CHAPTER 9.1

Summary
Treating PTSD in psychosis

The main objective of this thesis was to test the effectiveness and safety of evidence-based trauma-focused treatments in people with a psychotic disorder. **CHAPTER 1** presents an introduction into this research area. Both childhood trauma and posttraumatic stress disorder (PTSD) are highly prevalent in people with psychotic disorders and negatively affect psychiatric symptoms, prognosis, and social functioning. Trauma-focused treatments that include direct trauma memory exposure, such as prolonged exposure (PE) therapy and eye movement desensitization and reprocessing (EMDR) therapy, are amongst the most effective treatments in mental health care and have strong empirical support. However, childhood trauma is under-recognised in patients with psychosis, and although the prevalence of PTSD is between 12.4%-16.0% in this group, it goes undetected in virtually all cases. In the unlikely event that PTSD is diagnosed in patients with a psychotic disorder, most clinicians refrain from offering trauma-focused treatment. They believe that people with psychosis will not be able to benefit from trauma-focused treatment or fear that trauma-focused treatment will destabilise patients and induce all kinds of adversity, such as symptom exacerbation or suicide attempts. Little is known about the veracity of these harm expectancies of clinicians, because psychosis is the most frequently used exclusion criterion in randomised controlled trials (RCTs). When we started this research no RCT had tested the effects and safety of standard trauma-focused treatments in samples consisting entirely of patients with psychosis and PTSD. Consequently, it was unknown whether standard trauma-focused treatments with direct trauma memory exposure were effective and safe in people with a psychotic disorder.

In **CHAPTER 2** we tested the effectiveness and safety of six EMDR sessions in 27 outpatients with a psychotic disorder and PTSD. In this uncontrolled feasibility study with a baseline and a post-treatment assessment the drop-out rate was relatively low (18.5%) and there were no severe adverse events. PTSD symptoms decreased significantly and greatly in both the intention-to-treat and in the completers analyses. Of the completers, 77.3% no longer met full PTSD criteria at post-treatment. Auditory verbal hallucinations, delusions (measured with the Psychotic Symptom Rating Scales), anxiety, depression, and self-esteem improved significantly, while paranoid ideation severity (measured with the Green et al. Paranoid Thought Scale) and feelings of hopelessness did not. The preliminary conclusion was that EMDR appears to be an effective and safe treatment in people with a psychotic disorder, and that EMDR can be applied without adapting the protocol or preceding treatment with stabilizing psychotherapeutic interventions.
The findings from the feasibility study encouraged us to set up a large trial, which is described in CHAPTER 3. In this single-blind RCT we compared the effects of eight sessions of standard PE, eight sessions of standard EMDR, and waiting list for trauma-focused treatment (WL) in 155 participants with a psychotic disorder and current chronic PTSD that were all receiving treatment as usual for psychosis. Treatment was not preceded by stabilizing psychotherapeutic interventions. Blinded assessors performed baseline, posttreatment, and 6-month follow-up assessments. Both PE and EMDR were found to effectively reduce PTSD symptoms compared to WL (between group Cohen's $d$: PE $v.$ WL = 0.78; EMDR $v.$ WL = 0.65). Participants in the PE condition (56.6%) and in the EMDR condition (60.0%) were significantly more likely to achieve loss of PTSD diagnosis during treatment than those in the WL condition (27.7%). Participants receiving PE (28.3%), but not those in the EMDR condition (16.4%), had greater odds of achieving full remission of PTSD symptoms (Clinician-Administered PTSD Scale score < 20) than those in the WL condition (6.4%). Compared to WL, both PE and EMDR effectively reduced self-reported PTSD symptoms and negative posttraumatic cognitions. All posttreatment effects were maintained at 6-month follow-up. PE and EMDR did not differ significantly on any of the outcomes or in dropout rate (24.5% in PE and 20.0% in EMDR) and there were no differences in severe adverse events between conditions (2 in PE, 1 in EMDR, and 4 in WL). These findings suggest that it may not be justifiable to exclude people with psychotic disorders from standard PE and EMDR therapies, because these treatments appear to be effective, safe and feasible for this patient group.

In CHAPTER 4 we report the secondary outcomes of the RCT described in the previous chapter. Over time (with all the three assessments in the analyses) both PE and EMDR were associated with significant reductions in severity of paranoid ideation compared to WL. For PE this effect was observed both at both posttreatment and 6-month follow-up, for EMDR only at posttreatment. Neither PE nor EMDR significantly influenced auditory verbal hallucinations severity in the individuals that experienced auditory verbal hallucinations at any of the time points. Both PE and EMDR were associated with more patients remitting from schizophrenia than WL at posttreatment. These effects were however not significant at 6-month follow-up and were significant over time only for PE. Participants in the PE, but not in the EMDR condition, showed significant reductions of depression symptoms at post-treatment, 6-month follow-up, and over time compared to those in the WL condition. Neither PE nor EMDR influenced social functioning. These findings appear to suggest that trauma-focused treatments may have positive side effects in patients with psychosis.
In **CHAPTER 5** we explored the influence of trauma-focused treatment on symptom exacerbation, adverse events, and revictimization in people with both psychosis and PTSD within the RCT described in **CHAPTER 3**. In these analyses we compared trauma-focused treatment (PE or EMDR) to WL. Trauma-focused treatment did not cause symptom exacerbation, adverse events, or revictimization. In fact, any form of exacerbation of symptoms occurred in twice as many participants in the WL condition than in the trauma-focused treatment condition. Exacerbation of self-rated PTSD and paranoia symptoms was extremely rare in the trauma-focused treatment condition and showed a trend of occurring more in the WL condition. There were no differences in exacerbation of depression symptoms between the trauma-focused treatment condition and the WL condition. In this sample, PTSD symptom exacerbation in anticipation of the start of trauma-focused treatment was rare (7.1%) and virtually absent after the initiation of trauma-focused treatment (1.1%). In the first two trauma-focused treatment sessions there was no exacerbation of auditory verbal hallucinations, dissociative symptoms, or suicidal ideation. Paranoid ideation decreased significantly during this period. Dropout was not associated with PTSD symptom exacerbation. Compared with the WL condition, fewer participants in the trauma-focused treatment condition reported an adverse event (relative risk reduction = 27.9-34.6%). Participants in the trauma-focused treatment condition experienced half as many adverse incidents compared to those in WL. Participants receiving trauma-focused also appeared to be less likely to be revictimised during follow-up (relative risk reduction = 80.3%). This reduction of revictimization during follow-up was associated with a reduction in PTSD symptoms during treatment. We concluded that conventional trauma-focused treatment protocols appear to be safe in people with psychosis and may even reduce a range of adversities.

In **CHAPTER 6** we tested whether baseline PTSD severity and seven psychosis-specific baseline factors could predict what participants with a psychotic disorder and PTSD would benefit from trauma-focused treatment (with regard to a reduction in PTSD symptoms). We found baseline PTSD symptom severity to predict a small proportion (11.4%) of the variance in posttreatment outcome. More severe PTSD at baseline was however also significantly associated with greater PTSD symptom reduction during treatment. This means that that participants with more severe PTSD symptoms at baseline exhibited greater posttreatment PTSD symptom severity end state, but also showed a slightly greater reduction in PTSD symptoms. Besides the modest predictive value of baseline PTSD severity, we found few associations. After correction for baseline PTSD symptom severity, the model with the seven baseline variables (paranoia, auditory
verbal hallucinations, negative symptoms, suicide risk, the presence of recent adversities, working memory capacity, and chlorpromazine hydrochloride dose equivalents) did not significantly explain variance in posttreatment PTSD outcome. Within this non-significant model, the presence of auditory verbal hallucinations contributed uniquely to variance in posttreatment outcome; however, this factor had limited prognostic value as it explained only 5.4% of the variance of trauma-focused treatment outcome. We found no significant differences in any of the baseline variables between treatment completers and dropouts. The limited predictive utility of baseline psychosis-related factors in our sample adds to the notion that there appears to be no reason to exclude individuals with psychotic disorders from trauma-focused treatments. Also, we speculate that people with more severe baseline PTSD symptoms may primarily benefit from receiving more than eight sessions of trauma-focused treatment.

Little is known about how clinicians’ beliefs about the credibility, burden and harm of trauma-focused treatments can be influenced. In CHAPTER 7 we therefore explored the impact of the different stages of specialised trauma-focused treatment training on these beliefs among the therapists that participated in our RCT. In this feasibility study we assessed credibility, expected burden, and harm expectancies of trauma-focused treatment in 16 therapists that were novices to trauma-focused treatment at baseline. These beliefs were assessed before the start of training, post-theoretical training, post-technical training, post-supervised practical training, and at two-year follow-up. Therapists’ credibility and burden beliefs concerning the treatment of every specific patient that they treated in the trial (n = 79) were also assessed. Specialised trauma-focused treatment training with a subsequent trajectory of technical and supervised practical training was found to result in a significant increase in therapist-rated credibility, and a significant decrease in the expected burden and harm of trauma-focused treatment. These effects were sustained up to two-year follow-up. In treating PTSD in patients with psychotic disorders during the trial, pre-treatment symptom severity was not associated with therapist-rated credibility or expected burden of that specific treatment. Patient-specific credibility and expected burden of trauma-focused treatment did not change during treatment and both were not influenced by treatment outcome. The findings from this feasibility study lend support for the notion that specialised training, including practical training with supervision, has long-term positive effects on therapists’ credibility, burden, and harm beliefs concerning trauma-focused treatment. Future research may prove ongoing consultation after training to be an essential element in reducing therapists’ burden and harm expectancies.
In **CHAPTER 8** the findings that are reported in this thesis are discussed in the light of the scientific literature. General limitations and strengths of the work are discussed and future directions for both research and clinical practice are considered. Although the main findings in this thesis are quite clear and robust, replication by another research group is required before definite conclusions can be drawn. Moreover, there is need for a head-to-head comparison of trauma-focused treatments with and without direct trauma memory exposure. The available evidence does however tentatively suggest that specifically trauma-focused treatments with direct trauma memory exposure are effective in people with a psychotic disorder. In this chapter we also stress the importance of screening for childhood trauma and other negative life experiences in people with psychosis and to include these experiences in conceptualizing and planning treatment. Moreover, it is advocated that we should invest in order to greatly reduce and the duration of untreated PTSD in patients with psychosis. Important challenges concerning the dissemination of empirically supported trauma-focused treatments in mental healthcare services for people with psychotic disorders are discussed.