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Predictors of remission from PTSD symptoms after sexual and non-sexual trauma in the community: A mediated survival-analytic approach

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Abstract

Epidemiological data on the chronicity of posttraumatic stress disorder (PTSD) symptoms in relation to trauma type and underlying pathways are rare. The current study explored how PTSD symptoms change over time across different trauma types and examined mediators of their persistence. A trauma-exposed community sample, whereof approximately one quarter met diagnostic criteria for PTSD, provided retrospective data on the duration of PTSD symptoms. Those who remitted and those who had not at the time of assessment were compared regarding worst trauma, symptom severity, comorbidity, demographic and treatment-seeking variables. Time to remission was estimated using Cox proportional hazard models including candidate predictors of remission. A mediated survival analysis was used to explore indirect pathways that explain trauma-specific differences in remission times. Both the full sample and PTSD subgroup were analyzed separately. Overall, lower socio-economic status, lifetime and childhood sexual trauma, symptom severity, comorbid depression and past treatment were associated with non- and longer remissions. PTSD avoidance symptoms and comorbid depression were found to mediate longer remission times after lifetime or childhood sexual trauma. Our findings provide insight into the mechanisms and complicating factors of remission from PTSD symptoms after trauma, which might have important implications for therapeutic interventions.

Keywords: PTSD symptoms, remission, mediated survival analysis, hazard ratio, sexual and non-sexual trauma, avoidance, comorbid depression.

1. Introduction

Posttraumatic stress disorder (PTSD) is a chronic condition (Steinert et al., 2015); less than 40% of subjects remit from their symptoms without specific treatment within one to five years while the majority of subjects report symptoms for a much longer period (Chapman et al., 2012; Perez Benitez et al., 2012). Results from the National Comorbidity Survey (Kessler et al., 1995) suggest that PTSD is very unlikely to remit if it persists beyond 6 years. Females are at a greater risk than males to suffer from a chronic course of the disorder although the underlying mechanisms are not yet entirely clearly understood (Breslau, 2009; Breslau and Davis, 1992).

A recent meta-analysis indicated variable PTSD trajectories, whereof the nature of the traumatic event was identified as a major predictor of remission (Morina et al., 2014). Evidence from either clinical or epidemiological studies, using prospective or retrospective study designs, suggests that more severe trauma experiences, such as sexual abuse and childhood trauma, can cause more long-term adverse effects and are strong predictors of a chronic course of PTSD (Bremner, 2003; Chapman et al., 2012). In particular, exposure to sexual adversity in the early developmental stages substantially decreased the likelihood of long-term remission from PTSD (Zanarini et al., 2011; Zlotnick et al., 1999). However, the reasons for those associations remain largely unclear.

A possible explanation could be the existence of posttraumatic factors that shape underlying pathways to remission from PTSD. One such factor might be symptom severity. A large body of evidence suggests that individuals with personal exposure to interpersonal and abusive trauma, in particular sexual trauma, experienced a higher number of, more severe and persisting PTSD symptoms than those exposed to other types of trauma (Forbes et al., 2012; Loos et al., 2015; Norris, 1992; Smith et al., 2016). In particular, avoidance symptoms seem to play a critical role in this regard. Indeed, higher avoidance was found to be highly specific for those trauma types (Bal et al., 2003; Glover et al., 2010; Muller et al., 2015b) and was assumed to play an important role in the stability of PTSD (Cone et al., 2015; Davidson et al., 1991; North

and Oliver, 2013; Solomon et al., 2009). Another such posttraumatic factor is the development of a range of other mental health problems that occur with higher incidence after a traumatic event (Breslau, 2009). Thus, a recent meta-analysis has shown that sexual abuse experience more than other trauma types has clear ties to a higher incidence of mood, anxiety or substance use disorders, even independently from PTSD (Dworkin et al., 2017). Interestingly, these conditions were also found to be more likely among individuals with chronic PTSD than among those with faster symptom improvement (Chapman et al., 2012; McFarlane, 2000; Zlotnick et al., 2004; Zlotnick et al., 1999). This raises the question of whether those independent findings might represent specific pathways. In other words, the type of traumatic experience possibly represents a specific condition that affects the chronicity of PTSD symptoms, which, however, might be explained by specific posttraumatic determinants.

Therefore, based on the literature, sexual or childhood adversity and exposure to violence, the presence of avoidance symptoms and posttrauma psychiatric conditions could play a significant role in the persistence of PTSD. However, the mechanisms underlying these associations are not yet clear. Furthermore, most epidemiological studies on long-term effects of trauma exposure have only focused on individuals meeting diagnostic criteria for PTSD (Gradus, 2017), which restricts the view to exclusively severe cases and does not mirror the mechanisms of remission in those with a lower symptom load. Yet, it might be possible that different factors play a role in the remission of PTSD symptoms below the diagnostic level. To our knowledge, no epidemiological study to date has modeled the temporal course of PTSD symptoms along the continuum over the lifetime across a broader spectrum of trauma types. For this reason, we tried to broaden the view of symptom remission towards an unselected community sample of trauma-exposed individuals that have indexed one most upsetting lifetime trauma as well as symptoms of posttraumatic stress. In the current study we implemented a survival analytic approach from a lifetime perspective to determine whether the expected duration of time until PTSD symptom remission was related to a specific type of trauma and to identify factors that contribute to variation in this regard.

Thereby, we assumed that different types of trauma were differently associated with non-remission and we tested whether both the type of PTSD symptoms and comorbid conditions were also likely to be responsible for chronicity of PTSD symptoms. Specifically, this study aimed to: 1) examine the course of PTSD symptoms over the lifetime, 2) explore the relative impact of trauma type on time to remission from PTSD symptoms, and 3) investigate whether PTSD symptom types or posttrauma psychiatric comorbidity were possible mediators in the associations between trauma type and the time a subject needed to recover from the specific trauma experience. We studied these three issues both in a large sample of individuals with a lifetime history of trauma and in a subgroup of subjects diagnosed with PTSD, controlling our analyses for relevant covariates.

2. Methods

2.1. Sample and procedure

All data were collected within the PsyCoLaus study (Preisig et al., 2009), a subsample from the larger CoLaus study (Firmann et al., 2008), a randomly selected population-based cohort study conducted in Lausanne, in the French-speaking part of Switzerland. From 2003 to 2006, a community sample of N=6,734 subjects aged between 35 and 75 years was recruited for the first wave of CoLaus, an epidemiological study designed to assess the prevalence and determinants of cardiovascular risk factors and diseases. Sixty-seven percent of the subjects of the CoLaus study in the age range between 35 and 66 years (n=3720) accepted to participate in the psychiatric exam (PsyCoLaus; see Preisig et al. (2009) for a detailed description).

Twenty-six subjects were excluded due to missing data on the screening item for traumatic exposure, leading to a sample of n=3694 individuals. The study sample was restricted to those participants with a

self-reported history of lifetime trauma (n=783; 21.2%). From those, n=199 (25.4%) participants were further excluded due to missing data on symptom duration.

Accordingly, the final study sample consists of n=584 participants whereof 59.9% were females and the mean age was 50.5 years (SD=8.7). The majority of participants (58.2%) were married, around one quarter (23.6%) were divorced or separated, 14% were single and 22 participants (3.8%) were widowed. More than half of the sample (53.1%) had basic education (i.e. completion of basic schooling until the age of 16), 24.8% had higher education (i.e. completion of a school in which a certified profession was taught), and 20.4% had a university degree or equivalent. Ten participants (1.7%) reported that they had not completed compulsory school (i.e. they had left school before the age of 16). Socio-economic status (SES) was assessed according to the Hollingshead's index (Hollingshead, 1975). The mean SES was 3.3 (SD=1.3), indicating a middle class status on average. For more details on these sample characteristics please refer to Table 1a. A subgroup of individuals with PTSD (n=147; 25.17%) was selected for separate analyses. Sample characteristics for this subgroup are summarized in Table 1b.

The study was approved by the Ethics Committee of the Lausanne University. All participants provided written consent after being informed of the goal and funding of the study.

2.2. Measures

The data of the PsyCoLaus study were derived from the French version (Leboyer et al., 1995) of the semi-structured Diagnostic Interview for Genetic Studies (DIGS) (Nurnberger et al., 1994). In addition to demographic features, the DIGS comprises information on a broad spectrum of DSM-IV Axis I disorders as well as on some Axis II criteria and suicide behavior (Preisig et al., 2009). The PTSD and generalized anxiety disorders sections of the DIGS were based on the relevant sections of the French version of the Schedule for Affective Disorders and Schizophrenia – Lifetime and Anxiety disorder version (SADS-LA) (Endicott and Spitzer, 1978). The French version of the DIGS as well as the anxiety sections of the SADS-LA revealed

excellent inter-rater and fair to good test-retest reliability for major mood (Preisig et al., 1999), substance use (Berney et al., 2002) and anxiety disorders (Leboyer et al., 1991). The test-retest reliability for the PTSD diagnosis was estimated at Yule=0.69 from a sample of 176 psychiatric patients (Perrin et al., 2014).

Lifetime exposure to potentially traumatizing events was assessed using the question “Have you ever been exposed to any of the events from the following categories?”: 1.) accident, 2.) physical assault, 3.) combat and/or war, 4.) witness of murder, violence or death by an accident, and 5.) sexual trauma, defined as the experience of an event that a person judged as sexual and to which he/she did not consent, such as exhibitionism, being touched, threatened or raped. All trauma categories were binary coded as 1 “exposed” versus 0 “not exposed”. In the test-retest reliability study, only the events that were reported before the baseline assessment were analyzed, therefore excluding new events that occurred during the follow-up period. The three-year test-retest reliability coefficients in terms of Yule's Y for exposure to violent crime and sexual trauma in the sample of 176 adult psychiatric patients were as high as 0.84 and 0.57, respectively, although those for exposure to accidents and witnessing trauma to others were only 0.30 and 0.22, respectively (Perrin et al., 2014). The test-retest reliability for exposure to war could not be tested in this sample given its rareness (Perrin et al., 2014). For the current study, in case of more than one trauma exposure, the most upsetting event, as specified by the participant, was indexed. Trauma types, based on the worst event, were defined over lifetime. Finally, the recalled age of first exposure to the worst event was documented. Based on this information exposure, below the age of 16, to a worst event from categories 1 through 4 was additionally coded as “childhood non-sexual trauma”, from category 5 as “childhood sexual trauma, and then as “childhood trauma” in general, respectively.

In the current study, we used a symptom-based definition of remission, i.e. remission from PTSD symptoms was determined as the retrospectively reported end of duration of previously existing symptoms, irrespective of the number and severity of symptoms. Accordingly, time to remission was defined as the estimated duration of symptoms (in years) from the age of the worst event. Subjects either reported ongoing symptoms at the time of the interview or symptom offset in the past. Hence, if a participant

reported a symptom offset in the past he or she was designated as remitted. In contrast, in those respondents who reported ongoing symptoms at the time of survey, the data were censored for the models.

The following conditions were considered to be posttrauma comorbid disorders when an individual met DSM-IV definitions after the age of worst trauma exposure: (1) alcohol use disorders (AUD) (abuse or dependence), (2) other substance use disorders (SUD) (abuse or dependence) except nicotine use, (3) major depression, and (4) anxiety disorders including generalized anxiety disorder, panic disorder, agoraphobia and social phobia. Other conditions were not considered due to their low prevalence.

Participant covariates included sex, age, education, marital status, socio-economic status and treatment-related variables since these variables might have an impact on remission from PTSD symptoms. Treatment was assessed by asking the participants whether they had ever received professional treatment for mental health problems, and whether they had ever used psychotropic medication for mental health problems such as anxiolytics, antidepressants, antipsychotics, or others.

2.3. Statistical analyses

Bivariate comparisons were made between those who did and those who did not remit from PTSD symptoms regarding socio-demography, worst trauma type, multiple traumatizations, delayed symptom onset, posttrauma comorbidity, as well as retrospectively reported PTSD symptom type severity using Chi-Square tests for categorical variables and t-tests for continuous variables. Hazard ratios (HR) and 95% confidence intervals (95%CI) were calculated. Those variables that were at least marginally ($p<.25$) linked to remission were selected as candidate predictors for subsequent Cox proportional hazard models to estimate their raw impact on time to remission. Following the recommendations for a minimum number of events per variable (EPV), those candidates with fewer than 10 cases in one of their two categories were

excluded from further modeling in order to avoid an unstable selection and model overfitting (Peduzzi et al., 1995).

Candidate predictors from bivariate Cox regression models were selected for further multivariate and path modeling. Comorbid conditions and PTSD symptom clusters that were significantly correlated with trauma type predictors according to Pearson Product-Moment correlations or Cohen's Phi correlations, respectively, qualified as potential mediators.

In the next step, we focused on PTSD symptom clusters and comorbidity as potential mediators between relevant trauma types and time to remission. For this purpose, for each selected trauma type a separate Cox proportional hazard model (baseline model) was fitted and adjusted for selected covariates except the potential mediator variables. Then, baseline models were extended into path models, i.e. including mediator variables and containing time to remission as the discrete-time survival part as the outcome. Indirect effects for mediated paths were estimated using the product-of-coefficients approach, whilst total indirect effects were obtained by the sum of indirect effects and overall total effects were obtained by the sum of all indirect and total effects (Preacher and Hayes, 2008). When a PTSD cluster was uncorrelated with a type of trauma but associated to remission time no indirect path was considered; but this variable was kept in the model as a covariate only. By comparing full against baseline models, absolute (differences in HR) and relative changes (in %) were provided. HRs and 95%CIs were calculated for direct, indirect, sum of specific indirect and for total effects.

Descriptive statistics were conducted using STATA/SE v12 (StataCorp, 2011) and Cox proportional hazard models were calculated using MPlus (Muthen and Muthen, 1998-2011).

3. Results

The most frequently experienced most upsetting trauma type was witnessing murder, violence or death, followed by accidents and sexual trauma (Table 1a). About one third experienced their worst trauma before the age of 16, whereof non-sexual experiences were reported twice as often as sexual ones. Eighteen percent were exposed to more than one trauma type during their lives. Almost all subjects endorsed at least one posttraumatic stress symptom (94.01%), and one quarter met diagnostic criteria for full PTSD. Less than seven percent reported a PTSD symptom onset more than six months after exposure. Posttrauma comorbid conditions included depression, anxiety disorders, AUD and SUD in descending order of their prevalence. About 6 out of ten participants had received treatment for mental health problems over their lifetime, and about half had used psychotropic medication over their lifetime.

-Table 1a-

In the PTSD subgroup, witnessing trauma as well as sexual trauma were almost equally the most prevalent trauma types, followed by crime and accidents (Table 1b). More than one third experienced trauma before the age of 16 with a preponderance of sexual trauma. One quarter were exposed to multiple trauma types during their lives and less than five percent reported a delayed symptom onset that began six months or more after the time of exposure. Comorbid conditions were twice as prevalent as in the total sample. Three quarters of PTSD cases had received treatment for mental health problems over their lifetime and about two thirds had used psychotropic medication over their lifetime.

-Table 1b-

More than 70% of the total study sample (70.89%; n=414) reported remission from their PTSD symptoms within a median time of 0.31 years (interquartile range: 0.06-1.99 years) and a mean duration of 3.27 years (SD=6.93 years) (Figure 1a). Remission compared to non-remission was significantly associated with male gender, higher SES, lower lifetime prevalence of sexual trauma, any childhood trauma or childhood sexual trauma, less frequent AUD, SUD, depression, and anxiety disorders, less previous mental health treatment, lower use of psychotropic drugs for mental health problems, lower PTSD symptom load, particularly avoidance symptoms, as well as not having a fully expressed PTSD (Table 1a). Moreover, higher witnessing of trauma and less frequent delayed symptom onset were marginally ($p<.25$) linked to remission.

In those who remitted, Cox proportional hazards models were calculated for all these candidate predictors with sufficient EPV (see Methods section). Accordingly, this set of variables contributed significantly to a delayed time until PTSD symptom remission, except for SES and witnessing violence that were associated with a shorter remission time (Table 1a).

-Figure 1a -

In the subgroup of PTSD cases, about 55% (55.10%; n=81) reported a remission of their PTSD symptoms within a median time of 2.99 years (interquartile range: 0.50-9.97 years) and a mean duration of 5.91 years (SD=7.23 years) (Figure 1b). Higher SES, less frequent comorbid AUD, depression and anxiety disorders, less previous mental health treatment, and lower PTSD symptom load were significantly linked to symptom remission (Table 1b). Higher education, more frequent experience of criminal assault, less frequent experience of war and combat, less frequent overall or childhood sexual trauma as well as more frequent delayed symptom onset, and less comorbid SUD were marginally linked to remission.

In bi-variate Cox proportional hazard models all selected candidate predictors with sufficient EPV contributed significantly or marginally (Crime) to time until PTSD symptom remission. Education, SES and crime were associated to a faster remission time while sexual trauma (lifetime and childhood), comorbid depression, treatment for mental health problems and PTSD symptoms were associated with a delayed remission time (Table 1b).

-Figure 1b -

Correlations between relevant trauma types and PTSD symptom severity or posttrauma depression (i.e. all those variables that contributed at least marginally to the duration of PTSD symptom remission), are presented for the total sample (Table 2a) as well as for PTSD cases (Table 2b). Accordingly, in the total sample, lifetime and childhood sexual trauma were associated with all three PTSD symptom clusters while overall childhood trauma was linked to avoidance symptoms only. Overall and childhood sexual trauma and childhood trauma were also linked to posttrauma depression. In contrast, witnessing violence was negatively linked to hyperarousal symptoms and posttrauma depression (Table 2a). Among PTSD cases, overall and childhood sexual trauma were linked to avoidance and hyperarousal symptoms as well as posttrauma depression, whereas crime was unrelated to posttrauma factors (Table 2b).

-Tables 2a & 2b-

The results of the Cox proportional hazard models for examining the effects of trauma (before and after inclusion of posttraumatic factors) on time to remission are displayed for the total sample in Table 3a as

well as for the PTSD subsample in Table 3b. The full and subsample baseline models revealed significant negative associations between childhood or lifetime sexual trauma and time to remission. In addition, in the full sample, childhood trauma was negatively and witnessing violence positively linked to remission time. In the full models, i.e. after adjusting for posttraumatic factors, childhood or lifetime sexual trauma as well as childhood trauma (in the full sample only) revealed a loss of significance (and strength) in their relationships to time to remission compared to their baseline models. The size of change in direct effects of those trauma types indicate that posttraumatic factors have an additional effect on remission time. Indeed, the inspection of indirect paths suggested that, in the full sample, avoidance symptoms and comorbid depression mediated the trauma-remission time association, whereas in the PTSD subgroup comorbid depression emerged as a specific mediator in this association.

-Table 3a-

-Table 3b-

4. Discussion

In the current study, we explored the impact of worst-event trauma, PTSD symptom types and posttrauma comorbid conditions on time to remission from PTSD symptoms in a community sample of individuals with a lifetime history of trauma exposure as well as within a more focused subgroup of individuals diagnosed with PTSD. We used survival and path analytic techniques to explore whether worst-event trauma type was associated with varying PTSD symptom remission times, and whether symptom type severity and comorbid conditions were determining factors within these pathways.

Our study findings revealed that individuals diagnosed with PTSD have lower remission rates and were also slower to remit from their symptoms than the average of all individuals with lifetime trauma. The average remission time was almost twice as long when diagnosed with PTSD compared to the full sample,

and it took about 12-times as long for half of the sample to be free of symptoms. In the full and subsample, those with lifetime and/or childhood sexual trauma were less likely to remit from their symptoms and achieved remission more slowly than others, during which avoidance symptoms and posttrauma depression were identified as important mediators that contributed to a delayed remission time.

In general, our findings suggest that symptoms of posttraumatic stress are a common and normal reaction after exposure to significant trauma (Rothbaum and Davis, 2003). They further suggest that the majority of subjects often recovered within a short time period and that only a small proportion manifested their symptoms as a chronic condition. Indeed, only approximately one third of our full sample failed to remit from their symptoms before the time of the survey, which is very consistent with a range of epidemiological studies on individuals with PTSD (Breslau et al., 1998; Chapman et al., 2012; Gospodarevskaya, 2013; Kessler et al., 1995). However, our sample also included subjects with very low symptom levels. Therefore, it is not surprising that we found substantially lower projected median remission times than those reported in other studies (e.g. (Breslau, 2001; Kessler et al., 1995; McLaughlin et al., 2011)). Our subgroup analyses on individuals with PTSD revealed lower remission rates as well as a longer duration among those who remitted, implying that individuals with higher symptom severity in fact have a slower remission than those with lower severity. Although this has been well-confirmed in previous studies (Breslau and Davis, 1992; Chapman et al., 2012), this might also be the result of a thinning effect, i.e. when those with lower symptom severity remit earlier; the average symptom severity automatically increases over time among those who remain.

Although there was no formal focus on gender differences, our findings indicate that females generally remitted more slowly from their symptoms; this effect, however, was not observed in the PTSD subsample. This supports the results of previous research suggesting that both men and women do not differ in their recovery time from PTSD (Hu et al., 2015). Nevertheless, it raises the question as to why this effect disappeared among subjects with higher levels of posttraumatic stress in our sample, which clearly

deserves attention in future research. In fact, there is epidemiological evidence that males and females differ significantly in type and frequency of trauma exposure as well as prevalence and extent of posttraumatic psychopathology, in particular of PTSD but, however, evidence as well as research in general on gender-specific recovery processes is very limited (Blain et al., 2010).

Moreover, we found past treatment to be associated with non- or delayed remission, which, however, turned out to be non-significant in multivariate models when measures of symptom types and/or comorbidity were added (estimates of covariates were not tabulated). It is possible that treatment or help-seeking is simply another indicator of illness severity in those with a chronic symptom course (Maercker et al., 2013; Perkonigg et al., 2005; Sripada et al., 2015), which, however, becomes redundant when other measures of severity come into play. Actually, in a previous report from this study we found mental health service utilization to be linked to higher illness severity; an effect that was attenuated or even reversed after controlling for comorbidity (Muller et al., 2015a). On the other hand, especially in the case of sexual abuse, it is possible that health care providers are not aware of or have misunderstood the effect of the traumatic experience and it therefore remains untreated (Rosenberg et al., 2001), which, in the worst case, might lead to symptom exacerbation and finally to delayed recovery.

Our findings suggest that the type of traumatic experience was one of the strongest predictors of symptom remission. Thus, those who experienced any childhood and/or sexual trauma were less likely to remit from their symptoms and had delayed estimated remission times than those who experienced other types of trauma (Gospodarevskaya, 2013; Zlotnick et al., 1999). This is very consistent with earlier findings suggesting that the sequelae of early and abusive traumas in particular promote a chronic course of PTSD (Chapman et al., 2012). Another explanation might be that specific factors that delay recovery from PTSD symptoms specifically exist in individuals exposed to sexual trauma. According to this, we explored whether remission from PTSD symptoms was affected by either the types of symptoms themselves or by comorbid mental health problems. Indeed, we found comorbid depression and symptom types to be

bivariately linked to delayed remission times, which reflects earlier findings that especially mood, alcohol use and anxiety disorders are linked to PTSD chronicity (Breslau and Davis, 1992; Chapman et al., 2012; Chiba et al., 2016), and that a more severe illness has a longer recovery time (Chapman et al., 2012). Moreover, correlational analyses confirmed that both PTSD symptom types and comorbidity varied highly across trauma types. On the one hand, we found a link between the PTSD symptom type, especially avoidance symptoms, and lifetime and childhood sexual trauma, which is in line with an earlier report from this study (Muller et al., 2015b). This finding also received support in other research suggesting that avoidance symptoms are more frequently reported after chronic and abusive trauma (Fletcher, 2003; Polusny and Follette, 1995), and sexual abuse in particular (Bal et al., 2003; Silva et al., 1997), which points to their severity. On the other hand, we specifically found early and sexual trauma to be linked to depressive disorders, which is also known from the literature (Chiba et al., 2016; Vitriol et al., 2017).

Finally, we were interested in whether those associations might be parts of distinct and more complex pathways that are typical of illness course after specific traumatic experience. Indeed, path models suggest that symptom types mediated the relationship between (childhood) sexual trauma and the observed longer remission time from PTSD symptoms, whereof avoidance most specifically contributed to this association. As already known from previous research, avoidance symptoms might constitute a specific pathway for the manifestation of chronic PTSD (Davidson et al., 1991; North and Oliver, 2013; Perkonigg et al., 2005). The current study was able to show that avoidance symptoms, unlike other PTSD symptoms, particularly after sexual trauma, increase time to PTSD symptom remission. This assembles the fragmentary knowledge from previous research. Those, who were sexually traumatized, are more likely to avoid exposure to experience that may correct negative perceptions and beliefs, which persistently prevents recovery, while lower avoidance promotes remission (Foa et al., 2006; Larsen and Berenbaum, 2014). Therefore, avoidance, unlike other PTSD symptoms, rather tends to increase over time and is linked to overall symptom exacerbation (Karamustafalioglu et al., 2006; North and Oliver, 2013).

Moreover, path models further suggest that symptom remission after sexual trauma was further negatively affected (mediated) by depression that developed after the trauma. Thus, especially those with lifetime or childhood sexual trauma had a delayed remission from PTSD symptoms due to the higher prevalence of depression with onset after the trauma. This is in line with a recent study finding that the co-occurrence of PTSD and depression (Chiba et al., 2016; Rytwinski et al., 2013) was higher in those exposed to type II trauma, such as sexual abuse and childhood trauma, and required a longer duration of treatment. According to other research, childhood sexual abuse in particular was found to increase the risk for depression, which, due to a shared risk factor profile with PTSD, increases the likelihood of comorbid PTSD (Spinhoven et al., 2014). Moreover, the co-occurrence of PTSD and depression in particular, seems to promote a rather unfavorable symptom course. Thus, depressive symptoms often diminish social engagement, which is an important source of recovery from PTSD, and they hinder reappraisal of the traumatic experience due to the augmented negative cognitions that are frequently observed in depression (Priebe et al., 2013). In contrast, AUD and/or SUD did not affect the symptom remission time after traumatic experiences in our study - a finding that was somewhat surprising but may be an artifact of the small number of individuals with AUD/SUD in our sample. The specific role of any AUD or SUD in relation to sexual abuse and PTSD severity has been discussed in the literature (Cusack et al., 2013; Ullman et al., 2013), but requires further empirical evidence for the understanding of their complex interplay using larger samples.

This study has some limitations that have to be acknowledged when interpreting our findings. Most importantly, the reliance on retrospective reports is a potential limitation as recall bias cannot be excluded. Based on theoretical considerations, we selected factors that might be the cause of delayed remission times and were therefore not able to identify real causal effects. Then, individuals were asked to recall their ages of symptom onset and offset at any point during their lives. Thus, we cannot rule out that those subjects that reported PTSD symptoms far in the past might have under-estimated the duration of their

symptoms and therefore reported a shorter remission time. In contrast, those subjects with more recent symptoms of PTSD may have reported a longer duration, or they may have reported remission while symptoms still reappeared after the interview (i.e. we do not know if they were completely remitted or not). The study of time to remission is an important component of clinical epidemiology. Although prospective study designs are methodologically more appropriate and conceptually understandable, they are expensive to carry out – in particular across the lifetime - and it is difficult to obtain a representative sample from the general population. In contrast, retrospective studies in representative samples provide an economical opportunity to investigate broad population patterns, even if they cannot establish causation and only associations. Therefore, our findings have to be interpreted with caution and require replication in prospectively followed cohort studies. Then, a further weakness of our study was that our assessments did not include information on treatment specifically for PTSD or trauma. However, although treatment was assessed very broadly, this finding at least suggests that the majority of individuals with trauma experiences did not receive treatment that was effective enough to affect or to accelerate the recovery process. Furthermore, our symptom-based definition of remission makes our findings hardly comparable to other study findings. However, results from the National Epidemiologic Survey on Alcohol and Related Conditions suggest that subthreshold PTSD may similarly take a chronic course, which stresses the importance of viewing PTSD along a continuum (Pietrzak et al., 2011). Thus, the inclusion of individuals with subthreshold symptom levels allows to gain insight into the mechanisms that might promote remission from symptoms even below the level of clinical relevance. Then, another limitation is that we did not evaluate whether new traumatic events occurred after the worst event and whether they influenced the recovery process from PTSD symptoms. Especially those exposed to sexual victimization are at a higher risk of new victimization, which might have influenced the time (delay) to recovery from PTSD symptoms. Finally, we did not assess whether pre-existing mental health problems may have had an impact on the remission of PTSD symptoms, i.e. either due to the accumulating effect of mental health problems, which may have led to delayed remission time, or, the other way around, that other mental

health problems may have led to a faster remission due to ongoing treatment for these health problems and therefore a faster access to health care after severe traumatization. However, at least one study provided evidence that primary disorders, i.e. before the onset of PTSD, were not linked to an alteration in the likelihood and duration of remission from PTSD (Chapman et al., 2012).

Despite these limitations, for the first time, the current study provides data on the chronicity of PTSD symptoms after various types of exposure to traumas and the underlying mechanisms for non-remission. In particular, our study design extends the scope from a selected population of individuals with PTSD towards the broader population of individuals with traumatic experiences, including those with low symptom loads, which largely increases the generalizability of our findings. Our findings suggest that both symptom type and comorbid conditions are important (complicating) factors for recovery from posttraumatic stress, particularly after highly traumatic and stressful experiences, such as sexual trauma, even below the level of clinical relevance. The avoidance of trauma-related thoughts and comorbid depression are more common among individuals with (early) sexual adversity (Briere and Elliott, 1994) and were linked to a greater risk of failure or delay to recover from PTSD symptoms (North and Oliver, 2013). This might have important implications for therapeutic interventions. On the one hand, greater avoidance might hamper an adequate processing of or "working through" the traumatic event (Larsen and Berenbaum, 2014) and depression comorbid with PTSD, despite a considerable overlap in symptoms, on the other hand, increases clinical complexity and disability due to higher overall distress and impairment as additional therapeutic targets (Green et al., 2006; Nijdam et al., 2013; Ronconi et al., 2015). Therefore, clinically, our findings strongly suggest that among those presenting with a history of (early) sexual trauma, assessment of PTSD, but also of other conditions is essential. By recognizing specific factors (symptoms, comorbidity), therapeutic interventions can specifically target those factors that have an unfavorable effect on recovery in order to minimize the risk of chronification of mental health problems. Early and effective intervention for those with chronic PTSD might help, not only to decrease subjective

psychological distress, but also to reduce societal burden by reducing health care and other costs that are related to PTSD (Atwoli et al., 2013; Ferry et al., 2014).

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Conflict of interest

All authors declare that they have no conflicts of interest.

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Table 1a. Bi-variate associations of sociodemographic and clinical variables with status of PTSD symptom remission in the full sample and Cox proportional hazard models among those who remitted

						Cox proportional hazard model	
		Total N=584	No PTSD symptom remission N=170	PTSD symptom remission N=414	p-value	Unadjusted HR (95%CI)	p-value
		N (%)/M±SD	N (%)	N (%)			
	Gender female	350 (59.93)	118 (69.41)	232 (56.04)	**0.003**	0.59 (0.49,0.72)	<**0.001**
	Age	50.46±8.71	50.08±9.18	50.62±8.52	0.497	-	-
Civil status	Single	84 (14.38)	26 (15.29)	58 (14.01)	0.719	-	-
	Married	340 (58.22)	103 (60.59)	237 (57.25)		-	-
	Divorced/separated	138 (23.63)	35 (20.59)	103 (24.88)		-	-
	Widowed	22 (3.77)	6 (3.53)	16 (3.86)		-	-
Education	Compulsory school not completed	10 (1.71)	5 (2.94)	5 (1.21)	0.382	-	-
	Obligatory schooling or apprenticeship	310 (53.08)	92 (54.12)	199 (52.66)		-	-
	Professional school or technical higher education	145 (24.83)	43 (25.29)	95 (24.64)		-	-
	University-level education	119 (20.38)	30 (17.65)	78 (21.50)		-	-
	SES	3.30±1.31	3.12±1.27	3.37±1.32	**0.035**	1.10 (1.03,1.18)	**0.007**
Worst trauma	Accident (vs. other)	126 (21.58)	38 (22.35)	88 (21.26)	0.770	-	-
	Crime (vs. other)	100 (17.12)	25 (14.71)	75 (18.12)	0.320	-	-
	War (vs. other)	39 (6.68)	10 (5.88)	29 (7.00)	0.622	-	-
	Witnessing violence (vs. other)	230 (39.38)	59 (34.71)	171 (41.30)	**0.138**	1.37 (1.12,1.66)	**0.002**
	Sexual trauma (vs. other)	88 (15.07)	38 (22.35)	50 (12.08)	**0.002**	0.48 (0.37,0.61)	<**0.001**
	Childhood trauma (vs. adulthood trauma)	195 (33.39)	68 (40.00)	127 (30.68)	**0.030**	0.58 (0.47,0.71)	<**0.001**
	Childhood sexual trauma (vs. not)	65 (11.13)	26 (15.29)	39 (9.42)	**0.040**	0.53 (0.40,0.70)	<**0.001**
	Childhood non-sexual	130 (22.26)	42 (24.71)	88 (21.26)	0.363	-	-

	trauma (vs. not)						
Multiple victimizations - yes		103 (17.64)	32 (18.82)	71 (17.15)	0.630	-	-
Delayed symptom onset (later than 6 months posttrauma)		36 (6.56)	16 (9.47)	20 (5.26)	**0.066**	0.55 (0.38,0.81)	**0.002**
Post-trauma comorbid conditions	Alcohol use disorders	25 (4.30)	22 (12.94)	3 (0.73)	**<0.001[a]**	-	-
	Other substance use disorders	7 (1.21)	6 (3.59)	1 (0.24)	**0.001[a]**	-	-
	Depression	79 (13.55)	61 (35.88)	18 (4.36)	**<0.001**	0.13 (0.09,0.20)	**<0.001**
	Anxiety disorders	36 (6.16)	28 (16.47)	8 (1.93)	**<0.001[a]**	-	-
Past treatment	Treatment for mental health problems	343 (58.73)	113 (66.47)	230 (55.56)	**0.015**	0.69 (0.57,0.83)	**<0.001**
	Use of psychotropic medication for mental health problems	290 (49.66)	100 (58.82)	190 (45.89)	**0.005**	0.65 (0.54,0.79)	**<0.001**
PTSD symptoms	Re-experience	2.31±1.60	2.92±1.63	2.06±1.52	**<0.001**	0.78 (0.73,0.83)	**<0.001**
	Avoidance	2.19±2.03	3.05±2.27	1.84±1.82	**<0.001**	0.79 (0.75,0.84)	**<0.001**
	Hyperarousal	1.64±1.55	2.09±1.66	1.45±1.46	**<0.001**	0.82 (0.77,0.87)	**<0.001**
PTSD diagnosis		147 (25.17)	66 (38.82)	81 (19.57)	**<0.001**	0.47 (0.38,0.58)	**<0.001**

Note: SES = Socio-economic status by Hollingshead Index; PTSD = Posttraumatic stress disorder; HR = Hazard ratio; 95%CI = 95% confidence interval; a Variables not included in Cox proportional hazard models due to low numbers of events (cf. for EPV in Methods)

Table 1b. Bi-variate associations of sociodemographic and clinical variables with status of PTSD symptom remission in PTSD cases and Cox proportional hazard models among those who remitted

						Cox proportional hazard model	
		Total N=147	No PTSD symptom remission N=66	PTSD symptom remission N=81	p-value	Unadjusted HR (95%CI)	p-value
		N (%)/M±SD	N (%)	N (%)			
	Gender female	105 (71.43)	49 (74.24)	56 (69.14)	0.495	-	-
	Age	50.71±8.72	49.88±9.25	51.39±8.26	0.300	-	-
Civil status	Single	18 (12.24)	8 (12.12)	10 (12.35)	0.730	-	-
	Married	77 (52.38)	35 (53.03)	42 (51.85)		-	-
	Divorced/separated	44 (29.93)	18 (27.27)	26 (32.10)		-	-
	Widowed	8 (5.44)	5 (7.58)	3 (3.70)		-	-
Education	Compulsory school not completed	7 (4.76)	4 (6.06)	3 (3.70)	**0.081**	1.43 (1.11,183)	**0.005**
	Obligatory schooling or apprenticeship	80 (54.42)	41 (62.12)	39 (48.15)			
	Professional school or technical higher education	34 (23.13)	15 (22.73)	19 (23.46)			
	University-level education	26 (17.69)	6 (9.09)	20 (24.69)			
	SES	3.03±1.36	2.77±1.20	3.25±1.45	**0.035**	1.20 (1.02,1.42)	**0.030**
Worst trauma	Accident (vs. other)	21 (14.29)	9 (13.64)	12 (14.81)	0.839	-	-
	Crime (vs. other)	29 (19.73)	9 (13.64)	20 (24.69)	**0.094**	1.45 (0.93,2.27)	**0.103**
	War (vs. other)	5 (3.40)	6 (6.06)	1 (1.23)	**0.108**[a]	-	-
	Witnessing violence (vs. other)	47 (31.97)	19 (28.79)	28 (34.57)	0.455	-	-
	Sexual trauma (vs. other)	45 (30.61)	25 (37.88)	20 (24.69)	**0.084**	0.48 (0.30,0.77)	**0.002**
	Childhood trauma (vs. adulthood trauma)	55 (37.41)	27 (40.91)	28 (34.57)	0.429	-	-
	Childhood sexual trauma (vs. not)	32 (21.77)	18 (27.27)	14 (17.28)	**0.144**	0.51 (0.30,0.86)	**0.012**

	Childhood non-sexual trauma (vs. not)	23 (15.65)	9 (13.64)	14 (17.28)	0.545	-	-
Multiple victimizations - yes		37 (25.17)	17 (25.76)	20 (24.69)	0.883	-	-
Delayed symptom onset (later than 6 months posttrauma)		7 (4.79)	1 (1.54)	6 (7.41)	**0.099[a]**	-	-
Post-trauma comorbid conditions	Alcohol use disorders	14 (9.59)	13 (19.70)	1 (1.25)	**<0.001[a]**	-	-
	Other substance use disorders	4 (2.74)	3 (4.62)	1 (1.23)	**0.214[a]**	-	-
	Depression	36 (24.66)	26 (39.39)	10 (12.50)	**<0.001**	0.24 (0.13,0.42)	**<0.001**
	Anxiety disorders	18 (12.24)	14 (21.21)	4 (4.94)	**0.003[a]**	-	-
Past treatment	Treatment for mental health problems	110 (74.83)	56 (84.85)	54 (66.67)	**0.012**	0.51 (0.32,0.80)	**0.003**
	Use of psychotropic medication for mental health problems	100 (68.03)	48 (72.73)	52 (64.20)	0.270	-	-
PTSD symptoms	Re-experience	3.65±1.31	4.06±1.14	3.32±1.35	**<0.001**	0.76 (0.66,0.87)	**<0.001**
	Avoidance	4.71±1.39	5.14±1.42	4.36±1.26	**<0.001**	0.73 (0.62,0.86)	**<0.001**
	Hyperarousal	3.26±1.09	3.48±1.13	3.07±1.03	**0.023**	0.72 (0.59,0.89)	**0.002**

Note: SES = Socio-economic status by Hollingshead Index; PTSD = Posttraumatic stress disorder; HR = Hazard ratio; 95%CI = 95% confidence interval; a Variables not included in Cox proportional hazard models due to low numbers of events (cf. for EPV in Methods)

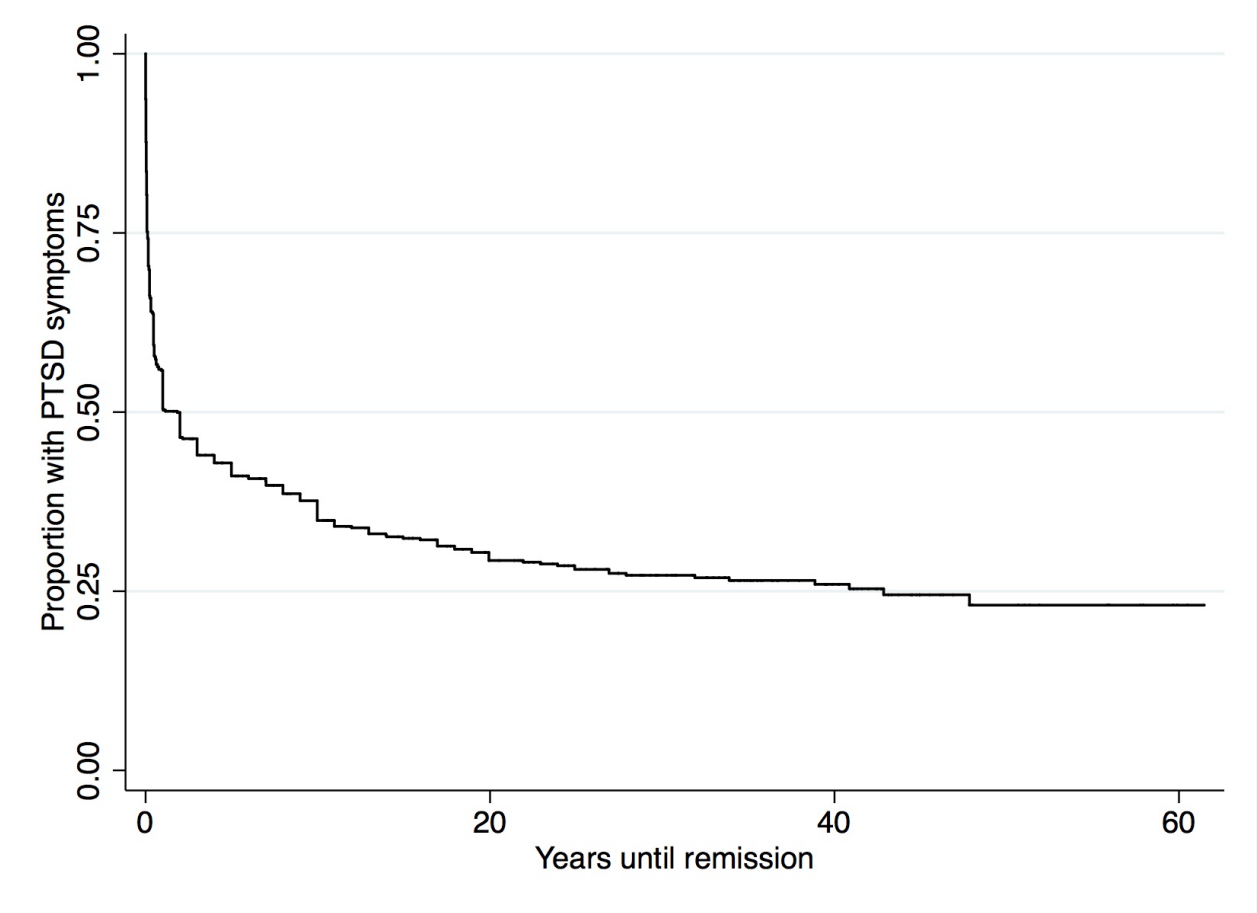

Figure 1a. Survival curve indicating years from age of exposure to worst event until remission from PTSD symptoms in a trauma-exposed population

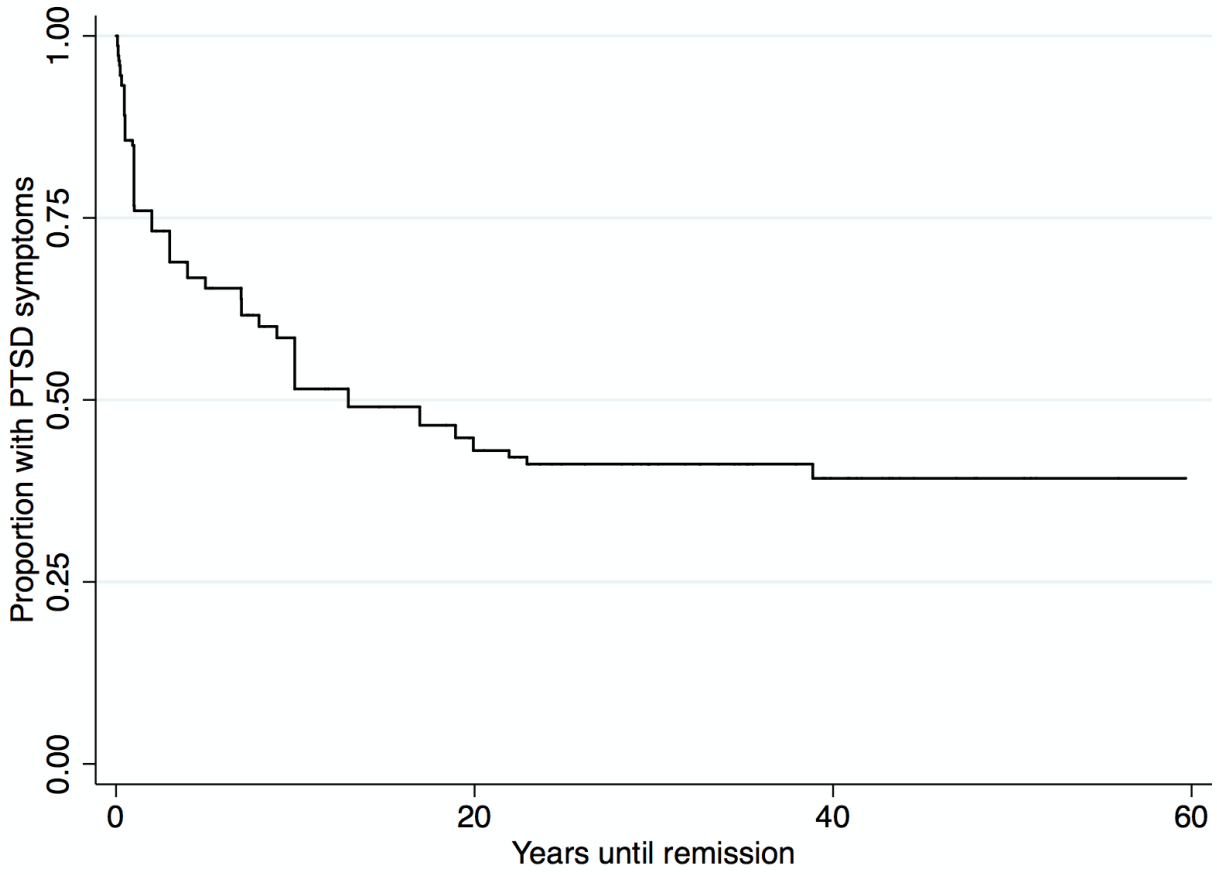

Figure 1b. Survival curve indicating years from age of exposure to worst event until remission from PTSD symptoms in PTSD cases

Table 2a. Bivariate associations of predictor and mediator candidates for Cox regression modeling in the full sample (N=584)

	Witnessing violence	Sexual trauma	Childhood trauma	Childhood sexual trauma
Re-experience symptoms	-0.05	0.14**	0.04	0.11**
Avoidance symptoms	-0.07	0.33***	0.11**	0.29***
Hyperarousal symptoms	-0.12**	0.24***	0.04	0.19***
Posttrauma depression	-0.12**	0.26***	0.20***	0.20***

Note: *** p<0.001; ** p<0.01

Table 2b. Bivariate associations of predictor and mediator candidates for Cox regression modeling in PTSD cases (N=147)

	Crime exposure	Sexual trauma	Childhood sexual trauma
Re-experience symptoms	-0.12	0.03	0.06
Avoidance symptoms	-0.11	0.25**	0.25**
Hyperarousal symptoms	-0.01	0.21*	0.19*
Posttrauma depression	-0.09	0.28***	0.25**

Note: *** p<0.001; ** p<0.01; * p<0.05

Table 3a. Results of the baseline and mediated models for time to remission by trauma type in the full sample

Trauma type	Baseline model	Full model adjusted for posttraumatic factors			
	Direct effect on time to remission HR (95% CI)	Direct effect on time to remission HR (95% CI)	Change against baseline model Absolute in HR (relative in %)	Indirect effects on time to remission HR (95% CI)	Total effect on time to remission HR (95% CI)
Witnessing violence	1.27 (1.03,1.58)*	1.25 (1.00,1.56)*	-0.02 (-2%)	Via hyperarousal: 0.99 (0.96,1.03) Via depression: 1.19 (1.07,1.32)** Total: 1.18 (1.05,1.32)**	1.47 (1.14,1.90)**
Sexual trauma	0.54 (0.42,0.71)***	0.83 (0.64,1.09)	0.29 (54%)	Via reexperience: 0.95 (0.90,1.01) Via avoidance: 0.76 (0.66,0.88)*** Via hyperarousal: 1.02 (0.93,1.10) Via depression: 0.64 (0.52,0.80)*** Total: 0.47 (0.36,0.62)***	0.39 (0.28,0.55)***
Childhood trauma	0.63 (0.51,0.79)***	0.72 (0.57,0.91)**	0.09 (14%)	Via avoidance: 0.94 (0.88,<1.00)* Via depression: 0.76 (0.66,0.87)*** Total: 0.71 (0.61,0.84)***	0.51 (0.39,0.68)***
Childhood sexual trauma	0.62 (0.47,0.82)**	0.89 (0.67,1.19)	0.27 (44%)	Via reexperience: 0.96 (0.90,1.01) Via avoidance: 0.75 (0.65,0.88)*** Via Hyperarousal: 1.01 (0.94,1.10) Via depression: 0.68 (0.53,0.86)** Total: 0.49 (0.37,0.66)***	0.44 (0.30,0.64)***

Note: All models adjusted for Sex, SES, delayed onset, treatment and use of psychotropic medication; HR = Hazard ratio; 95%CI = 95% confidence interval; *** p<0.001; ** p<0.01; * p<0.05.

Table 3b. Results of the baseline and mediated models for time to remission by trauma type in PTSD cases

Trauma type	**Baseline model**	**Full model adjusted for posttraumatic factors**			
	Direct effect on time to remission **HR (95% CI)**	**Direct effect on time to remission** **HR (95% CI)**	**Change against baseline model** **Absolute in HR (relative in %)**	**Indirect effects on time to remission** **HR (95% CI)**	**Total effect on time to remission** **HR (95% CI)**
Sexual trauma	0.54 (0.34,0.86)*	0.69 (0.41,1.14)	0.15 (28%)	Via avoidance: 0.84 (0.69,1.03) Via hyperarousal: 0.96 (0.84,1.09) Via depression: 0.69 (0.53,0.91)** Total: 0.56 (0.40,0.79)**	0.38 (0.22,0.68)**
Childhood sexual trauma	0.59 (0.35,0.99)*	0.85 (0.51,1.40)	0.26 (44%)	Via avoidance: 0.81 (0.64,1.02) Via hyperarousal: 0.94 (0.82,1.09) Via depression: 0.70 (0.51,0.95)* Total: 0.53 (0.36,0.78)**	0.45 (0.25,0.81)**

Note: Baseline model adjusted for education, SES and treatment; PTSD = Posttraumatic stress disorder; HR = Hazard ratio; 95%CI = 95% confidence interval; ** p<0.01; * p<0.05.