: 6-12	Baseline Post treatment	Remission rate Retention rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
92.	Marcus et al, 1997	USA	DSM-III-R Mixed trauma	EMDR	TAU	Format: Individual Frequency: 8 sessions Duration: 50-90 minutes Days of week: 1 x/week Total times: 6-12 hours	Total: 67 E: 34 C: 33 Male: 14 Female: 53	Mean age: 39.98 Range age: 18-73	Baseline Post treatment	Remission rate Depression Anxiety
93.	Meentken et al, 2020	Netherlands	DSM-IV-TR CRTI Injury & threatening illness related trauma	EMDR	TAU	Format: Individual Frequency: 8 sessions Duration: 50-90 minutes Days of week: 1 x/week Total times: 6-12 hours	Total: 74 E: 37 C: 37 Male: 49 Female: 25	Mean age: 9.6 Range age: 4-15	Baseline Post treatment	Retention rate Depression Anxiety
94.	Osorio et al, 2018	Mexico	DSM-5 PCL-5 Injury & threatening illness related trauma	EMDR	No treatment	Format: Individual Frequency: 6 sessions Duration: 50-100 minutes Total day: 2 days Total times: 2.5-10 hours	Total: 23 E: 11 C: 12 Male: 13 Female: 10	Mean age: 16.71 Range age: 13-22	Baseline Post treatment 3 months	Retention rate Depression Anxiety
95.	Power et al, 2002	United Kingdom	DSM-IV SI-PTSD Mixed trauma	EMDR	No treatment	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 15 hours	Total: 51 E: 27 C: 24 Male: 29 Female: 32	Mean age: 39.24 Range age: 18-65	Baseline Post treatment	Retention rate Depression Anxiety
96.	Rogers et al, 1999	USA	DSM-III-R IES War & terrorist related trauma	EMDR	PE	Format: Individual Frequency: 1 session Duration: 60-90 minutes Days of week: 1 x/week Total times: 1-1.5 hours	Total: 12 E: 6 C: 6 Male:12 Female: -	Mean age: NA Range age: 47-53	Baseline Post treatment	Retention rate
97.	Rothbaum, 1997	USA	DSM-III-R Assaults & Abuse	EMDR	No treatment	Format: Individual Frequency: 3 sessions Duration: 90 minutes Days of week: 1x/week Total times: 4.5 hours	Total: 18 E: 10 C: 8 Male: Female: 18	Mean age: 34.22 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
98.	Shapiro et al, 2015	Israel	DSM-IV IES-R War & terrorist	EMDR	No treatment	Format: Individual/group Frequency: NA Duration: 90 minutes Days of week: 2 days	Total: 17 E: 8 C: 9 Male:16	Mean age: 39.83 Range age: 19-57	Baseline Post treatment	Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
			related trauma			Total times: NA	Female:1			
99.	Shapiro et al, 2018	Israel	DSM-5 PCL-5 War & terrorist related trauma	EMDR	No treatment	Format: Individual Frequency: 3 sessions Duration: 90 minutes Days of week: NA Total times: 4.5 hours	Total: 25 E: 13 C: 12 Male: 3 Female: 22	Mean age: 39.06 Range age: 20-65	Baseline Post treatment	Retention rate
100.	Tarquinio et al, 2016	France	SCID DSM-IV Assaults & Abuse	EMDR	No treatment	Format: Individual Frequency: 1 session Duration: 90-120 minutes Days of week: 1 day Total times: 1.5-2 hours	Total: 37 E: 19 C: 18 Male: 22 Female: 15	Mean age: 34.38 Range age: NA	Baseline Post treatment	Remission rate Retention rate
101.	TerHeide 2016	Netherlands	DSM-IV-TR War & terrorist related trauma	EMDR	TAU	Format: Individual Frequency: 9 sessions Duration: 60-90 minutes Days of week: NA Total times: 12 hours	Total: 72 E: 36 C: 36 Male: 52 Female: 20	Mean age: 41.45 Range age: 8-17	Baseline Post treatment	Remission rate
102.	Yurtsever et al, 2018	Turkey	IES-R War & terrorist related trauma	EMDR	No treatment	Format: Group Frequency: 2 sessions Duration: 120 minutes Days of week: NA Total times: 4 hours	Total: 47 E: 18 C: 29 Male: 11 Female: 36	Mean age: NA Range age: NA	Baseline Post treatment 1 months	Remission rate Retention rate Depression
103.	Sack et al, 2016	Germany	DSM-IV CAPS Mixed trauma	EMDR + PE	PE	Format: Individual Frequency: 8 sessions Duration: NA Days of week: NA Total times: NA	Total: 92 E: 47 C: 45 Male: 29 Female: 63	Mean age: 39.3 Range age: 18-70	Baseline Post treatment	Remission rate Retention rate Depression
104.	Adenauer et al, 2011	Germany	DSM-IV War & terrorist related trauma	NET	No treatment	Format: Individual Frequency: 12 sessions Duration: 90-120 minutes Days of week: 1 x/week Total times: 18-24 hours	Total: 19 E: 11 C: 8 Male: NA Female: NA	Mean age: 33.52 Range age: 16-56	Baseline Post treatment	Retention rate Depression
105.	Ertl et al, 2011	Germany	DSM-IV Mixed trauma	NET	No treatment	Format: Individual Frequency: 8 sessions Duration: 90-120 minutes Days of week: 3 x/week Total times: 12-16 hours	Total: 57 E: 29 C: 28 Male: 29 Female: 28	Mean age: 18.37 Range age: 12-25	Baseline 3 months (FU) 12 months (FU)	Retention rate Depression

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
106.	Hijazi et al, 2014	USA	HTQ Mixed trauma	NET	No treatment	Format: Individual Frequency: 3 sessions Duration: 60-90 minutes Days of week: 3 x/week Total times: 3-4.5 hours	Total: 66 E: 41 C: 22 Male: 28 Female: 38	Mean age: 48.2 Range age: NA	Baseline 4 months (FU)	Retention rate Depression
107.	Jacob et al, 2014	Germany	DSM-IV-TR CAPS Mixed trauma	NET	No treatment	Format: Individual Frequency: 8 sessions Duration: 90-150 minutes Days of week: 2 x/week Total times: 12-20 hours	Total: 76 E: 38 C: 38 Male: 6 Female: 70	Mean age: 37.57 Range age: NA	Baseline 3 months (FU)	Retention rate
108.	Lely et al, 2019	Netherlands	DSM-IV-TR CAPS Mixed trauma	NET	PCT	Format: Individual Frequency: 11 sessions Duration: 90 minutes Days of week: 1-2 x/week Total times: 16.5 hours	Total: 33 E: 18 C: 15 Male: 24 Female: 9	Mean age: 63.81 Range age: NA	Baseline Post treatment 4 months	Remission rate Retention rate
109.	Morath et al, 2014a	Switzerland	DSM-IV-TR CAPS War & terrorist related trauma	NET	No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 18 hours	Total: 38 E: 19 C: 19 Male: 26 Female: 12	Mean age: 29.4 Range age: NA	Baseline Post treatment 8 months	Retention rate
	Morath et al, 2014b	Switzerland	DSM-IV War & terrorist related trauma	NET	No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 18 hours	Total: 34 E: 17 C: 17 Male: 20 Female: 14	Mean age: 29.5 Range age: 16-47	Baseline Post treatment	Retention rate Depression
110.	Neuner et al, 2008	Uganda	DSM-IV PDS Mixed trauma	NET	No treatment	Format: Individual Frequency: 6 sessions Duration: 60-120 minutes Days of week: 2 x/week Total times: 6-12 hours	Total: 166 E: 111 C: 55 Male: 83 Female: 83	Mean age: 34.8 Range age: NA	Baseline 3 months (FU)	Retention rate
111.	Neuner et al, 2010	Uganda	DSM-IV Mixed trauma	NET	TAU	Format: Individual Frequency: 12 sessions Duration: 90-120 minutes Days of week: 2 x/week Total times: 18-24 hours	Total: 32 E: 16 C: 16 Male: 22 Female: 10	Mean age: 31.35 Range age: NA	Baseline Post treatment	Retention rate Depression

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
112.	Orang et al, 2018	Iran	DSM-IV PSS-I Assaults & Abuse	NET	TAU	Format: Individual Frequency: 12 sessions Duration: 120-150 minutes Days of week: 1 x/week Total times: 24-30 hours	Total: 34 E: 17 C: 17 Male: - Female: 34	Mean age: 37.88 Range age: NA	Baseline Post treatment 3 months	Retention rate
113.	Park et al, 2020	Korea	DSM-5 UCLA Mixed trauma	NET	TAU	Format: Individual Frequency: 10 sessions Duration: 90-120 minutes Days of week: 1 x/week Total times: 15-20 hours	Total: 20 E: 9 C: 11 Male: NA Female: NA	Mean age: 19 Range age: 16-24	Baseline 3 months (FU) 6 months (FU)	Depression
114.	Peltonen & Kangaslampi 2019	Finland	CRIES Mixed trauma	NET	TAU	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 15 hours	Total: 36 E: 22 C: 16 Male: NA Female: NA	Mean age: 13.2 Range age: 9-17	Baseline Posttreatment	Remission rate Retention rate Depression
115.	Ruf et al, 2010	Germany	DSM-IV UCLA Mixed trauma	NET	No treatment	Format: Individual Frequency: 8 sessions Duration: 90-120 minutes Days of week: 1 x/week Total times: 12-16 hours	Total: 26 E: 13 C: 13 Male: 14 Female: 12	Mean age: 11.45 Range age: 7-16	Baseline 12 months (FU)	Retention rate
116.	Zang et al, 2013	China	DSM-IV IES-R Injury & threatening illness related trauma	NET	No treatment	Format: Individual Frequency: 4 sessions Duration: 60-90 minutes Days of week: 2 x/week Total times: 4-6 hours	Total: 22 E: 11 C: 11 Male: 5 Female: 17	Mean age: 55.73 Range age: NA	Baseline Posttreatment	Retention rate Depression Anxiety
117.	Zang et al, 2014	China	DSM-IV IES-R Injury & threatening illness related trauma	NET	No treatment	Format: Individual Frequency: 3 sessions Duration: 60-120 minutes Days of week: 1-2 x/week Total times: 3-6 hours	Total: 20 E: 10 C: 10 Male: 3 Female: 17	Mean age: 52.20 Range age: NA	Baseline Posttreatment	Retention rate Depression Anxiety
118.	Ford et al, 2011	USA	DSM-IV SCID-P Mixed trauma	PCT	No treatment	Format: Individual Frequency: 12 sessions Duration: Days of week: x/week Total times: hours	Total: 98 E: 53 C: 45 Male: - Female: 98	Mean age: 30.7 Range age: 18-45	Baseline Posttreatment	Remission rate Depression Anxiety

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
119.	Asukai et al, 2010	Japan	DSM-IV CAPS Mixed trauma	PE	TAU	Format: Individual Frequency: 8-15 sessions Duration: 90 minutes Days of week: 1x/week Total times: 12-22.5 hours	Total: 24 E: 12 C: 12 Male: 3 Female: 21	Mean age: 29.25 Range age: NA	Baseline Post treatment	Retention rate Depression
120.	Cigrang et al, 2017	USA	DSM-IV PCL-S Mixed trauma	PE	TAU	Format: Individual Frequency: 4 sessions Duration: 30 minutes Days of week: 1x/week Total times: 2 hours	Total: 67 E: 34 C: 33 Male: 50 Female: 17	Mean age: 38.9 Range age: 29.9-47.9	Baseline Post treatment 2 months 6 months	Retention rate
121.	Feske et al, 2008	USA	DSM-IV SCID Mixed trauma	PE	TAU	Format: Individual Frequency: 9-12 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 13.5-18 hours	Total: 200 E: 101 C: 99 Male: - Female: 21	Mean age: 43.1 Range age: 29-55	Baseline Post treatment 6 months	Retention rate Depression Anxiety
122.	Foa et al, 1991	USA	DSM-III Assaults & Abuse	PE	No treatment	Format: Individual Frequency: 9 sessions Duration: 90 minutes Days of week: 2 x/week Total times: 13.5 hours	Total: 20 E: 10 C: 10 Male: - Female: 20	Mean age: 32.35 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
123.	Foa et al, 1999	USA	DSM-III-R SCID Assaults & Abuse	PE	No treatment	Format: Individual Frequency: 9 sessions Duration: 90 minutes Days of week: 2 x/week Total times: 13.5 hours	Total: 38 E: 23 C: 15 Male: - Female: 38	Mean age: 34.9 Range age: NA	Baseline Post treatment	Remission rate Retention rate
124.	Foa et al, 2005	USA	DSM-IV PSS-I Mixed trauma	PE	No treatment	Format: Individual Frequency: 9 sessions Duration: 90-120 minutes Days of week: 1 x/week Total times: 13.5-18 hours	Total: 105 E: 79 C: 26 Male: - Female: 105	Mean age: 31.3 Range age: NA	Baseline Post treatment	Retention rate Depression
125.	Foa et al, 2018	USA	DSM-IV-TR PSS-I Mixed trauma	PE	No treatment	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1-2 x/week	Total: 149 E: 109 C: 40 Male: 137 Female: 12	Mean age: 32.84 Range age: 18-65	Baseline Post treatment 2 weeks	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Total weeks: 8 weeks Total times: 15 hours				
126.	Franklin et al, 2016	USA	DSM-IV CAPS Mixed trauma	PE	TAU	Format: Individual Frequency: 10 sessions Duration: NA Days of week: 1 x/week Total weeks: 12 weeks Total times: NA	Total: 10 E: 3 C: 7 Male: NA Female: NA	Mean age: 46.1 Range age: NA	Baseline Post treatment 1 month	Retention rate Depression Anxiety
127.	Gilboa-Schechtman et al, 2010	Israel	DSM-IV CPSS Mixed trauma	PE	PDT	Format: Individual Frequency: 12-15 sessions Duration: 60-90 minutes Days of week: 1 x/week Total weeks: 12-15 weeks Total times: 12-22.5 hours	Total: 38 E: 19 C: 19 Male: 14 Female: 24	Mean age: 14.05 Range age: 12-18	Baseline Post treatment Month Month	Remission rate Retention rate Depression
128.	Hien et al, 2017	USA	DSM-IV-TR CAPS Mixed trauma	PE	No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 18 hours	Total: 67 E: 39 C: 28 Male: 43 Female: 24	Mean age: 44.8 Range age: NA	Baseline Post treatment	Retention rate
129.	Laugharne et al, 2016	Australia	DSM-IV CAPS Mixed trauma	PE	EMDR	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 2 x/week Total times: 18 hours	Total: 20 E: 10 C: 10 Male: 6 Female: 14	Mean age: 42.8 Range age: NA	Baseline Post treatment	Retention rate
130.	Lee et al, 2002	Australia	DSM-III-R SI-PTSD Mixed trauma	PE	EMDR	Format: Individual Frequency: 7 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 10.5 hours	Total: 24 E: 12 C: 12 Male: 13 Female: 11	Mean age: 35.3 Range age: NA	Baseline Post treatment 3 months	Remission rate Retention rate Depression
131.	Marks et al, 1998	UK	DSM-III-R CAPS Mixed trauma	PE	1: CT 2: CBT	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 15 hours	Total: 66 E: 23 C1: 19 C2: 24 Male: 56 Female: 10	Mean age: 38 Range age: 16-65	Baseline Post treatment 3 months 6 months	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
132.	Nacasch et al, 2011	USA	DSM-IV PSS-I Mixed trauma	PE	PDT	Format: Individual Frequency: 9-15 sessions Duration: 90-120 minutes Days of week: 1 x/week Total times: 13.5-30 hours	Total: 30 E: 15 C:15 Male: 30 Female: 0	Mean age: 34.25 Range age: NA	Baseline Post treatment	Retention rate Depression Anxiety
133.	Pacella et al, 2012	USA	DSM-IV PDS Injury & threatening illness related trauma	PE	No treatment	Format: Individual Frequency: 10 sessions Duration: 90-120 minutes Days of week: 2 x/week Total times: 15-20 hours	Total: 65 E: 40 C: 25 Male: 41 Female: 24	Mean age: 46 Range age: 31-61	Baseline Post treatment 3 months	Remission rate Retention rate Depression
134.	Rauch et al, 2015	USA	CAPS Mixed trauma	PE	PCT	Format: Individual Frequency: 10-12 sessions Duration: 80 minutes Days of week: 1 x/week Total times: 13.3-16 hours	Total: 36 E: 18 C: 18 Male: 33 Female: 3	Mean age: 31.9 Range age: NA	Baseline Post treatment	Retention rate
135.	Reger et al, 2016	USA	DSM-IV-TR CAPS Mixed trauma	PE	No treatment	Format: Individual Frequency: 10 sessions Duration: 90-120 minutes Days of week: 2 x/week Total times: 15-20 hours	Total: 79 E: 32 C: 47 Male: NA Female: NA	Mean age: 30.89 Range age: NA	Baseline Post treatment	Remission rate Retention rate Depression Anxiety
136.	Rossouw et al, 2016	South Africa	DSM-IV PSS-I Mixed trauma	PE	TAU	Format: Individual Frequency: 14 sessions Duration: 60-90 minutes Days of week: 1 x/week Total times: 14-21 hours	Total: 11 E: 6 C: 5 Male: 1 Female: 10	Mean age: 16 Range age: 14-18	Baseline Post treatment 12 months	Retention rate Depression
137.	Schnurr et al, 2007	USA	DSM-IV CAPS Mixed trauma	PE	PCT	Format: Individual Frequency: 10 sessions Duration: 90 minutes Days of week: 1 x/week Total times: 15 hours	Total: 284 E: 141 C: 143 Male: - Female: 284	Mean age: 44.75 Range age: NA	Baseline Post treatment 3 months 6 months	Retention rate Depression Anxiety
138.	Shalev et al, 2012	Israel	DSM-IV Mixed trauma	PE	C1:CT C2: No treatment	Format: Individual Frequency: 12 sessions Duration: 90 minutes Days of week: 1 x/week	Total: 158 E: 51 C1: 30 C2: 77	Mean age: 38.66 Range age: NA	Baseline Post treatment	Remission rate Retention rate

No	Author (year)	Nationality	Diagnostic criteria & Trauma background	T1	T2/T3	Intervention	Sample size	Age	Measurement time	Secondary outcomes
						Total times: 18 hours	Male: NA Female: NA			
139.	Vandenberg et al, 2015	Netherlands	DSM-IV-TR CAPS Mixed trauma	PE	C1: EMDR C2: No treatment	Format: Individual Frequency: 8 sessions Duration: 90 minutes Days of week: 1x/week Total weeks: 10 weeks Total times: 12 hours	Total: 155 E: 53 C1: 55 C2: 47 Male: 71 Female: 84	Mean age: 41.2 Range age: 18-65	Baseline Post treatment	Remission rate Retention rate
140.	Wells et al, 2014	United Kingdom	DSM-IV-TR IES Mixed trauma	PE	No treatment	Format: Individual Frequency: 8 sessions Duration: 60 minutes Days of week: 1 x/week Total times: 8 hours	Total: 20 E: 10 C: 10 Male: 12 Female: 8	Mean age: 41.42 Range age: 18-65	Baseline Post treatment	Remission rate Retention rate Depression Anxiety

Note. Diagnostic criteria: Diagnostic and Statistical Manual for Mental Disorders (DSM) 3rd Version (DSM-III), 4th Version (DSM-IV), 4th edition Revision (DSM-IV-R), 4th Edition Text Revision (DSM-IV-TR), 5th Edition (DSM-5); Structured Interview for PTSD (SI-PTSD); Impact Event Scale (IES); Impact Event Scale-Revision (IES-R); Clinical Administered PTSD Scale (CAPS); Clinical Administered PTSD Scale 2nd edition (CAPS-2); PTSD symptoms scale (PSS); PTSD symptoms Scale Interview (PSS-I); Structural Clinical Interview for DSM-IV-TR patient edition (SCID-I/P); Structural Clinical Interview Diagnostic (SCID); The Children Impact of Event Scale 13 (CRIES-13); Kiddie schedule for affective disorders and schizophrenia, present and lifetime version (K-SADS-PL); The UCLA PTSD reaction index (PTSD-RI); Clinical Administered PTSD Scale for children and adolescents (CAPS-CA); Posttraumatic Diagnostic Scale (PDS); Harvard Trauma Questionnaire (HTQ); PTSD symptoms scale self-report (PSS-SR); Child report of post-traumatic symptoms (CROPS); Parent Report of Post-traumatic Stress Symptoms (PROPS); Child PTSD Symptoms Scale (CPSS); Kiddie schedule for affective disorders and schizophrenia (K-SADS); Anxiety disorders interview schedule for DSM-IV (ADIS); Children's PTSD inventory (CPTSDI); University of California Los Angeles PTSD (UCLA-PTSD); Clinical Administered PTSD Scale DSM-5 (CAPS-5); Diagnostic Interview schedule for children version 2.3 (DISC-2.3); The Anxiety Disorder Interview Schedule-for Children and Parent (ADIS-CP);Posttraumatic stress disorder checklist-civilian version (PCL-C); Mini international neuropsychiatric interview-PTSD subscale (MINI); Post-traumatic cognition inventory (PTCI); PTSD checklist stressor specific version (PCL-S); The diagnostic interview for children and adolescence (DICA); The Short Post-Traumatic Stress Disorder Rating Interview (SPRINT); Children responses to trauma inventory (CRTI); Therapy or treatment of intervention group (T1); Therapy or treatment of control group (T2/T3): Brief eclectic psychotherapy (BEP); Cognitive behavior therapy (CBT); Cognitive processing therapy (CPT); Cognitive therapy (CT); Eye movement desensitization and reprocessing (EMDR); Narrative exposure therapy (NET); No treatment (NT); Present centered therapy (PCT); Psychodynamic therapy (PDT); Prolonged exposure (PE); Therapy as usual (TAU); Not available (NA); and Follow up (FU).

4.2.2. NMA Model Fit

The network plot of posttreatment meta-analysis showed the nodes along with direct and indirect effects of interventions and comparisons. The width of the lines is proportional to the number of trials involved in each comparison. CBT had the majority of studies compared to other comparisons either in the posttreatment, short-term and long-term follow-up analyses. Pairwise meta-analysis conducted on 27 comparisons (9 treatments) in posttreatment showed that all interventions were superior compared to NT and TAU. Most of the psychotherapies showed direct evidence compared to controls condition (NT and TAU). In the analysis between psychotherapies, direct comparisons were relatively few and not strongly attached to the network, as is the combination among them (**Figure 8**). The loop inconsistency check showed that all the p-values were more than 0.05. The result of inconsistency check using the design by treatment interaction model also reported p-value of more than 0.05. It can be concluded that there was no inconsistency between direct and indirect effects in this study. This result showed that the NMA model had a good model fit.

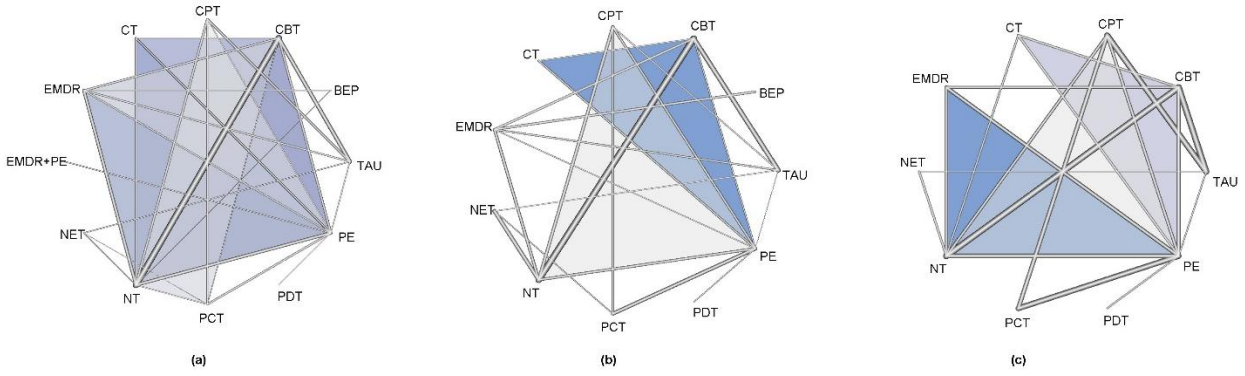

Figure 8. Network map of psychotherapies for PTSD

4.2.3. Network Meta-analysis

4.2.3.1. Primary Outcome

Baseline to Endpoint

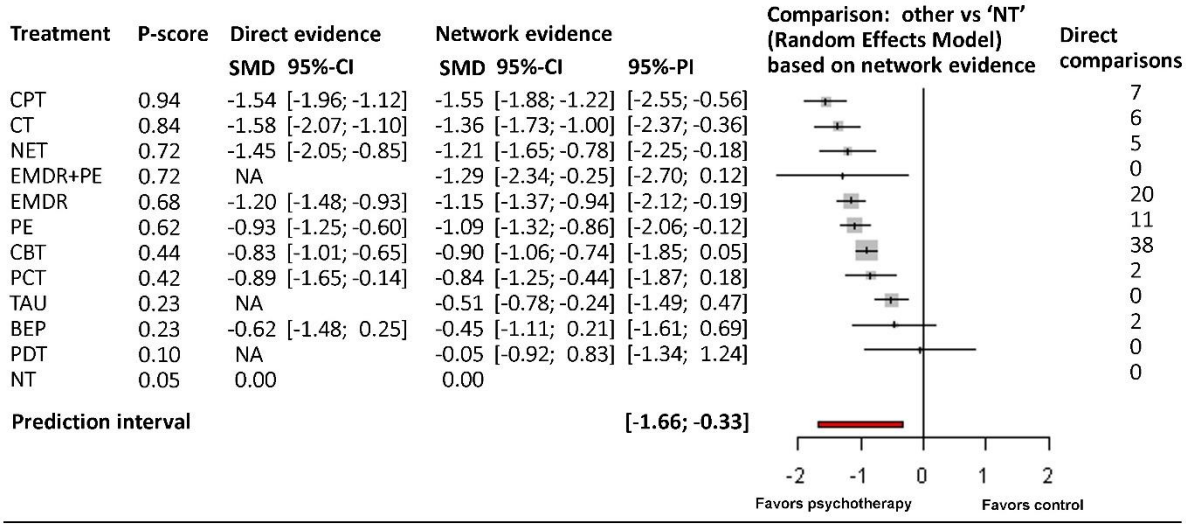

Figure 9. Forest plot NMA of psychotherapies effectiveness toward PTSD at posttreatment

Evidence from 135 studies were retrieved for analysis of PTSD symptoms in posttreatment. According to figure 9, CPT, CT, NET, EMDR+PE, EMDR, PE, CBT, and PCT had significant effect with a large effect size (SMD range -1.55 to -0.88), while BEP and PDT showed no significant effect. Rank analysis found CPT and CT as the most effective therapies (upper quartile) with respect to NET, EMDR+PE, EMDR, and PE (second quartile) and CBT and PCT (third quartile). In addition, BEP and PDT (lower quartile) showed less effective as psychotherapies for people with PTSD. Heterogeneity test showed moderate inconsistency (I^2=74.4%; τ^2=0.234). PrI score shows that future new studies were predicted to have effect size

ranged between SMD -1.67 to -0.34 (**Figure 9**). Detailed effect size of all comparison's psychotherapies including TAU and NT were provide in the league table (**Figure 10**).

	CPT	CT	EMDR	EMDR+PE	NET	PE	CBT	PCT	BEP	PDT	TAU	NT
CPT	CPT	-0.19 (-0.67 to 0.29)	**-0.40 (-0.78 to -0.02)**	-0.26 (-1.35 to 0.82)	-0.34 (-0.86 to 0.18)	**-0.47 (-0.84 to-0.09)**	**-0.65 (-1.01 to-0.30)**	**-0.71 (-1.14 to-0.28)**	**-1.10 (-1.80 to-0.36)**	**-1.20 (-1.83 to-0.37)**	**-1.04 (-1.42 to-0.66)**	**-1.55 (-1.88 to-1.22)**
CT	1.169 (0.779 to 1.81)	CT	-0.21 (-0.62 to 0.20)	-0.07 (-1.16 to 1.01)	-0.15 (-0.71 to 0.41)	-0.28 (-0.65 to 0.10)	**-0.46 (-0.84 to-0.09)**	-0.52 (-1.05 to 0.01)	**-0.91 (-1.66 to-0.16)**	**-1.32 (-2.24 to-0.39)**	**-0.85 (-1.28 to-0.42)**	**-1.36 (-1.73 to-1.00)**
EMDR	1.01 (0.72 to 1.41)	0.84 (0.60 to 1.29)	EMDR	0.14 (-0.92 to 1.19)	0.06 (-0.41 to 0.53)	-0.07 (-0.34 to 0.21)	**-0.25 (-0.49 to-0.02)**	-0.31 (-0.75 to 0.13)	**-0.70 (-1.36 to-0.04)**	**-1.11 (-1.99 to-0.22)**	**-0.64 (-0.94 to-0.35)**	**-1.15 (-1.37 to-0.94)**
EMDR+PE	1.15 (0.62 to 2.14)	0.96 (0.52 to 1.77)	1.14 (0.64 to 2.04)	EMDR+PE	-0.08 (-1.20 to 1.05)	-0.20 (-1.22 to 0.81)	-0.39 (-1.44 to 0.66)	-0.45 (-1.55 to 0.65)	-0.84 (-2.07 to 0.39)	-1.24 (-2.57 to 0.08)	-0.78 (-1.84 to 0.28)	**-1.29 (-2.34 to-0.25)**
NET	**2.45 (1.16 to 5.14)**	2.05 (0.94 to 4.47)	**2.43 (1.17 to 5.06)**	2.13 (0.86 to 5.29)	NET	-0.13 (-0.60 to 0.35)	-0.31 (-0.76 to 0.13)	-0.37 (-0.92 to 0.18)	-0.76 (-1.55 to 0.03)	**-1.17 (-2.13 to-0.20)**	**-0.70 (-1.15 to-0.25)**	**-1.21 (-1.65 to-0.78)**
PE	1.16 (0.84 to 1.61)	0.97 (0.72 to 1.32)	1.16 (0.91 to 1.47)	1.01 (0.60 to 1.71)	0.47 (0.23 to 1.00)	PE	-0.19 (-0.43 to 0.06)	-0.24 (-0.66 to 0.18)	-0.63 (-1.32 to 0.06)	**-1.04 (-1.88 to-0.19)**	**-0.58 (-0.88 to-0.27)**	**-1.09 (-1.32 to-0.86)**
CBT	1.12 (0.81 to 1.54)	0.93 (0.68 to 1.30)	1.11 (0.91 to 1.37)	0.97 (0.55 to 1.72)	0.46 (0.22 to 0.94)	0.96 (0.76 to 1.22)	CBT	-0.06 (-0.47 to 0.36)	-0.45 (-1.12 to 0.23)	-0.85 (-1.73 to 0.03)	**-0.39 (-0.65 to-0.13)**	**-0.90 (-1.06 to-0.74)**
PCT	1.23 (0.75 to 2.00)	1.03 (0.57 to 1.85)	1.22 (0.71 to 2.09)	1.07 (0.50 to 2.26)	0.50 (0.22 to 1.14)	1.05 (0.62 to 1.82)	1.10 (0.65 to 1.84)	PCT	-0.39 (-1.16 to 0.38)	-0.80 (-1.74 to 0.16)	-0.33 (-0.79 to 0.12)	**-0.84 (-1.25 to-0.44)**
BEP	0.84 (0.28 to 2.5)	0.70 (0.24 to 2.08)	0.83 (0.29 to 2.44)	0.73 (0.22 to 2.44)	0.34 (0.09 to 1.23)	0.72 (0.25 to 2.13)	0.75 (0.276 to 2.17)	0.68 (0.21 to 2.22)	BEP	-0.41 (-1.50 to 0.69)	0.06 (-0.65 to 0.76)	-0.45 (-1.11 to 0.21)
PDT	2.16 (0.89 to 5.23)	1.81 (0.75 to 4.35)	2.15 (0.91 to 5.05)	1.88 (0.71 to 4.98)	0.88 (0.29 to 2.67)	1.85 (0.81 to 4.17)	1.93 (0.82 to 4.54)	1.76 (0.66 to 4.69)	2.57 (0.67 to 9.93)	PDT	0.46 (-0.43 to 1.36)	-0.305 (-0.92 to 0.83)
TAU	**1.60 (1.15 to 2.22)**	1.34 (0.90 to 1.99)	**1.59 (1.19 to 2.12)**	1.39 (0.75 to 2.57)	0.65 (0.33 to 1.29)	**1.37 (1.00 to 1.89)**	**1.43 (1.09 to 1.86)**	1.30 (0.76 to 2.23)	1.90 (0.64 to 5.64)	0.74 (0.31 to 1.79)	TAU	**-0.51 (-0.78 to-0.24)**
NT	**3.14 (2.28 to 4.32)**	**2.63 (1.90 to 3.63)**	**3.12 (2.48 to 3.92)**	**2.73 (1.53 to 4.86)**	1.28 (0.62 to 2.67)	**2.70 (2.13 to 3.42)**	**2.80 (2.33 to 3.37)**	**2.56 (1.52 to 4.31)**	**3.74 (1.31 to10.66)**	1.45 (0.62 to 3.42)	**1.96 (1.46 to 2.65)**	NT

Figure 10. League table of psychotherapies effectiveness toward PTSD at posttreatment and remission rate

White (▭) represents nodes of therapies included in the analysis. Light grey (▭) represents the effect size given as network SMD and 95% CI. Network evidence SMD was based on pooled direct and indirect evidence from all studies included. Lower scores SMD indicate better effectiveness in decreasing PTSD symptoms. Instruction to read: the upper side of league table (PTSD symptoms) should be start from row then compared to column therapy, e.g. CT showed more effective in decreasing PTSD symptom as big as -0.21 (-0.62 to 0.20) compared to EMDR. Dark grey (▭) represent remission rate given as RR and 95% Confidence Interval. Results are represented as RR for remission rate and retention rate. Higher scores of RR indicate better effectiveness in remitted the participants. Instruction to read: the lower side of league table (remission rate) should be start from column then compared to row therapy, e.g. CT showed less effective in remission rate of PTSD diagnosis as big as 0.84 (0.60 to 1.29) compared to EMDR. Statistically significant data are shown in bold. Cognitive processing therapy (CPT); Cognitive therapy (CT); Eye movement desensitization and reprocessing (EMDR); Narrative exposure therapy (NET); No treatment (NT); Present centered therapy (PCT); Psychodynamic therapy (PDT); Prolonged exposure (PE); Therapy as usual (TAU); Brief eclectic psychotherapy (BEP); Cognitive behavior therapy (CBT); Standardized mean different (SMD); and 95% confidence interval (95% CI); Risk ratio (RR). Figure was created by the author.

Baseline to Longitudinal Follow-Up

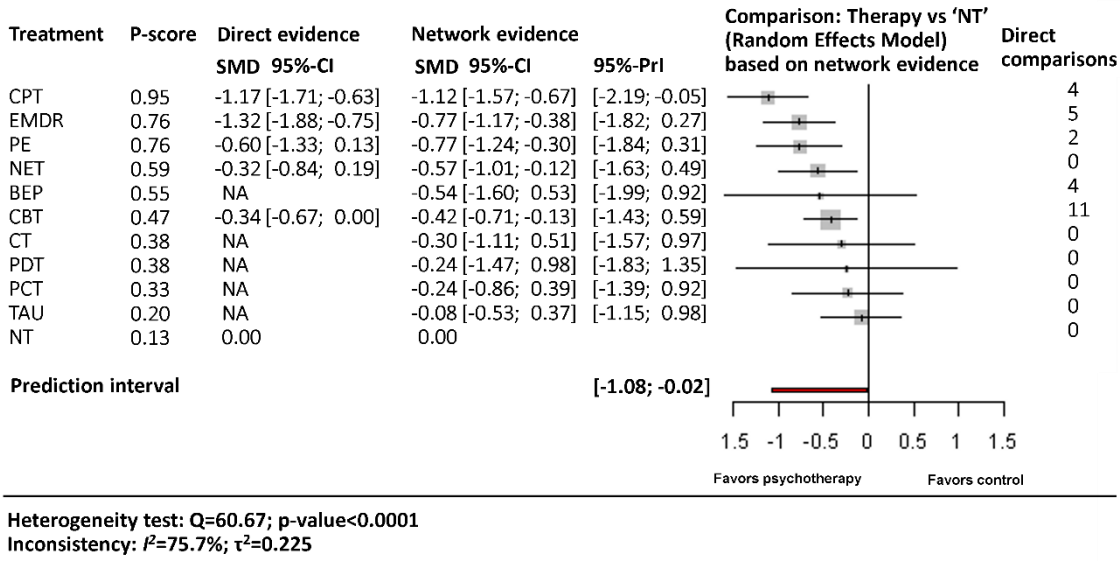

Figure 11. Forest plot NMA of psychotherapies effectiveness toward PTSD at short-term follow-up

In the short-term effectiveness analysis, 45 studies were included in the analysis. The results revealed that CPT, EMDR, and PE showed significant results with large effect size (SMD range -1.14 to -0.90), BEP and NET showed moderate effect size (SMD range -0.58 to -0.67), and CBT showed low effect size (SMD -0.45). According to rank analysis, CPT and EMDR were most effective therapies (upper quartile) followed PE, BEP and NET (second quartile) CBT, CT, PDT, and PCT (third quartile) (see Appendix 8). PrI score showed future new studies will have effect size ranged between SMD -1.15 to -0.04. Heterogeneity test showed moderate inconsistency (I^2=77%; τ^2=0.2468). (**Figure 11**).

Twenty-nine studies were included in long-term follow-up analysis. The results found that only CPT, NET, and EMDR showed significantly greater efficacy than no treatment with large effect size (SMD range -1.00 to -0.58), PE with moderate effect size (SMD -0.38). While PCT, CBT, CT, and PDT showed no significant results. Rank analysis found that CPT and NET

(upper quartile) were the most effective therapies, with regards EMDR, PE (second quartile) PCT, CBT, CT, and PDT (third quartile) for PTSD. PrI score showed future new studies will have effect size ranged between SMD -0.96 to 0.27. Heterogeneity test showed moderate inconsistency (I^2=68%; τ^2=0.1327). (**Figure 12**).

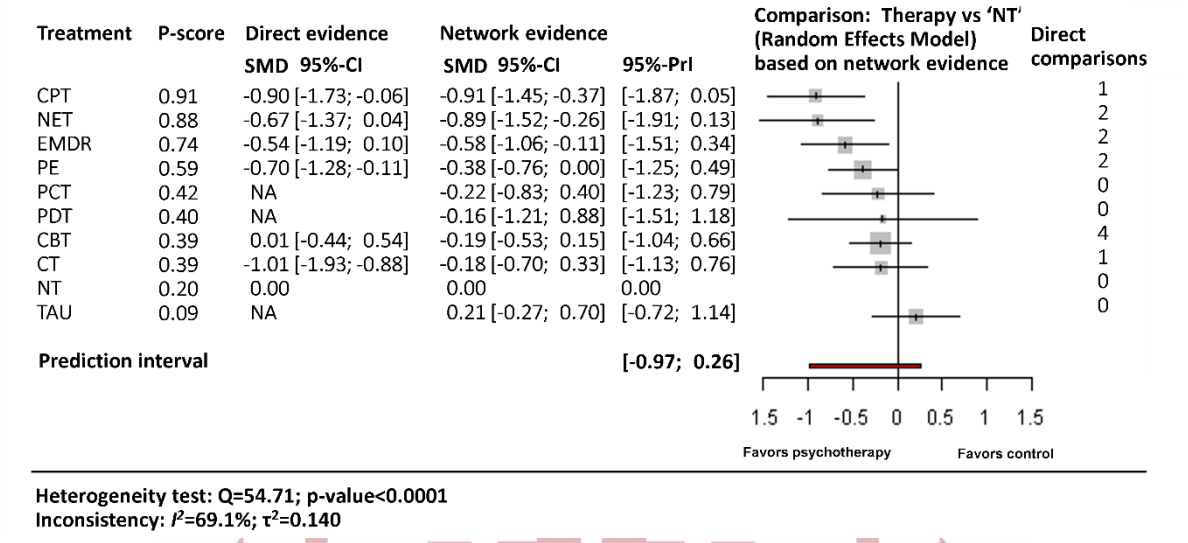

Figure 12. Forest plot NMA of psychotherapies effectiveness toward PTSD at long-term follow-up

4.2.3.2. Secondary Outcome

In terms of remission rates, 70 studies were included in the analysis. According to figure 13, EMDR, BEP, CPT, CBT, EMDR+PE, PE, CT, PCT, and PDT showed large significantly different remission rates (RR range 3.18 to 2.38) compared to NT. On the contrary, NET was not significant. Our rank analysis found that EMDR, CPT, and BEP (upper quartile) were the most effective therapy in remission rate with regards to EMDR+PE, PE, CBT, CT, PCT (second quartile), PDT (third quartile), and NET (fourth quartile). The detailed effect sizes of all

comparison psychotherapies including TAU and NT are provided in the league table (see Appendix 6). According to PrI score, it is predicted that future new studies would have higher remission rates than NT ranged between RR 2.22 to 3.31 Heterogeneity test showed moderate inconsistency (I^2=50.7%; τ^2=0.0637) (**Figure 13**).

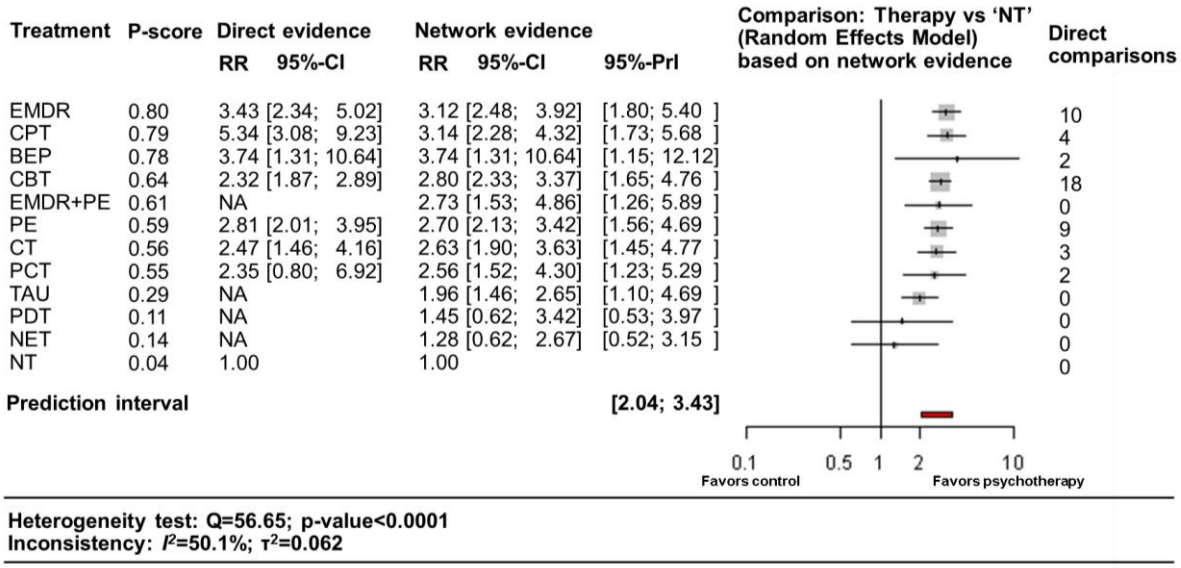

Figure 13. Forest plot NMA of psychotherapies effectiveness toward PTSD remission rate

4.2.4. Quality of Study

The assessment of risk of bias using Cochrane RoB 2.0 showed 32.9%, 39%, and 28% of studies had low, some concern, and high risk of bias, respectively. About 85.7% were based on intention-to-treat (ITT) analysis (**Figure 14**).

Twenty-seven comparisons were performed to evaluate the certainty based on contribution matrix risk of bias, inconsistency, indirectness, imprecisions, and publication bias of each comparison. Studies included were subject to the risk of bias, particularly in selection and measurement, some inconsistencies, serious indirectness, and wide confidence intervals. Indirect evidence was taken from the lowest certainty among two highest contribution loops

found for each comparison. One study showed no direct effect (PDT vs NT) and indirect effect (EMDR+PE vs PE). GRADE NMA analysis from direct, indirect, and network evidence revealed that 6, 6, 8, and 7 studies showed high, moderate, low, and very low certainty (**Table 5**). Cohen kappa test of GRADE analysis for all domains showed 92.6% (25 out of 27) agreement among raters.

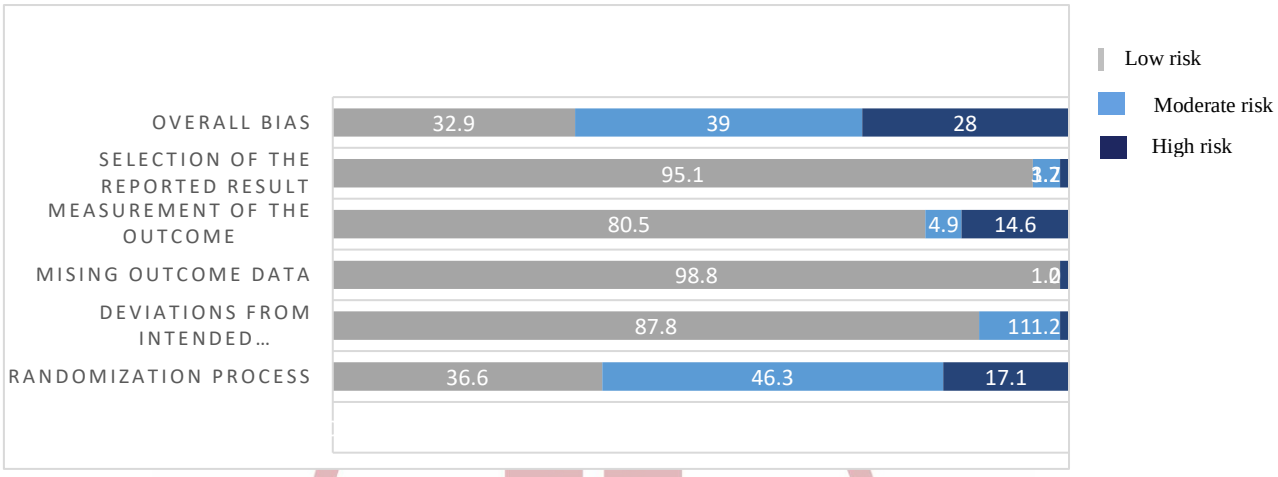

Figure 14. Risk of Bias Assessment based on Cochrane 2.0

4.2.5. Publication Bias

Publication bias assessment was conducted on posttreatment measurement of PTSD by adjusting the covariates. We hypothesize that in addition to small sample size publication bias and negative outcome publication bias, there might be bias based on more publications of recommended therapies according to guidelines. Therapies were arranged based on APA recommendation order prior with control groups (no treatment and TAU) followed by PCT, PDT, PDT, EMDR, NET, EMDR+PE, CT, CPT, and CBT. Results are reported with Begg-Mazumdar test, this study found a publication bias with Egger $p = 0.0196$; and Thompson-Sharp $p<0.0001$ (**Figure 15**).

Table 5. Study quality of pairwise psychotherapies by GRADE analysis

Comparison	Direct evidence		Indirect evidence		Network evidence	
	SMD (95%CI)	Certainty	SMD (95%CI)	Certainty	SMD (95%CI)	Certainty
CT vs NT	-1.59 (-2.08 to -1.10	⊕⊕◯◯ LOW	-1.12 (-1.67 to -0.58)	⊕◯◯◯ VERY LOW	-1.38 (-1.75 to -1.02)	⊕⊕◯◯ LOW
CT vs PE	-0.02 (-0.56 to 0.51)	⊕◯◯◯ VERY LOW	-0.49 (-1.03 to 0.55)	⊕◯◯◯ VERY LOW	-0.26 (-0.64 to 0.12)	⊕◯◯◯ VERY LOW
EMDR+PE vs PE	-0.20 (-1.24 to 0.83)	⊕⊕◯◯ LOW		NA	-0.20 (-1.24 to 0.83)	⊕⊕◯◯ LOW
EMDR vs NT	-1.25 (-1.53 to -0.98)	⊕⊕⊕⊕ HIGH	-1.09 (-1.43 to -0.76)	⊕◯◯◯ VERY LOW	-1.19 (-1.40 to -0.97)	⊕⊕⊕⊕ HIGH
EMDR vs TAU	-0.33 (-0.79 to 0.13)	⊕⊕⊕◯ MODERATE	-0.85 (-1.19 to -0.51)	⊕◯◯◯ VERY LOW	-0.66 (-0.94 to -0.39)	⊕⊕⊕◯ MODERATE
EMDR vs PE	-0.24 (-0.74 to 0.27)	⊕◯◯◯ VERY LOW	0.01 (-0.31 to 0.33)	⊕◯◯◯ VERY LOW	-0.06 (-0.33 to 0.21)	⊕◯◯◯ VERY LOW
EMDR vs CBT	-0.19 (-0.26 to 0.63)	⊕◯◯◯ VERY LOW	0.30 (0.02 to 0.57)	⊕◯◯◯ VERY LOW	0.27 (0.03 to 0.50)	⊕◯◯◯ VERY LOW
EMDR vs BEP	0.91 (-0.10 to 1.93)	⊕◯◯◯ VERY LOW	0.56 (-0.34 to 1.46)	⊕◯◯◯ VERY LOW	0.72 (0.05 to 1.39)	⊕◯◯◯ VERY LOW
PE vs NT	-0.93 (-1.26 to -0.59)	⊕⊕◯◯ LOW	-1.30 (-1.60 to -0.99)	⊕◯◯◯ VERY LOW	-1.12 (-1.35 to -0.90)	⊕⊕◯◯ LOW
PE vs TAU	-1.03 (-1.58 to -0.49)	⊕⊕⊕⊕ HIGH	-0.44 (-0.77 to -0.10)	⊕⊕◯◯ LOW	-0.60 (-0.89 to -0.32)	⊕⊕⊕⊕ HIGH
PE vs CPT	-0.20 (-1.21 to 0.81)	⊕◯◯◯ VERY LOW	-0.48 (-0.87 to -0.08)	⊕⊕◯◯ LOW	-0.44 (-0.81 to -0.07)	⊕⊕◯◯ LOW
PE vs CBT	-0.01 (-0.58 to 0.56)	⊕◯◯◯ VERY LOW	0.25 (-0.02 to 0.52)	⊕⊕◯◯ LOW	0.20 (-0.04 to 0.45)	⊕⊕◯◯ LOW
PE vs PCT	0.36 (-0.31 to 1.03)	⊕◯◯◯ VERY LOW	0.15 (-0.36 to 0.66)	⊕⊕◯◯ LOW	0.23 (-0.18 to 0.63)	⊕⊕◯◯ LOW
PE vs PDT	1.04 (0.19 to 1.90)	⊕⊕⊕◯ MODERATE	0.34 (-0.68 to 1.35)	⊕◯◯◯ VERY LOW	0.75 (0.10 to 1.40)	⊕⊕⊕◯ MODERATE
NET vs NT	-1.46 (-2.06 to -0.85)	⊕⊕⊕⊕ HIGH	-0.98 (-1.61 to -0.34)	⊕⊕◯◯ LOW	-1.23 (-1.67 to -0.79)	⊕⊕⊕⊕ HIGH
NET vs TAU	-0.72 (-1.40 to -0.04)	⊕⊕⊕◯ MODERATE	-0.70 (-1.29 to -0.10)	⊕◯◯◯ VERY LOW	-0.71 (-1.16 to -0.26)	⊕⊕⊕◯ MODERATE
NET vs PCT	0.58 (-0.60 to 1.75)	⊕◯◯◯ VERY LOW	-0.58 (-1.19 to 0.04)	⊕⊕⊕◯ MODERATE	-0.33 (-0.88 to 0.21)	⊕⊕⊕◯ MODERATE
CPT vs NT	-1.55 (-1.97 to -1.12)	⊕⊕⊕⊕ HIGH	-1.59 (-2.10 to -1.08)	⊕◯◯◯ VERY LOW	-1.57 (-1.89 to -1.24)	⊕⊕⊕⊕ HIGH
CPT vs TAU	-0.85 (-1.50 to -0.20)	⊕⊕⊕⊕ HIGH	-1.13 (-1.57 to -0.69)	⊕◯◯◯ VERY LOW	-1.04 (-1.41 to -0.68)	⊕⊕⊕⊕ HIGH
CPT vs PCT	-0.87 (-1.50 to -0.25)	⊕⊕⊕⊕ HIGH	-0.49 (-1.07 to 0.09)	⊕◯◯◯ VERY LOW	-0.67 (-1.09 to -0.24)	⊕⊕⊕⊕ HIGH
PCT vs NT	-0.89 (-1.65 to -0.13)	⊕⊕⊕◯ MODERATE	-0.90 (-1.36 to -0.44)	⊕⊕◯◯ LOW	-0.90 (-1.29 to -0.50)	⊕⊕⊕◯ MODERATE
CBT vs NT	-0.86 (-1.05 to -0.66)	⊕⊕◯◯ LOW	-1.10 (-1.42 to -0.78)	⊕◯◯◯ VERY LOW	-0.92 (-1.09 to 0.75)	⊕⊕◯◯ LOW
CBT vs TAU	-0.46 (-0.78 to -0.13)	⊕⊕⊕◯ MODERATE	0.25 (-0.02 to 0.52)	⊕⊕◯◯ LOW	0.20 (-0.04 to 0.45)	⊕⊕⊕◯ MODERATE
CBT vs CT	0.15 (-0.66 to 0.96)	⊕◯◯◯ VERY LOW	0.55 (0.12 to 0.98)	⊕◯◯◯ VERY LOW	0.46 (0.08 to 0.84)	⊕◯◯◯ VERY LOW
CBT vs PCT	0.24 (-0.86 to 1.34)	⊕◯◯◯ VERY LOW	-0.06 (-0.51 to 0.38)	⊕⊕◯◯ LOW	-0.02 (-0.43 to 0.39)	⊕⊕◯◯ LOW
BEP vs NT	-0.62 (-1.49 to 0.26)	⊕◯◯◯ VERY LOW	-0.26 (-1.30 to 0.77)	⊕◯◯◯ VERY LOW	-0.47 (-1.14 to 0.20)	⊕◯◯◯ VERY LOW
PDT vs NT	NA	NA	-0.38 (-1.04 to 0.29)	⊕⊕◯◯ LOW	-0.38 (-1.04 to 0.29)	⊕⊕◯◯ LOW

[a] Direct evidence SMD represent the relative effect of two comparisons that directly determined in study. Direct evidence certainty was estimate based on five domains in GRADE analysis (risk of bas, inconsistency, indirectness, imprecision, and other consideration). Indirect evidence SMD and certainty was taken from the lowest certainty among two highest contribution loops found for each comparison. Network evidence SMD was based on pooled direct and indirect evidence from all studies included. Network evidence certainty were estimates based on agreement between direct and indirect evidence with consideration to level up or level down the certainty based on several reasons. The certainty was categorized into four levels: ⊕ as very low, ⊕⊕ as low, ⊕⊕⊕ as moderate, and ⊕⊕⊕⊕ as high certainty.

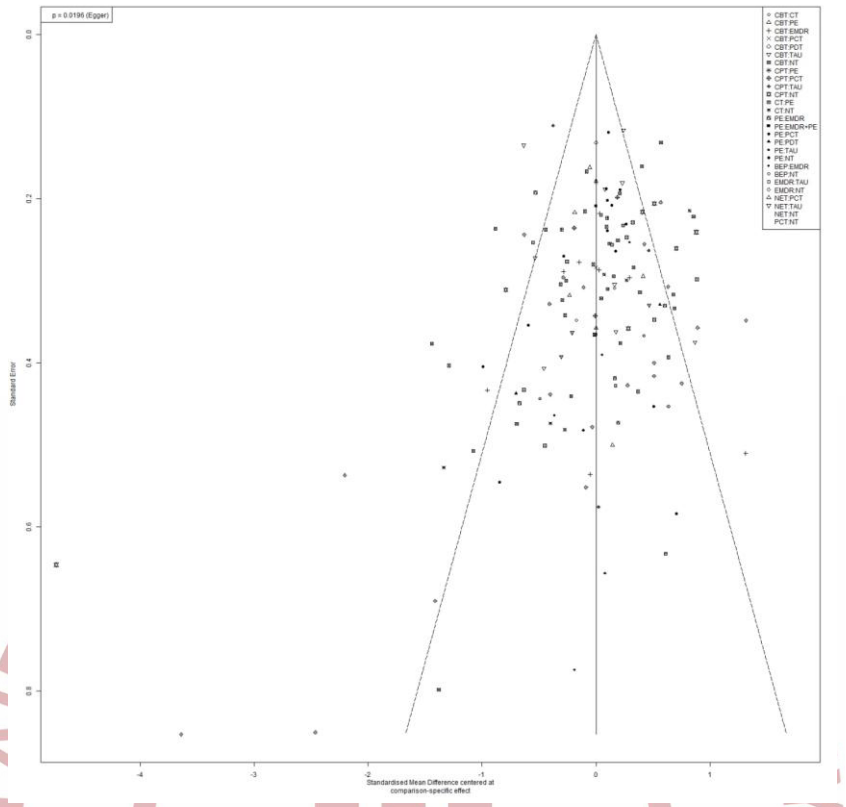

Figure 15. Funnel Plot of network meta-analysis of PTSD psychotherapies

4.2.6. Sensitivity Analysis

The sensitivity analyses based on combinations of CBT were performed to evaluate the robustness of the included therapies. Sensitivity analyses based on treatments combinations were performed in four different formats. Although the change of DIC scores from the initial model (DIC=287.08), the combination of CBT+CT (DIC=298.38), CBT+CT+CPT (DIC=301.32), and combination CBT+CT+CPT+PE (DIC=287.49) were significant statistically, we found combining psychotherapies into a broader category was not superior model (**Table 6**).

Table 6. Models fit of combined CBT therapies

Model	DIC initial model	ES of therapy compared to NT MD [95% CI[	DIC
All intervention: Original classification (11 therapies)	-		287.08
CPT		-1.54 [-1.89 to -1.24]	
CT		-1.28 [-1.63 to -0.93]	
EMDR+PE		-1.33 [-2.39 to -0.27]	
NET		-1.23 [-1.67 to -0.79]	
EMDR		-1.19 [-1.40 to -0.97]	
PE		-1.13 [-1.35 to -0.90]	
CBT		-0.91 [-1.07 to -0.74]	
PCT		-0.90 [-1.29 to -0.50]	
BEP		-0.52 [-0.77 to -0.27]	
PDT		-0.47 [-1.14 to -0.20]	
TAU		-0.37 [-1.04 to -0.30]	
Combined CBT and CT (10 therapies)	287.08		298.38
CPT		-1.60 [-1.90 to -1.20]	
EMDR+PE		-1.20 [-2.30 to -0.16]	
NET		-1.30 [-1.70 to -0.78]	
EMDR		-1.20 [-1.40 to -0.98]	
PE		-1.10 [-1.30 to -0.89]	
CBT		-0.96 [-1.10 to -0.79]	
PCT		-0.92 [-1.30 to -0.52]	
BEP		-0.50 [-1.20 to -0.28]	
TAU		-0.53 [-0.79 to -0.29]	
PDT		-0.36 [-1.10 to -0.32]	
Combined CBT, CT, and CPT (9 therapies)	285.57		301.32
EMDR+PE		-1.20 [-2.50 to -0.09]	
EMDR		-1.20 [-1.50 to -1.00]	
NET		-1.20 [-1.70 to -0.98]	
PE		-1.10 [-1.30 to -0.85]	
CBT		-1.10 [-1.20 to -0.91]	
PCT		-0.73 [-1.20 to -0.32]	
BEP		-0.46 [-1.30 to -0.27]	
PDT		-0.35 [-1.10 to -0.34]	
TAU		-0.52 [-0.79 to -0.22]	
Combined CBT, CT, CPT, and PE (8 therapies)	269.77		287.49
EMDR+PE		-1.30 [-2.50 to -0.05]	
NET		-1.20 [-1.70 to -0.79]	
EMDR		-1.20 [-1.40 to -0.98]	
CBT		-1.10 [-1.20 to -0.92]	
PCT		-0.78 [-1.20 to -0.29]	
BEP		-0.50 [-1.30 to -0.21]	
PDT		-0.39 [-1.00 to -0.44]	
TAU		-0.52 [-0.83 to -0.28]	

Note. Different types of CBT therapies (CT, CPT, and PE) were combined as CBT in each model to evaluate its effectiveness. Unadjusted MD and DIC value were obtained using Bayesian NMA without adjusting for specific risk factors. Adjusted MD and DIC value were obtained after adjusting for different risk factors. We choose the adjusted model if there was DIC value difference more than 10 points between adjusted and unadjusted model. β coefficient represent the effect of moderator in the NMA result. Example: at the second model analysis, the DIC at initial model was 287.08, While after CBT and CT was combined together, the DIC change into 298.38. There was a significant different between initial and after combined since the different was more than 10 points.

Further sensitivity analysis was conducted by excluding studies that combine psychotherapies with medication. Eighty-two studies without additional medication or stable dose before and during study, consist of CPT (10 studies), CT (6 studies), NET (5 studies), EMDR (15 studies), PE (17 studies), PCT (1 studies), CBT (25 studies), BEP (3 studies), and PDT (1 studies) were included in the analysis. The results found CPT, CT, and NET as the first quartile therapies that effective in decreasing PTSD symptoms at immediate posttreatment measurement with high network estimates (-1.58 to -1.29). While in the second quartile was EMDR and PE with high network evidence (-1.24 to -1.22), followed by PCT and CBT in the third quartile (-0.88 to -0.78). BEP and PDT found not significantly effective toward PTSD symptoms at immediate posttreatment measurement (**Figure 16**).

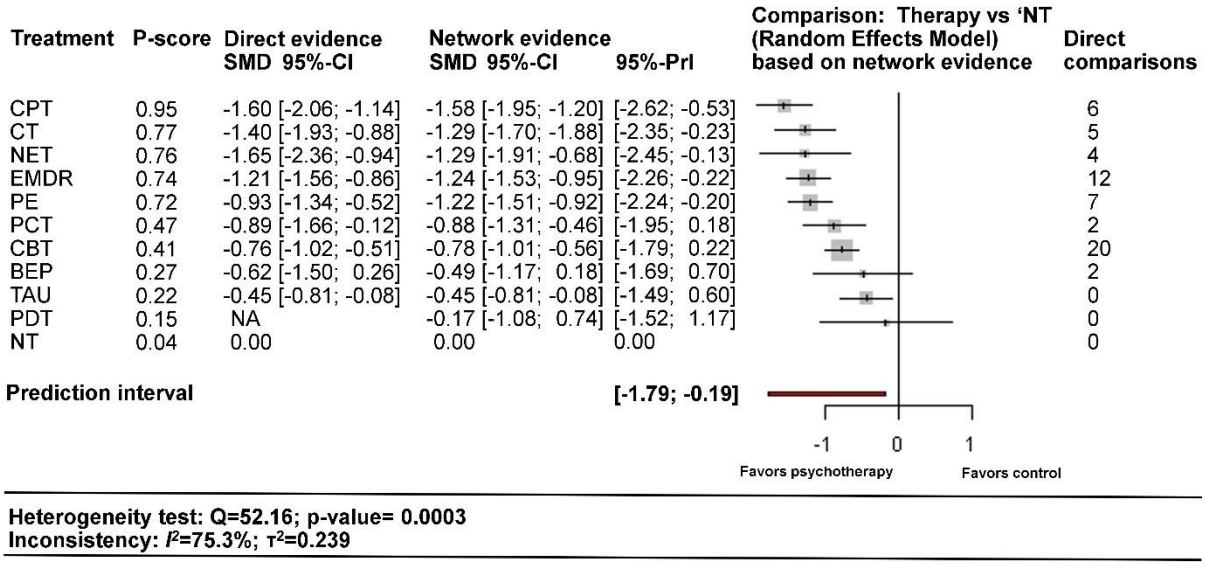

Figure 16. Forest plot of sensitivity analysis of PTSD psychotherapies effectiveness without or with stable medication

4.2.7. Moderator Analysis

Our study utilized five different models for moderator analysis that include age groups. Among all models of moderator analysis, only age-adjusted models showed lower DIC than the initial model and significant coefficient of age (β=-7.78; 95%CI = -13.30 to -2.82). Based on this result, a subgroup analysis was conducted for two age groups, children-adolescent, and adults (**Table 7**).

Table 7. Model fit based on age group (children-adolescent vs adults)

Therapies	**Unadjusted**		**Adjusted by age**		**β (95%CI)**
	MD (95% CI)	**DIC**	**MD (95% CI)**	**DIC**	
CPT	-22 (-29 to -17)	**558.28**	-22 (-28 to -16)	**555.68**	**-7.78 (-13.30 to -2.82)**
CT	-22 (-28 to -15)		-21 (-27 to -15)		
EMDR+PE	-21 (-40 to -0.39)		-21 (-41 to -2.3)		
NET	-18 (-26 to -11)		-18 (-24 to -9.8)		
EMDR	-17 (-21 to -14)		-17 (-21 to -14)		
PE	-17 (-21 to -13)		-17 (-21 to -12)		
PCT	-16 (-23 to -8.8)		-15 (-23 to -7.4)		
CBT	-13 (-16 to -10)		-13 (-16 to -10)		
BEP	-4.2 (-15 to 7.2)		-3.1 (-15 to 7.0)		
TAU	-8.6 (-13 to -3.7)		-8.6 (-13 to -3.9)		
PDT	-7 (-18 to 5.4)		-6.1 (-18 to 4.5)		
NT	ref		ref		

Beta coefficients (β) represent the effect of moderator in the NMA result from meta-regression using Bayesian approach of NMA. Unadjusted value was obtained using Bayesian NMA without adjusting for specific risk factors. Adjusted value was obtained after adjusting for different risk factors. We choose the adjusted model if there was DIC value difference more than 10 point between adjusted and unadjusted model.

[a] Model A using percentage of female as moderator; Model B using age group as moderator variable, adult (mean age ≥18 years old) compared with children-adolescents (mean age <18 years old); Model C using six different type of continent as moderator variable (North America, South America, Asia, Europe, Australia, and Africa); Model D using study's power as moderator, low (<80%) and high (≥80%) power of study; Model E using study's risk of bias (low, some concern, and high) as moderator variable.

Further analysis related to different age groups showed different effectiveness and rank of therapies for each group. CT, CBT, and EMDR showed as significant psychotherapies to children and adolescents (SMD range -1.25 to -0.69). While CPT, EMDR, CT, EMDR+PE, NET, PE< CBT, and PCT were significant therapies for adults (SMD range -1.57 to -0.91) (**Figure 17**). The detailed effect sizes of all comparison's psychotherapies including TAU and NT across different age group are provided in the league table (**Figure 18).**

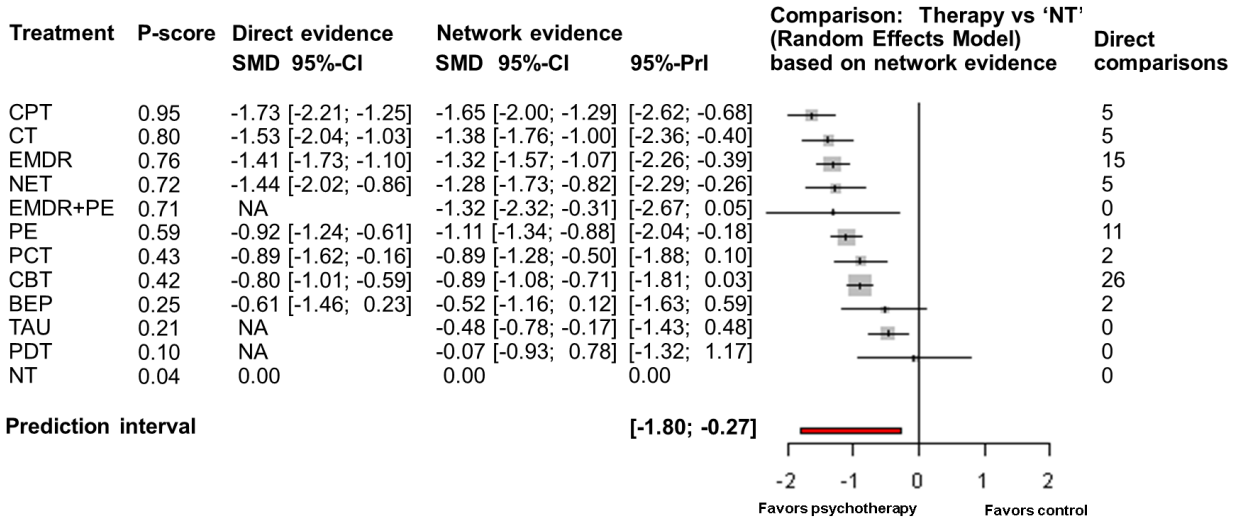

Figure 17. Forest plot of PTSD psychotherapies effectiveness for adult

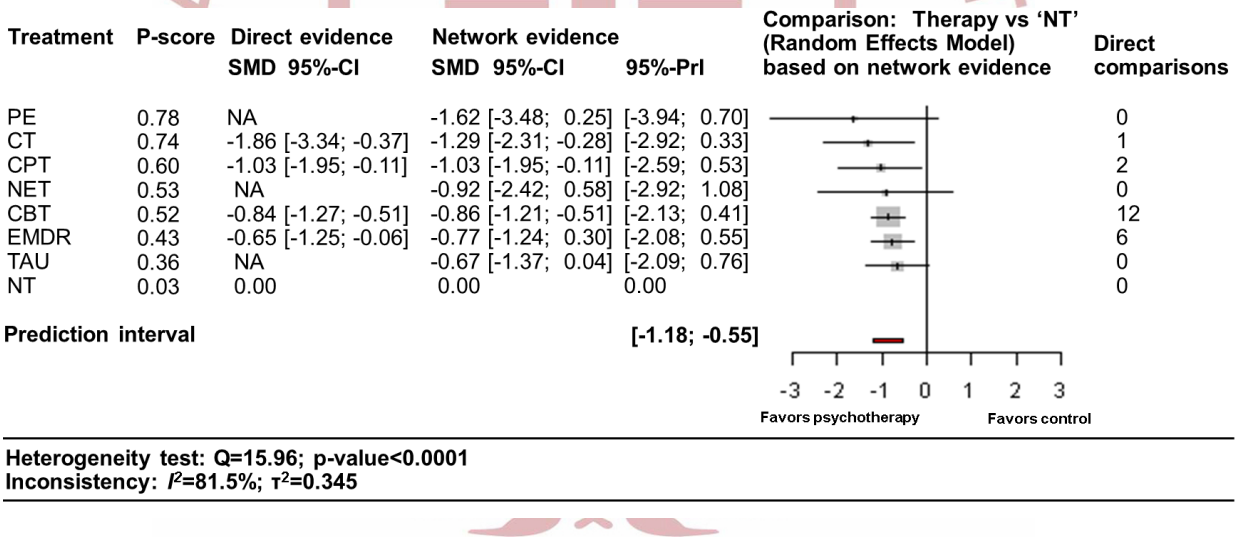

Figure 18. Forest plot of PTSD psychotherapies effectiveness for children and adolescent

CHAPTER 5 – Discussion

This study's found overall pooled PTSD prevalence higher than the prevalence rate during the SARS pandemic. A study from China in 2009 found the prevalence rate of PTSD among SARS patients was about 4% and 5% at one and three months after discharge, respectively (Wu et al., 2005). Although the mortality rate of COVID-19 less than SARS (15%) (Chan-Yeung & Xu, 2003) and MERS (35%) (WHO, 2019a), yet the reproduction number of COVID-19 is relatively high (2-2.5) (WHO, 2019b) when compared to SARS (1.7-1.9) and MERS (<1) (Petrosillo et al., 2020). Furthermore, a longer duration of COVID-19 might also play an important role in increasing its serious impact. According to WHO, the COVID-19 is currently longer than previous coronavirus outbreaks. Whereas the SARS outbreak ended eight months after the first case was reported (WHO, 2015b), while for COVID-19, the pandemic is still spreading after two years since the first reported case.

The current study results indicate that there are similar and considerable rates of PTSD for both those who are directly and indirectly exposed to COVID-19. This result is supported by previous studies, which showed that either direct or indirect exposure to trauma could lead to PTSD (Lee et al., 2017; May & Wisco, 2016; Szogi & Sullivan, 2018). This meta-analysis found PTSD prevalence among health professionals was higher compared to patient or survivors of COVID-19. Surprisingly, it also demonstrated a higher prevalence of PTSD (15.5%) among health professionals compared to a previous study (11.9%) (Chirico et al., 2021).

Although patients/survivors who directly exposed to COVID-19 could experience trauma from the disease affect, health professionals faced higher number of traumatic incidences. They play an essential role in the pandemic as the frontline responders in hospitals and clinics

and the service centers for patients affected by the COVID-19 infection. Compared to other professionals in the social and trading sectors, health professionals confronted with high traumatic situations (Magnavita, Capitanelli, et al., 2021). Initially, Overcrowding the case counts leaves health professionals with high stress without enough resources, uncertainty about COVID-19 and the lack of guidelines for taking care of the patients resulted in feelings of frustration and anger among health professionals. This may have generated moral injury that could be considered as a serious threat to mental stability (Chirico et al., 2020). The prevalence of PTSD among the population at large or those not directly exposed was also quite high compared to the average global prevalence (Kessler et al., 2017). Although this population was not exposed to COVID-19 directly, stressful situations such as lockdowns, economic instability, social isolation, and media reporting of information during the pandemic most likely had a negative effect on their psychological well-being.

Further moderator analysis found age as significant moderator to PTSD during COVID-19 pandemic. Although the elderly was considered as a vulnerable population, they were more likely to have less negative psychological affect than other age groups. A study by Ditlevsen and Elklit (2010) found that the prevalence of PTSD among adults tends to be higher than the elderly. It is also supported by another study by Robert et al. (2012) that found the PTSD prevalence among older adults was 4.5%, which was lower than reported rates of younger age. The elderly is believed has cumulated life experiences offering them a higher resilience to post-traumatic events including COVID -19 pandemic compared to younger age groups. Resiliency is the ability to adapt and being flexible and persistently toward hard situations and as well as ability to tolerate negative emotions and failures. It have been recognized as a protective factor against the experienced negative life events (Oginska-Bulik & Kobylarczyk, 2016). Further,

from a biological perspective, because people's prefrontal cortex is not fully mature until the age of 20, they have difficulty coping with traumas after they experience them (Johnson et al., 2009).

In terms of health professionals' characteristics, moderator analysis found those who worked in COVID-19 units showed five times greater to develop PTSD than those who did not work in COVID-19 units. Being exposed to highly stressful situations such as witnessing death, trauma, and working overtime, and overcrowded settings could be a major reason for the psychosomatic problems in the COVID-19 units during the pandemic. The general director of WHO, Tedros Adhanom Ghebreyesus, notes that "many (health professionals) have themselves become infected, and while reporting is scant, we estimate that at least 115,000 health care workers have paid the ultimate price in the service of others" (Euronews, 2021). The current study findings also indicate that nurses were at high risk of having PTSD than other health professionals. Similarly, nurses who work in COVID-19 units have shown to have a 0.8 times higher risk of developing PTSD (Moon et al., 2021). As part of the frontline health workers, nurses are facing high stress in taking care of people with COVID-19. At the start of the pandemic, armed only with limited information about COVID-19 and basic training of universal precautions, nurses tended to have more direct contact with patients and work more than eight hours every day. The shortage of nurses and personal protective equipment could have led to an increased number becoming infected and dying from COVID-19. Nurses experience fear of their own deaths or the deaths of loved ones that could result in the development of PTSD (Marshall, 2020).

Subgroup analysis and meta-regression also revealed that there were significant differences PTSD prevalence among different continents. Although different strategies were applied for each country, yet the COVID-19 pandemic was the center of government policies

on 2020 (Konig & Winkler, 2021). Countries in European continent, such as Italy, Spain, and France, were significantly late in implementing national restriction and badly impacted to COVID-19 pandemic. As consequence, the uncontrolled situation likely causes high mortality rate (Oksanen et al., 2020). As the largest contributor to new COVID-19 cases and death (Smith-Spark et al., 2020), people who live in Europe countries have higher risk to develop pandemic-related PTSD. Surprisingly, this study found people who live in European continent showed the highest number of PTSD compared to Asia and America. Furthermore, the social restriction caused businesses struggle to survive (Konig & Winkler, 2021), unemployment due to COVID-19 pandemic has demonstrated to cause significant health loss in high-income countries and these situations have collectively impacted on people's mental health condition including development of PTSD (WHO, 2020). Since the outbreak of COVID-19 in Europe, the level of stress and anxiety have risen significantly (Nation, 2020). However, this finding should be interpreted with caution, as only three studies reported the prevalence rates of PTSD in low-income countries. Thus, more studies are needed to further explore the prevalence of PTSD in more countries and continents to have a comprehensive view and better understanding of the global pandemic-related PTSD.

Subgroup analyses found that the PTSD assessment tool among the included studies was a significant moderator. Studies that used CAPS-5 and PCL-5/S/C/C2 as instruments to measure PTSD showed the highest and lowest prevalence, respectively. Of all the instruments, the CAPS-5, PCL-5/S/C/C2, and IES-R/6 showed high validity and reliability (Blevins et al., 2015; Creamer et al., 2003; Weathers et al., 2018). CAPS-5 is the gold standard for PTSD assessment (F W Weathers et al., 2013) which is an interview-based instrument, while PCL-5/S/C/C2 and IES-R/6 are self-reported ones. Different thresholds used in several studies might have also

influenced the pooled PTSD prevalence in studies that used PCL-5/S/C/C2 as the assessment tool. Furthermore, different rates of PTSD among three different populations might also be related to the instrument used. About 72.7% of studies that measured PTSD among patients/survivors of COVID-19 used PCL-5/S/C/C2. In addition, studies that measured PTSD on health professionals and the population at large dominantly use IES-R/6 More comprehensive assessments using interview and self-report-based instruments are needed instead rely on one specific type of assessment tool only.

Providing information on essential elements of the COVID-19 pandemic to the population at large to reduce stress for trauma including increasing the sense of safety, staying connected, promoting calm and sense of self, collective efficacy, and remaining hopeful could also be an effective method in reducing PTSD. Health care providers should ensure periodic comprehensive screening and occupational health surveillance of possible mental disorders to ensure peoples' well-being and prompt treatment is provided (Chirico & Magnavita, 2020). Furthermore, it is essential to develop adequate psychological support to help people through the challenges of the COVID-19 pandemic. Mental health supports are needed to be given to those who suffer from PTSD related to COVID-19 pandemic. In-person or virtual in-service training on essential elements related to COVID-19 and treatments should be available and accessible including to patients/survivors of COVID-19, health professionals, and population at large.

Undetected PTSD, indeed, have substantial impact due untreated burden. Prolonged morbidity, low quality of life, and higher cost of care are some problems that emerge among people with unthreatened PTSD (Priebe et al., 2009). In addition, it will also lead to others mental health problems. People with untreated PTSD are more likely to conduct suicidal

attempted, abused, developed complex PTSD, and have physical and mental health complication (Armenta et al., 2018; Flannery, 2001; Fox et al., 2021) as well as poor treatment prognosis (Priebe et al., 2009). Therefore, it is important to figure out the prevalence of PTSD as well as provide its treatment.

Among numerous psychotherapies to treat people with PTSD, our analyses showed that based on posttreatment analysis, CPT and CT were in the upper quartile in our model which means it has the highest likelihood of being ranked first for treating people with PTSD. The longitudinal analysis found CPT and EMDR as the upper quartile therapies in short-term follow-up measurements while CPT and NET were in the upper quartile in long-term follow-up measurements. In terms of secondary outcomes, EMDR, CPT, and BEP were found as upper quartile therapies for remission rates. While CT was the most effective in retaining the participants in studies. Both CPT and EMDR were consistently in the highest quartile in decreasing anxiety and depression symptoms. If we consider all outcomes—primary and secondary—then we suggest that CPT, CT, EMDR, and NET as the four most recommended therapeutic approaches.

Of these approaches with superior performance, it is worth noting that CPT outperforms others in most categories. In secondary measures, CPT also outperforms other treatments in reducing anxiety and depressive symptoms. Our analyses show that CPT and EMDR both rank quite well in primary and secondary outcomes. This may possibly provide some useful guidance for the clinicians when deciding which psychotherapy to be more suitable: where CPT is most effective in decreasing PTSD and anxiety/depression symptoms, EMDR is more well-rounded when remission rate is taken into account. Therefore, CPT is recommended if the remission rate

is not of immediate concern. Or alternatively, one may even consider CPT as first-line treatment, then gradually switch to options like EMDR as patients improve to a state ready for remission.

As noted above, CPT, CT, EMDR, and NET all show very good efficacy in the current analysis. CPT and CT aim to improve a person's ability to accommodate and decrease rumination by targeting specific thoughts and beliefs, NET aims to develop a coherent narrative of the trauma autobiographical memory. On the other hand, EMDR applies bilateral stimulation as the patients recall specific events from the trauma—which has also been shown to have better remission rates in previous NMA (Mavranezouli, Megnin-viggars, Dally, & Dias, 2020). Despite the seemingly different natures of these approaches, one notable commonality is that CPT, EMDR, and NET all require some form of re-exposure and reprocessing of the traumatic memory. Therefore, re-exposure and (more importantly) subsequent reprocessing may be crucial elements to effective treatment. Indeed, these elements are also present in most psychotherapies in the top two quartiles in the primary outcome, though CBT is one notable (and perhaps surprising) exception. We take this variability to suggest a slightly more nuanced view: perhaps re-exposure and reprocessing of traumatic events are necessary, though not sufficient in and of themselves, components to effective psychotherapy. As of now, it does seem that all forms of treatment are capable of reducing anxiety and depression. This is consistent with a previous component NMA by Coventry et al. (2020) that showed psychological interventions to be effective in the reduction of anxiety (SMD = −1.02; −1.72 to −0.32) and depression (SMD= −0.60; −1.06 to −0.14) symptoms. However, potential harms need to be acknowledged and put into consideration when designing treatment plans.

Some clinicians that these trauma-focused therapies could be destabilizing for participants and cause negative effects. For specific therapies, such as PE, the treatment could

provoke panic as the therapy is based on having participants re-experience the trauma until desensitization occurs naturally (Foa & Meadows, 1997). In clinical trials, there have been reports of negative side effects for PE such as those for Pitman et al. (1991) where 30% in the PE group experience side effects such as depression, panic attacks, drug/alcohol relapse, suicidal ideations and early terminations.

Previous NMA conducted by Mavranezouli, Megnin-viggars, Dally and Dias (2020) found that CT, TF-CBT consistently showed a large effect in reducing PTSD symptoms among youth. This result is similar to our subgroup analyses where we found CT, CBT, and EMDR to be the most effective for children and adolescents. Another NMA conducted for adults with PTSD showed slightly different results where EMDR, CT, TF-CBT, and self-help with support were the most effective therapies (Mavranezouli, Megnin-viggars, Dally, & Dias, 2020). While our current study found CPT, CT, NET, and EMDR as the most recommend therapies. Our results were slightly different when compared to some previous meta-analyses, which found no significant differences among psychotherapies comparisons (Bisson et al., 2020; Powers et al., 2010). Different meta-analyses also had different categorizations for grouping interventions; for example, Chen et al. (2015) grouped BEP and PE into CBT and found that EMDR was slightly better than the grouped CBT category. However, when interventions are analyzed separately and not grouped into CBT, CPT also showed significant effect size (SMD −1.40; 95%CI -1.95 to −0.85) in Cusack et al. (2016)'s meta-analysis of psychological treatments for adults with PTSD. Our sensitivity analysis of grouping different interventions into CBT, has different results than Gerger et al. (2014)'s NMA. Although the different formats of CBT therapies (CT, CPT, and PE) were put into the CBT group, our study found that the difference of the DIC was lower than 10 in the combination model from the original one, which means the combination

model did not change the original model. There needs to be further research for how best to approach grouping different interventions in categories of comparison in meta-analysis and network meta-analysis.

Recently, APA's PTSD guideline strongly recommends CBT, CPT, CT, and PE as psychotherapies for treating people with PTSD while BEP, EMDR, and NET were suggested psychotherapies (APA, 2017). While the Veteran Affairs/DoD clinical practice guidelines recommended PE, CPT, EMDR, BEP, and NET as trauma-focused psychotherapies for full PTSD (Departement of Veterans Affairs, 2017). Putting our results in the context of these guidelines, our results help to refine the list of those guidelines. This appears rather surprising at first, as one would expect that the inclusion of more studies should yield a more diverse line-up of psychotherapies. However, it is important to note that *all* therapeutic approaches in our NMA showed efficacy over the NT group. Therefore, by focusing on the top quartiles, a shorter recommended list in the present study merely means that CPT, CT, EMDR, and NET seem to be most effective in a list of psychotherapies that are all proven effective. Though, of course, meta-analyses are by nature biased towards therapies that enjoy more clinical data and studies, which are often the case in RCTs.

Thus, we also recommend caution when interpreting the present results because the numbers here simply cannot replace the therapists' insights of a client/patient that is gained through mutual understanding and long-term rapport. Our point above is also akin to one concern raised by Norcross and Wampold (2019), who pointed out that the importance of therapist-client relationship seems to be missing in the current versions of the guidelines. We wholeheartedly agree with this point, while we would also suggest that our analyses here do show that not all therapies are created equal. Therefore, perhaps a middle ground for this issue

is that the guidelines and the concerns raised are not mutually exclusive; rather, by combining therapist-client relationship with the most efficacious psychotherapies such as CPT, EMDR, and NET, treatment efficacy can likely be maximized. As such, we anticipate that as more studies and data on the catalytic and therapeutic effects of therapist-client relationship (not necessarily in the form of RCT) become available, these data should be able to help better strengthen and expand the scope of APA and VA/DOD guidelines.

CHAPTER 6 – Conclusions

This study found considerable PTSD prevalence rates was found in patients/survivors of COVID-19, health professionals, and the population at large. Moderator analysis found age, unit of work, health profession, continent, and PTSD assessment tool as significant moderators. In term of PTSD treatments, CPT, CT, NET, EMDR+PE, EMDR, PE, CBT, PCT showed as effective therapies on PTSD with moderate to large effect in immediate measurement. The remission rates showed all specific psychological treatments tend to decrease the number of people who meet PTSD diagnosis at the treatment endpoint. Moderator analyses found age as significant moderator. The psychotherapies showed different effectiveness rank between children-adolescent and adults.

Clinical Implication

The findings from this study can be used to develop programs needed to offer support for people who are at high risk for developing PTSD, especially in adults under the age of 65, health professionals who work in the COVID-19 units, nurses, and those who live in the European countries. Further psychological support as part of health services for those who suffer from PTSD due to COVID-19 is needed. Lastly, CPT, EMDR, and NET can be prioritized options as effective psychotherapies to treat people with PTSD.

Limitation

Regarding the PTSD prevalence meta-analysis, not all studies provide demographic characteristics of those with PTSD or information prior to the pandemic such as previous mental

disorder diagnosis that could be associated with PTSD; subgroup analyses were measured based on available data only. Elderly, countries in American's continent, countries with low-income GDP, and study used CAPS as the screening instrument were underrepresented. This situation might be contributed to the moderator analysis results and should interpret with cautious. Therefore, future studies meeting the diagnostic criteria of PTSD and better reporting of demographic and study characteristics for more accurate measurement of prevalence are needed. As the pandemic is not yet over, more studies are needed to explore the long-term impact of the COVID-19 pandemic on PTSD.

The network meta-analysis results there could be limited network connectivity due to the limited number of studies available. The different number of studies included in the analysis for each therapy node could also be an influential factor in determining grading recommendations of final results. Therapy nodes without closed loop will have limited indirect evidence used to create NMA estimate from pooled direct and indirect evidence. As there are limited studies included in the analysis, there are potential for low statistical power and publication bias risk (Veer et al., 2019). More robust studies are needed to inform future recommendations and guidelines. As such, an integrative view using all outcome measures is a better way to interpret the present data and results as it avoids the pitfalls of focusing too narrowly on a specific measurement without the overall context.

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